

Real-world post-treatment durability of esketamine nasal spray effectiveness in treatment resistant depression: results from the ECHO, non-interventional cohort study

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Introduction

- Esketamine nasal spray (NS) is approved by the European Medicines Agency, in combination with a selective serotonin reuptake inhibitor (SSRI) or serotonin-norepinephrine reuptake inhibitor (SNRI), for patients with treatment resistant depression (TRD).
- After depressive symptoms improve, treatment is recommended for at least 6 months; however, data on the durability of treatment effects and the risk of symptom recurrence or relapse following treatment cessation in real-world practice remain limited.
- This analysis presents the first structured real-world post-treatment follow-up data on clinical outcomes after esketamine NS cessation, evaluating the durability of clinical outcomes after esketamine NS cessation in adults with TRD in the Esketamine CoHoRT (ECHO) study.
- Here, we also assess whether outcomes differed by clinical status at esketamine NS cessation and by duration of esketamine NS exposure.

Methods

- ECHO was a prospective, non-interventional study in Belgium, Germany, Israel, Italy, Netherlands, Spain and Sweden.
- Esketamine NS was prescribed per local prescribing information, independent of study participation.
- The study included a variable-length esketamine NS treatment period, followed by a 6-month post-treatment follow-up period after esketamine NS cessation.
- Clinical outcomes in the post-treatment follow-up included Montgomery-Åsberg Depression Rating Scale (MADRS) total score, relapse rate and time to first relapse.
- Outcomes are reported for all patients and stratified by status at the end of the esketamine NS treatment period: remission (MADRS ≤10), response without remission (≥50% improvement in MADRS from treatment initiation and MADRS >10) or no remission/response. Outcomes are also stratified by duration of esketamine NS exposure.
- Relapses in the follow-up period were defined by patients' treating clinicians; definitions included relapse per the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria, hospitalisation, suicide attempt or by a confirmed MADRS total score of ≥22 for all patients.²

Results

- Overall, 301/570 patients enrolled in the study continued to the post-treatment follow-up.

Durability of effectiveness

- After esketamine NS cessation, mean MADRS total score remained stable throughout the 6-month post-treatment period, with no clear evidence of rebound in depressive symptoms (Figure 1).
- Patients who achieved remission or response at the end of esketamine NS treatment demonstrated lower MADRS scores throughout the follow-up period compared with non-responders (Figure 1).
- Lower mean MADRS scores and higher remission rates were observed for patients with >6 months esketamine NS exposure compared with ≤6 months esketamine NS exposure (Figures 2 and 3).
- At the beginning of the follow-up period, 25.0% of patients were in remission; these proportions were maintained to Week 24 (27.9%; Figure 3).

Relapse rates in the post-treatment follow-up

- At any point during esketamine NS treatment and the follow-up period, 166/301 patients achieved remission or response; 81.3% (135/166) of these patients remained relapse-free during the follow-up.
- Of the 31 patients who relapsed, mean (standard deviation [SD]) time to first relapse in the follow-up period was 52.4 (47.9) days (Table 1).
- Among patients with response (N=50) and remission (N=74) at the end of esketamine NS treatment, 74.0% (37/50) and 93.2% (69/74) remained relapse-free during the follow-up period, respectively.
- Of the patients who relapsed after achieving response or remission at the end of esketamine NS treatment, mean time to first relapse was 57.1 and 66.6 days, respectively.

Concomitant treatments

- Most patients continued background treatment after stopping esketamine NS.
- At the end of the follow-up period, 97.7% were receiving antidepressant treatment and 35.2% were receiving psychosocial treatment that had been started during the esketamine NS treatment period (Table 2).
- During the follow-up period, 21.3% of patients ended an antidepressant treatment that had been received together with esketamine NS. As patients could receive multiple concomitant treatments, patients who ended one treatment during the follow-up may have continued receiving additional concomitant treatments.

Strengths and limitations

- ECHO represents the varied populations of patients with TRD, demonstrating esketamine NS' effectiveness in real-world settings.
- The ECHO study was limited by the single-arm design and the high flexibility in frequency of assessments and treatment cessation, representing real-world clinical settings.
- Of 570 patients enrolled in the ECHO treatment period, only 301 (52.8%) continued into the post-treatment follow-up period.

Figure 1. MADRS total score in the post-treatment follow-up period by patient status at end of esketamine NS treatment

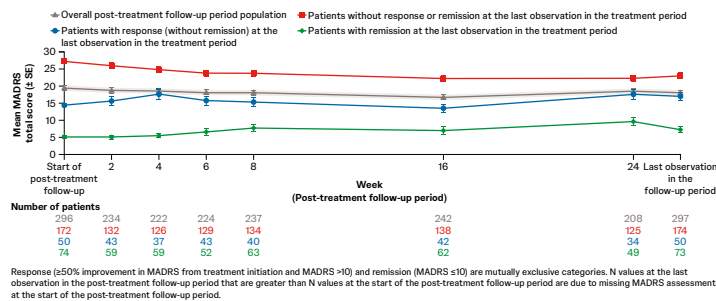


Figure 2. MADRS total score in the post-treatment follow-up period stratified by duration of esketamine NS exposure

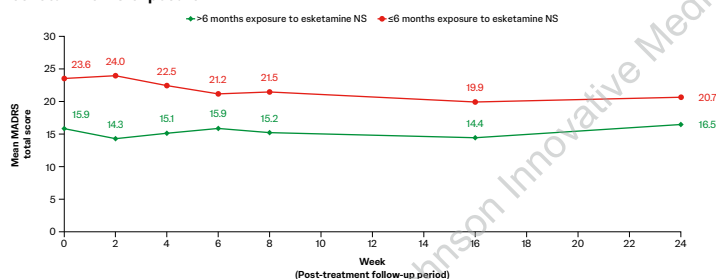


Figure 3. Remission rate in the post-treatment follow-up period: overall population and stratified by duration of esketamine NS exposure

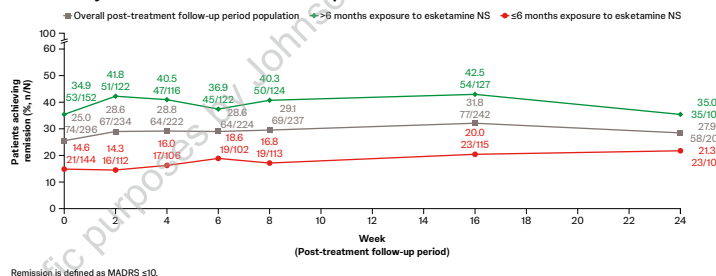


Table 1. Relapse rates during the post-treatment follow-up period

n (%), unless otherwise stated	Patients with response/remission at any time during the treatment period or follow-up period (N=166)	Patient status at end of treatment period	
		Response (N=50)	Remission (N=74)
≥1 relapse	31 (18.7)	13 (26.0)	5 (6.8)
Time to first relapse,* days (mean, SD)	52.4 (47.9)	57.1 (49.3)	66.6 (52.5)
Definition of first relapse, n/N (%)			
As defined by DSM-5 criteria	18/31 (58.1)	8/13 (61.5)	5/5 (100.0)
Confirmed MADRS total score ≥22 ^a	13/31 (41.9)	5/13 (38.5)	0
Suicide attempt	0	0	0
Hospitalisation	0	0	0

Response (≥50% improvement in MADRS from treatment initiation and MADRS >10) and remission (MADRS ≤10) are mutually exclusive categories. *Time to first relapse from Day 1 in the post-treatment follow-up period. ^aWorsening of depressive symptoms as indicated by MADRS total score ≥22. MADRS was evaluated by an additional assessment conducted ≥5 days from the previous assessment; the date of the second MADRS assessment was recorded as the date of relapse.

Table 2. Background antidepressant and psychosocial treatments during the post-esketamine NS follow-up period

Treatment, n (%)	(N=301)
Concomitant treatments initiated during esketamine NS treatment and ongoing at end of post-treatment follow-up period	
≥1 antidepressant treatment	294 (97.7)
≥1 psychosocial treatment	106 (35.2)
Concomitant treatments received together with esketamine NS treatment and ended during post-treatment follow-up period	
≥1 new antidepressant treatment	64 (21.3)
≥1 psychosocial treatment	3 (1.0)
Treatment initiated at/after the start of post-esketamine NS follow-up	
≥1 antidepressant treatment	81 (26.9)
≥1 psychosocial treatment	3 (1.0)

As patients could receive multiple concomitant treatments, patients who ended one treatment during the follow-up may have continued receiving additional concomitant treatments.

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- European Medicines Agency. 2025. SPRAVATO® (esketamine NS) Summary of Product Characteristics. Available from: https://www.ema.europa.eu/en/documents/product-information/spravato-epar-product-information_en.pdf [Accessed: June 2026].
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Key takeaways



- The ECHO study demonstrates the durability of esketamine NS' clinical benefit following treatment cessation.
- Overall, these results provide evidence that achievement of remission during esketamine NS treatment can be maintained over the long term following treatment cessation, with patients demonstrating very low relapse rates during the follow-up period.
- In particular, longer exposure to esketamine NS was associated with improved outcomes and durability in the post-esketamine NS follow-up period such as lower MADRS score, and patients who achieved remission at the end of the treatment period demonstrated low relapse rates in the follow-up.
- This highlights the importance of providing sufficient esketamine NS treatment duration and aiming for high efficacy targets during treatment to maximise its therapeutic benefit.

Conclusions



- In this real-world cohort, patients who achieved remission by the end of esketamine NS treatment demonstrated lower mean MADRS scores throughout the post-treatment follow-up period compared with non-responders.
- Longer duration of exposure to esketamine NS was associated with higher remission rates and lower mean MADRS scores following esketamine NS cessation.
- Most patients who achieved remission or response with esketamine NS remained relapse-free during the 6 months after treatment cessation, supporting the clinical relevance of achieving high efficacy thresholds before treatment cessation.
- These data thus provide important clinical insights into TRD clinical trajectories following esketamine NS treatment cessation.

Abbreviations

DSM-5: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; ECHO: Esketamine CoHoRT; MADRS: Montgomery-Åsberg Depression Rating Scale; NS: nasal spray; SD: standard deviation; SE: standard error; SNRI: serotonin-norepinephrine reuptake inhibitor; SSRI: selective serotonin reuptake inhibitor; TRD: treatment resistant depression.

Author contributions

Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: CRL, SDF, YG, AL, TI, EO, MP, TWK, DZ, EC; drafting of the publication, or reviewing it critically for important intellectual content: CRL, SDF, YG, AL, TI, EO, MP, TWK, DZ, EC; final approval of the publication: CRL, SDF, YG, AL, TI, EO, MP, TWK, DZ, EC.

Disclosures

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