Deutetrabenazine Is Associated With an Improvement in Involuntary Movements in Patients With Tardive Dyskinesia (TD) as Seen by the High Proportion of Responders to Deutetrabenazine Treatment in the AIM-TD Study

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BACKGROUND
- Tardive dyskinesia (TD), an involuntary movement disorder caused by exposure to dopamine receptor antagonists (DRA)s, can affect any part of the body and be debilitating.
- The symptoms of TD, which may cause social stigma and physical disability, are often masked and can be exacerbated by continuing treatment with the causative agent.
- Clinicians typically manage TD by lowering the dose or discontinuing the causative treatment, which can permanently worsen psychiatric symptoms in the chronically ill.
- This approach is recommended as a first line of treatment, but is not possible in many cases and patients may effectively treat TD, as it is often irreversible.
- TD is a heterogeneous disorder with diverse aetiologies and a lack of effective treatment.
- A platform presentation on Friday, April 28, 2017, by Anderson KE et al. (ISEE 2017) will summarize the efficacy and safety of deutetrabenazine in treating TD.

OBJECTIVE
- To assess treatment response rates based on percentage reduction in Abnormal Involuntary Movement Scale (AIMS) score from baseline to Week 12 between patients receiving deutetrabenazine and placebo in the AIM-TD trial.

METHODS
AIM-TD: Addressing involuntary movements in tardive dyskinesia
- Phase 3, double-blind, placebo-controlled, parallel-group study.
- Evaluated the efficacy, safety, and tolerability of deutetrabenazine in patients with TD.

Patient Population
- Key inclusion criteria:
  - AIMS score ≥1 at screening and confirmed at baseline by a blinded central rater.
  - Clinical diagnosis of TD (must have been both Previously known as basal functional impairment) for ≥3 months prior to screening.
  - History of DRA use for ≥3 months (≥3 months in patients ≥40 years old).
  - Patients with stable psychiatric illness on stable psychoactive medication for ≥30 days before screening, antipsychotic dose must have been stable for ≥45 days before screening.

Key exclusion criteria:
- A neurological condition other than TD that may interfere with assessment of TD severity.
- History of or current idiosyncratic idiosyncrasy within 6 months of screening, or active suicidal ideation at screening or baseline.
- A score ≥11 on the depression subscale of the Hospital Anxiety and Depression Scale (HADS) at screening or baseline.

Study Treatment and Design
- Eligible patients were randomized to baseline Tardive Dyskinesia (TD) 1-1-1-1-1-1 as shown in Figure 2.
- For deutetrabenazine 24 mg/day or 36 mg/day, deutetrabenazine was started at 12 mg/day and titrated up to a fixed dose escalation phase after 4 weeks.

RESULTS
- Baseline characteristics of the mITT population are presented in Table 1.
- AIMS score reductions of ≥50% were observed in 35% and 33% of patients taking deutetrabenazine 24 mg/day and 36 mg/day, respectively.
- Higher proportions of patients receiving deutetrabenazine 24 mg/day and 36 mg/day were responders versus placebo at the 10–70% response levels.
- Additionally, higher proportions of patients taking deutetrabenazine 36 mg/day were responders at the ≥80% and ≥90% response levels.

CONCLUSIONS
- In AIM-TD, there was a higher proportion of patients treated with deutetrabenazine 24 mg/day and 36 mg/day compared with placebo, as defined by percentage improvement in AIMS score from baseline to Week 12.
- The odds of response to deutetrabenazine 24 mg/day and 36 mg/day were higher than the odds of response to placebo at the 50% response level, indicating a clear benefit in reducing the severity of involuntary movements.
- Deutetrabenazine had a favourable safety and tolerability profile, with low rates of dose reductions, suspensions, and discontinuations due to AEs, including in patients with concomitant ORA treatment, allowing for the uninterrupted treatment of underlying psychiatric conditions.
- The analysis provides additional support for the clinical benefit of deutetrabenazine 24 mg/day and 36 mg/day in patients with TD, as indicated by reduction in AIMS score at levels ranging from 15% to 70%.

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REFERENCES
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Figure 1: Study Design
Figure 2: Patient Disposition
Figure 3: Odds Ratios of AIMS Responder Rates in Deutetrabenazine 24 mg/day in Placebo Groups
Figure 4: Odds Ratios of AIMS Responder Rates in Deutetrabenazine 36 mg/day in Placebo Groups
Figure 5: Proportion of Responders Based on AIMS Scores by Treatment Group

Table 1. Patient Baseline Characteristics by Treatment Group in the mITT Population

Table 2. Adverse Event Summary by Treatment Group