

PLS: Response and Remission Following Esketamine Nasal Spray Initiation in Treatment-Resistant Depression: Real-World Evidence From a Multi-Site Practice

What do these results mean for individuals with treatment-resistant depression (TRD)?

Esketamine nasal spray (ESK) shows early improvement, with continuous gains observed. The improvements were consistent across patient reported and clinician reported measures. These findings provide real-world evidence supporting the long-term effectiveness of ESK in routine clinical practice.

What was the purpose of the study?

To describe time to response to ESK and remission of depressive symptoms within 2 years after its initiation among patients with TRD in real-world settings.

Who was in the study and how was it carried out?

Who: 1,201 adult patients who initiated ESK treatment on or after 3/5/ 2019, with ≥ 1 assessment for PHQ-9 and ≥ 1 assessment for MADRS prior to and after ESK initiation.

When: Data time window was from 3/5/2019 to 8/4/2025.

How: This is a retrospective, observational study using electronic medical records data from Mindful Health Solutions (MHS) clinics.

Outcomes evaluated: The study evaluated the response and remission after ESK initiation based on PHQ-9 and MADRS scores separately among patients with moderate-to-severe depression with the following definition:

PHQ-9

- Response: $\geq 50\%$ reduction in PHQ-9 score from baseline
- Remission: follow-up PHQ-9 score < 5

MADRS

- Response: $\geq 50\%$ reduction in MADRS score from baseline
- Remission: follow-up MADRS score ≤ 12

What were the results of the study?

Most patients with TRD achieved response, and a substantial proportion achieved remission within 2 years of ESK initiation. Outcomes were consistent across clinician and patient-reported measures.

Based on PHQ-9, the proportion of patients that responded to treatment were 53.3%, 76.6%, and 86.4% at 3, 12, and 24 months, respectively.

Based on MADRS, the proportion of patients that responded to treatment were 41.8%, 80.1%, and 90.3% at 3, 12, and 24 months, respectively.

Based on PHQ-9, the remission rates were 16.9%, 38.4%, 44.6% at 3, 12, and 24 months, respectively.

Based on MADRS, the remission rates were 17.5%, 48.5%, 60.4% at 3, 12, and 24 months, respectively.

What were the limitations of the study?

A limited number of patients were still monitored at 24 months, particularly for response analyses, due to either rapid response, discontinuation, or end of follow-up; findings should be interpreted with caution. Additionally, results of this study may not be generalizable to patients who receive ESK treatment in non-MHS clinics, the uninsured, or patients covered under Medicaid insurance.

Glossary

Treatment-resistant depression: Major depressive disorder that has not adequately responded to at least two antidepressants.

Esketamine: A nasal spray approved for treatment-resistant depression in adults.

Montgomery-Åsberg Depression Rating Scale (MADRS): Clinician-rated scale measuring depression severity, scores range 0-60.

Patient Health Questionnaire-9 item (PHQ-9): Patient-reported questionnaire assessing depressive symptoms, scores range 0-27.