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: AlthoughTBZ was not approved by the FDA for chorea associated with HD until 2008, it has been used at the Parker’s Disease Center and Movement Disorder Clinic (PDCMDC), Baylor College of Medicine (BCM) since 1979.

Methods: In an open-label, Phase 8b study conducted through an Investigational New Drug Application (IND) granted to Dr. Jankovic in 1979, patients with HD-related movement disorders were evaluated at PDCMDC. TBZ was used as a ‘last resort’ when other medications failed to provide satisfactory symptom control. For HD patients, all chorea treatments were discontinued before TBZ initiation. Patients were initially hospitalized and TBZ was started at 12.5 mg/day (153 mg/kg body weight). Dosage was increased every 3–6 days to a maximum of 600 mg/day (900 mg/kg body weight) achieved if tolerated. TBZ was then gradually tapered and every 3 months thereafter. Responses were rated on a scale of 1–5, that provided best possible efficacy with no or tolerable AEs. Visits were 6 weeks after hospitalization and every 3 months thereafter. Responses were rated on a scale of 1–5, with 1 = marked chorea reduction, excellent improvement in function; 2 = moderate chorea reduction, very good improvement in function; 3 = fair chorea reduction, good improvement in function; 4 = poor or no response for chorea and function; and 5 = worsening chorea and some functional deterioration. Dosage, efficacy, and AEs were collected at each visit.

Results: By 2004, 170 HD-choreo patients had been treated with TBZ for a mean of 3.1±2.5 years (range: <1 to 11.4 years on TBZ); 54% had received TBZ >2 years. The mean age at HD diagnosis was 44±7 years (range: 21–68 years). The patients were 89% Caucasian (79/89) and 23% of the patients were African American (20/89). 78% of the patients had HD-related chorea (41/89), while the remaining 22% (20/89) had other chorea. The most common AEs possibly/probably related to TBZ were somnolence (31%), depression (28%), akathisia (10%), and anorexia (9%). 37% of patients reported 1 or more AEs, which was significantly higher than the overall rate of AEs reported in other chronic HD clinical trials. AEs were reported more frequently at dosages greater than optimal dosage (Figure 4).

Conclusions: The PDCMDC has the longest history with TBZ for the treatment of chorea associated with HD and the largest patient database for this population.

OBJECTIVE

To assess long-term safety and efficacy of TBZ for HD-related chorea.

METHODS

Background: Although TBZ was not approved by the FDA for HD-related chorea until 2008, it has been used at the PDCMDC, BCM since 1979.

Methods: In an open-label, Phase 8b study conducted through an Investigational New Drug Application (IND) granted to Dr. Jankovic in 1979, patients with HD-related movement disorders were evaluated at PDCMDC. TBZ was used as a ‘last resort’ when other medications failed to provide satisfactory symptom control. For HD patients, all chorea treatments were discontinued before TBZ initiation. Patients were initially hospitalized and TBZ was started at 12.5 mg/day (153 mg/kg body weight). Dosage was increased every 3–6 days to a maximum of 600 mg/day (900 mg/kg body weight) achieved if tolerated. TBZ was then gradually tapered and every 3 months thereafter. Responses were rated on a scale of 1–5, with 1 = marked chorea reduction, excellent improvement in function; 2 = moderate chorea reduction, very good improvement in function; 3 = fair chorea reduction, good improvement in function; 4 = poor or no response for chorea and function; and 5 = worsening chorea and some functional deterioration. Dosage, efficacy, and AEs were collected at each visit.

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BACKGROUND

• Tetrabenazine (TBZ) selectively and reversibly depletes monoamines from nerve terminals by inhibiting the vesicular monoamine transporter type 2 (VMAT2).
• Prior to approval of TBZ by the US Food and Drug Administration (FDA) for the treatment of chorea associated with Huntington’s disease (HD), over 1000 US patients were able to obtain the drug from abroad, while others received TBZ physician-investigational New Drug Applications (INDs).
• The Parker’s Disease Center and Movement Disorder Clinic (PDCMDC) at Baylor College of Medicine administered TBZ under Dr. Jankovic’s IND, issued in 1979.

• Patients were enrolled and treated at the PDCMDC under Protocol H-721, approved by the Institutional Review Board of BCM. Patients were treated as HD patients with chorea as defined. Efficacy and AEs were collected at each visit.

• The PDCMDC has the longest history with TBZ for the treatment of chorea associated with HD.

RESULTS

• Treatment with TBZ was started at 12.5 mg/day and the dosage was gradually increased every 3–6 days to a maximum of 600 mg/day (900 mg/kg body weight) achieved if tolerated. TBZ was then gradually tapered and every 3 months thereafter. Responses were rated on a scale of 1–5, with 1 = marked chorea reduction, excellent improvement in function; 2 = moderate chorea reduction, very good improvement in function; 3 = fair chorea reduction, good improvement in function; 4 = poor or no response for chorea and function; and 5 = worsening chorea and some functional deterioration.

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REFERENCES