Once-Daily Valbenazine Is Effective for Tardive Dyskinesia in Elderly Patients (≥65 Years)

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ABSTRACT DESCRIPTION

Older patients taking a dopamine-receptor blocking agent have increased risk for tardive dyskinesia (TD), a persistent and potentially disabling movement disorder. These analyses, being the first to assess the effects of an approved TD medication in elderly patients (≥65 years), indicate that long-term once-daily valbenazine is appropriate for this population.

INTRODUCTION

- TD is a persistent and potentially disabling movement disorder associated with prolonged exposure to antipsychotics and other dopamine-receptor blocking agents (DRBAs)[1]
- Compared to younger adults, older adults (≥55 years) have a higher risk of developing TD after a shorter duration of DRBA treatment[2]
- Valbenazine, a highly selective vesicular monoamine transporter 2 (VMAT2) inhibitor, is the only approved TD medication with once-daily dosing and enough clinical trial data to specifically indicate no required dosing adjustments in elderly patients (≥65 years)[3]
- To date, no results have been reported for the effects of VMAT2 inhibitors on TD in elderly patients using the more conventional threshold of 65 years
- Therefore, data from 2 long-term trials of valbenazine were analyzed post hoc to evaluate treatment outcomes in elderly study participants (≥65 years) versus a younger cohort (<65 years)

OBJECTIVES

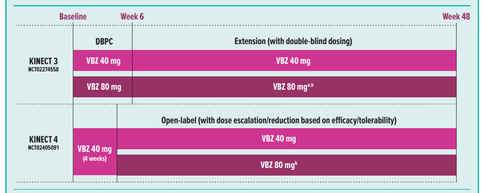
- Understand the increased risk for TD in older patients taking antipsychotics or other DRBAs
- Describe results from the first analyses to assess the effects of an approved medication (valbenazine) on TD in elderly patients (≥65 years)
- Apply the substantial and clinically meaningful improvements found in this analysis to the real-world management of TD in elderly patients

METHODS

STUDY DESIGN

- Participants in KINECT 3 and KINECT 4 received up to 48 weeks of once-daily treatment with valbenazine 40 mg or 80 mg (**Figure 1**)
- All valbenazine dose groups were pooled for this analysis; participants who initially received placebo in KINECT 3 were excluded

Figure 1. Study Design



[a]Participants who were randomized to 80 mg were initiated at 40 mg for 1 week.
[b]Includes participants who had a dose reduction to 40 mg due to tolerability issues.
DBPC, double-blind, placebo-controlled; VBZ, valbenazine.

PARTICIPANTS

- Key inclusion criteria:
  - *Diagnostic and Statistical Manual of Mental Disorders* (e.g., DSM-IV) diagnosis of schizophrenia, schizoaffective disorder, or mood disorder and psychiatrically stable prior to study entry (e.g., Brief Psychiatric Rating Scale score <50 at screening)
  - DSM-IV diagnosis of neuroleptic-induced TD for ≥3 months prior to screening
  - Moderate or severe TD as qualitatively assessed by an external reviewer at screening; no threshold for Abnormal Involuntary Movement Scale (AIMS) total score (sum of items 1-7) was required at baseline
- Key exclusion criteria:
  - Active, clinically significant, and unstable medical condition within 1 month prior to screening
  - Comorbid movement disorder more prominent than TD
  - Significant risk for active suicidal ideation, suicidal behavior, or violent behavior
- Stable doses of concomitant medications to treat psychiatric disorders were permitted

ANALYSES

- Analyses were conducted in participants who received ≥1 dose of study drug and had ≥1 post-baseline efficacy assessment
- Mean change from baseline in AIMS total score was assessed at Week 48
- Response was also assessed at the following thresholds:
  - AIMS total score: ≥30% improvement from baseline ("clinically meaningful" response) or ≥50% improvement from baseline ("protocol-defined" response)
  - Clinical Global Impression of Change-Tardive Dyskinesia (CGI-TD): score ≤2 ("much improved" or better) or score ≤3 ("minimally improved" or better)
  - Patient Global Impression of Change (PGIC): score ≤2 ("much improved" or better) or score ≤3 ("minimally improved" or better)
- Treatment-emergent adverse events (TEAEs), serious TEAEs, and TEAEs leading to study discontinuation were summarized
- All outcomes were analyzed for comparison between age subgroups (≥65 years vs <65 years)

RESULTS

- Demographics and baseline characteristics are presented in **Table 1**

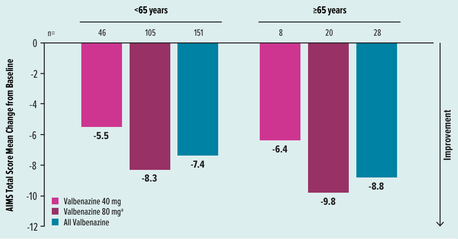
Table 1. Demographics and Baseline Characteristics by Age

	<65 Years		≥65 Years	
	VBZ 40 mg (n=89)	VBZ 80 mg[a] (n=160)	VBZ 40 mg (n=18)	VBZ 80 mg[a] (n=37)
Age, years				
Mean (SD)	53.5 (7.5)	54.1 (7.6)	69.8 (4.3)	69.8 (4.5)
Median (min, max)	55 (26, 64)	55 (32, 64)	69 (65, 80)	69 (65, 83)
Male, n (%)	47 (52.8)	89 (55.6)	11 (61.1)	15 (40.5)
Race, n (%)				
White	49 (55.1)	98 (61.3)	12 (66.7)	30 (81.1)
Black/African-American	34 (38.2)	57 (35.6)	5 (27.8)	7 (18.9)
Other[b]	6 (6.7)	5 (3.1)	1 (5.6)	0 (0)
Body mass index, mean (SD), kg/m^2	28.3 (5.9)	28.5 (5.5)	29.2 (5.2)	27.9 (5.8)
Psychiatric diagnosis, n (%)				
Schizophrenia/schizoaffective disorder	63 (70.8)	110 (68.8)	12 (66.7)	24 (64.9)
Mood disorder[c]	26 (29.2)	50 (31.3)	6 (33.3)	13 (35.1)
BPRS total score, mean (SD)	30.6 (7.6)	27.9 (6.7)	26.8 (5.0)	28.9 (6.9)
AIMS total score, mean (SD)	11.3 (5.4)	13.1 (4.8)	10.6 (3.9)	12.6 (4.5)

[a]Includes participants who had a dose reduction from 80 to 40 mg.
[b]Includes Asian, American Indian/Alaska Native, Native Hawaiian/Pacific Islander, other (unspecified), and multiple (unspecified).
[c]Includes bipolar disorder and major depressive disorder.
AIMS, Abnormal Involuntary Movement Scale; BPRS, Brief Psychiatric Rating Scale; SD, standard deviation; VBZ, valbenazine.

- Substantial mean improvements from baseline in AIMS total score were found at Week 48 (end of treatment), with no statistically significant differences between the age subgroups (**Figure 2**)

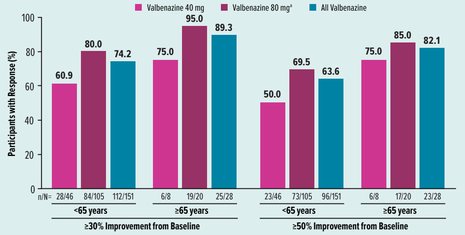
Figure 2. AIMS Total Score Change from Baseline to Week 48 by Age Subgroup



No statistically significant differences were observed between age subgroups.
[a]Includes participants who had a dose reduction from 80 to 40 mg.
AIMS, Abnormal Involuntary Movement Scale.

- High rates of clinically meaningful AIMS response (≥30% total score improvement) and the more robust, protocol-defined AIMS response (≥50% total score improvement) were found at Week 48, with no statistically significant differences between age subgroups (**Figure 3**)

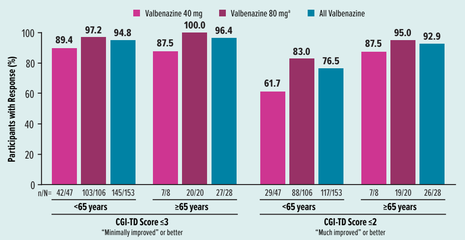
Figure 3. AIMS Response Rates at Week 48 by Age Subgroup



No statistically significant differences were observed between age subgroups.
[a]Includes participants who had a dose reduction from 80 to 40 mg.
AIMS, Abnormal Involuntary Movement Scale.

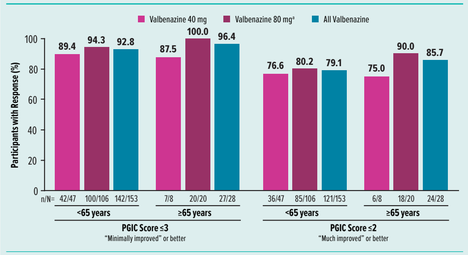
- Both subgroups also had high rates of clinician- and patient-reported improvement (CGI-TD and PGIC response) at Week 48, which trended in the same direction (**Figures 4 and 5**)
  - >90% of participants in both subgroups had a global rating of "minimally improved" or better (CGI-TD or PGIC score ≤3)
  - >75% achieved a stricter global rating of "much improved" or better (CGI-TD or PGIC score ≤2)

Figure 4. CGI-TD Response Rates at Week 48 by Age Subgroup



No statistically significant differences were found between age subgroups.
[a]Includes participants who had a dose reduction from 80 to 40 mg.
CGI-TD, Clinical Global Impression of Change-Tardive Dyskinesia.

Figure 5. PGIC Response Rates at Week 48 by Age Subgroup



No statistically significant differences were found between age subgroups.
[a]Includes participants who had a dose reduction from 80 to 40 mg.
PGIC, Patient Global Impression of Change.

- No statistically significant differences between age subgroups were found for overall TEAEs (<65 years, 71.5%; ≥65 years, 72.7%) or serious TEAEs (<65 years, 16.5%; ≥65 years, 18.2%); however, discontinuations due to TEAEs were more common in elderly participants (<65 years, 13.3%; ≥65 years, 25.5%; $P<0.05$)

CONCLUSIONS

- These analyses, based on data pooled from 2 long-term studies, are the first to assess the effects of an approved TD medication in an elderly study population (≥65 years), and the results indicate that long-term treatment with once-daily valbenazine is appropriate and beneficial for this age group
- In both age subgroups (≥65 years, <65 years), substantial and clinically meaningful improvements in TD were found after 48 weeks of once-daily valbenazine treatment
- Statistical analyses generally indicated no statistically significant differences between age subgroups, although the comparisons may have been limited by relatively smaller numbers of elderly study participants
- The results of these analyses may provide clinicians with important information about the management of TD in elderly patients

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Please contact medinfo@neurocrine.com with any questions.

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