Supplementary Online Content

Nikayin S, Rhee TG, Cunningham ME, et al. Evaluation of the trajectory of depression severity with ketamine and esketamine treatment in a clinical setting. *JAMA Psychiatry*. Published online May 11, 2022. doi:10.1001/jamapsychiatry.2022.1074

eMethods

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods

All patients treated at Yale IPS receive a consultation/assessment by an IPS physician before initiating either IV ketamine or esketamine; during this evaluation the diagnosis and appropriateness for treatment is ascertained. As part of IPS standard clinical practice, each patient's non-interventional treatment continues to be managed by their primary psychiatric provider, with the IPS team encouraging continuation of current medications, and/or optimization of medication treatment during the course of ketamine/esketamine treatment. In this analysis, we included adults with a major depressive episode receiving an initial acute treatment course (defined as multiple treatments each ≤7 days apart for up to 8 total treatments). The primary outcome was group differences in trajectory of depression severity over time, as measured by Montgomery-Åsberg Depression Rating Scale (MADRS). Secondary outcomes included group differences in depression severity as measured by Quick Inventory of Depressive Symptomatology-Self Report (QIDS-SR), response (≥50% improvement), and remission (MADRS≤10) rates. Additionally, sensitivity analyses were conducted using data from the first 6 treatments of each group; this was done because early in the clinic history (prior to FDA approval of esketamine), a full course of ketamine was considered to be 6 treatments. A logarithmic-transformed, multivariable-adjusted model was used as primary outcome based on the best model fit, with other models (linear and square-root) explored. We set a two-sided $p<0.05$ as the threshold of statistical significance. All analyses were conducted using SAS v.9.4 and Stata v.16.