

# An Interim Blinding Integrity Analysis of a Randomized, Double-Blind, Midazolam-Controlled Phase II Clinical Trial Investigating Repeated Ketamine Infusions for Treatment Resistant Bipolar Depression

<b>Submission ID</b>	3005744
<b>Submission Type</b>	Individual Research Report
<b>Topic</b>	Bipolar Disorders
<b>Status</b>	Submitted
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## SUBMISSION DETAILS

### Request for Proposals Psychedelics

**Abstract:** Introduction: Psychedelic therapies have emerged as promising treatments for a range of psychiatric disorders, including treatment-resistant bipolar depression (TRBD). However, the lack of robust results in psychedelic studies has often been attributed to issues with functional unblinding, where participants are able to guess their treatment allocation based on subjective experiences. This can lead to biased outcomes and undermine the reliability of clinical trial results. Despite these challenges, the potential of psychedelics, particularly intravenous ketamine, for treating TRBD warrants further investigation, especially under conditions that minimize bias. Methods: A randomized, double-blind, midazolam-controlled phase II clinical trial will investigate repeated ketamine infusions for TRBD (NCT05004896). An interim blinding integrity analysis will be completed using participants' Blinding Assessment Tool responses after the first infusion to evaluate midazolam's suitability as an active control for ketamine.

Results: A total of 34 participants (N=34) with TRBD have completed treatment making this the largest randomized control trial investigating ketamine for TRBD to date. After the first infusion, 44.1% of participants correctly guessed their treatment allocation. Participants correctly guessed what medication they received 26.7% of the time in the ketamine arm and 57.9% of the time in the midazolam arm.

Discussion: Our results suggest midazolam is a suitable active control for ketamine to minimize bias. Future investigation of the relationship between Clinician-Administered Dissociative States scores and Blinding Assessment Tool results is encouraged to understand the influence of a strong dissociative experience to participants' treatment allocation guesses. Understanding of participants' expectancy bias may offer more insight into this relationship.

### Learning Objectives:

**Learning Objective 1** Describe the need for randomized control trials investigating psychedelic pharmacotherapies that minimize bias.

**Learning Objective 2** Evaluate the suitability of midazolam to act as an active control for ketamine.

## **DISCLOSURE**

### Financial Relationships

**Disclosure** No, I have nothing to disclose.