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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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 binge-related obsessions and compulsions.

METHOD: Patients with moderate-to-severe BED, based on DSM-5 criteria, were randomized to 12 weeks of double-blind, placebo controlled, treatment with flexible doses of dasotraline (4, 6, and 8 mg/d). The primary efficacy measure was number of binge-eating days/week; secondary measures included the Binge Eating Clinical Global Impression of Severity (BE-CGI-S) score and the Yale-Brown Obsessive-Compulsive Scale Modified for Binge-Eating (Y-BOCS-BE), a validated, 10-item interviewer-administered measure designed to assess the severity of obsessional thoughts and compulsive behaviors related to binge eating. Change from baseline in efficacy measures in the Intent-to-treat (ITT) population were analyzed using a mixed model for repeated measures (MMRM) analysis.

RESULTS: The ITT population consisted of 317 patients (female, 84%; mean age, 38.2 years). LS mean reduction from baseline in number of Binge Eating (BE) days per week was significantly greater for dasotraline vs. placebo at week 12 (-3.74 vs. -2.75; P<0.0001; effect size [ES] = 0.74; primary endpoint); week 12 change was significantly greater for dasotraline vs. placebo on the Y-BOCS-BE total score (-17.05 vs. -9.88; P<0.0001; ES, 0.96), the obsession subscale score (-8.32 vs. -4.58; P<0.0001; ES, 0.95), and the compulsion subscale score (-8.69 vs. -5.35; P<0.0001; ES, 0.87). All 10 YBOCS-BE items were significantly improved on dasotraline vs. placebo at week 12 (P<0.001 for all comparisons; with effect sizes ranging from 0.54 to 0.90). At Week 12 (LOCF), for dasotraline and placebo, 52.3% and 18.4% of patients, respectively, had a BE-CGI-S score of 1 ("normal; not at all ill"; NNT=3). At endpoint, for patients with a global illness severity score of 1, the corresponding mean Y-BOCS-BE total scores were 0.5 and 0.7 for dasotraline and placebo, respectively, indicating that when BED illness severity approaches "normal, not at all ill", binge-related obsessions and compulsions demonstrate comparably low levels of severity.

CONCLUSION: In this placebo-controlled, 12-week study of patients with moderate-to-severe binge eating disorder, treatment with dasotraline (4-8 mg/d) was associated with significant and clinically meaningful reduction in binge-related obsessional thoughts and compulsive behaviors.

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Efficacy and Safety of Dasotraline in Adults with Binge-Eating Disorder: A Randomized, Double-blind, Fixed-dose Trial

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ABSTRACT: Background: Dasotraline is a long-acting dopamine/norepinephrine reuptake inhibitor with a PK profile characterized by slow absorption and a t½ of 47-77 hours, permitting once-daily dosing. In a previous flexible dose study, dasotraline demonstrated significant efficacy in the treatment of binge-eating disorder (BED). The aim of this confirmatory fixed-dose study was to evaluate efficacy and safety of dasotraline in the treatment of patients with BED.

METHODS: Patients meeting DSM-5 criteria for BED were randomized to 12 weeks of double-blind treatment with dasotraline (4 mg/d or 6 mg/d), or placebo. The primary efficacy endpoint was change in number of binge-eating days per week at week 12. Secondary efficacy endpoints included changes at Week 12 on the Binge Eating Clinical Global Impression of Severity Scale (BE-CGI-S), the Yale-Brown Obsessive-Compulsive Scale Modified for Binge Eating (Y-BOCS-BE), and the proportion of patients with 100% cessation of binge-eating episodes during the final 4 weeks of treatment. Efficacy was assessed using an MMRM analysis (and a logistic regression model for cessation) with a pre-specified sequential testing procedure used to control overall type I error rate.

RESULTS: A total of 486 were in the ITT population (dasotraline 6 mg/d (N=162), 4 mg/d (N=161), or placebo (N=163). At week 12, treatment with dasotraline was associated with significant reduction in number of binge-eating days per week in the 6 mg/d group vs. placebo (-3.5 vs. -2.9; P=0.0045), but non-significant improvement in the 4 mg/d group vs. placebo (-3.2; P=0.12). Greater improvement was observed vs. placebo for dasotraline 6 mg/d and 4 mg/d, respectively, on the BE-CGI-S (P<0.01 and P<0.03) and the Y-BOC-BE (P<0.001 and P<0.02; all P-values were nominal, not adjusted for multiplicity). The proportion of patients who achieved 4-week cessation of binge-eating episodes was only significant for the