Valbenazine Improves Physical, Social, and Emotional Impacts on the Tardive Dyskinesia Impact Scale (TDIS): Post Hoc Analyses of KINECT-PRO™ Data

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INTRODUCTION

- Once-daily valbenazine is a uniquely selective vesicular monoamine transporter 2 (VMAT2) inhibitor approved for the treatment of tardive dyskinesia (TD), a potentially debilitating movement disorder associated with prolonged exposure to antipsychotics and dopamine-receptor blocking agents[1-2]
- TD has been shown to negatively affect social, emotional, and physical functioning, even in patients with "mild" movement severity[3-5]
- KINECT-PRO™ is the first clinical trial to comprehensively assess and report the effects of an approved TD medication (valbenazine) on quality of life and functionality using multiple validated patient-reported outcomes (PROs)
  - Among these was the Tardive Dyskinesia Impact Scale (TDIS), the only PRO specifically developed and psychometrically validated to measure the physical and socio-emotional impacts of TD[6]
- The mean change in TDIS total score at Week 24 (end of treatment) was a primary endpoint in KINECT-PRO, as analyzed in the overall population and in subgroups of participants categorized by psychiatric diagnosis and TD movement severity
  - Robust and clinically meaningful improvements in TDIS total score were observed at Week 24, regardless of primary psychiatric condition or TD movement severity
  - Even patients with milder TD movements, as measured by item 8 of the Abnormal Involuntary Movement Scale (AIMS) at baseline, were impacted by their movements
  - Mean changes in TDIS total score exceeded the minimal clinically important difference (MCID) of -4 points[7] in the overall population and in all subgroups, including participants with milder TD movement severity
- The objective of this post hoc analysis was to provide more detailed insights into the impacts of TD by focusing on change in individual items from the TDIS

METHODS

STUDY DESIGN AND PARTICIPANTS

- This multicenter, US-based, phase 4 study included 24 weeks of treatment, with valbenazine dosing as follows:
  - Initiation at 40 mg (4 weeks)
  - Continuation with 40 mg or increase to 60 or 80 mg (12 weeks)
  - Stable dosing with 40, 60, or 80 mg (8 weeks)
- Stable doses of concomitant medications were allowed to manage comorbid psychiatric and medical conditions
- Key eligibility criteria included:
  - Men and women (aged ≥18 years) with confirmed psychiatric diagnosis (schizophrenia, schizoaffective disorder, bipolar disorder, or major depressive disorder) and TD diagnosis for ≥3 months before screening
  - Mild-to-severe TD movement severity, per AIMS item 8 and Schooler-Kane criteria[8] for AIMS items 1-7
  - Awareness of dyskinetic movements with mild-to-severe associated distress, per AIMS item 10

POST HOC ANALYSES

- The TDIS is composed of 11 items that are organized into 6 conceptual scales representing physical and socio-emotional domains: Mouth/Throat Function (3 items), Dexterity (2 items), Mobility (2 items), Emotional (2 items), Pain (1 item), and Social (1 item)
- Each item assesses the level or frequency of TD impact over the previous 7 days, with each item scored from 0 ("not at all" or "never") to 4 ("extremely" or "all the time")
- For each TDIS item, the mean change from baseline was analyzed at Week 24 in both absolute (i.e., raw score) and percent terms

RESULTS

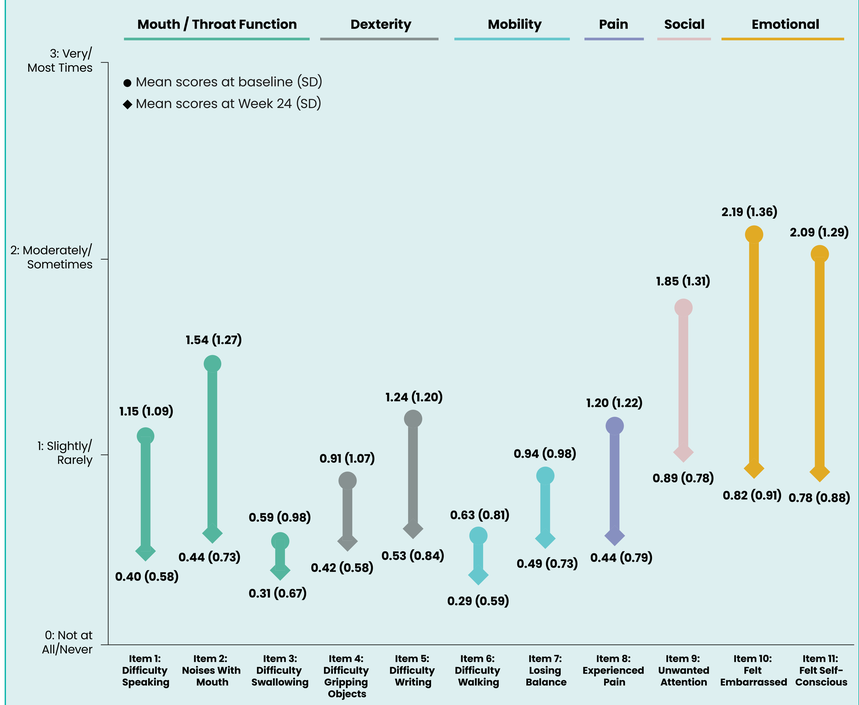
STUDY PARTICIPANTS

- Among the 59 enrolled participants, mean (±SD) age was 61.3 (±12.0) years, 34 (57.6%) were female, and 38 (64.4%) were White
  - 27 (45.8%) participants had schizophrenia or schizoaffective disorder, and 32 (54.2%) had major depressive disorder or bipolar disorder
  - 24 (40.7%) participants had mild TD at baseline per AIMS item 8; 35 (59.3%) had moderate or severe TD

TDIS ITEMS

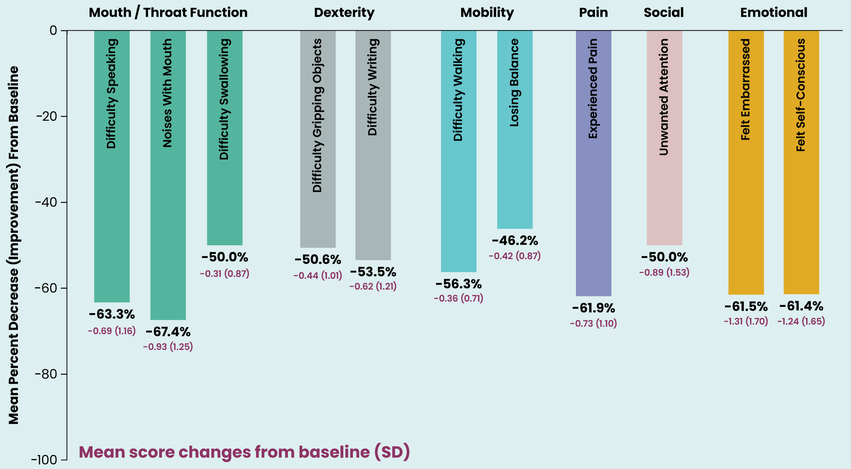
- Mean TDIS scores at baseline indicated TD impacts across physical and socio-emotional domains (**Figure 1**)
  - Items with the highest mean scores at baseline (i.e., greatest impact) were found in the Emotional, Social, and Mouth/Throat Function scales
- At Week 24, mean scores were reduced relative to baseline in all 11 TDIS items, indicating improvements in all domains
- At Week 24, substantial mean percent decreases (improvements) from baseline were observed in all 11 TDIS items, ranging from -46.2% (losing balance) to -67.4% (noises with mouth) (**Figure 2**)
  - The 5 TDIS items with the largest magnitude of improvement (i.e., mean score change from baseline) were: felt embarrassed (-1.31), felt self-conscious (-1.24), noises with mouth (-0.93), unwanted attention (-0.89), and experienced pain (-0.73)

Figure 1. Mean TDIS Item Scores at Baseline and at Week 24[a]



[a]Mean scores were analyzed in participants with available data at baseline (n=54) and at Week 24 (n=45). Item scores indicate level or frequency of impact over the 7 previous days, ranging from 0 ("not at all" or "never") to 4 ("extremely" or "all the time").
SD, standard deviation; TDIS, Tardive Dyskinesia Impact Scale.

[Figure 2. Percent Decrease (Improvement) From Baseline to Week 24 in TDIS Item Scores[a]



[a]Mean percent changes and mean score changes from baseline were analyzed in participants with available data at baseline and Week 24 (n=45).
BL, baseline; CFB, change from baseline; SD, standard deviation; TDIS, Tardive Dyskinesia Impact Scale.

CONCLUSIONS

- Results of these post hoc analyses showcase the use of TDIS to evaluate the physical and socio-emotional impacts of TD, which are not captured by existing clinician-rated TD scales such as the AIMS
- Mean TDIS item scores at baseline showed impact across all conceptual scales, with the largest impacts in the Emotional (felt embarrassed, felt self-consciousness), Social (unwanted attention), and Mouth/Throat Function (noises with mouth) scales, with mouth noises likely due to orofacial movements associated with TD (e.g., lip smacking, puckering, chewing)
- Items with the highest mean baseline scores tended to have the largest magnitudes of change
- The percent changes from baseline indicated that participants experienced substantial improvements across all 11 TDIS items (range, 46% to 67% improvement in 24 weeks)
- These data, in conjunction with the substantial improvements found in the primary PRO endpoints and secondary AIMS endpoint, show valbenazine to be the first VMAT2 inhibitor to demonstrate robust improvements in quality of life, functionality, and TD movement severity in patients with TD

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Please email medinfo@neurocrine.com if you have any questions on this presentation.

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