Ventura Real-World Evidence (RWE) Study

Esketamine Nasal Spray (NS) and Anhedonia/Functional Outcomes

Healthcare Provider Study Summary

Study at a glance: A 12-month prospective, non-interventional study of a subgroup of 49 patients with major depressive disorder (MDD), anhedonia, and inadequate response to ongoing antidepressant treatment who initiated esketamine NS in addition to their oral antidepressant (OAD) treatment.

What is the purpose of this study?

This study evaluated whether esketamine NS added to an OAD improves depressive symptoms, anhedonia, functioning, and health-related quality of life in patients with MDD who had an inadequate response to prior antidepressant treatment.

How was the study conducted?

Ventura-RWE was a prospective, non-interventional, 12-month study. Patients with MDD and anhedonia who had inadequate response to a selective serotonin reuptake inhibitor (SSRI) or serotonin-norepinephrine reuptake inhibitor (SNRI) with physician-initiated adjunctive treatment options including esketamine NS as a subgroup of the population. Depression, anhedonia, functioning, and health-related quality of life (HRQoL) measures were assessed through Month 12.

What were the results of the study?

In this post-hoc analysis, the outcomes of the esketamine NS treatment subgroup are presented. Patients receiving esketamine NS plus an OAD showed improvements in overall depression severity, anhedonia, functional impairment, and HRQoL. Improvements in anhedonia were correlated with improvements in functioning and multiple HRQoL measures.

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

These findings suggest that esketamine NS may help improve not only depressive symptoms in general, but also anhedonia and everyday functioning. Because anhedonia is linked to poor outcomes in MDD, addressing this core symptom and a subdomain of depression may contribute to broader clinical and functional recovery.[1]

What is the design of the study?

Ventura-RWE (NCT05841030) was a prospective, observational, non-interventional, 12-month real-world evidence study. Adults with MDD and anhedonia who had an inadequate response to ongoing OAD therapy, including an SSRI or SNRI, initiated adjunctive treatment based on physician choice, including esketamine NS according to approved prescribing information. The presented post-hoc analysis included patients who started esketamine NS at baseline using an intention-to-treat (ITT) approach. Outcomes were evaluated at baseline, Week 6, Month 6, and Month 12 using validated assessments of depression severity (MADRS, PHQ-9), anhedonia (SHAPS, DARS, MADRS item 8, PHQ-9 item 1, PGI-S anhedonia, MADRS anhedonia subscale),

functional impairment (WPAI), and HRQoL (EQ-5D-5L, EQ-5D visual analogue scale [VAS]). Descriptive and Spearman correlation analyses were performed. The esketamine NS plus OAD cohort included 49 patients.

What were the limitations of the study?

This was an observational real-world study without a randomized control group, limiting causal conclusions. The esketamine NS cohort was relatively small (N=49), and patient numbers decreased over time. The authors also noted that small sample sizes for some WPAI work-related outcomes limited assessment of functional associations at later timepoints.

Reference

1. Cutler AJ, Clayton AH, Krystal AD, Maletic V, McIntyre RS, Nemeroff CB. Anhedonia in patients with major depressive disorder (MDD): State-of-the-art consensus review. *Psychiatry Res*. 2026 Oct;364:117225. doi: 10.1016/j.psychres.2026.117225.

Glossary of Technical Terms

Term	Plain-language definition
Anhedonia	Reduced ability to experience pleasure or interest in normally enjoyable activities.
MDD	Major depressive disorder, a mood disorder characterized by persistent depressive symptoms that impair daily functioning.
Esketamine NS	Esketamine nasal spray, an intranasal formulation of esketamine used for specific depressive disorders.
OAD	Oral antidepressant, an antidepressant medication taken by mouth.
RWE	Real-world evidence, where clinical information has been generated from routine healthcare settings rather than controlled clinical trials.
Prospective study	A study that follows participants forward in time after enrollment.
Noninterventional study	A study in which treatment decisions are made as part of routine clinical care rather than assigned by investigators.
ITT	Intention-to-treat, an analysis approach that includes all patients according to initial treatment assignment or initiation.
MADRS	Montgomery-Asberg Depression Rating Scale, a clinician-rated measure of depression severity.
MADRS item 8	One of 10 items on the MADRS, item 8 measures the inability to feel.
PHQ-9	Patient Health Questionnaire-9, a 9-question, patient-reported depression screening and severity measure.
PHQ-9 item 9	Item 9 on the PHQ-9 measures whether an individual has little interest or pleasure in doing things.
SHAPS	Snaith-Hamilton Pleasure Scale, a questionnaire assessing anhedonia severity.
DARS	Dimensional Anhedonia Rating Scale, a measure of interest, motivation, effort, and enjoyment. Higher scores indicate less severe anhedonia.
MADRS anhedonia subscale	A subset of 5 items of the MADRS used to assess anhedonia-related depressive symptoms.
PGI-S anhedonia	Patient Global Impression of Severity scale focused on anhedonia symptoms.
WPAI	Work Productivity and Activity Impairment questionnaire, measuring the impact of illness on work and daily activities.
HRQoL	Health-related quality of life, describing how health affects well-being and functioning.
EQ-5D-5L	EuroQoL 5-dimension, 5-level standardized instrument evaluating mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.
EQ-5D VAS	The visual analogue scale component of EQ-5D on which patients rate overall health status.
SSRI	Selective serotonin reuptake inhibitor, a class of antidepressants.
SNRI	Serotonin-norepinephrine reuptake inhibitor, a class of antidepressants.
Spearman correlation	A statistical measure describing the strength and direction of association between two variables.

Interpretive note

The poster reports outcomes among patients with inadequate response to prior antidepressants. It does not state that every participant met a formal definition of treatment-resistant depression, although esketamine NS is discussed in the context of approved use for treatment-resistant depression and related depressive conditions.

Source

Cutler AJ, Jain R, Henry K, et al. Esketamine Nasal Spray on Anhedonia and Functional Outcomes: Findings from the Ventura Real-World Evidence Study. Poster prepared for Psych Congress 2026. Summary based on the attached poster dated August 31, 2026.