Methodology for a Randomized, Double-blinded, Active-controlled Clinical Trial to Determine the Safety, Efficacy, and Durability of MDMA-Assisted Therapy for Military Service Members with PTSD

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INTRODUCTION

- Posttraumatic stress disorder (PTSD) is the most common psychiatric cause of medical discharges in the military.[1]
- Current gold-standard treatments such as Prolonged Exposure (PE) and Cognitive Processing Therapy (CPT) lead to loss of PTSD diagnosis in 28-40% of participants. However, about 40% drop out of treatment.[2]
- With midomafetamine-assisted therapy (MDMA-AT), 67-71% are no longer diagnosable with PTSD and <10% drop out despite the longer course of treatment.[1,3,4]
- Evidence of MDMA-AT for Active Duty, National Guard, or Reserve Service Members (SMs) with PTSD does not exist.

METHODS

- We intend to conduct a randomized, double-blind, active-controlled clinical trial of MDMA-AT for SMs with PTSD.
- The Randomized cohort would receive either a variable high-dose or low-dose MDMA combined with Acceptance and Commitment Therapy (ACT) for PTSD.
- We intend to recruit **86 SMs** with moderate to severe PTSD. Total duration of study engagement for a participant will be approximately **7-8 months** (see Figure 1).

FIGURE 2. Simultaneous Dosing Model

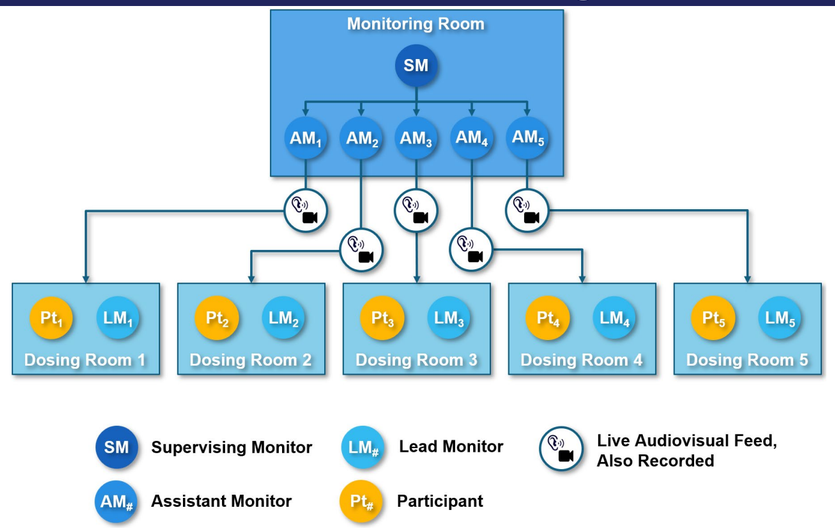
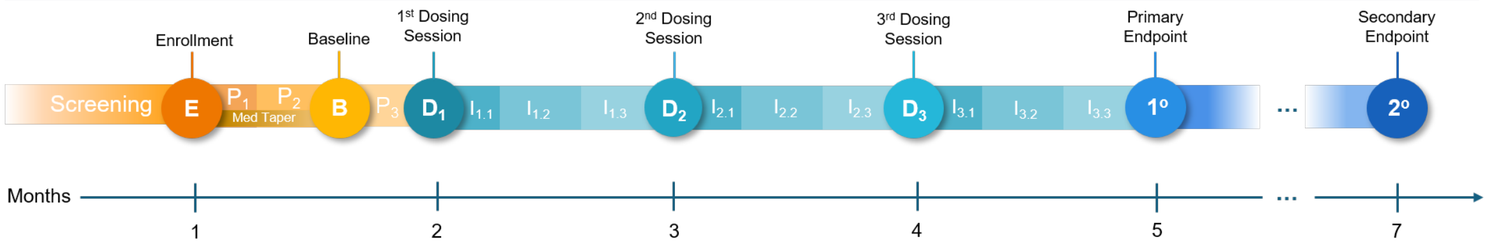


FIGURE 1. Study Schema Diagram



- E Enrollment
- B Baseline Measures
- Screening
- Medication Taper
- P_1 Preparatory Session 1 (90 min) – 0-12 days after Enrollment
- P_2 Preparatory Session 2 (90 min) – 2-21 days after P_1
- P_3 Preparatory Session 3 (90 min) – 3-14 days after Baseline
- D_1 1st Dosing Session (6-8 hours) – Within 15 days after Baseline
- D_2 2nd Dosing Session (6-8 hours) – Within 21-35 days after D_1
- D_3 3rd Dosing Session (6-8 hours) – Within 21-35 days after D_2
- $I_{N.1}$ 1st Integration Sessions (90 min) – Morning after dosing
- $I_{N.2}$ 2nd Integration Sessions (90 min) – 3-14 days after dosing
- $I_{N.3}$ 3rd Integration Sessions (90 min) – 20-34 days after dosing
- 1º Primary Endpoint – 14 weeks after Baseline
- 2º Secondary Endpoint – 13 weeks after D_3
- One safety follow-up call

STUDY TIMELINE

- Each participant will undergo three dosing sessions each one month apart, with live audio-video monitoring.
- The first dosing session is preceded by three 90-minute preparatory ACT sessions. Each of the three dosing sessions is followed by three 90-minute integration ACT sessions.
- Follow-up will occur at one month (primary endpoint) and three months (secondary endpoint) after the last dosing session (see Figure 1).

SIMULTANEOUS DOSING MODEL

- There will be up to five rooms conducting dosing sessions simultaneously (see Figure 2).
- One therapist will be in the dosing room with the participant, with an Assistant Monitor monitoring each room and a Supervising Clinician monitoring all rooms.
- Support Events (when a study team member enters the dosing room to assist) will be analyzed to evaluate the Simultaneous Dosing Model's safety and feasibility.

CONCLUSIONS

- With PTSD being the leading psychiatric cause of medical discharges, establishing safe treatment options with high efficacy and durability is a major opportunity to improve retention and readiness.
- The Simultaneous Dosing Model approach aims to improve resource-efficiency and treatment access if it is implemented within clinical settings.
- Our study will gather data from the military health system and inform Department of War PTSD treatment policies.

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