Long-Term Deutetrabenazine Treatment Is Associated With Continued Improvement in Tardive Dyskinesia in the Completed 3-Year Open-Label Extension Study

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Abstract

Background. The 12-week ARM-TD and AIM-TD studies in tardive dyskinesia (TD) patients showed statistically significant improvements in TD symptoms with deutetrabenazine. The completed open-label extension (OLE) study (SD-809-C−20) evaluated long-term efficacy and safety of deutetrabenazine in TD.

Methods. Patients who completed ARM-TD or AIM-TD enrolled in the OLE study, with deutetrabenazine dose titrated based on dyskinesia control and tolerability. Change from baseline in Abnormal Involuntary Movement Scale (AIMS) score was assessed by local site raters. Treatment success was evaluated locally as patients being "much improved" or "very much improved" on Clinical Global Impression of Change (CGIC).

Results. 343 patients enrolled in the OLE study; 6 patients were excluded from analyses. At Week 54 (n=249; dose [mean±SE]: 38.7±0.66mg/day), mean change from baseline in AIMS score was −4.8±0.28; 66% of patients experienced treatment success. At Week 106 (n=194; dose: 39.3±0.75mg/day), mean change from baseline in AIMS score was −5.4±0.33; 65% of patients experienced treatment success. At Week 145 (n=160; dose: 39.4±0.83mg/day), mean change from baseline in AIMS score was −6.6±0.37; 73% of patients experienced treatment success. Treatment was generally well tolerated across 723 patient-years of exposure through Week 158, and exposure-adjusted incidence rates (incidence/patient-years) for akathisia/restlessness were 0.01, somnolence/sedation were 0.07, and symptoms which may represent parkinsonism or depression were 0.08 each.

Conclusions. Patients who received long-term treatment with deutetrabenazine achieved sustained improvement in AIMS scores. Findings from this open-label trial with response-driven dosing suggest the possibility of increasing benefit over time.

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Evaluation of the Safety of Deutetrabenazine at Higher Doses to Treat Chorea in Huntington's Disease

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Abstract

Background. In the First-HD pivotal trial, the maximum deutetrabenazine dose evaluated to treat chorea associated with Huntington's disease (HD chorea) was 48 mg/d, which is the approved maximum dose for this population. In ARC-HD, an open-label extension study evaluating the long-term efficacy and safety of deutetrabenazine to treat HD chorea, dosage ranged from 6 mg/d to 72 mg/d, with doses ≥12 mg/d administered twice daily. Doses in ARC-HD were increased by 6 mg/d per week in a response-driven manner based on efficacy and tolerability until 48 mg/d (Week 8). At the investigator's discretion, further increases were permitted by 12 mg/d per week to a maximum of 72 mg/d. This post-hoc analysis evaluates the safety and tolerability of deutetrabenazine >48 mg/d compared to ≤48 mg/d to treat HD chorea in ARC-HD.

Methods. Patient counts and safety assessments were attributed to patients when they received a dose of either ≤48 mg/d or >48 mg/d. For 9 selected adverse events (AEs), we compared AE rates adjusted for duration of drug exposure (as number of AEs/year) at ≤48 mg/d or >48 mg/d. The AE rates were determined after titration when participants were on stable doses of deutetrabenazine.

Results. All 113 patients were exposed to doses ≤48 mg/d (177.1 patient-years) and 49 patients were ever exposed to doses >48 mg/d (74.1 patient-years). In patients taking deutetrabenazine >48 mg/d compared to ≤48 mg/d after the titration period, there were no apparent differences in exposure-adjusted AE rates.

Conclusions. Based on clinical experience, some patients with HD may benefit from doses higher than 48 mg/d to adequately control chorea. These doses were tolerated without apparent increase in the exposure-adjusted rates of selected AEs after titration. This analysis does not address the occurrence of other

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