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Comparison of Safety and Tolerability of Deutetrabenazine During Titration and Maintenance in Patients with Tardive Dyskinesia

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Abstract

Background. Deutetrabenazine is approved to treat tardive dyskinesia (TD) in adults and is titrated weekly by 6 mg/day, from 12 to 48 mg/day, based on dyskinesia control and tolerability. This analysis compared the safety of deutetrabenazine during titration versus maintenance.
Methods. Safety was assessed during titration versus maintenance using integrated data from two 12-week placebo-controlled studies (ARM-TD and AIM-TD) and the open-label extension study. Rates were compared for overall and serious adverse events (AEs), AEs leading to discontinuation, treatment-related AEs, common AEs (≥4%), and specific AEs (parkinsonism, suicidal ideation, akathisia, restlessness).
Results. In titration versus maintenance, AE rates with placebo (n=130) were: overall, 43.1% vs 25.4%; serious, 4.6% vs 2.3%; leading to discontinuation, 3.1% vs 0; treatment-related, 26.9% vs 10.0%. For placebo, common AEs during titration were somnolence, headache, nausea, fatigue, and dry mouth; none occurred during maintenance. In titration versus maintenance, AE rates in fixed-dose deutetrabenazine 12–36 mg (n=216) were: overall, 33.3–38.9% vs 22.2–29.2%; serious, 2.8–6.9% vs 0–1.4%; leading to discontinuation, 2.8–5.6% vs 0; treatment-related, 8.3–16.7% vs 8.3–13.9%. For fixed-dose deutetrabenazine, common AEs during titration were headache, diarrhea, nasopharyngitis, depression, hypertension, and dry mouth; headache was the only common AE during maintenance. In titration versus maintenance, AE rates with flexible-dose deutetrabenazine (n=168) were: overall, 49.4% vs 32.7%; serious, 3.6% vs 2.4%; leading to discontinuation, 2.4% vs 0.6%. For flexible-dose deutetrabenazine, the only common AE during titration was somnolence; none occurred during maintenance. Rates of parkinsonism, suicidal ideation, akathisia, and restlessness were low and comparable in titration and maintenance.
Conclusions. Deutetrabenazine was well-tolerated, with AE rates similar to placebo during both phases; AE rates were higher during titration and decreased during maintenance.
Funding. Teva Pharmaceutical Industries Ltd., Petach Tikva, Israel

Long-Term Efficacy and Safety of Deutetrabenazine for Chorea in Huntington's Disease: Results From the ARC-HD Open-label Study

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Abstract

Background. Chorea is a prominent motor dysfunction in Huntington's disease (HD). Deutetrabenazine, a vesicular monoamine transporter 2 (VMAT2) inhibitor, is FDA-approved for the treatment of chorea in HD. In the pivotal, 12-week First-HD trial, deutetrabenazine treatment reduced the Unified Huntington's Disease Rating Scale (UHDRS) total maximal chorea (TMC) score versus placebo. ARC-HD, an open-label extension study, evaluated long-term safety and efficacy of deutetrabenazine dosed in a response-driven manner for treatment of HD chorea.
Methods. Patients who completed First-HD (Rollover) and patients who converted overnight from a stable dose of tetrabenazine (Switch) were included. Safety was assessed over the entire treatment period; exposure-adjusted incidence rates (EAIRs; adverse events [AEs] per person-year) were calculated. A stable, post-titration time point of 8 weeks was chosen for efficacy analyses.
Results. Of 119 patients enrolled (Rollover, n=82; Switch, n=37), 100 (84%) completed ≥1 year of treatment (mean [SD] follow-up, 119 [48] weeks). End of study EAIRs for patients in the Rollover and Switch cohorts, respectively, were: any AE, 2.6 and 4.3; serious AEs, 0.13 and 0.14; AEs leading to dose suspension, 0.05 and 0.04. Overall, 68% and 73% of patients in Rollover and Switch, respectively, experienced a study drug–related AE. Most common AEs possibly related to study drug were somnolence (17% Rollover; 27% Switch), depression (23%; 19%), anxiety (9%; 11%), insomnia (10%; 8%), and akathisia (9%; 14%). Rates of AEs of interest include suicidality (9%; 3%) and parkinsonism (6%; 11%). In both cohorts, mean UHDRS TMC score and total motor score (TMS) decreased from baseline to Week 8; mean (SD) change in TMC score (units) was –4.4 (3.1) and –2.1 (3.3) and change in TMS was –7.1 (7.3) and –2.4 (8.7) in Rollover and Switch, respectively. While receiving stable dosing from Week 8 to 132 (or end of treatment), patients showed minimal change in TMC score (0.9 [5.0]), but TMS increased compared to Week 8 (9.0 [11.3]). Upon drug withdrawal, there were no remarkable AEs and TMC scores increased 4.4 (3.7) units compared to end of treatment.
Conclusions. The type and severity of AEs observed in long-term deutetrabenazine exposure are consistent with the previous study. Efficacy in reducing chorea persisted over time. There was no unexpected worsening of HD or chorea associated with HD upon deutetrabenazine withdrawal.
Funding. Teva Pharmaceutical Industries Ltd., Petach Tikva, Israel

Challenges in Treating Tardive Dyskinesia: Assessing the Impact of Virtual Medical Education

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Abstract

Introduction. Tardive Dyskinesia (TD) refers to abnormal, involuntary, choreoathetoid movements of the tongue, lips, face, trunk, and extremities and is associated with long-term exposure to dopamine-blocking agents, such as antipsychotic medications. Once established, these movements usually persist. The movements are disfiguring and can bring unwanted attention to affected individuals. When severe, especially if the respiratory muscles are affected, the movements can be disabling, limit activity, and reduce quality of life. The prevalence is 7.2% in individuals on newer antipsychotics who have never been exposed to older neuroleptics. Until recently, there were no effective treatments for TD. In recent years, many new treatments have been investigated for the treatment of TD, including valbenazine, deutetrabenazine, and branched chain amino acids. Valbenazine first, followed by deutetrabenazine are FDA approved to treat TD. A virtual broadcast was developed to assess the ability of continuing medical education (CME) to improve awareness of the recognition and treatment of TD among psychiatrists.
Methods. The virtual broadcast (May 9, 2020) consisted of a two-hour, live-streamed discussion between two expert faculty. Impact of the educational activity was assessed by comparing psychiatrists' responses to four identical questions presented before and directly after activity participation. A follow-up survey was sent to all participants six-weeks post-activity to measure performance in practice changes. A chi-square test was used to identify significant differences between pre- and post-assessment responses. Cohen's *d* was used to calculate the effect size of the virtual broadcast.
Results. Activity participation resulted in a noticeable educational effect among psychiatrists (n=621; d=6.12, P<.001). The following areas showed significant (P<0.05) pre- vs post-educational improvements: recognition of movements in patients with TD, rate of TD in SGA exposed patients, treatment options for TD (on and off-label), and treatment of TD using VMAT inhibitors. Additionally, 54% of psychiatrists reported a change in practice performance as a result of the education received in the activity, including utilization of a standard scale to evaluate movement disorders and educate patients and family members about potential for TD, how to recognize symptoms, and when to treat.
Conclusions. The results indicated that a CME-certified two-hour virtual broadcast was effective at improving knowledge among psychiatrists for the recognition and treatment of TD. This knowledge also resulted in positive changes in practice performance post-activity. Future education should continue to address best practices in the diagnosis, treatment and management of patients with TD, as there remains an increased need for tailored CME among psychiatrists.
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Quantifying Psychopathology in Rapid Readmissions

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