fatigue vs PBO after 6 months of treatment. Reduced severity in insomnia symptoms with LEM5 and LEM10 also translated to improved daytime functioning.
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Post Market Rate of Seizures During TMS Treatment with NeuroStar® System Appears to Be Lower than Previously Estimated

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ABSTRACT: Objective: NeuroStar® Advanced Therapy System is a transcranial magnetic stimulation (TMS) device with FDA-clearance for the treatment of Major Depressive Disorder (MDD) in adult patients who have failed to receive satisfactory improvement from prior antidepressant medication in the current episode. With TMS, magnetic pulses are transmitted into the brain. Though the exact mechanism of action is unknown, it is postulated that resulting neuronal depolarization and changes in brain functional activity may be associated with various physiologic changes that lead to relief of depression in the indicated population. The type of magnetic field generated with TMS is not intended to induce a seizure during therapeutic use, but unintentional seizures have been reported during TMS treatment.
No seizures were reported with the use of the NeuroStar® system in clinical trials conducted prior to FDA clearance. The estimated risk of seizure in the NeuroStar® label is approximately 1 in 30,000 treatments or 1 in 1,000 patients. Since introduction of the NeuroStar® system into clinical practice, the rate at which seizures have been reported is even lower.

METHODS: We conducted a review of literature that named the NeuroStar® Advanced Therapy System as the device used for TMS treatment and reviewed all seizure events reported to Neuronetics, Inc., directly or through FDA MedWatch through June 30, 2019. Articles reporting seizures in subjects with epilepsy during TMS treatment were excluded.

RESULTS: Previous comprehensive reviews of seizures induced by treatment with any TMS device by Wasserman et al. (1998) and Rossi et al. (2009) revealed that the rate of seizures is low. Many subjects that developed seizures during TMS had either received stimulation at parameters beyond current recommendations or had been predisposed to develop seizures in some way. Some of the events reported as seizures may, in fact, have been non-epileptic events.
Our literature review and analysis of seizures reported to Neuronetics, Inc. revealed that the rate of seizures during TMS treatment with the NeuroStar® appears to be lower than the rate that is published in the NeuroStar® Advanced Therapy prescribing information.

CONCLUSIONS: Seizures that take place during TMS treatment with the NeuroStar® system are rare. The rate of seizures reported directly to Neuronetics, Inc. is lower than that included in the NeuroStar® prescribing information. Our literature review validated seizures during TMS treatment with the NeuroStar® system reported in published literature have described either non-epileptic events (syncope) or occurred with risk factors for seizure induction, such as other predisposing clinical factors or treatment parameters outside the guideline recommend "safe" ranges.
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Randomized, Double-Blind, Active-Controlled Study of Starting Aripiprazole Lauroxil with 1-Day Initiation in Acutely Ill Patients with Schizophrenia

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ABSTRACT: Objective: Evaluate efficacy and safety of a 2-month dose of aripiprazole lauroxil (AL) with a 1-day initiation regimen during hospitalization for an acute exacerbation of schizophrenia.

METHODS: In the phase 3b double-blind ALPINE study, adults with schizophrenia were randomized to AL (AL NanoCrystal® Dispersion + oral aripiprazole 30 mg day 1; AL 1064 mg day 8 and every 8 weeks) or paliperidone palmitate (PP 234 mg day 1; PP 156 mg day 8 and every 4 weeks). Patients were discharged after 2 weeks of hospitalization and followed through week 25. Primary

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endpoint was within-group changes in PANSS total score from baseline to week 4 (observed cases). Secondary analyses included within-group changes at weeks 9 and 25 (observed) and between-group comparisons at weeks 4, 9, and 25 (MMRM). Adverse events (AEs) were monitored throughout the study.

RESULTS: 200 patients were randomized (AL, n=99; PP, n=101); 56.6% and 42.6%, respectively, completed the study. Within-group changes from baseline in PANSS were −17.4 for AL and −20.1 for PP at week 4 (both groups, P<0.001) and continued to decline at weeks 9 (AL, −19.8; PP, −22.5) and 25 (AL, −23.3; PP, −21.7). The change in PANSS over time was similar between groups. AEs occurring in ≥10% of patients in either group were injection site pain (AL, 17.2%; PP, 24.8%), akathisia (AL, 9.1%; PP, 10.9%), and weight increased (AL, 9.1%; PP, 16.8%).

CONCLUSIONS: AL and PP were effective and well-tolerated for initiating treatment of schizophrenia in the hospital and continuing in the outpatient setting.

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Effect of Dasotraline on Body Weight in Patients with Binge-Eating Disorder

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ABSTRACT: Background: Binge-eating disorder (BED) is associated with obesity (BMI ≥30) in approximately 40-45% of patients. Dasotraline is a long-acting dopamine/norepinephrine reuptake inhibitor with a PK profile characterized by slow absorption and an elimination half-life of 47-77 hours, permitting once-daily dosing. In a recent placebo-controlled, flexible-dose study, dasotraline demonstrated significant efficacy in patients with BED. We now report an analysis from this study of the effect of dasotraline on body weight.

METHOD: Patients with moderate-to-severe BED, based on DSM-5 criteria, were randomized to 12 weeks of double-blind flexible-dose treatment with dasotraline (4-8 mg/d) vs. placebo. The primary efficacy outcome was number of binge-eating days/week. Mean change in body weight at Week 12 (assessed as a safety outcome) was analyzed by baseline body mass index (BMI, kg/m2) category. Inferential statistics were not performed.

RESULTS: The safety population consisted of 317 patients (female, 84%; mean age, 38.2 years; mean weight, 97.3 kg). At baseline, the proportions of patients in each BMI category were as follows: normal (<25 kg/m2: 5.7%), overweight (25 to <30 kg/m2: 18.3%), obesity class I (30 to <35 kg/m2: 24.9%), class II (35 to <40 kg/m2: 29.3%), and class III (≥40 kg/m2: 21.8%). For the overall patient sample, treatment with dasotraline significantly reduced the number of binge-eating days per week vs. placebo (-3.74 vs. -2.75; P<0.0001; effect size = 0.74). Mean changes at Week 12 in weight (kg) for completers treated with dasotraline vs. placebo, by baseline BMI category, were as follows: normal weight (-4.6 vs. -0.2), overweight (-5.8 vs. +1.3), and combined obesity classes I-III (-6.2 vs. +0.3). Among obese patients (Class I-III, combined) treated with dasotraline, weight reduction (≥5%) was observed in 45.3% of patients (vs. 4.1% on placebo); and weight reduction ≥10% in approximately 13.7% of patients (vs. none on placebo). Weight-related adverse events, for dasotraline vs. placebo, consisted of decreased appetite (19.7% vs. 6.9%), decreased weight (12.1% vs. 0%), and increased weight (0.6% vs. 1.3%).

CONCLUSION: Among patients completing 12 weeks of treatment with dasotraline, weight reduction ≥5% was observed in 45% of obese patients with a BMI ≥30. The most frequent weight-related adverse event was decreased appetite, reported in approximately one in five patients treated with dasotraline.

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Dasotraline for Treatment of Adults with Binge-Eating Disorder: Effect on Binge-related Obsessions and Compulsions

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ABSTRACT: Background: Binge-eating disorder (BED), the most common eating disorder in the US, is frequently associated with impairment in quality of life and functioning. Dasotraline, a long-acting dopamine/norepinephrine reuptake inhibitor, has a PK profile characterized by slow absorption and an elimination half-life of 47-77 hours, and is dosed once-daily. In a recent placebo-controlled,

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