Real-World Change in Depressive Symptoms Among Patients With Treatment-Resistant Depression Initiated on Esketamine Nasal Spray

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Introduction

- Esketamine nasal spray (ESK), approved for treatment-resistant depression (TRD) in the United States (US) on March 5, 2019, has demonstrated efficacy and safety in multicenter, randomized, phase 3 trials[1,2]
- Real-world evidence of ESK effectiveness remains limited

Objective

- To evaluate the real-world effectiveness of ESK among US patients with TRD using health insurance claims data augmented with 9-item Patient Health Questionnaire (PHQ-9) scores

Methods

Data source

- Closed claims from Komodo Research Database and PHQ-9 scores from Komodo Clinical Observations Database were used during January 2016 to June 2023
- Data was de-identified and complied with requirements of the Health Insurance Portability and Accountability Act

Study design

- A retrospective observational design was used
- The intake period spanned from March 5, 2019 (ESK approval date for TRD in the US) to end of data; the index date was the date of ESK initiation
- The baseline period was the 12 months before the index date
- The follow-up period spanned the index date until the end of continuous insurance eligibility or data availability

Study population

- ≥1 MDD diagnosis (International Classification of Disease, Tenth Revision, Clinical Modification [ICD-10-CM]: F32.X [excluding F32.A and F32.8], F33.X [excluding F33.8])
- Initiation of ESK during the intake period
- Evidence of TRD before the index date (i.e., ≥2 unique antidepressants of adequate dose and duration during the major depressive episode in which ESK was initiated)
- ≥18 years old on the index date
- ≥12 months of continuous insurance eligibility before the index date
- ≥1 PHQ-9 score during the baseline period or on the index date (i.e., baseline score) and during the follow-up period up to 30 days after the last ESK claim (i.e., score while on ESK treatment)

Subgroup

- Patients with baseline PHQ-9 ≥10 indicating moderate-to-severe depression were analyzed separately

Outcome measures

- PHQ-9 is a patient-reported tool with a recall of 2 weeks; the score ranges from 0 to 27, with higher scores indicating higher severity[3]
- Depression severity was measured using most recent baseline PHQ-9 score (mean [median] time to index date: 78.5 [30] days) and the most recent score while on ESK treatment (mean [median] time to last treatment session: 91.0 [24] days) as follows:
  - Mean change in PHQ-9 score
  - Proportion of patients with moderately severe or severe depression (PHQ-9 score ≥15)
  - Time to substantial clinical improvement (mean reduction in score of ≥6 points among those with baseline PHQ-9 score of ≥6 points)[4] in the follow-up period

Statistical analysis

- Generalized estimating equations adjusted for repeated measurements of PHQ-9 score for the same patient were used to estimate mean change in PHQ-9 score and compare proportions of patients with moderately severe or severe depression in follow-up versus baseline periods
- Time to substantial clinical improvement was described using Kaplan-Meier analysis

Results

TABLE 1: Patient baseline characteristics

Mean ± SD [median] or n (%)	ESK cohort N = 103	Subgroup with baseline PHQ-9 ≥10 N = 80
Age at index date (years)	41.5 ± 14.2 [38.0]	41.0 ± 14.3 [37.0]
Female	67 (65.0)	53 (66.3)
Insurance plan		
Commercial	71 (68.9)	54 (67.5)
Medicaid	21 (20.4)	18 (22.5)
Medicare Advantage	8 (7.8)	5 (6.3)
Unknown	3 (2.9)	3 (3.8)
Year of index date		
2019	5 (4.9)	3 (3.8)
2020	12 (11.7)	11 (13.8)
2021	36 (35.0)	27 (33.8)
2022	35 (34.0)	26 (32.5)
2023	15 (14.6)	13 (16.3)
DSM-5 comorbidities		
Anxiety disorders	87 (84.5)	69 (86.3)
Sleep-wake disorders	52 (50.5)	43 (53.8)
Physical comorbidities		
Hypertension	36 (35.0)	28 (35.0)
Obesity	32 (31.1)	27 (33.8)

DSM-5, Diagnostic and Statistical Manual of Mental Disorders, 5th Edition; ESK, esketamine nasal spray; SD, standard deviation.

Demographics and baseline characteristics

- A total of 103 patients were identified in the ESK cohort, among who 80 had baseline PHQ-9 ≥10. Baseline characteristics of these patients are reported in **Table 1**

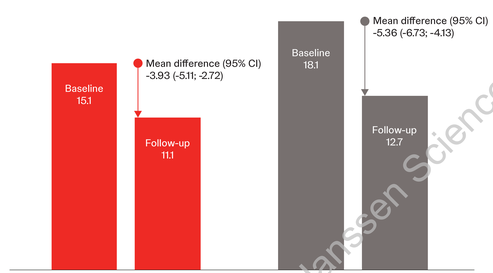
Change in depression severity

- Mean duration of follow-up period was 17.0 months in the ESK cohort and 15.7 months in the subgroup with baseline PHQ-9 ≥10
- Mean number of ESK sessions was 19.7 in the ESK cohort and 21.7 in the subgroup with baseline PHQ-9 ≥10
- From baseline to follow-up:
  - Mean PHQ-9 score decreased by statistically significant 3.93 points in the esketamine cohort and by 5.36 points in the subgroup (all $P < 0.001$; **Figure 1**)
  - Odds of reporting moderately severe or severe depression were significantly reduced (by 65% in the esketamine cohort and by 74% in the subgroup, all $P < 0.001$; **Figure 2**)
  - Mean decrease in PHQ-9 score appeared larger in patients completing ESK induction, i.e., the first 8 treatment sessions (**Figure 3**)

Time to substantial clinical improvement

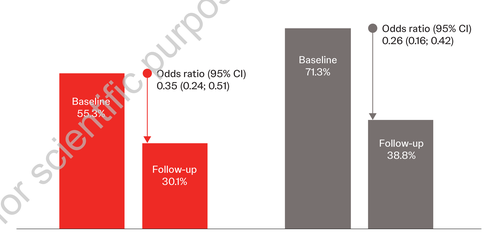
- The probability of achieving substantial clinical improvement 12 months post-index was 71.0% in the ESK cohort and 81.8% in the subgroup with baseline PHQ-9 ≥10 (**Figure 4**)

FIGURE 1: Mean PHQ-9 scores in baseline and follow-up periods



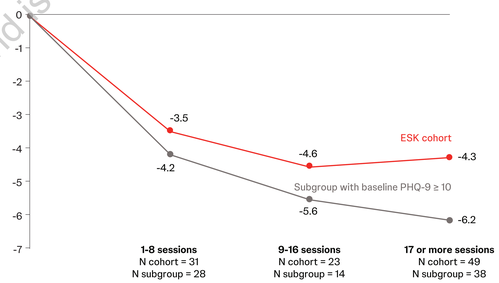
CI, confidence interval; ESK, esketamine nasal spray; PHQ-9, 9-item Patient Healthcare Questionnaire.

FIGURE 2: Proportion of patients with moderately severe or severe depression in baseline and follow-up periods



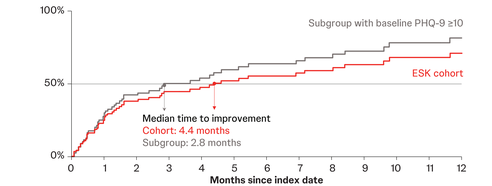
CI, confidence interval; ESK, esketamine nasal spray; PHQ-9, 9-item Patient-Health Questionnaire.

FIGURE 3: Mean change from baseline in PHQ-9 score by number of ESK sessions completed



ESK, esketamine nasal spray; PHQ-9, 9-item Patient Health Questionnaire.

FIGURE 4: Time to substantial clinical improvement



	3 months	6 months	9 months	12 months
ESK cohort, N = 92				
Patients at risk, n (%)	40 (43.5)	26 (28.3)	15 (16.3)	10 (10.9)
Kaplan-Meier rates (95% CI)	44.6 (34.8, 55.8)	55.5 (44.8, 66.9)	63.2 (51.8, 74.5)	71.0 (58.7, 82.3)
Subgroup with baseline PHQ-9 ≥10, N = 80				
Patients at risk, n (%)	30 (37.5)	17 (21.3)	10 (12.5)	5 (6.3)
Kaplan-Meier rates (95% CI)	50.3 (39.5, 62.3)	63.8 (52.0, 75.6)	72.6 (60.5, 83.6)	81.8 (68.9, 91.6)

CI, confidence interval; ESK, esketamine nasal spray; PHQ-9, 9-item Patient Health Questionnaire; SD, standard deviation.

Limitations

- PHQ-9 scores are patient-reported and subject to bias; further, PHQ-9 score measures were limited, and time between the most recent score and the last treatment session exceeded 2 weeks in some patients, potentially rendering results conservative
- TRD was identified based on pharmacy claims; pharmacy claims do not guarantee that the medication dispensed was taken as prescribed
- Results may not be generalizable to patients without health insurance

Conclusions

- Initiation of ESK was associated with significant clinical benefits among patients with TRD, which is consistent with evidence from clinical trials
- Patients, on average, reached clinically meaningful reduction in depressive symptoms (≥3 points) and more than two-thirds achieved substantial clinical improvement (≥6 points) within 12 months after initiating ESK
- Clinical benefits appeared larger in patients completing ESK induction, as well as in patients with baseline PHQ-9 score indicating moderate-to-severe depression

Disclosures

KC has served on an advisory board for Janssen Pharmaceuticals. MZ, DP, AV, ATS, and FJ are employees of Analysis Group, Inc., a consulting company that has provided paid consulting services to Janssen Scientific Affairs, LLC, a Johnson & Johnson company, which funded the development and conduction of this study. AT and KJ are employees of Janssen Scientific Affairs, LLC, a Johnson & Johnson company, and stockholders of Johnson & Johnson.

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References

1. Reif A et al. *N Engl J Med.* 2023;389:1298-1309. **2.** Popova V et al. *Am J Psychiatry.* 2019;176:428-438. **3.** American Psychological Association. Patient Health Questionnaire (PHQ-9 & PHQ-2). 2020. **4.** Turkoz I et al. *Acta Psychiatrica Scandinavica.* 2021;143:253-263.