PLS: Real-World Prescribing Patterns of Esketamine Monotherapy vs Adjunctive Therapy in Routine Psychiatric Care

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

Following the January 2025 FDA approval of esketamine monotherapy, 23% of patients initiating esketamine nasal spray in routine psychiatric care were prescribed monotherapy at treatment initiation. Treatment choice is related to individual patient characteristics such as prior medication burden, patient sex, psychiatric comorbidities, and geographic region.

What was the purpose of the study?

This study evaluates clinical and demographic differences between patients prescribed esketamine monotherapy versus adjunctive therapy at treatment initiation in real-world settings.

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

Who: Adults with major depressive disorder who received ≥ 1 dose of esketamine treatment.

When: Patients who received esketamine on or after 4/30/2025 were included in the study.

How: Retrospective study of electronic health record data from outpatient psychiatric clinics. Statistical analysis was performed to evaluates the association between patient characteristics and treatment choice.

What were the results of the study?

Of the 2,095 patients who initiated esketamine, 1,620 received esketamine as adjunctive therapy and 475 as monotherapy.

Female patients or patients treated in the North Central geographic region were significantly more likely to receive adjunctive esketamine therapy.

Male patients were significantly more likely to receive esketamine monotherapy.

PHQ-9 scores were modestly higher in the monotherapy group.

Patients starting on adjunctive esketamine treatment had lower rates of psychiatric comorbidities including anxiety disorders, recurrent depressive disorder, and depressive episode, but had significantly greater historic use of antidepressants and antipsychotics.

What were the limitations of the study?

This is a retrospective, observational design and cannot exclude the impact of unmeasured factors. Therefore, causality cannot be inferred from group differences.

Concurrent oral antidepressant use was inferred from EHR documentation, which may not fully capture active versus discontinued prescriptions at the time of esketamine initiation.

Some relevant variables (race, ethnicity, Montgomery-Åsberg Depression Rating Scale score, insurance type, body mass index, etc) had missing data, limiting interpretation and generalizability for those subgroups.

The sample is drawn from clinics using the Osmind platform, which may not be representative of all outpatient clinical practices in the US.

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.