Response and Remission on Esketamine Nasal Spray in Patients With Treatment-Resistant Depression Overall and Among TMS-Naive Subgroup

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Introduction

- Esketamine nasal spray and transcranial magnetic stimulation (TMS) are treatments indicated for treatment-resistant depression (TRD) with proven efficacy in clinical trials[1-5]
- There are no guidelines on the sequence of use of these treatments in TRD
- To inform decision-making in treatment choice, this analysis used Patient Health Questionnaire (PHQ-9) data from a large US group psychiatric practice to measure response and remission on esketamine depending on previous TMS experience

Methods

Data source

- Retrospective de-identified electronic medical records data including patient demographics, esketamine and TMS treatment information, and PHQ-9 scores were obtained from Mindful Health Solutions (MHS) clinics from 05/02/2018 to 01/15/2024
- Institutional review board exemption status under Exemption 45 CFR 46.104(d)(4) was granted prior to commencement of the study[6]

Study design

- The study had a retrospective observational design
- The intake period spanned from 03/05/2019 to the end of data; the index date was the date of esketamine initiation
- Adults who initiated esketamine for TRD in MHS clinics during the intake period and had ≥1 baseline PHQ-9 score were included in the overall cohort; the TMS-naive subgroup included patients without history of TMS treatment before or on the index date
- Baseline PHQ-9 score was the most recent score before or on the index date and follow-up PHQ-9 scores were observed after the index date until the end of patient clinical activity or end of data

Outcomes

- PHQ-9 is a patient-reported measure of depression severity; it has a recall period of 2 weeks; scores range from 0 to 27, and higher scores indicate higher severity[7]
- Response was defined as PHQ-9 score decrease from baseline by ≥50% and was assessed among patients with a baseline PHQ-9 score ≥10[8]
- Remission was defined as PHQ-9 score <5 and was assessed among patients with a baseline PHQ-9 score ≥5[9]

Statistical analysis

- Kaplan-Meier survival analysis was used to describe time from the index date to response and remission; patients without an outcome were censored at the last PHQ-9 score in the data

Results

Demographics and baseline characteristics

- 911 patients were included in the overall cohort out of which 512 (56.2%) were TMS-naive; baseline characteristics are reported in **Table 1**

Clinical outcomes

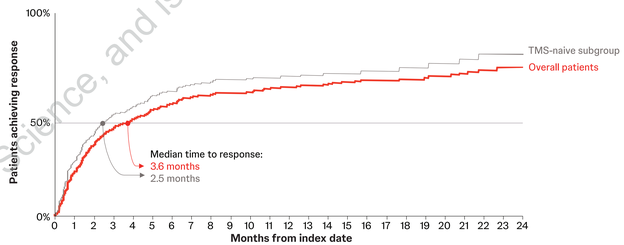
- Patients in the overall cohort completed a mean of 24.9 esketamine sessions over a mean of 12.8 months of follow-up and patients in the TMS-naive subgroup completed a mean of 23.8 sessions over a mean of 12.5 months of follow-up
- Time to response (**Figure 1**):
  - At 12 months after the index date, the probability of achieving response was 69.6% in the overall cohort and 75.4% in the TMS-naive subgroup
  - The median time to response was 3.6 months among the overall cohort and 2.5 months among the TMS-naive subgroup
- Time to remission (**Figure 2**):
  - At 12 months post-index date, the probability of achieving remission was 37.3% in the overall cohort and 44.3% in the TMS-naive subgroup
  - The median time to remission was not reached among the overall cohort and was 15.1 months among the TMS-naive subgroup

TABLE 1. Baseline characteristics

Mean ± SD [median] or n (%)	Overall esketamine cohort (N = 911)	TMS-naive subgroup (n = 512)
Age at index date (years)	43.7 ± 13.7 [42.0]	42.6 ± 13.7 [40.0]
Female	516 (56.6)	278 (54.3)
State		
California	894 (98.1)	501 (97.9)
Washington	17 (1.9)	11 (2.1)
Year of index date		
2021	190 (20.9)	107 (20.9)
2022	394 (43.2)	228 (44.5)
2023-2024	327 (35.9)	177 (34.6)
PHQ-9 scores		
Baseline PHQ-9 score (out of 27)	16.3 ± 6.1 [17.0]	15.6 ± 6.3 [16.0]
Time from baseline score to index date (days)	3.6 ± 12.6 [0.0]	3.0 ± 11.9 [0.0]
Patients with PHQ-9 score ≥10	773 (84.9)	419 (81.9)
MADRS scores		
Patients with a MADRS score	849 (93.2)	461 (90.0)
Baseline MADRS score (out of 60)	34.9 ± 7.9 [36.0]	35.3 ± 7.7 [36.0]

MADRS, Montgomery–Åsberg Depression Rating Scale; PHQ-9, Patient Health Questionnaire; SD, standard deviation, TMS, transcranial magnetic stimulation.

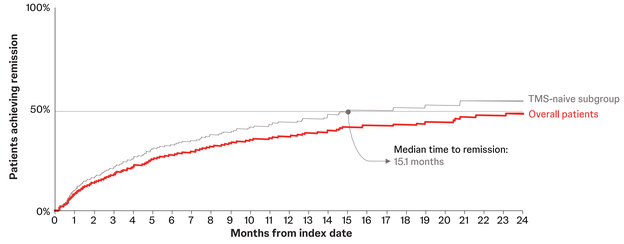
FIGURE 1. Time to response (decrease from baseline PHQ-9 score of ≥50%)



Patients at risk, n (%)	1 month	3 months	6 months	12 months
Overall esketamine cohort	542 (71.4)	335 (44.1)	210 (27.7)	96 (12.7)
TMS-naive subgroup	270 (65.9)	152 (37.1)	91 (22.2)	38 (9.3)
Kaplan-Meier rates, % (95% CI)				
Overall esketamine cohort	23.6 (20.6-26.8)	46.9 (43.3-50.7)	60.4 (56.7-64.3)	69.6 (65.7-73.5)
TMS-naive subgroup	29.2 (25.0-34.0)	54.4 (49.4-59.6)	67.5 (62.5-72.5)	75.4 (70.3-80.2)

CI, confidence interval; PHQ-9, Patient Health Questionnaire; TMS, transcranial magnetic stimulation.

FIGURE 2. Time to remission (PHQ-9 score <5)



Patients at risk, n (%)	1 month	3 months	6 months	12 months
Overall esketamine cohort	732 (85.8)	584 (68.5)	421 (49.4)	219 (25.7)
TMS-naive subgroup	395 (83.7)	304 (64.4)	216 (45.8)	105 (22.3)
Kaplan-Meier rates, % (95% CI)				
Overall esketamine cohort	8.2 (6.5-10.3)	17.6 (15.1-20.4)	27.9 (24.8-31.4)	37.3 (33.5-41.3)
TMS-naive subgroup	10.0 (7.6-13.2)	21.1 (17.6-25.3)	33.0 (28.6-37.9)	44.3 (39.1-49.8)

CI, confidence interval; PHQ-9, Patient Health Questionnaire; TMS, transcranial magnetic stimulation.

Limitations

- PHQ-9 score is a patient-reported outcome and subject to recall bias
- Results may not be generalizable to patients receiving esketamine in non-MHS clinics, from states other than California and Washington, with public insurance or the uninsured

Conclusions

- Within a year of esketamine initiation, over two-thirds of patients achieved response and over one-third of patients achieved remission of self-reported depression symptoms measured by the PHQ-9
- This descriptive analysis suggests that TMS experience does not preclude response to esketamine, however, there is a trend of TMS-naive patients responding and reaching remission faster

Disclosures
TM is and JG was, at the time of the study, an employee and stockholder of Mindful Health Solutions, as well as an honorarium speaker for Janssen Scientific Affairs, LLC. MZ, AS, DP, BM, and FJ are employees of Analysis Group, Inc., a consulting company that has provided paid consulting services to Janssen Scientific Affairs, LLC, which funded the development and conduction of this study. KJ is an employee and stockholder of Johnson & Johnson.

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