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ABSTRACT: Objectives: Binge eating disorder (BED) is the most common eating disorder in the US, with a lifetime prevalence of 2.8%. Disturbances in reward circuitry have been implicated in its pathogenesis. Dasotraline is a novel and potent dopamine and norepinephrine reuptake inhibitor with slow absorption and a long half-life resulting in stable plasma concentrations over 24 hours with once-daily dosing. This study evaluated the efficacy and safety of flexibly-dosed dasotraline (4, 6, and 8 mg/day) vs placebo in adults with moderate to severe BED over a 12-week period (NCT02564588).

METHODS: Key inclusion criteria included moderate to severe BED based on a history of ≥2 binge eating days/week for ≥6 months prior to screening, and ≥3 binge eating days for each of2 weeks prior to randomization, as documented in participant's binge eating diary. Patients were randomized 1:1 to flexibly-dosed dasotraline (4, 6, 8 mg/day) or placebo. Theprimary endpoint was change from baseline (CFB) in the number of binge eating days per week at Week 12. Key secondary endpoints were: CFB in Clinical Global Impression–Severity (CGI-S) Scale at Week 12; CFB in Yale-Brown Obsessive Compulsive Scale Modified for Binge Eating (YBOCS-BE) at Week 12; and the percentage ofsubjects with a 4-week cessation from binge eating prior to Week 12 or end of treatment (EOT). Except for 4-week cessation, the other three variables were analyzed using amixed model for repeated measures (MMRM).

RESULTS: 317 subjects (84% female) received ≥1 dose of study medication (mean age was 38.2 years; mean number of binge eating days per week, 4.25; mean CGI-S score, 4.5; mean BMI, 34.7). The MMRM analysis of CFB at Week 12 in the number of binge days/week yielded a significant mean difference of –0.99 (95% CI: –0.65 to –1.33; $p < 0.001$) infavour of dasotraline (–3.74 in the dasotraline group vs –2.75 in the placebo group). All three key secondary endpoints were met at Week 12 or EOT: 46.5% of subjects in thedasotraline group achieved at least 4 consecutive weeks' cessation from binge eating vs 20.6% in the placebo group ($p < 0.001$); CFB in CGI-S and YBOCS-BE scores were also statistically significant in favour of dasotraline ($p < 0.001$). The treatment-emergent adverse events (TEAEs) that occurred more frequently with dasotraline vs placebo at >2% incidence included: insomnia (44.6% vs 8.1%), dry mouth (27.4% vs 5.0%), decreased appetite (19.7% vs 6.9%), anxiety (17.8% vs 2.5%), nausea (12.7% vs 6.9%) and decreased body weight (12.1% vs 0%). Discontinuation due to AEs occurred in 11.5% of patients taking dasotraline vs 2.5% taking placebo.

CONCLUSIONS: In adults with moderate to severe BED, there were highly significant and clinically meaningful reductions with dasotraline vs placebo in the frequency of binge eating, global severity of illness, and obsessive-compulsive symptoms related to binge eating. These results suggest dasotraline may offer a novel, well-tolerated and efficacious treatmentfor BED.

FUNDING ACKNOWLEDGEMENTS: Study sponsored by Sunovion Pharmaceuticals Inc.

116
Retrospective Analysis of Clozapine Augmentation in Treatment-Resistant Schizophrenia in an Outpatient Setting

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ABSTRACT: Study Objectives: This retrospective analysis hopes to add to the literature about Treatment Resistant Schizophrenia (TRS), augmentation strategies with antipsychotics used in our patient population with the hopes of clarifying what possibilities should be further studied. In addition, we aim to emphasize the need for focusing on individualized treatment and multidisciplinary efforts to ensure compliance and appropriate disposition options.

METHOD: We reviewed retrospectively 3025 charts of patients between January 2017 to March 2017 in our outpatient department establishing which antipsychotic clozapineaugmentation strategies were being used. We also did a literature review to establish what augmentation strategies are recommended. These patients will then be compared to a random sample of patients in the clinic who were not prescribed clozapine and compared for readmission rate, side effect profile, length of stay while admitted, frequency of clinic attendance and compliance with outpatient appointments.

https://doi.org/10.1017/S1092852918000147 Published online by Cambridge University Press

RESULTS: Out of 3025 patients 35 were prescribed Clozapine as monotherapy and 5 patients had clozapine plus psychopharmacological augmentation. Ages ranged from 21-86. Out of the 39 patients, there were 13 male and 26 female. The predominant diagnosis was mood disorder or MDD with psychotic features followed by schizophrenia. The augmentation antipsychotics used were aripiprazole and risperidone. In the literature, the most frequent augmentation strategy for TRS is adding another antipsychotic with more D2 receptor blockade. Other strategies involve identifying and treating the symptoms not controlled by clozapine.

CONCLUSIONS: Currently augmentation of Clozapine in TRS is highly individualized due to lack of supporting evidence to state the contrary. When working with treatmentresistant patients who are not responding to clozapine alone, it is imperative to thoroughly review and consider all treatment options and augmentation strategies. More studies should be done in controlled settings to better evaluate possibilities as well as more evaluations to be done on other ways of augmentation of clozapine. Literature has stated between 20-60% of patients are defined as TRS. Clozapine is considered as one of the most effective treatment available at present time for TRS. Recent literature suggests despite its superior efficacy, as many as 70% of those suffering from TRS on clozapine continue to suffer from positive, negative or cognitive symptoms. The literature has abundant adjunctive treatment strategies such as the addition of antipsychotics, mood stabilizers, antidepressants, or even with the use of electroconvulsive therapy. We emphasize the importance of correctly identifying TRS patients who may benefit from the initiation of clozapine, what would be beneficial for them if they do not respond, how to tailor their treatment to target symptoms not being ameliorated, and recommend treatment in these complex cases be multidisciplinary.

FUNDING ACKNOWLEDGEMENTS: No funding.

117
RE-KINECT: Real-World Dyskinesia Screening Study and Registry in Patients Taking Antipsychotic Agents: Interim Baseline Burden of Illness Results

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ABSTRACT: Background: Tardive dyskinesia (TD) is associated with prolonged exposure to dopamine receptor blockers including antipsychotics. This registry describes the prevalence and impact of involuntary movements (possible TD) in a real-world population of patients taking antipsychotics.

METHODS: RE-KINECT (NCT03062033) aims to enroll 1,000 patients from 70 US psychiatric practices. Adults with ≥3 months lifetime exposure to antipsychotic(s) and ≥1 psychiatric disorder are eligible for two-tier screening: informal observation, and then clinician observation of abnormal involuntary movements in general body regions (head/face, neck/trunk, upper/lower limbs) and confirmation of possible TD. Based on clinician assessment, patients are assigned to Cohort 1 or Cohort 2 (without or with abnormal involuntary movements, respectively). In both cohorts, the following baseline assessments are included: clinician's assessment of clinical psychiatric severity, patient perceived health-related quality of life (EuroQOL 5-Dimensions), social burden/disability questionnaire (Sheehan Disability Scale), and 12-month retrospective chart review ofmedical and treatment history. Cohort 2 also participate in 12-month longitudinal evaluation. Interim baseline data are available from four sites.

RESULTS: Baseline data are currently available for 116 patients—mean age, 49.6 years; female, 60.3%; schizophrenia/schizoaffective disorder, 32.8%; at least 1 mood disorder, 84.5%, and 10.4 years mean cumulative lifetime exposure to antipsychotic(s). The most concerning health condition for both cohorts is their mental health (69.0%), followed by physical activity and nutrition (33.6%). 32.8% of subjects had clinician confirmation of possible TD.

CONCLUSION: This novel registry aims to evaluate the real-world potential impact/burden of TD. Preliminary analyses suggest that TD is common in patients with schizophrenia and mood disorders taking antipsychotics. Further analyses will explore the burden of illness in this population.

FUNDING ACKNOWLEDGEMENTS: This study was funded by Neurocrine Biosciences, Inc.