LONG-TERM SAFETY AND EFFICACY OF TETRABENAZINE IN THE TREATMENT OF CHOREA ASSOCIATED WITH HUNTINGTON’S DISEASE

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ABSTRACT (UPDATED)

Objective: To assess long-term safety and efficacy of tetrabenazine (TBZ) for chorea associated with Huntington’s disease (HD).

Background: Although TBZ was not approved by the FDA for chorea associated with HD until 2002, it had been used at the Parkinson’s Disease Center and Movement Disorders Clinic (PDCMDC), Baylor College of Medicine (BCM) since 1979.

Methods: In an open-label, Phase IIIb study conducted through the Investigational New Drug Application (IND) center in St. James, TX, patients with hyperkinetic movement disorders were evaluated at PDCMDC. TBZ was used as a “last resort” when other medications failed to provide satisfactory symptom control. For HD chorea patients, all previous chorea treatments were discontinued before TBZ initiation. Patients were initially treated at 12.5 mg/day and titrated up to a target dosage of 50–100 mg/day if tolerated.

Dosage was increased every 2 days until a troublesome adverse event (AE) occurred. TBZ was then down-titrated to the optimal dosage, defined as dosage that provided maximum possible efficacy with no or tolerable AEs. Visits were every 2 weeks thereafter and every 3 months thereafter. Pharmacists were instructed to stop dosage escalation if patients reported a tolerable level of akathisia or insomnia, or nausea and constipation approaches. TBZ dosage was reduced if patients experienced a worsening of chorea or functional deterioration, or if patients experienced other severe AEs. Dosage, efficacy, and AEs were collected at each visit.

Results: By 2004, 98 HD-chorea patients had been treated with TBZ for a mean of 4.9 years (range, 4.9–10.2 years). The most common HD-related AEs possibly related to TBZ were somnolence (51%), insomnia (19%), depression (13%), akathisia (13%), and constipation (12%). Of those patients with valid data, 25% of patients had no change in chorea and function, whereas 30% of patients improved by more than 2 units on the CHQ (choreography) scale; 35% of patients showed worsening of chorea or functional deterioration.

Conclusions: TBZ provided sustained improvement in chorea and function with AE rates depression (13%), akathisia (11%), and nervousness (10%). Of those patients with valid data, 25% of patients had no change in chorea and function, whereas 30% of patients improved by more than 2 units on the CHQ (choreography) scale; 35% of patients showed worsening of chorea or functional deterioration. Dosage, efficacy, and AEs were collected at each visit.

Areas of championship

RESULTS

Demographics and Patient Disposition

• Patient demographics are shown in Table 1.

Table 1. Demographics and Patient Disposition

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Mean (SD): 49.5 (13.3)</td>
</tr>
<tr>
<td>Gender</td>
<td>Male: 59%, Female: 41%</td>
</tr>
<tr>
<td>Race</td>
<td>Caucasian: 81%, African American: 12%, Asian: 5%, Other: 3%</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Hispanic or Latino: 6%, Asian: 6%, Native Hawaiian or Pacific Islander: 2%</td>
</tr>
<tr>
<td>Number of previous HD-related chorea treatments</td>
<td>Mean (SD): 4.9 (2.9)</td>
</tr>
<tr>
<td>Number of previous HD-related chorea AEs</td>
<td>Mean (SD): 4.9 (2.9)</td>
</tr>
</tbody>
</table>

Efficacy

• All AEs had complete efficacy data.
• Among the 98 HD-chorea patients, 83% of patients had a “marked or moderate” improvement in chorea and function (Figure 2).
• Twenty-five percent of patients had worsening of symptoms at any time/dosage.

Safety

• The most commonly reported AEs possibly or probably related to TBZ were somnolence, insomnia, depression, akathisia, and worsening of chorea or functional deterioration.

LEADING TO STUDY WITHDRAWAL

• 80 of 98 patients (81%) had withdrawn because of AEs.

LIMIITATIONS

• Although the data were prospectively collected, the analysis was retrospective.
• Not a double-blind, placebo-controlled, randomized study.

CONCLUSIONS

• All patients who had long-term HD. HD. The data from Bayes’ TBZ-PCD study provides valuable insights into the long-term efficacy and safety of TBZ treatment of HD-induced chorea.

• TBZ provided sustained improvement in chorea and function.

• The most frequent AEs were somnolence, insomnia, depression, akathisia, and worsening of chorea or functional deterioration.

• All patients who had long-term HD. HD. The data from Bayes’ TBZ-PCD study provides valuable insights into the long-term efficacy and safety of TBZ treatment of HD-induced chorea.

REFERENCES


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