ABSTRACT (UPDATED)

Objective: To assess efficacy, safety, and utility of tetrabenazine (TBZ) for patients with moderate vs. severe/disabling chorea associated with Huntington’s disease (HD).

Methods: In an open-label study, patients with hyperkinetic movement disorders were evaluated at the Parkinson’s Disease Center and Movement Disorders Clinic (PDCMDC), Baylor College of Medicine. TBZ was used “as need” when other medications failed to provide satisfactory symptom control. For HD-chorea patients, all previous chorea treatments were discontinued before TBZ initiation. Dosage was increased every 3 days, until a dosage limiting AE occurred. TBZ was then titrated to optimal dosage. Visits were 6 weeks after hospitalization, and every 3 months thereafter. Responses were rated until a dosage-limiting AE occurred. TBZ was then down-titrated to optimal dosage. Visits were evaluated at the Parkinson’s Disease Center and Movement Disorders Clinic (PDCMDC).

Results: By 2004, 98 HD-chorea patients had participated. At baseline, 44 had moderate and 54 severe/disabling chorea. 45% with moderate vs. 67% with severe/disabling chorea received TBZ 12 years of age. Average daily dosage (SD) range of mean doses) were 60.5 mg (±25.9) and 74.8 mg (±45.0) for moderate and severe/disabling chorea, respectively. On optimal dosage, 71% of moderate chorea patients vs. 86% for severe/disabling chorea achieved a “marked or moderate” response (any time point) vs. 78% for severe/disabling chorea.

Conclusions: TBZ dosage was similar across severity groups. Response to TBZ and AEs were similar for patients grouped by baseline chorea severity.

BACKGROUND

Prior to approval of tetrabenazine (TBZ) for the treatment of chorea associated with Huntington’s disease (HD) in the United States, some US patients were able to obtain the drug from abroad, while others received TBZ under physician Investigational New Drug (IND) requests.

TBZ was initially studied and treated in the PDCMDC and/or Protocol H-721, “Compassionate Use of TBZ in the Treatment of Hyperkinesias,” a single-center, open-label, individualized-dosage study.

Over 25 years (January 1979–February 2004), a total of 98 patients with HD-chorea were treated and had complete records available for analysis. At baseline was 60.5 (±25.9) mg/day and 74.8 (±45.0) mg/day, respectively for moderate and severe/disabling chorea. The average daily dosage (SD; range of mean doses) were 60.5 mg (±25.9) and 74.8 mg (±45.0) for moderate and severe/disabling chorea, respectively. On optimal dosage, 71% of moderate chorea patients vs. 86% for severe/disabling chorea received TBZ >2 years. Average daily dosages (SD; range of mean doses) were 60.5 mg (±25.9) and 74.8 mg (±45.0) for moderate and severe/disabling chorea, respectively. On optimal dosage, 71% of moderate chorea patients vs. 86% for severe/disabling chorea achieved a “marked or moderate” response (any time point) vs. 78% for severe/disabling chorea.

RESULTS

Demographics and Patient Disposition

Patients

Patients with hyperkinetic disorders underwent a detailed neuropsychological examination until a time recording beginning to capture the phenomenology and severity of the disorder that began from abstraction, while others received TBZ under physician Investigational New Drug (INDs)

TBZ Treatment

TBZ dosage was highly individualized and independent of chorea severity. Response to TBZ and AEs were similar for patients grouped by baseline chorea severity.

Efficacy

At any dosage and time during the trial, 72% of patients with moderate chorea achieved a “marked or moderate” response compared with 78% for patients with severe/disabling chorea (Figure 3).

CONCLUSIONS

The incidence of somnolence and depression for patients with moderate chorea at baseline (45% and 27%) was notably different from the incidence for patients with severe/disabling chorea at baseline (22% and 11%, respectively) (Figure 6).

REFERENCES


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TETRABENAZINE FOR MODERATE VS. SEVERE/DISABLING CHOREA ASSOCIATED WITH HUNTINGTON’S DISEASE

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