Een studie naar de veiligheid en effecten van psychotherapie in combinatie met MDMA als behandeling voor zware post-traumatische stress stoornis

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON27176

Source
Nationaal Trial Register

Brief title
M-PSY-PTSD, MDMA4PTSD

Health condition

Post-Traumatic Stress Disorder

Sponsors and support

Primary sponsor: K.P.C. Kuypers,
Maastricht University
Source(s) of monetary or material Support: Multidisciplinary Association for Psychedelic Studies (MAPS)
1115 Mission Street
Santa Cruz, CA 95060

Intervention

Outcome measures

Primary outcome

The primary objective of this study is to evaluate the effect of MDMA-assisted psychotherapy on PTSD, as measured by the estimand of change in CAPS-5 Total Severity Score from Baseline (Visit 3) to 18 weeks post Baseline (Visit 19).

Secondary outcome

The overall safety objective is to assess severity, incidence and frequency of AEs, AEs of Special Interest (AESIs), and Serious Adverse Events (SAEs), concomitant medication use, suicidal ideation and behavior, and vital signs to support the package insert for MDMA-assisted psychotherapy. The following safety objectives will evaluate the safety of MDMA-assisted psychotherapy.

Study description

Background summary

Post-traumatic stress disorder is a very debilitating disease, impairing the quality of life of people suffering from it. Current treatments are not effective in a large number of cases, pressing the need for alternative treatments . MDMA has been shown to reduce defenses and fear of emotional injury, enhance communication, and increase empathy, and it may enhance fear extinction learning in humans. These subjective effects of MDMA create a productive psychological state that enhances the therapeutic process for the treatment of PTSD and other anxiety disorders. This novel treatment package consists of three once-monthly Experimental Sessions of psychotherapy combined with a flexible dose of MDMA, along with non-drug preparatory and integrative psychotherapy. This is supported by data from an international series of Phase 2 pilot studies of MDMA-assisted psychotherapy conducted by MAPS, the sponsor, providing preliminary evidence that chronic PTSD, independent of cause, is treatable with two to three sessions of MDMA-assisted psychotherapy and associated non-drug preparatory and integrative psychotherapy. The results from multiple independent studies in Phase 2 efficacy analyses demonstrate superiority of MDMA-assisted psychotherapy over psychotherapy with placebo or low dose MDMA. The acceptable risk-benefit ratio in early trials justifies further study.

This open-label lead-in Phase 2 study is intended to gather supportive data on the safety and effect of manualized MDMA-assisted psychotherapy as a treatment for PTSD. The Primary Outcome measure, the change in Clinician Administered PTSD Scale for DSM-5 (CAPS-5) from Baseline, evaluates changes in PTSD symptom severity and is assessed by a centralized Independent Rater (IR) pool in this study and in planned Phase 3 clinical trials. This study will gather supportive data on the safety and effect of manualized MDMA-assisted psychotherapy as a treatment for PTSD and provide clinical supervision to planned Phase 3 therapy teams.

This study will explore reproducibility of findings gathered at another research site to further confirm the Phase 3 study design.

In this Phase 2 study, a therapy team without previous experience on a MAPS-sponsored MDMA-assisted psychotherapy study will have the opportunity for clinical supervision from the sponsor prior to their roles in Phase 3 studies. Only sites planned for Phase 3 will participate in this study. The sponsor conducts group and individual training programs to teach therapy team members about techniques and procedures for conducting MDMA-assisted psychotherapy for PTSD. These programs are designed to support and expand the knowledge and skills of therapy team members who will be working on MDMA research studies.

Study design

Baseline, visit 3, visit 19 (18 weeks post-baseline)

Intervention

This study will compare the effects of three open-label manualized Experimental Sessions of psychotherapy assisted by flexible doses of MDMA. Initial doses per Experimental Session include 80 mg or 120 mg of MDMA compounded with lactose, followed 1.5 to 2 hours later by a supplemental half-dose (40 mg or 60 mg). Total amounts of MDMA to be administered per Experimental Session range from 80 mg to 180 mg.

Contacts

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Eligibility criteria

Inclusion criteria

At the completion of Screening, participants must meet all eligibility criteria (except Inclusion Criterion #13) and agree to all lifestyle modifications to be enrolled. Each participant will then enter the Preparatory Period which includes medication tapering, if needed, and non-drug Preparatory Sessions. The Preparatory Period ends with Enrollment Confirmation. A participant’s enrollment will be confirmed if they have completed medication tapering, have a confirmed PTSD diagnosis per the CAPS-5 assessment and a Total Severity Score of 35 or greater, continue to agree to all lifestyle modifications, and continue to meet all eligibility criteria (those criteria marked with an * below will only be assessed at Screening, since they will not change).

Potential participants are eligible to enroll in the protocol if they:

1. *Are at least 18 years old

2. *Are fluent in speaking and reading the predominantly used or recognized language of the study site

3. *Are able to swallow pills

4. Agree to have study visits recorded, including Experimental Sessions, Independent Rater assessments, and non-drug psychotherapy sessions

5. Must provide a contact (relative, spouse, close friend or other caregiver) who is willing and able to be reached by the investigators in the event of a participant becoming suicidal or unreachable

6. Must agree to inform the investigators within 48 hours of any medical conditions and procedures

7. If of childbearing potential, must have a negative pregnancy test at study entry and prior to each Experimental Session, and must agree to use adequate birth control through 10 days after the last Experimental Session. Adequate birth control methods include intrauterine device (IUD), injected or implanted hormonal methods, abstinence, oral hormones plus a barrier contraception, or double barrier contraception. Two forms of contraception are required with any barrier method or oral hormones (i.e. condom plus diaphragm, condom or diaphragm plus spermicide, oral hormonal contraceptives plus spermicide or condom). Not of

childbearing potential is defined as permanent sterilization, postmenopausal, or assigned male at birth.

8. Agree to the following lifestyle modifications (described in more detail in Section 4.3 Lifestyle Modifications): comply with requirements for fasting and refraining from certain medications prior to Experimental Sessions, not participate in any other interventional clinical trials during the duration of the study, remain overnight at the study site after each Experimental Session and be driven home after, and commit to medication dosing, therapy, and study procedures

Medical History

9. *At Screening, meet DSM-5 criteria for current PTSD with a symptom duration of 6 months or longer

10. *At Screening, have at least severe PTSD symptoms in the last month based on PCL-5 total score of 50 or greater

11. *At Screening, may have well-controlled hypertension that has been successfully treated with anti-hypertensive medicines, if they pass additional screening to rule out underlying cardiovascular disease

12. *At Screening, may have asymptomatic Hepatitis C virus (HCV) that has previously undergone evaluation and treatment as needed

13. At Baseline, have at least severe PTSD per CAPS-5 and symptoms in the last month constituting a CAPS-5 Total Severity Score of 35 or greater.

Exclusion criteria

Potential participants are ineligible to enroll in the protocol if they:

1. *Are not able to give adequate informed consent

2. Are currently engaged in compensation litigation whereby financial gain would be achieved from prolonged symptoms of PTSD or any other psychiatric disorders

3. Are likely, in the investigator’s opinion and via observation during the Preparatory Period, to be re-exposed to their index trauma or other significant trauma, lack social support, or lack a stable living situation

4. Have used Ecstasy (material represented as containing MDMA) more than 10 times within the last 10 years or at least once within 6 months of the first Experimental Session; or have previously participated in a MAPS-sponsored MDMA clinical trial

5. Have any current problem which, in the opinion of the investigator or Medical Monitor, might interfere with participation

Psychiatric History

6. *Have received Electroconvulsive Therapy (ECT) within 12 weeks of enrollment

7. *Have a history of, or a current primary psychotic disorder, bipolar affective disorder type 1 assessed via MINI or dissociative identity disorder assessed via DDIS

8. *Have a current eating disorder with active purging assessed via MINI

9. *Have current major depressive disorder with psychotic features assessed via MINI

10. *Meet DSM-5 criteria for active substance use disorder for any substance other than caffeine or nicotine in the past 60 days assessed via MINI, AUDIT, DUDIT, drug test, and blood %carbohydrate-deficient transferrin (%CDT)

11. Have current Personality Disorders Cluster A (paranoid, schizoid, schizotypal), Cluster B (antisocial, borderline, histrionic, narcissistic), or Cluster C (avoidant, dependent, obsessive-compulsive) assessed via SCID-5-PD. Diagnoses will be confirmed via clinical interview

12. Any participant presenting current serious suicide risk, as determined through psychiatric interview, responses to C-SSRS, and clinical judgment of the investigator will be excluded; however, history of suicide attempts is not an exclusion. Any participant who is likely to require hospitalization related to suicidal ideation and behavior, in the judgment of the investigator, will not be enrolled

13. Would present a serious risk to others as established through clinical interview and contact with treating psychiatrist

14. Require ongoing concomitant therapy with a psychiatric medication with exceptions described in Section 12.0: Concomitant Medications.

Medical History

15. *Have evidence or history of significant (controlled or uncontrolled) hematological, endocrine, cerebrovascular, cardiovascular, coronary, pulmonary, renal, gastrointestinal, immunocompromising, or neurological disease, including seizure disorder, or any other medical disorder judged by the investigator to significantly increase the risk of MDMA administration (participants with hypothyroidism who are on adequate and stable thyroid replacement will not be excluded). Note: if participants present with a history of glaucoma, enrollment would be allowed only with the approval of their ophthalmologist

16. *Have uncontrolled hypertension using the standard criteria of the American Heart

Association (values of 140/90 milligrams of Mercury [mmHg] or higher assessed on three separate occasions)

17. *Have a marked baseline prolongation of QT/QTc interval (e.g., repeated demonstration of a QTc interval >450 milliseconds [ms] corrected by Bazett's formula)

18. *Have a history of additional risk factors for Torsade de pointes (e.g., heart failure, hypokalemia, family history of Long QT Syndrome)

19. *Require use of concomitant medications that prolong the QT/QTc interval during Experimental Sessions. Refer to Section 12.0 Concomitant Medications.

20. *Have symptomatic liver disease

21. *Have history of hyponatremia or hyperthermia

22. *Weigh less than 48 kilograms (kg)

23. Are pregnant or nursing, or are of childbearing potential and are not practicing an effective means of birth control.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Non controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-12-2017
Enrollment:	0
Type:	Anticipated

Ethics review

Not applicable
Application type: Not applicable

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL6483
NTR-old	NTR6670
Other	: P101

Study results

Summary results
Mithoefer, M. C., Wagner, M. T., Mithoefer, A. T., Jerome, L., Martin, S. F., Yazar-Klosinski, B., . . . Doblin, R. (2013). Durability of improvement in post-traumatic stress disorder symptoms and absence of harmful effects or drug dependency after 3,4-methylenedioxymethamphetamine-assisted psychotherapy: a prospective long-term follow-up study. Journal of Psychopharmacology, 27, 28-39.

Ricaurte, G. A., Yuan, J., Hatzidimitriou, G., Cord, B. J., & McCann, U. D. (2003). "MDMA ("Ecstasy") and neurotoxicity": Response.

Wagner, M. T., Mithoefer, M. C., Mithoefer, A. T., MacAulay, R. K., Jerome, L., Yazar-Klosinski, B., & Doblin, R. (2017). Therapeutic effect of increased openness: Investigating mechanism of action in MDMA-assisted psychotherapy. Journal of Psychopharmacology, 0269881117711712. doi: 10.1177/0269881117711712