

$\Delta\Delta\text{QTcF}$ were <10 msec. The by-time-point analysis showed the maximum least squares mean difference in ΔQTcF (90% CI) between CTN and PBO was 1.64 (−1.40, 4.68) msec at 24 hours postdose. No CTN-treated participants had a QTcF increase of >30 msec; no relevant increases in PR or QRS interval or HR were observed. Four participants had $>25\%$ decrease in HR and <50 beats per minute. No abnormal U waves were observed; 1 participant had abnormal T-wave morphology. No serious TEAEs or deaths were reported. The most frequently reported TEAEs with CTN were nausea (24.1%), dizziness (24.1%), and decreased appetite (13.8%).

Conclusions. In this TQT trial, centanafadine, a potential first-in-class NDSRI in development for treatment of ADHD, had no clinically meaningful effect on cardiac repolarization and was generally safe and well tolerated.

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Change in Depressive Symptoms Following Esketamine Initiation among Patients with Treatment-Resistant Depression in a Real-World Setting

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Introduction. Treatment-resistant depression (TRD) is commonly defined as non-response to ≥ 2 antidepressant treatment courses of adequate doses and durations in the current episode in patients with major depressive disorder (MDD). Esketamine (ESK) nasal spray was approved by the Food and Drug Administration in March 2019 for the treatment of TRD in adults in conjunction with an oral antidepressant (AD). This study assessed changes in depressive symptoms following ESK initiation among patients with TRD in a real-world setting.

Methods. The study was a retrospective longitudinal observational cohort study of adults with TRD who initiated esketamine treatment between March 2019 and June 2022. Data were sourced from the PremiOM™ MDD Dataset (OM1, Boston, MA), a continuously updated cohort of over 440,000 patients with MDD in the United States with linked claims and electronic medical record data. Patients were classified as having TRD if they had ≥ 1 diagnosis of MDD during the 6 months prior to or on the index date (defined as ESK initiation) and a record of ≥ 2 unique ADs of adequate dose and duration at any time prior to the index date within the same major depressive episode (MDE; defined as no clean period of ≥ 180 days without ADs and/or MDD diagnoses).

The Patient Health Questionnaire-9 (PHQ-9) was used to measure depressive symptoms. A machine learning model was used to estimate PHQ-9 scores for patients with no documented scores. The latest PHQ-9 score among questionnaires administered in the six months prior to or on the date of first ESK treatment was used as the baseline score. Baseline scores were compared to the latest scores in the 0–3-month and 3–6 month windows after first ESK treatment. A sensitivity analysis excluding the estimated scores was conducted. Marginal models were used to test for differences in post-treatment scores relative to baseline.

Results. The study cohort included 163 patients with a mean age of 49.5 years (standard deviation [SD]=15.4). Most patients were female (58.3%). At baseline, the mean PHQ-9 score was 15.0 (SD=6.7) and 55.8% of patients had either moderately severe or severe depression (PHQ-9 ≥ 15). Patients experienced statistically significant reductions in PHQ-9 scores of 2.9 points (95% CI: 1.7 to 4.1, $p<0.001$) in the 0–3-month interval and 4.4 points (95% CI: 3.2 to 5.6, $p<0.001$) in the 3–6-month interval relative to baseline. The percentage of patients with moderately severe or severe depression (PHQ-9 ≥ 15) decreased to 34.4% at the 0–3 month interval and 20.9% at the 3–6 month interval. Results were consistent when estimated PHQ-9 scores were excluded.

Conclusions. Among patients with TRD in a real-world setting, PHQ-9 scores significantly decreased in the 6 months following initiation of ESK treatment. Further investigation of longer-term effectiveness of ESK and among key subgroups is warranted.

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Kandinsky Clerambault Syndrome Manifesting as Tinnitus

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Introduction. Tinnitus not heretofore been described as the only manifestation of delusional possession in Kandinsky-Clerambault syndrome. Such a case is presented.

Methods. Case Report: A 70-year-old left handed (pathological) man, eight years prior to presentation, noted gradual onset of decreased hearing and high-pitched constant tinnitus AU made worse with stress. Initially only present in quiet, it intensified, ultimately present in all situations, even with ambient background noise. He believed that the Devil was inside of his head, had been there for many years, and was making his life unbearable by subjecting him to the tinnitus. Other than the tinnitus, the devil did not cause any other symptoms, nor did it communicate with him in any fashion. In an effort to eliminate the Devil-induced tinnitus, he twice attempted suicide through self-strangulation. The tinnitus persisted despite treatment with mirtazapine and lumateperone.