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Confirmed Safety of Deutetrabenazine for Tardive Dyskinesia in a 2-Year Open-label Extension Study

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ABSTRACT: Study Objective: To evaluate the long-term safety and tolerability of deutetrabenazine in patients with tardive dyskinesia (TD) at 2 years.

BACKGROUND: In the 12-week ARM-TD and AIM-TD studies, deutetrabenazine showed clinically significant improvements in Abnormal Involuntary Movement Scale scores compared with placebo, and there were low rates of overall adverse events (AEs) and discontinuations associated with deutetrabenazine.

METHOD: Patients who completed ARM-TD or AIM-TD were included in this open-label, single-arm extension study, in which all patients restarted/started deutetrabenazine 12 mg/day, titrating up to a maximum total daily dose of 48 mg/day based on dyskinesia control and tolerability. The study comprised a 6-week titration period and a long-term maintenance phase. Safety measures included incidence of AEs, serious AEs (SAEs), and AEs leading to withdrawal, dose reduction, or dose suspension. Exposure-adjusted incidence rates (EAIRs; incidence/patient-years) were used to compare AE frequencies for long-term treatment with those for short-term treatment (ARM-TD and AIM-TD). This analysis reports results up to 2 years (Week 106).

RESULTS: 343 patients were enrolled (111 patients received placebo in the parent study and 232 received deutetrabenazine). There were 331.4 patient-years of exposure in this analysis. Through Week 106, EAIRs of AEs were comparable to or lower than those observed with short-term deutetrabenazine and placebo, including AEs of interest (akathisia/restlessness [long-term EAIR: 0.02; short-term EAIR range: 0–0.25], anxiety [0.09; 0.13–0.21], depression [0.09; 0.04–0.13], diarrhea [0.06; 0.06–0.34], parkinsonism [0.01; 0–0.08], somnolence/sedation [0.09; 0.06–0.81], and suicidality [0.02; 0–0.13]). The frequency of SAEs (EAIR 0.15) was similar to those observed with short-term placebo (0.33) and deutetrabenazine (range 0.06–0.33) treatment. AEs leading to withdrawal (0.08), dose reduction (0.17), and dose suspension (0.06) were uncommon.

CONCLUSIONS: These results confirm the safety outcomes seen in the ARM-TD and AIM-TD parent studies, demonstrating that deutetrabenazine is well tolerated for long-term use in TD patients.

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Sustained Functional Recovery and Symptom Remission After Maintenance Treatment with Aripiprazole Once-Monthly for Patients with Bipolar I Disorder

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ABSTRACT: Study Objectives: To report functional recovery, symptomatic remission, and sustained symptomatic remission rates after treatment with aripiprazole once-monthly 400 mg (AOM 400) administered every 4 weeks for up to 52 weeks as maintenance treatment in a mixed cohort of AOM 400 naïve (de novo) and experienced adults (rollover) with bipolar I disorder (BP-I).

METHOD: This open-label study (NCT01710709) enrolled de novo patients with a diagnosis of BP-I and ≥1 previous manic or mixed episode and rollover patients who completed a randomized, double-blind, placebo-controlled study assessing the efficacy and safety of AOM 400 (NCT01567527). Efficacy was assessed by mean changes from baseline in Young-Mania Rating Scale (YMRS), Montgomery-Asberg Depressive Rating Scale (MADRS), and Clinical Global Impression- Bipolar Version-Severity of Illness (CGI-BP-S) scores. Sustained functional recovery was defined as a total score of ≤11 on the Functioning Assessment Short Test (FAST) for ≥8 consecutive weeks. Remission was defined as YMRS and MADRS total scores ≤12, and sustained remission was defined as meeting criteria for remission for 8 consecutive weeks. The study included a screening phase (6 weeks) for de novo patients, an oral aripiprazole conversion phase (4–6 weeks), an oral stabilization phase (4–12 weeks), and an AOM 400 maintenance phase (up to 52 weeks). Rollover patients entered directly into the AOM 400 maintenance phase.

RESULTS: A total of 464 subjects entered the maintenance phase and 63% (291/464) completed the trial. Of patients entering the maintenance phase, 379 (82%) were de novo and 85 (18%) were rollover. The most frequent reasons for discontinuation were withdrawal of consent (11%) and adverse events (AEs) (10%). Weight increase (1.5%, 7/464) and BP-I (0.9%, 4/464) were the most common reasons for discontinuation due to AEs. Improvements in mean YMRS, MADRS, CGI-BP-S, and FAST scores achieved in previous phases were maintained over 52 weeks. Treatment-emergent AEs experienced by >10% of the patients were akathisia (14.7%), weight increased (13.4%), nasopharyngitis (12.1%), and insomnia (11.0%). A high proportion of de novo patients met the criteria for symptomatic remission (87.2%, 328/376) and sustained remission (77%, 292/379) by last visit. Rollover patients' remission rate remained stable (98.8%, 84/85) by last visit. Of the rollover patients, 35/85 (43%) and 35/116 (36%) of de novo subjects met the criteria for sustained functional recovery after study completion.

CONCLUSIONS: Patients treated with AOM 400 maintained symptomatic and functional stability for up to 52 weeks. Importantly, more than one-third of patients achieved sustained functional recovery using a strict criterion. Overall, AOM 400 was safe and well tolerated in patients with BP-I. Results support AOM 400 as a viable once-monthlyoption for maintenance treatment of BP-I.

These data were previously presented at the 31st ECNP Congress, 2018, Barcelona, Spain.
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Combinatorial Pharmacogenomics to Guide Treatment Selection for Major Depressive Disorder: A Large, Blinded, Randomized Controlled Trial

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