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Factors Associated With Completion of the Induction Phase and Persistence to Esketamine Nasal Spray Among Individuals With Major Depressive Disorder (MDD): Role of Social Determinants and Distance From Treatment Centers

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BACKGROUND

- SPRAVATO® (esketamine) nasal spray, CIII, is indicated, in conjunction with an oral antidepressant, for the treatment of treatment-resistant depression (TRD) in adults and depressive symptoms in adults with major depressive disorder (MDD) with acute suicidal ideation or behavior (MDSI)[1]
- Esketamine must be self-administered under the supervision of a certified healthcare provider at a certified treatment center in accordance with the approved Risk Evaluation and Mitigation Strategy[1]
- Induction requires twice-weekly visits for 4 weeks. After induction, TRD patients transition to the maintenance phase of weekly administration for 4 weeks followed by biweekly administration; for MDSI patients, evidence of therapeutic benefit should be evaluated to determine the need for continued treatment. The use of esketamine, in conjunction with an oral antidepressant, beyond 4 weeks has not been systematically evaluated in the treatment of depressive symptoms in adult MDSI patients

OBJECTIVE

- To measure the association of social determinants of health and distance to certified treatment center with completion of the induction phase and 6-month persistence to esketamine

METHODS

Study Design

- This study was an observational retrospective cohort among 308 US adults who initiated esketamine between 10/11/2019 and 12/31/2020

Data Sources

- Medical and pharmacy claims licensed from Clarivate
- Social determinants of health data from the Area Health Resources Files, a public dataset that compiles county-level information from >50 databases, available at https://data.hrsa.gov/topics/health-workforce/ahrf

Study Periods and Outcomes

- The 12 months prior to initiation (baseline) were used to profile demographics, healthcare utilization, social determinants, and comorbidities
- The 6-month period following initiation (follow-up) was used to measure completion of induction (8 administrations within 45 days of initiation) and persistence (defined by continuous use without a >60-day gap)

Populations

- All 308 individuals were included in the analysis to assess completion of the induction phase, which applies to individuals with either TRD or MDSI. 275 individuals with no evidence of MDSI (probable TRD) were included in the persistence analysis

Covariables

- Distance was derived from the individual's assigned zip code centroid to the certified esketamine treatment center and was categorized by tertile (≤2.5, 2.6-7.2, and >7.2 miles)
- Social determinants (employment, education, health insurance coverage, population density, and race/ethnicity), healthcare access variables, and distance to certified treatment center were included in multivariable analyses, logistic regression (completed induction phase), and the Cox proportional hazards model (time to discontinuation)

RESULTS

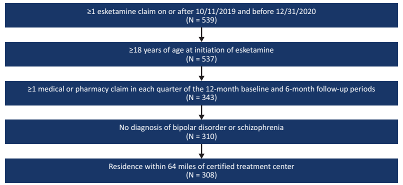
Overall Sample

- A total of 308 of the 539 patients who initiated esketamine were selected as eligible users in the study (**Figure 1**)

Demographic and Baseline Characteristics

- The study population had a mean age of 48.8 years and was predominantly female (61.4%) and commercially insured (57.8%; **Table 1**)
- Average distance to certified treatment center was 7.0 miles (standard deviation: 9.4 miles)
- A total of 43.2% of the population completed induction and, of the probable TRD population, 34.2% were persistent with esketamine therapy

Figure 1. Flow Diagram for the Selection of Eligible Users



≥1 esketamine claim on or after 10/11/2019 and before 12/31/2020
(N = 539)
≥18 years of age at initiation of esketamine
(N = 537)
≥1 medical or pharmacy claim in each quarter of the 12-month baseline and 6-month follow-up periods
(N = 343)
No diagnosis of bipolar disorder or schizophrenia
(N = 310)
Residence within 64 miles of certified treatment center
(N = 308)

Table 1. Distribution of Demographic and Social Determinants of Health Characteristics Among the Total Population

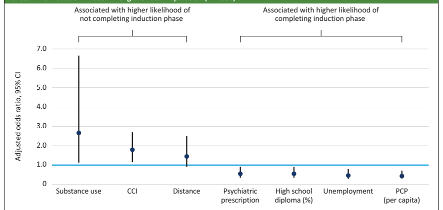
Demographic or social characteristic, n (%)	Patients N = 308
Female	189 (61.4)
Age, mean ± SD[a]	48.8 ± 16.9
Insurance plan	
Commercial	178 (57.8)
Medicaid	39 (12.7)
Medicare	81 (26.3)
VA/other	10 (3.2)
Comorbidities	
GAD	97 (31.5)
Sleep/wake disorders	71 (23.1)
Substance disorder	35 (11.4)
CCI, mean (SD)	
0	262 (85.1)
≥1	46 (14.9)
Service utilization	
Psychiatry visit >3	152 (49.4)
Psychiatric prescription fills (yes)	145 (47.1)
Social determinants of health	
Population density per square mile ≥912.9	172 (55.8)
High school graduation rate ≥90.8	154 (50.0)
Mental health providers per 100,000 population ≥17.7	165 (53.6)
PCPs per 100,000 population ≥100.8	155 (50.3)
Unemployment rate >8.3	155 (50.3)
Non-Hispanic White percentage >58.1	151 (49.0)
Non-Hispanic Black percentage ≥8.0	168 (54.5)
Hispanic percentage ≥9.9	165 (53.6)
Asian percentage ≥4.7	154 (50.0)
Rural (yes)	75 (24.4)
Distance to certified treatment center (miles), mean (SD)	7.0 (9.4)
Completed induction (yes)	133 (43.2)
Persistent[a] (yes)	94 (34.2)

CCI: Charlson Comorbidity Index; GAD: generalized anxiety disorder; MDSI: major depressive disorder and suicidal ideation or behavior; PCP: primary care physician; SD: standard deviation; VA: Veterans Administration.
[a]Includes 275 participants not defined as MDSI.

Association Between Select Characteristics and Not Completing the Esketamine Induction Phase Among the Total Population

- County-level factors associated with completing the esketamine induction phase were rates of primary care physicians (PCPs) per capita, unemployment, and high school graduation (**Figure 2**)
- Individual factors associated with the completion of the esketamine induction phase were psychiatric medication use in the baseline period, which was associated with a greater likelihood of completion, and Charlson Comorbidity Index (CCI) and comorbid substance use, which were associated with a greater likelihood of not completing induction

Figure 2. Adjusted Odds Ratios and 95% CIs for the Association Between Select Characteristics and Not Completing the Esketamine Induction Phase Among the Total Population (N = 308)



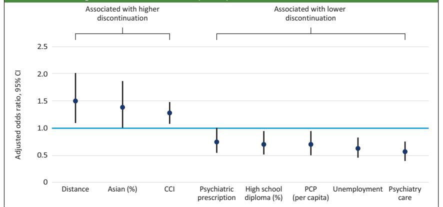
Associated with higher likelihood of not completing induction phase
Associated with higher likelihood of completing induction phase
Adjusted odds ratio, 95% CI
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
Substance use
CCI
Distance
Psychiatric prescription
High school diploma (%)
Unemployment
PCP (per capita)

CCI: Charlson Comorbidity Index; CI: confidence interval; PCP: primary care physician.

Association Between Select Characteristics and Treatment Discontinuation Among Individuals With Probable TRD

- Distance >7.2 miles, higher proportion of Asian population, and CCI were associated with a higher risk of esketamine discontinuation (**Figure 3**)
- Baseline psychiatric medication use, baseline psychiatry visit, county-level PCPs per capita, high school graduation rate, and unemployment rate were all associated with a lower risk of discontinuation

Figure 3. Adjusted Odds Ratios and 95% CIs for the Association Between Select Characteristics and Treatment Discontinuation Among Individuals With Probable TRD (N = 275)

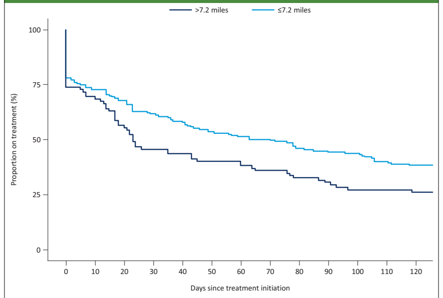


CCI: Charlson Comorbidity Index; CI: confidence interval; PCP: primary care physician; TRD: treatment-resistant depression.

Association Between Distance to Treatment Center and Treatment Persistence Among Esketamine Users With Probable TRD

- Living >7.2 miles away from the nearest certified treatment center was negatively associated with persistence in the first 30 days of treatment initiation (**Figure 4**)

Figure 4. Time to Treatment Discontinuation Among Esketamine Users With Probable TRD (N = 275), by Distance to Treatment Center



TRD: treatment-resistant depression.

CONCLUSIONS

- **Social determinants of health (race/ethnicity, employment, and education), prior psychiatric care, psychiatric medication use, substance use disorder, and distance to certified treatment center were associated with esketamine use**
- **Given that equitable access to mental health-related healthcare services is a significant challenge, social determinants of health and distance to site of care may be associated with challenges to esketamine treatment regimens**
- **Referring providers, who play an essential role in care continuity, may need to consider social determinants of health and distance to certified treatment center to help patients overcome any barriers to access**
- **Similarly, providers of esketamine treatment may need to consider social determinants of health and distance to certified treatment center when providing scheduling and support services**

REFERENCE

1. SPRAVATO® (esketamine) nasal spray, CIII [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; 2020.

DISCLOSURES

This research was sponsored by Janssen Scientific Affairs, LLC.
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