(40% and 42%, respectively) compared to those who did not achieve early PGIC and CGI-TD improvement (39% and 38%, respectively).

CONCLUSIONS: Results from this long-term valbenazine trial indicate that many participants achieved at least minimal patient- and clinician-reported improvement at Week 2. AIMS outcomes at Week 48 demonstrated long-term reductions in TD severity regardless of early response. More research is needed to understand the association between early improvement and long-term treatment effects, but early non-improvement based on subjective measures may not be predictive of long-term treatment failure.

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Effects of Long-Term Valbenazine on Tardive Dyskinesia in KINECT 4: Post Hoc Response and Shift Analyses

Stephen R. Marder, MD[1]; Cynthia L. Comella, MD[2]; Carlos Singer, MD[3]; Khodayar Farahmand, PharmD[4]; and Roland Jimenez, MS[5]

[1] Professor, Department of Psychiatry and Biobehavioral Sciences, University of California Los Angeles, David Geffen School of Medicine, Los Angeles, CA
[2] Professor, Department of Neurological Sciences, Rush University Medical Center, Chicago, IL
[3] Professor, Department of Neurology, University of Miami Miller School of Medicine, Miami, FL
[4] Director, Head of Medical Communications, Neurocrine Biosciences, Inc., San Diego, CA
[5] Sr. Director, Clinical Development, Neurocrine Biosciences, Inc., San Diego, CA

ABSTRACT: Study Objective: Valbenazine (VBZ) is a highly selective vesicular monoamine transporter 2 (VMAT2) inhibitor approved for the treatment of tardive dyskinesia (TD), a persistent and potentially disabling movement disorder associated with prolonged antipsychotic exposure. Post hoc response and shift analyses were conducted using Abnormal Involuntary Movement Scale (AIMS) data from KINECT 4 (NCT02405091), a long-term open-label study in which participants received up to 48 weeks of open-label treatment with once-daily VBZ (40 or 80 mg).

METHODS: KINECT 4 included participants who met the following criteria: ages 18 to 85 years; DSM-IV diagnosis of schizophrenia, schizoaffective disorder, or mood disorder; neuroleptic-induced TD for ≥3 months prior to screening; stable psychiatric status (Brief Psychiatric Rating Scale score <50); no high risk of active suicidal ideation or behavior. Stable doses of concomitant medications to treat psychiatric and medical disorders were allowed. VBZ dosing was initiated at 40 mg, with escalation to 80 mg at Week 4 based on clinical assessment of TD and tolerability; a dose reduction to 40 mg was allowed if 80 mg was not tolerated. AIMS responses, ranging from ≥10% to 100% improvement from baseline in AIMS total score (sum of items 1-7), were analyzed at Week 48 based on scoring by site investigators. AIMS shift, conducted for each item (representing 7 different body regions), was defined as an improvement from a score ≥3 (moderate/severe) at baseline to a score ≤2 (none/minimal/mild) at Week 48.

RESULTS: 103 participants had an available AIMS assessment at Week 48 (40 mg, n=20; 80 mg, n=83 [including 9 with a dose reduction]). At Week 48, 94.2% of participants had ≥30% total AIMS score improvement (40 mg, 90.0%; 80 mg, 95.2%) and 86.4% had ≥50% improvement (40 mg, 90.0%; 80 mg, 85.5%). The percentage of participants meeting the remaining AIMS response thresholds ranged from 9.7% (for 100% response) to 97.1% (for ≥10% response). In participants who had an AIMS item score ≥3 at baseline, shifts to a score ≤2 at Week 48 were as follows: 100% for lips, upper extremities, and lower extremities (VBZ 40 mg and 80 mg). Shift rates for the remaining regions were as follows (40 mg, 80 mg): face (100% [9/9], 96.9% [31/32]), jaw (100% [10/10], 97.6% [40/41]), tongue (100% [11/11], 97.9% [47/48]), trunk (87.5% [7/8], 88.9% [16/18]).

CONCLUSIONS: After 48 weeks of treatment with once-daily VBZ (40 or 80 mg), >85% of KINECT 4 participants had a clinically meaningful AIMS response (≥30% total score improvement), a robust AIMS response (≥50% total score improvement), or an AIMS shift (from item score ≥3 at baseline to score ≤2 at Week 48). These results suggest that VBZ is an appropriate long-term treatment for many adults with TD.
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Moderating Perspectives of Long Acting Injectable Use of Antipsychotics: A Literature Review

Kathy Riedford

Associate Professor, Director of Psychiatric Mental Health Nurse Practitioner Specialty
ANE Primary Care/Mental Health Integrated Model Project Director
College of Nursing and Health Professions, University of Southern Indiana, Evansville, IN

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ABSTRACT: Long acting injectable (LAI) antipsychotics are indicated for individuals suffering from schizophrenia, delusional disorder, schizoaffective disorder and bipolar disorder. Even though LAIs have traditionally been used for a subgroup of patients who were not compliant with oral treatments or who were a high risk to others, current trends are changing with increased options and availability of these treatments. A number of factors are implicated in the reversal of this trend including perspectives of patients and perspectives of providers. There is not abundant literature available regarding robust studies to examine these perspectives, but this presentation provides a current summary of available literature.

Some factors that influence perspectives of both patients and providers include knowledge about LAIs, cost of LAIs and the traditional views of these agents as being used under coercive circumstances. Altering perspectives has been a primary barrier to increase the use of these agents. Evidence clearly supports the use of early intervention for individuals with first episode psychosis, and poor medication compliance results in poorer treatment outcomes. With the potential improvement in quality of life and potentially decreasing the cost burden of this illness in society, this avenue for treatment must be a strong consideration for all involved in the treatment of the aforementioned disorders.

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Withdrawal Symptom Assessment in an Esketamine Safety Study in Patients with Treatment-resistant Depression

Leah Aluisio, PhD[1]; Lynn Yieh, PhD[1]; Ewa Wajs, MD, PhD[2]; Allitia DiBernardo, MD[3]; Andrew Krystal, MD[4]; Wayne Drevets, MD[1]; Yun Wu, PhD[5]; Jagadish Gogate, PhD[5]; Ella Daly, MD[3]; Peter Zannikos, PhD[3]; Valerie Curran, PhD[6]; Guang Chen, MD, PhD[1]; and Jaskaran Singh, MD[1]

[1] Janssen R&D, San Diego, CA US
[2] Janssen R&D, Beerse BE
[3] Janssen R&D, Titusville, NJ US
[4] UCSF, San Francisco, CA US
[5] Janssen R&D, Raritan, NJ US
[6] University College London, London UK

ABSTRACT: Background: SUSTAIN-2 (NCT02497287) was an open-label, phase III trial evaluating the safety of esketamine (ESK) nasal spray plus a newly initiated oral antidepressant (AD) for up to 1 year in adults with treatment-resistant depression (TRD). ESK is a schedule III drug that acts via glutamate receptor modulation. ESK is rapidly cleared from the plasma, and with intermittent dosing there is no accumulation. Thus, no withdrawal syndrome is expected. The current analysis assessed potential withdrawal symptoms in patients who discontinued ESK after long-term, intermittent use. In the absence of a glutamatergic-specific withdrawal scale, the Physicians Withdrawal Checklist1 (PWC-20) was used. The PWC-20 was designed to assess new or worsening benzodiazepine-like discontinuation symptoms after stopping non-SSRI anxiolytics.

METHODS: ESK nasal spray was administered two times per week during a 4-week induction phase (IND). Responders entered the optimization/maintenance phase (O/M) where ESK nasal spray was dosed either weekly or every two weeks for up to 48 weeks. Patients entered a 4-week follow up period (F/U) after discontinuation from either phase, during which continuation of the AD was recommended. PWC-20 assessments were conducted at the last ESK dosing (endpoint of IND or O/M) and at weeks 1, 2 and 4 of F/U. Symptoms were rated using a 0-3-point scale (Not present = 0, Mild = 1, Moderate = 2, Severe = 3). To account for worsening of underlying depression, subset calculations were performed for depressive symptoms (PWC-DS: loss of appetite; anxiety or nervousness; irritability; dysphoric mood or depression; insomnia; fatigue, lethargy or lack of energy; restlessness or agitation; headaches; muscle aches or stiffness; weakness; difficulty concentrating or remembering; depersonalization-derealization) and withdrawal symptoms (PWC-WS: nausea and/or vomiting; diarrhea; poor coordination; diaphoresis; tremor or tremulousness; dizziness or light-headedness; increased acuity of sound, smell, or touch; paresthesias).

RESULTS: Data on 357 patients entering F/U were included in the analysis (91 completed treatment during the IND phase and 141 were treated during O/M). The mean (SD) PWC-20 total scores (range 0-60) at treatment endpoint, Week 1, 2 and 4 were 7.2 (6.8), 7.5(7.0), 7.4 (7.1) and 7.2 (6.9), respectively. At these same assessment times, mean PWC-WS scores (range 0-24) were 0.9 (1.7), 1.0 (1.7), 1.0 (1.8), and 0.9 (1.8). Mean PWC-DS scores (range 0-36) were 6.3 (5.6), 6.5 (5.7), 6.5 (5.8), and 6.3 (5.7), respectively. Complete analysis of data from the entire SUSTAIN-2 dataset will be presented.

CONCLUSIONS: No indication of drug-specific withdrawal symptoms was seen after stopping up to 1-year of intermittent treatment with ESK nasal spray for TRD.

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