Treatment Patterns and Persistence Among Patients With Treatment-Resistant Depression Initiated on Esketamine Nasal Spray

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Introduction

- Esketamine nasal spray (ESK), approved in 2019 for treatment-resistant depression (TRD) in the United States (US), must be administered at certified treatment centers with a US Prescribing Information recommended frequency of twice weekly during the first 4 weeks (induction phase) and later weekly or bi-weekly[1]
- While ESK may provide rapid relief from depression symptoms, durability of clinical benefits may correlate with treatment sessions completed and therapy persistence[2]
- This analysis provides recent real-world data on ESK use patterns needed to contextualize its clinical performance

Objective

- To describe ESK pattern of use and persistence among real-world US patients with TRD

Methods

Data source

- Closed claims from Komodo Research Database and Patient Health Questionnaire (PHQ-9) scores from Komodo Clinical Observations Database were used (January 2016 to June 2023)
- Data have been de-identified and complied with the Health Insurance Portability and Accountability Act

Study design

- Retrospective observational cohort study
- 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 the index ESK claim
- The baseline period included the 12 months before the index date; the follow-up period spanned the index date until the earliest of end of continuous healthcare insurance eligibility or data availability

Study population

- ≥1 major depressive disorder 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])
- ESK initiation 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 that includes ESK initiation)
- ≥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 index date and ≥1 PHQ-9 score during the follow-up period while on ESK treatment (for the assessment of treatment effectiveness performed separately)

Outcome measures

- ESK use based on pharmacy and medical claims, including number, frequency and dose of treatment sessions (i.e., ESK claims on unique days), and induction completion (≥8 sessions)
- ESK persistence defined as an absence of a gap ≥60 days between consecutive ESK treatment sessions

Statistical analysis

- Descriptive statistics were used to report ESK use; persistent time or time to ESK discontinuation was described using Kaplan-Meier analysis

Results

Demographics and baseline characteristics

- The sample included 103 patients with TRD initiated on ESK. Baseline characteristics are available in **Table 1**

TABLE 1: Patient baseline characteristics

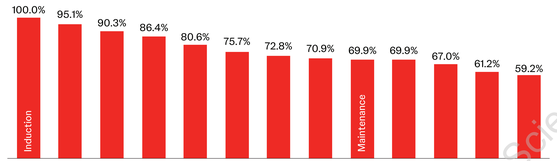
Mean ± SD [median] or n (%)	ESK cohort N = 103
Age at index date (years)	41.5 ± 14.2 [38.0]
Female	67 (65.0)
Insurance plan	
Commercial	71 (68.9)
Medicaid	21 (20.4)
Medicare Advantage	8 (7.8)
Unknown	3 (2.9)
Year of index date	
2019	5 (4.9)
2020	12 (11.7)
2021	36 (35.0)
2022	35 (34.0)
2023	15 (14.6)
PHQ-9 score[a]	15.1 ± 7.2 [16.0]
Common DSM-5 conditions	
Anxiety disorders	87 (84.5)
Sleep-wake disorders	52 (50.5)
Common physical conditions	
Hypertension	36 (35.0)
Obesity	32 (31.1)
Use of ≥3 unique antidepressants	68 (66.0)
Use of antipsychotics	48 (46.6)
Duration of follow-up period	15.7 ± 11.0 [12.8]

DSM-5, Diagnostic and Statistical Manual of Mental Disorders, 5th Edition; PHQ-9, 9-item Patient Health Questionnaire; SD, standard deviation.
[a]Depression severity was based on the most recent PHQ-9 score during the baseline period or on the index date. A score of 0 to 4 corresponds to minimal depression, a score of 5 to 9 corresponds to mild depression, a score of 10 to 14 corresponds to moderate depression, a score of 15 to 19 corresponds to moderately severe depression, and a score of 20 to 27 corresponds to severe depression.

ESK use

- During a mean (median) follow-up of 15.7 (12.8) months, patients completed a mean (median) of 21.7 (15.0) ESK sessions
- More than two-thirds of patients completed ESK induction (**Figure 1**); among them, half completed it within 64.0 days (per label, 28 days). The median frequency of induction sessions was lower than recommended per label (**Figure 2**)
- More than two-thirds of patients completed ≥12 sessions (i.e., induction and ≥4 maintenance sessions); the median frequency of the first 4 maintenance sessions was 7-8 days (per label, 7 days)
- During the first ESK session, 64.1% were administered 56 mg dosage and 35.9% with 84 mg dosage, while these proportions were 20.5% and 79.5% by end of induction, respectively (**Figure 3**)
- Patients accessed ESK through both pharmacy benefits (55.3%) and medical benefits (57.3%; **Figure 4**)

FIGURE 1: Patients with ESK treatment sessions



Mean [median] number of ESK sessions: 21.7 [15.0]

FIGURE 2: Median frequency of ESK treatment sessions

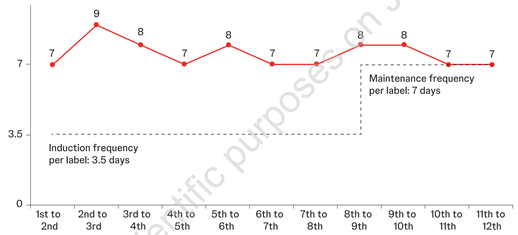


FIGURE 3: Dose of ESK during induction phase

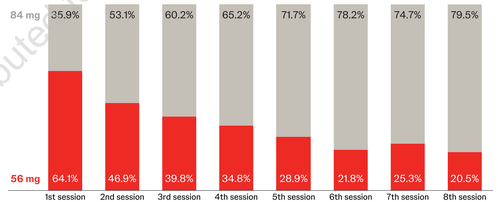
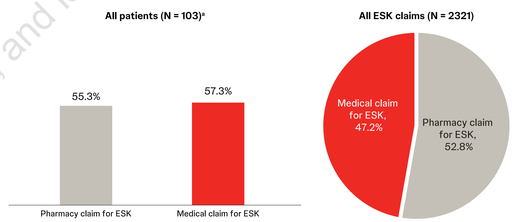
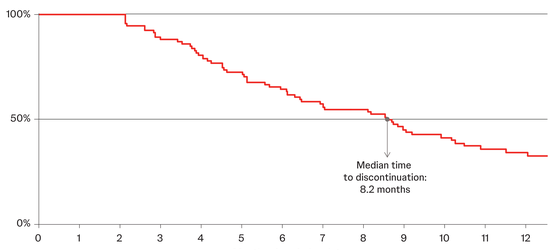


FIGURE 4: Share of ESK pharmacy and medical claims



[a]Patient-level categories are not mutually exclusive (i.e., a patient can have both pharmacy and medical claims for ESK during the follow-up period).

FIGURE 5: Persistence on ESK treatment



	3 months	6 months	9 months	12 months
Patients on treatment, n (%)	81 (78.6)	52 (50.5)	35 (34.0)	18 (17.5)
Kaplan Meier rate of persistence (95% CI)	88.1 (79.5, 93.2)	61.7 (50.7, 70.9)	42.4 (31.8, 52.6)	32.0 (21.9, 42.5)

CI, confidence interval.
ESK persistence is defined as an absence of a gap ≥60 days between consecutive ESK treatment sessions.

Persistence on ESK Treatment

- Half of patients persisted on ESK for 8.2 months (i.e., median time to discontinuation)
- The probabilities of ESK persistence at 6 and 12 months after ESK initiation were 61.7% and 32.0%, respectively (**Figure 5**)

Limitations

- TRD was determined based on pharmacy claims. However, pharmacy claims do not guarantee that the medication dispensed was taken as prescribed
- Dates of ESK pharmacy claims may not correspond to the dates of ESK administration; time between ESK treatment sessions may be misestimated
- Results may not be generalized to patients without health insurance

Conclusions

- In the real-world setting, most patients initiating ESK completed the induction phase, but session frequency was lower than per label; session frequency of the first 4 maintenance sessions aligned with label
- Most patients persisted on ESK for 8.2 months, an increase of over 4-5 months of median persistence on ESK reported in earlier studies[3,4]
- Collaboration among payers, providers, and patients is needed to ensure adherence and persistence with ESK treatment dosing schedule and duration of therapy to optimize its clinical benefits

Disclosures
KC has served on an advisory board for Janssen Pharmaceuticals. AT and KJ are employees of Janssen Scientific Affairs, LLC, a Johnson & Johnson company and stockholders of Johnson & Johnson. MZ, AV, ATS, FJ, and DP 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.

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