Long-Term Effects of Valbenazine on Tardive Dyskinesia in Patients with Schizophrenia/Schizoaffective Disorder or Mood Disorder: Results from an Open-Label, Rollover Study

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INTRODUCTION

Tardive Dyskinesia (TD) is a persistent and often irreversible movement disorder associated with prolonged exposure to antipsychotics and other dopamine receptor blocking agents.1

Valbenazine (VBZ) is a novel and highly selective vesicular monoamine transporter 2 (VMAT2) inhibitor that is approved for the treatment of TD in adults.2

The long-term efficacy and safety of valbenazine was demonstrated in two phase 3 studies: KINET 3 (n=373) and KINET 4 (n=378).3,4 In which participants received 40 or 80 mg of valbenazine daily (VBZ 40 mg or VBZ 80 mg) in the active valbenazine period.

Completions from KINET 3 and KINET 4 led to eligibility of 190 participants in a rollover study (NCT02736955), for further treatment after a variable valbenazine-free period

Data from the rollover study were assessed post hoc to further assess the long-term safety and tolerability of daily valbenazine in patients with schizophrenia/schizoaffective disorder or a mood disorder.

METHODS

STUDY DESIGN

The open-label study included patients who completed KINET 3 or KINET 4 (40 mg of treatment) and a 4-week washout (Figure 1).

- KINET 3 included 104 participants from an earlier phase 2 study
- All participants received ≥1 daily valbenazine for at least 5 weeks.4
- Discharge was evaluated at 80 mg of the end of Week 4 based on clinical judgment of stability and patient readiness to continue TD treatment.
- One dose reduction to 40 mg was allowed if 80 mg was not tolerated.
- Patients unable to tolerate 40 mg were discontinued from the study

Participants received continued treatment for up to 12 weeks or until valbenazine became commercially available.

Stable doses of concomitant medications to treat psychiatric disorders and comorbid medical conditions were allowed

PARTICIPANTS

Key inclusion criteria:
- Adults with neuroleptic-induced TD and a psychiatric diagnosis and TD diagnosis
- Participants unable to tolerate 40 mg were discontinued from the study
- One dose reduction to 40 mg was allowed if 80 mg was not tolerated
- Participants unable to tolerate 40 mg were discontinued from the study

Key exclusion criteria:
- Significant risk for active suicidal ideation or suicidal behavior (Columbia-Suicide Severity Rating Scale (C-SSRS) or violent behavior
- Participants who had no previous exposure to valbenazine (a washout period of 0-324 days)
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There were no clinically important changes in laboratory parameters, vital signs, or ECG tests, vital sign measurements, electrocardiograms (ECGs), and the C-SSRS

Participants who received >1 year of treatment with once-daily valbenazine had any worsening in C-SSRS score at any time during treatment

Most of these participants continued to have no emergence of suicidal ideation at any time during treatment

There were no clinically important changes in laboratory parameters, vital signs, or ECG tests, vital sign measurements, electrocardiograms (ECGs), and the C-SSRS

RESULTS

Table 2: Baseline Characteristics by Diagnosis Subgroup

<table>
<thead>
<tr>
<th>Diagnosis Subgroup</th>
<th>n</th>
<th>Age (mean, SD)</th>
<th>Sex (M/F)</th>
<th>BMI (mean, SD)</th>
<th>Gender (M/F)</th>
<th>C-SSRS</th>
<th>BPRS</th>
<th>CGI</th>
<th>CGI-S</th>
<th>CGI-TD</th>
<th>CGI-SD</th>
<th>CGI-SSR</th>
<th>CGI-TG</th>
<th>CGI-SS</th>
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</thead>
<tbody>
<tr>
<td>Schizophrenia/Schizoaffective Disorder</td>
<td>52</td>
<td>28.6 (5.8)</td>
<td>27 (26.0)</td>
<td>5 (21.7)</td>
<td>6 (8.0)</td>
<td>51.8 (10.3)</td>
<td>46.3 (11.5)</td>
<td>33.9 (13.3)</td>
<td>3 (5.6)</td>
<td>1 (1.3)</td>
<td>8 (15.4)</td>
<td>1 (1.9)</td>
<td>1 (1.9)</td>
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<tr>
<td>Mood Disorder</td>
<td>75</td>
<td>28.2 (4.6)</td>
<td>55.9 (9.4)</td>
<td>26.7 (5.7)</td>
<td>2 (4.8)</td>
<td>55.9 (9.4)</td>
<td>46.3 (11.5)</td>
<td>33.9 (13.3)</td>
<td>3 (5.6)</td>
<td>1 (1.3)</td>
<td>8 (15.4)</td>
<td>1 (1.9)</td>
<td>1 (1.9)</td>
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</table>

Table 3: CGI-TD Rollover Study

<table>
<thead>
<tr>
<th>Period</th>
<th>CGI-TD (mean ± SD)</th>
<th>n</th>
<th>CGI-TD (mean ± SD)</th>
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<tbody>
<tr>
<td>Baseline</td>
<td>33.9 ± 13.3</td>
<td>103</td>
<td>Baseline</td>
<td>33.9 ± 13.3</td>
</tr>
<tr>
<td>Week 72</td>
<td>25.0 ± 5.6</td>
<td>103</td>
<td>Week 4</td>
<td>33.9 ± 13.3</td>
</tr>
<tr>
<td>Week 4</td>
<td>33.9 ± 13.3</td>
<td>103</td>
<td>Week 72</td>
<td>25.0 ± 5.6</td>
</tr>
</tbody>
</table>

Table 4: CGI-TD Rollover Study

<table>
<thead>
<tr>
<th>Week</th>
<th>CGI-TD (mean ± SD)</th>
<th>n</th>
<th>CGI-TD (mean ± SD)</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>33.9 ± 13.3</td>
<td>103</td>
<td>0</td>
<td>33.9 ± 13.3</td>
</tr>
<tr>
<td>4</td>
<td>25.0 ± 5.6</td>
<td>103</td>
<td>4</td>
<td>33.9 ± 13.3</td>
</tr>
<tr>
<td>72</td>
<td>25.0 ± 5.6</td>
<td>103</td>
<td>72</td>
<td>33.9 ± 13.3</td>
</tr>
</tbody>
</table>

CONCLUSIONS

Clinical-based assessments indicated ongoing and meaningful TD improvements in patients who received ≥1 year of once-daily treatment with valbenazine

Valbenazine was generally well tolerated and no new safety signals were observed

Valbenazine may be an appropriate long-term treatment for managing TD in adults with schizophrenia/schizoaffective disorders and mood disorders.

REFERENCES

UPDATE FOR THE NEVADA PSYCHIATRIC ASSOCIATION

FEBRUARY 13-16, 2019

SD, standard deviation; VBZ, valbenazine.