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Clinical Trials Update

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Esketamine Nasal Spray Effective in Treatment-Resistant Depression

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sketamine nasal spray combined with an oral antidepressant was more effective in treating refractory depression than placebo plus a newly initiated antidepressant, according to a phase 3 trial published in the *American Journal of Psychiatry*.

The 277 adults with moderate to severe depression, who had not responded to at least 2 antidepressants prior to the study, were randomized to 1 of 2 groups. Patients in 1 group were switched from their current antidepressant to esketamine nasal spray (56 or 84 mg twice weekly) plus a newly initiated antidepressant (duloxetine, escitalopram, sertraline, or extended-release venlafaxine). Patients in the other group were switched from their current treatment to a placebo nasal spray and a new antidepressant.

At day 28, the esketamine group had a significantly greater improvement in depression severity than did the comparator group. Clinically meaningful improvements were seen in the esketamine group 24 hours after a single dose. In the esketamine group, 7% discontinued the study drug due to adverse events compared with 0.9% of the comparator group. Esketamine-related adverse events, including nausea, dissociation, vertigo, and dizziness, usually resolved by 1.5 hours.

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