Onset and Resolution of Key Adverse Events in Valbenazine-Treated Patients with Tardive Dyskinesia: Pooled Analyses from Two Long-Term Clinical Trials

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Abstract

Objective. Tardive dyskinesia (TD) is a persistent and potentially disabling movement disorder associated with prolonged exposure to antipsychotics and other dopamine receptor blocking agents. Long-term safety of the approved TD medication, valbenazine, was demonstrated in 2 clinical trials (KINECT 3 [NCT02274558], KINECT 4 [NCT02405091]). Data from these trials were analyzed post hoc to evaluate the onset and resolution of adverse events (AEs).

Methods. Participants in KINECT 3 and KINECT 4 received up to 48 weeks of once-daily valbenazine (40 or 80 mg). Data from these studies were pooled and analyzed to assess the incidence, time to first occurrence, and resolution for the following AEs of potential clinical interest: akathisia, balance disorder, dizziness, parkinsonism, somnolence/sedation, suicidal behavior/ideation, and tremor.

Results. In the pooled population (N=314), all AEs of potential clinical interest occurred in <10% of participants, with somnolence (9.6%), suicidal behavior/ideation (6.4%), and dizziness (5.7%) being the most common AEs. Mean time to first occurrence ranged from 36 days (akathisia [n=9]) to 224 days (parkinsonism [n=2]). By end of study (or last study visit), resolution of AEs was as follows: 100% (suicidal ideation/behavior, parkinsonism); >85% (somnolence/sedation, dizziness); >70% (akathisia, balance disorder, tremor).

Conclusions. In long-term clinical trials, the incidence of AEs of potential clinical interest was low (<10%) and most were resolved by end of treatment (>70–100%). All patients taking valbenazine should be routinely monitored for AEs, particularly those that may exacerbate the motor symptoms associated with TD.

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Clinician-Reported Patient Awareness of Symptoms and Severity of Tardive Dyskinesia in Patients Prescribed VMAT2 Inhibitors

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Abstract

Objective. Vesicular monoamine transporter 2 (VMAT2) inhibitors including valbenazine are first-line therapies for tardive dyskinesia (TD), a persistent movement disorder associated with antipsychotic exposure. This real-world study was performed to assess the association between patient awareness of TD symptoms and clinician-assessed symptom severity.

Methods. Clinicians who treated antipsychotic-induced TD with a VMAT2 inhibitor within the past 24 months were asked to extract demographic/clinical data from patients charts and complete a survey for additional data, including patient awareness of TD (yes/no) and TD symptom severity (mild/moderate/severe).

Results. Data for 601 patients were provided by 163 clinicians (113 psychiatrists; 46 neurologists; 4 primary care physicians). Patient demographics: 50% male; mean age 50.6 years; 55% schizophrenia/schizoaffective disorder; 29% bipolar disorder; 16% other psychiatric diagnoses. Positive relationships were seen between patient awareness and clinician-assessed symptom severity. Awareness was highest in patients with severe symptoms in specific body regions: face (88% vs 78%/69% [awareness by severe vs moderate/mild symptoms]); jaw (90% vs 80%/67%); wrists (90% vs 69%/63%). In other regions, awareness was similar in patients with severe or moderate symptoms: lips (85%/86% vs 68% [severe/moderate vs mild]); tongue (81%/80% vs 73%); neck (80%/78% vs 68%); arms (67%/66% vs 62%); knees (67%/67% vs 53%).

Conclusions. In patients prescribed a VMAT2 inhibitor for TD, patient awareness was generally higher in those determined to have moderate-to-severe symptom severity as assessed by the clinician. More research is needed to understand how awareness and severity contribute to TD burden, and whether different treatment strategies are needed based on these factors.

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