Expanded Analysis of MM120 (Lysergide) for Generalized Anxiety Disorder: Updated Findings on Quality of Life and Depressive Symptoms

Submission ID 3006027

Submission Type Late Breaking Poster

Topic Anxiety Disorders (other than OCD)

Status Submitted

Submitter Daniel Karlin, MD, MA

Affiliation Mind Medicine Inc., Department of Psychiatry, Tufts University School of Medicine

SUBMISSION DETAILS

Abstract Introduction: Generalized anxiety disorder (GAD) and major depressive disorder (MDD) are common, highly morbid conditions and manifest as a range of chronic and episodic psychiatric and somatic symptoms. Patients with a primary diagnosis of GAD often exhibit comorbid depressive symptoms, underscoring the 80% construct overlap of GAD and MDD diagnostic criteria. For both disorders, management is limited by the inefficacy of available treatments and treatment-associated adverse events (AEs). Contemporary drug development for GAD should place increased priority on quality-of-life (QoL), well-being, and depressive symptoms. Primary and key secondary outcomes from a phase 2b (NCT05407064) dose-finding study of a single treatment with MM120 (lysergide D-tartrate) suggest a rapid, safe, and durable dose-dependent response in participants with a primary GAD diagnosis and moderate-to-severe-anxiety. Prespecified secondary analyses showed improvements in co-morbid depressive symptoms.2 Herein, we provide additional results from analyses of functional and QoL assessments and a post hoc analysis of depressive symptoms.

Methods: This phase 2b multicenter, randomized, double-blind, placebo-controlled study of a single dose of 25, 50, 100, or 200µg MM120 (freebase equivalent) vs placebo has previously been described. The effects of MM120 on functional disability, QoL, and sexual dysfunction were assessed throughout the trial by the Sheehan Disability Scale (SDS); the EQ-5D-5L and the Pittsburgh Sleep Quality Index (PSQI); and the Arizona Sexual Experiences Questionnaire (ASEX), respectively. Changes from baseline for each of these measures were analyzed descriptively. Montgomery-Åsberg Depression Rating Scale (MADRS) was collected as a key secondary endpoint. Post hoc analyses examining MADRS change from baseline were performed using a subset of participants with a baseline MADRS of >26 and at least 1 post-baseline MADRS. Definitionally, these participants had comorbid depressive symptoms in the upper range of moderate to severe. Results for the dose with optimal level of clinical activity on the HAM-A are reported.

Results: The phase 2b study enrolled 198 participants. Placebo-adjusted improvements in functional

outcome scales were observed with MM120 100µg at weeks 4 (primary endpoint) and persisted through weeks 12 across the SDS (-6.0 and -6.9), EQ-5D-5L (0.111 and 0.116), EQ VAS of the EQ5 (4.0 and 6.0), and PSQI (-1.6 and -1.6). Most measures showed improvements as early as week 1. At week 12, there was a considerable decrease from baseline in the proportion of male participants who reported sexual dysfunction with MM120 100µg (29.2% at baseline vs 10% at week 12) compared with placebo (15.4 at baseline vs 12.5% at week 12). Similar decreases from baseline were observed in the proportion of female participants who reported sexual dysfunction (75% at baseline vs 46.2% at week 12) compared with placebo (50% at baseline vs 33.3% at week 12). At post hoc analysis, 22 participants of the 40 randomized to receive MM120 100µg had baseline MADRS >26 (mean baseline MADRS of 32.5 ± 4.6) and a mean change from baseline of -23.3 ± 11.3 and -25.0 ± 9.2 at weeks 4 and 12.

Conclusion: Single treatment with MM120 represents a promising new potential treatment option that demonstrated anxiety reduction and improvement of functional outcome measures in patients with moderate-to-severe GAD, regardless of the presence of comorbid depressive symptoms. Efficacy is also being explored in patients with a primary diagnosis of MDD in a planned Phase 3 program.

Author Listing

* Presenting Author

First Name	Last Name	Affiliation
Daniel *	Karlin, MD, MA *	Mind Medicine Inc., Department of Psychiatry, Tufts University School of Medicine
Todd M.	Solomon, PhD	Mind Medicine Inc.
Paula L.	Jacobsen, PhD	Mind Medicine Inc.
Sarah M.	Karas, PsyD	Mind Medicine Inc.
Jamie M.	Freedman, BS	Mind Medicine Inc.

Signature Daniel Rollings Karlin