

# Real-world esketamine nasal spray treatment duration and dosing in patients with treatment resistant depression: findings from ECHO, a non-interventional study

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## Introduction

- Esketamine nasal spray (NS), in combination with a selective serotonin reuptake inhibitor (SSRI) or serotonin-norepinephrine reuptake inhibitor (SNRI), is indicated for use in adults with treatment resistant depression (TRD).
- Evaluating patients' treatment patterns with esketamine NS across real-world clinical settings can facilitate improved understanding of current trends in clinical decision-making, including treatment duration and dosing.
- Furthermore, assessing the impact of treatment patterns on patient outcomes is important for informing treatment guidance for clinicians.
- Here, this analysis aimed to assess the real-world treatment patterns of patients with TRD who were initiating esketamine NS as a new antidepressive treatment regimen, including duration, dosing and frequency, and reasons for treatment discontinuation.
- Secondly, post-hoc analyses to evaluate the impact of treatment regimens on patient outcomes were conducted.

## Methods

- Esketamine CoHort (ECHO) was a long-term, prospective, international, non-interventional study investigating esketamine NS long-term effectiveness and safety in real-world clinical settings.
- Esketamine NS was prescribed per the local prescribing information, in accordance with local reimbursement criteria independent of the study. Clinical management, including treatment duration and dosing, was reflective of local practice and at the sole discretion of the treating physician.
- ECHO comprised a treatment period of variable duration; the duration of esketamine NS exposure, dosing and frequency changes, and reasons for discontinuation are reported.
- Time to treatment discontinuation after achieving response (≥50% improvement in Montgomery-Åsberg Depression Rating Scale [MADRS] total score) and remission (MADRS total score ≤10), and response/remission rates stratified by treatment patterns, are reported.

## Results

- In total, 570 patients, aged 19–95 years, from 7 countries (Belgium, Germany, Italy, Israel, the Netherlands, Spain and Sweden) started the treatment period in ECHO.
- Baseline characteristics have been reported previously; patients had severe and chronic TRD<sup>2</sup>.

### Treatment duration

- The mean and median esketamine NS treatment durations were 267 days (~9 months) and 190 days (~6 months), respectively.
  - Of 570 patients, 23.2% received esketamine NS for >12 months.
  - Following study completion, 10.7% of patients continued esketamine NS treatment (Table 1).

- The most common reasons for treatment discontinuation for all patients were patients no longer requiring treatment (28.9%; mainly due to depressive symptom resolution), lack of efficacy (20.4%) and patient preference (19.1%; Table 1).

### Treatment dosing and frequency

- The most common dosing frequency was once per week following the first 8 weeks of treatment (38.2% of patients) and once every 2 weeks for the last dosing frequency before stopping treatment (37.2% of patients; Figure 1).
- Of the three doses of esketamine NS (28, 56 and 84 mg), 84 mg was the most frequently administered dose in 67.4% of patients, the highest dose taken in 79.3% of patients and the final dose taken in 66.8% of patients (Figure 2).
- At baseline, 75.1% of patients received a dose of 56 mg, 23.9% received 28 mg and 1.1% received 84 mg (Figure 3).
- At Week 2, 51.1% of patients received a dose of 84 mg, increasing to 56.5% at Week 4.
- By Week 20, the esketamine NS dose had been up-titrated to 84 mg at least once for 88.9% of patients.

### Esketamine NS cessation following response and remission

- Of the patients without remission (N=118) during the treatment phase, the mean time from first response to the end of the treatment phase was 203.0 days (Table 2).
- Among all patients, the mean time from first remission and first response to the end of the treatment phase was 286.9 and 296.6 days, respectively (Table 2).

### Impact of treatment regimens on patient outcomes

- Of reported treatment regimens, the greatest proportions of patients achieving response and/or remission at any point during the treatment period were reported for patients who received >9 months of treatment, with a modal dose of 84 mg, modal weekly treatment and early up-titration to 84 mg at Week 2 (N=48).
- Among these patients, 77.1% and 50.0% achieved response and remission at any time during the treatment regimen, respectively (Table 3).

- The proportions of patients who achieved response at any time during the treatment period were generally greater amongst patients with a modal esketamine NS dose of 84 mg compared with ≤56 mg, including for patients with later up-titration to 84 mg (i.e. after Week 2; Table 3).

### Strengths and limitations

- ECHO data represent the broad and diverse populations of patients with TRD, reflecting the heterogeneity of patients' experiences.
- Esketamine NS was prescribed in accordance with local labels and reimbursement criteria, and at the treating physician's discretion; as such, differences across regions may have influenced clinicians' selection of patients for treatment and decision-making regarding treatment regimens.
- High variability in treatment adherence observed in real-world evidence studies represents a potential limitation of this analysis.

**Table 1. Treatment disposition and duration of esketamine NS exposure**

| n (%)                                                                              | Esketamine NS + SSRI/SNRI (N=570) |
|------------------------------------------------------------------------------------|-----------------------------------|
| Ongoing esketamine NS treatment at the time of study completion or discontinuation | 61 (10.7)                         |
| Discontinuing esketamine NS treatment                                              | 509 (89.3)                        |
| Continuing into post-treatment follow-up                                           | 301 (52.8)                        |
| <b>Reasons for esketamine NS treatment discontinuation</b>                         |                                   |
| Patient no longer requiring treatment                                              | 165 (28.9)                        |
| Lack of efficacy                                                                   | 116 (20.4)                        |
| Patient preference                                                                 | 109 (19.1)                        |
| Other                                                                              | 59 (10.4)                         |
| Adverse event                                                                      | 47 (8.2)                          |
| Lack of compliance                                                                 | 6 (1.1)                           |
| Lack of tolerability                                                               | 4 (0.7)                           |
| Death                                                                              | 3 (0.5)                           |
| <b>Duration of esketamine NS exposure</b>                                          |                                   |
| <3 months                                                                          | 174 (30.5)                        |
| 3–6 months                                                                         | 100 (17.5)                        |
| 6–9 months                                                                         | 114 (20.0)                        |
| 9–12 months                                                                        | 50 (8.8)                          |
| >12 months                                                                         | 132 (23.2)                        |

**Table 2. Time after response/remission to end of treatment**

|                                                                     | Population (n)                   | Mean (SD)     | Median | Minimum maximum |
|---------------------------------------------------------------------|----------------------------------|---------------|--------|-----------------|
| Time from first response <sup>a</sup> to the end of treatment, days | All patients (206)               | 286.9 (293.2) | 202    | 1, 1437         |
|                                                                     | All patients (323)               | 296.6 (299.9) | 199    | 1, 1437         |
| Time from first response <sup>a</sup> to the end of treatment, days | Patients without remission (118) | 203.0 (240.3) | 129    | 1, 1303         |
|                                                                     |                                  |               |        |                 |

<sup>a</sup>MADRS total score ≤10; <sup>b</sup>≥50% improvement in MADRS from treatment initiation.

**Table 3. Response and remission for the five most frequent dosing patterns during the treatment period**

| Treatment duration, frequency and dosing pattern |                              |                                    |                           |  | Total patients, n (%) <sup>a</sup> | Remission at any time during the treatment regimen, n (%) <sup>b</sup> | Response at any time during the treatment regimen, n (%) <sup>b</sup> |
|--------------------------------------------------|------------------------------|------------------------------------|---------------------------|--|------------------------------------|------------------------------------------------------------------------|-----------------------------------------------------------------------|
| Treatment duration                               | Modal esketamine NS dose, mg | Up-titration                       | Modal treatment frequency |  |                                    |                                                                        |                                                                       |
| 3–9 months                                       | 84                           | Up-titration to 84 mg at Week 2    | Weekly                    |  | 63 (11)                            | 19 (30.2)                                                              | 36 (57)                                                               |
| >9 months                                        | 84                           | Up-titration to 84 mg at Week 2    | Weekly                    |  | 48 (8.4)                           | 24 (50.0)                                                              | 37 (77)                                                               |
| 3–9 months                                       | 84                           | Up-titration to 84 mg at Week 2    | Every 2 weeks             |  | 40 (7.0)                           | 14 (35.0)                                                              | 24 (60.0)                                                             |
| >9 months                                        | 84                           | Up-titration to 84 mg after Week 2 | Weekly                    |  | 33 (5.8)                           | 16 (48.5)                                                              | 24 (72.7)                                                             |
| 3–9 months                                       | ≤56                          | N/A                                | Weekly                    |  | 29 (5.1)                           | 10 (34.5)                                                              | 14 (48.3)                                                             |

<sup>a</sup>N=570 and percentages are calculated accordingly; <sup>b</sup>The total numbers of patients with each reported treatment regimen were used as the denominator to calculate the percentages of patients with response or remission at any time during the treatment regimen for each treatment regimen.

**Figure 1. Modal dosing frequency following the first 8 weeks of treatment and last dosing frequency before stopping esketamine NS treatment**

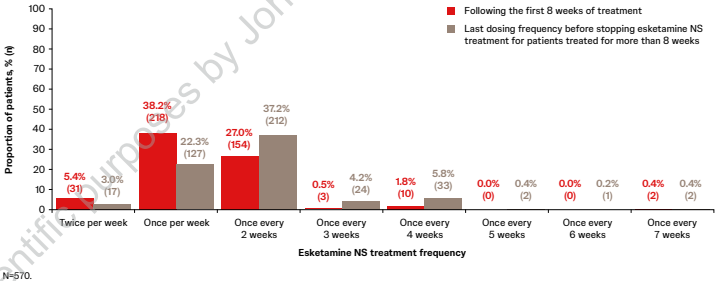
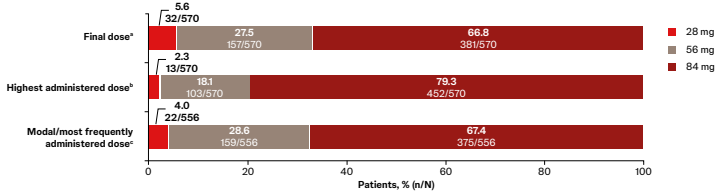
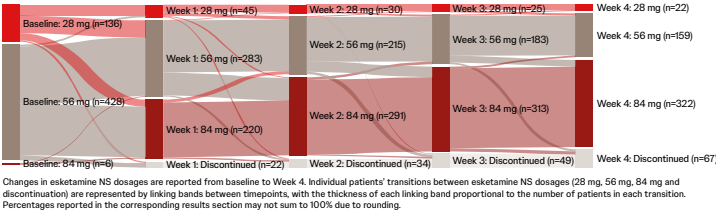


**Figure 2. Esketamine NS treatment dosing during the treatment period**



\*The final dose is the last non-zero dose received; \*Two patients (0.4%) received a highest administered dose of 112 mg; \*If a patient received only one dose or two doses with different dose amounts, then the modal/most frequently administered dose was not calculated.

**Figure 3. Changes in esketamine NS dose from baseline to Week 4**



## References:

1. European Medicines Agency. 2025. SPRAVATO® (esketamine NS) Summary of Product Characteristics. Available from: [https://www.ema.europa.eu/en/documents/product-information/spravato-spar-product-information\\_en.pdf](https://www.ema.europa.eu/en/documents/product-information/spravato-spar-product-information_en.pdf) [Accessed: June 2026]. 2. Rosso G, et al. Poster presented at EPA 2026; EPPO15.

## Key takeaways



- These results indicate that clinicians may employ a multifactorial approach to decision-making with esketamine NS treatment, considering patient characteristics and perspectives, and the anticipated impact of treatment frequency, duration and dose on patient outcomes, to select the most suitable treatment regimens for their patients.
- Patients who received adequate doses of esketamine NS (i.e. 84 mg) generally achieved higher rates of response at any point during the treatment regimen compared with patients who received lower doses; response rates were generally greater with 84 mg even among patients with later up-titration.

## Conclusions



- Real-world use of esketamine NS in patients with TRD was characterised by marked heterogeneity in treatment duration, reflecting individualised clinical decision-making, patient preferences and differences in reimbursement criteria across regions.
- Dose optimisation, including escalation to the highest approved dose (84 mg), was commonly employed and may be central to achieving and sustaining clinical benefit in routine practice.
- Importantly, treatment discontinuation was most frequently driven by symptom resolution, underscoring the clinical effectiveness of personalised esketamine NS regimens in real-world settings.

## Abbreviations

ECHO: Esketamine CoHort; MADRS: Montgomery-Åsberg Depression Rating Scale; N/A: not applicable; NS: nasal spray; SNRI: serotonin-norepinephrine reuptake inhibitor; SSRI: selective serotonin reuptake inhibitor; SD: standard deviation; TRD: treatment resistant depression.

## Author contributions

Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: EC, KF, CvH, JMO, MPe, MKS, TWK, DZ, LH. Drafting of the publication, or reviewing it critically for important intellectual content: EC, KF, CvH, JMO, MPe, MKS, TWK, DZ, LH. Final approval of the publication: EC, KF, CvH, JMO, MPe, MKS, TWK, DZ, LH.

## Disclosures

EC: Received honoraria, advisory board fees and travel support from AstraZeneca, Bristol Myers Squibb, Eli Lilly and Company, Janssen-Cilag, Lundbeck, Pfizer, Servier, Teva, Viatris and Wyeth. KF: Received honoraria from Janssen-Cilag, Eli Lilly and Sigma and travel support from Brainway, Janssen-Cilag and Liva-Nova. CvH, MKS: Employees of Johnson & Johnson; hold Johnson & Johnson company stock/stock options. JMO: Received grants and served as consultant, advisor or CME speaker for AstraZeneca, Bristol Myers Squibb, Eli Lilly and Company, Glaxo-Smith-Kline, Johnson & Johnson, Lundbeck, Novartis, Otsuka, Pfizer and Sanofi-Aventis. MPe: Received travel support from Johnson & Johnson; participated in clinical studies on esketamine NS. MKS: Received honoraria in the past five years for lectures and advisory board membership or has engaged in clinical trial activities with AbbVie, Angelini Pharma, Boehringer Ingelheim, EG Stada, Fidia, Johnson & Johnson, Lundbeck, Merck Sharp and Dohme, Neopharm Gentili, Newron, Otsuka, Pfizer, Recordati, Rovi, Teva and Viatris Corporation, all of which are unrelated to this work. DZ: Received speaker's honoraria, advisory board fees and travel support from Johnson & Johnson and Lundbeck over the last 3 years; participated in clinical trials on esketamine NS. TWK: Formerly an employee of Johnson & Johnson and held Johnson & Johnson company stock/stock options. LH: Participated in advisory boards and received speaker's honoraria over the last 3 years from Johnson & Johnson and Lundbeck; participated in clinical studies on esketamine NS.

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