ΔΔQTcF 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.

Previous presentation: 2023 ACCP Annual Meeting, September 10–12, 2023, Bellevue, WA

Funding. Otsuka

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

Carl D. Marci, MD[1,2], Swapna Karkare, MS[3], Manish K. Jha, MD[4], Stevan Geoffrey Severtson, PhD[1] and Kruti Joshi, MPH, BS[3]

[1]OM1, Inc., Boston, MA, USA; [2]Massachusetts General Hospital, Harvard Medical School; [3]Janssen Scientific Affairs, LLC, Titusville, NJ, USA and [4]UT Southwestern Medical Center, Dallas, TX, USA

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.

Funding. Janssen Pharmaceuticals, the manufacturer of esketamine

Kandinsky Clerambault Syndrome Manifesting as Tinnitus

Vasudha Sharma, MD[1], Luai Shaaban, MD[2], Taseen Ali[3] and Alan R Hirsch, MD[4]

[1]Dayanand Medical College & Hospital, Ludhiana, India; [2]Baskent University, Ankara, Turkey; [3]Windsor University School of Medicine, Saint Kitts & Nevis and [4]Smell & Taste Treatment and Research Foundation, Chicago, IL

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.

https://doi.org/10.1017/S1092852924001962 Published online by Cambridge University Press

Results. Abnormalities in physical examination: General: Decreased blink frequency. Continuous fidgeting and generalized tremulousness. Neurological examination: Mental status examination: Hypoverbal. Able to remember 5 digits forwards and 3 digits backwards. Unable to remember any of four objects in 3 minutes with and without reinforcement. Presidents as follows: Biden, Obama, ?. Animal Fluency Test: 7 (Abnormal). Cranial Nerve (CN) Examination: CN I Alcohol Sniff Test: 0 (Anosmia). CN VIII Calibrated Finger Rub Auditory Screening Test: Strong 2 AU. Motor Examination: 1+ cogwheel rigidity in the right upper extremity. Gait Examination: Unstable tandem gait. Reflexes: 1+ throughout. Other: Tinnitus Severity Questionnaire : 38/40 (Severe tinnitus). Tinnitus Handicap Inventory: 94/100 (Grade 5- Catastrophic handicap).

Discussion. While Kandinsky Clerambault Syndrome, Delusion of Possession Syndrome is uncommon in the United States (Dimkov, 2020; Enoch, 2020), 46% of Italians believe in the Devil (Marra, 1990) and 0.6% of Canadians believe that they have been possessed by a demon (Ross & Joshi, 1992). Although the most common neurological presentation of Kandinsky Clerambault syndrome is glossolalia, sensory phenomenon of anosmia (Chand et al, 2000; Medeiros De Bustos et al, 2014), ageusia (Chand et al, 2000), kinaesthesia (Gedevani et al, 2022), allochiria (Medeiros De Bustos et al, 2014), synesthetic neuralgia (Medeiros De Bustos et al, 2014), cenesthesia (Medeiros De Bustos et al, 2014), pain (Medeiros De Bustos et al, 2014) and anaesthesia (Yap, 1960) have also been described. While tinnitus has not been reported with Kandinsky Clerambault, it has been noted to occur with depression, anxiety (Zöger et al, 2006; Salviati et al, 2013), and psychosis (Frankenburg & Hegarty, 1994; Jain et al, 2017). Given the widespread belief in the general population of the Devil and possession by external entities, assessment of presence of Kandinsky Clerambault Syndrome in those with intractable tinnitus may be worthwhile.

Funding. No Funding

Proportion of Patients with Severe Postpartum Depression Achieving Response and Remission of Depressive and Anxiety Symptoms in the SKYLARK Study

Kristina M. Deligiannidis, MD[1,2], E. Quinn, Peeper, MD[3], Bridgette Leclair, PharmD[4], Theresa Vera, PhD[5], Ming-Yi Huang, PhD[5], Catherine Mak[4], Deidre Kile[6] and James Doherty, PhD[5]

[1]Department of Psychiatry, Zucker Hillside Hospital, Glen Oaks, NY, USA; [2]Feinstein Institutes for Medical Research, Northwell Health, Manhasset, NY, USA; [3]Touro Infirmary and Best Clinical Trials, New Orleans, LA, USA; [4]Biogen, Inc., Cambridge, MA, USA; [5]Sage Therapeutics, Inc., Cambridge, MA, USA and [6]Lenox Executive Search, Boston, MA, USA

Introduction. Postpartum depression (PPD) is a serious illness where patients (pts) experience depressive symptoms that start during or after pregnancy. Concurrent anxiety symptoms in PPD are common and are associated with poorer outcomes. The Edinburgh Postnatal Depression Scale (EPDS) is a patient-reported instrument used for PPD and may be used concurrently with the clinician-administered Hamilton Rating Scale for Anxiety (HAM-A). Zuranolone (ZRN) is an investigational oral positive allosteric modulator of synaptic and extrasynaptic $GABA_A$ receptors and neuroactive steroid for the treatment of PPD and major depressive disorder in adults. The phase 3, double blind, randomized, placebo (PBO)-controlled SKYLARK study evaluating the efficacy and safety of ZRN 50 mg (ZRN50) in pts with severe PPD met its primary endpoint of change from baseline (CFB) in the 17-item Hamilton Rating Scale for Depression (HAMD-17) total score at Day (D)15 (−15.6 vs −11.6 for placebo; p<0.001). The percentages of pts achieving HAMD-17 response (≥50% CFB in HAMD-17 total score) and remission (HAMD-17 total score ≤7) were higher in the ZRN group vs PBO. We report a post hoc analysis of the EPDS and HAM-A response and remission rates to assess the effects of ZRN50 on depressive and anxiety symptoms in the SKYLARK study.

Methods. Adults aged 18-45 years with severe PPD (baseline HAMD-17 ≥26) were randomized 1:1 to oral once-daily ZRN50 or PBO for 14 days and followed through D45. EPDS and HAM-A response (≥50% CFB in EPDS or HAM-A total score, respectively) and remission (EPDS total score <10 or HAM-A total score ≤7) rates were recorded at D3, D8, D15, D21, D28, and D45. Response and remission rates were modeled using generalized estimating equations for binary responses. Statistical testing was not adjusted for multiplicity; p values and statements of significance are considered nominal. D15 and D45 results are reported.

Results. Among 196 pts randomized and dosed, 170 completed the 45-day study. Significantly greater percentages of pts treated with ZRN achieved EPDS response (52.7% vs 33.7%; p=0.0178) and remission (49.5% vs 33.7%; p=0.0192) at D15 vs PBO and achieved HAM-A response (54.3% vs 37.8%, p=0.0338) and remission (34.8% vs 15.6%; p=0.0050) at D15 vs PBO. Numerically greater percentages of pts achieved EPDS response (57.1% vs 50.6%; p=0.3020) and remission (56.0% vs 47.1%; p=0.0812) at D45 with ZRN vs PBO and achieved HAM-A response (65.5% vs 60.0%; p=0.3066) and remission (44.0% vs 37.6%; p=0.3662) at D45 with ZRN vs PBO.

Conclusions. ZRN50 was associated with improvements in both depressive and anxiety symptoms, which commonly co-occur in individuals with PPD. These results suggest treatment with ZRN may lead to improvements in measures of both depression and anxiety and support the potential role of ZRN as a novel, oral, rapid-acting, 14-day treatment course for PPD.

Funding. Sage Therapeutics, Inc. and Biogen Inc. Medical writing and editorial support were provided by Meditech Media, Ltd. and Parexel, and funded by Sage Therapeutics, Inc. and Biogen Inc.

https://doi.org/10.1017/S1092852924001962 Published online by Cambridge University Press