Clinically Meaningful Long-Term Improvements With Valbenazine 40 mg in Adults With Tardive Dyskinesia

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ABSTRACT DESCRIPTION

Valbenazine, available in 3 once-daily doses (40, 60, and 80 mg) and 2 formulations (capsule, sprinkle capsule), is approved for tardive dyskinesia (TD) and Huntington's disease (HD) chorea. Data from 3 long-term TD studies, which included patients who took valbenazine for >2 years, indicate substantial improvements with valbenazine 40 mg.

INTRODUCTION

- TD is a persistent and often debilitating hyperkinetic movement disorder associated with prolonged exposure to antipsychotics[1]
- Once-daily valbenazine, approved for the treatment of TD and chorea associated with HD, is available in 3 doses (40 mg, 60 mg, and 80 mg) and 2 formulations (capsule and sprinkle capsule)[2]
- For TD patients starting valbenazine, treatment with 40 mg is recommended for the first week, after which patients can remain on 40 mg or increase to 60 or 80 mg
- In the 6-week, double-blind, placebo-controlled phase of KINECT® 3 (K3, NCT02274558), a significantly greater mean improvement in the Abnormal Involuntary Movement Scale (AIMS) total score (sum of items 1-7) was found with valbenazine 80 mg versus placebo (the primary endpoint)[3]; treatment with valbenazine 40 mg also showed greater improvement in AIMS total score compared with placebo (nominal $P<0.05$ per fixed-sequence testing procedure)
- The long-term effects of once-daily valbenazine (40 and 80 mg) have been assessed in two phase 3 studies (K3 extension and KINECT® 4 [K4, NCT02405091]) in which participants received up to 48 weeks of treatment[4,5] and in a rollover study (1506, NCT02736955) in which completers from prior valbenazine studies received additional treatment[6]
  - In K4, a mean 10-point improvement was found at end of the 48-week treatment period[5]
- To assess the long-term effectiveness of the lowest approved dose (40 mg) in patients with TD, pooled AIMS and Clinical Global Impression of Change-Tardive Dyskinesia (CGI-TD) data from K3 and K4, as well as Clinical Global Impression of Severity-Tardive Dyskinesia (CGIS-TD) data from 1506, were analyzed post hoc in participants who received valbenazine 40 mg or had a dose reduction from 80 to 40 mg

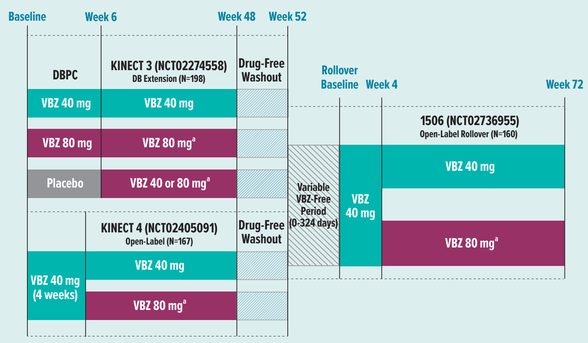
OBJECTIVES

- Recognize that all 3 available doses of valbenazine (40, 60, and 80 mg once-daily) can be safe and effective
- Communicate to patients that valbenazine 40 mg is an effective dose and that reduction to 40 mg can be tried if they are unable to tolerate a higher dose (60 or 80 mg)

METHODS

- Data from 3 long-term valbenazine studies were analyzed (**Figure 1**)
  - Few participants in 1506 had reached Week 60 (n=4) and none reached the final planned visit (Week 72) when the study was terminated due to commercial availability of valbenazine
- Analyses focused on valbenazine 40 mg in 2 populations:
  - K3/K4: participants who received valbenazine 40 mg throughout K3 or K4 (40 mg group) or had a dose reduction from 80 mg to 40 mg during K3 extension or after Week 4 in K4 (80/40 mg group)
  - 1506: participants who received valbenazine 40 mg from beginning of K3 or K4 to their last study visit in 1506 (40 mg group) or had a dose reduction during K3 extension after Week 4 in K4 or after Week 4 in 1506 (80/40 mg group)
  - Participants who initially received placebo in K3 were not included in either population

Figure 1. Study Designs



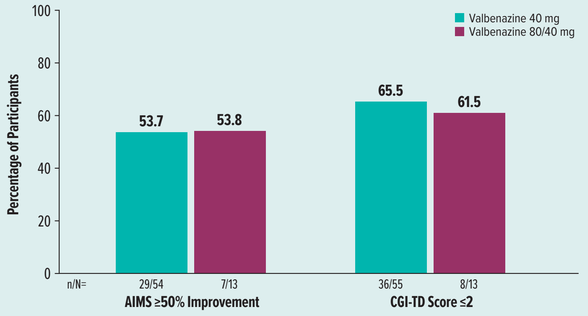
[a]Participants could have a dose reduction from 80 mg to 40 mg based on tolerability.
DB, double-blind; DBPC, double-blind placebo-controlled; VBZ, valbenazine.

- The following outcomes were assessed at Week 48 for the K3/K4 population:
  - Percentage of participants who met the protocol-defined AIMS response threshold (≥50% total score improvement from baseline); scored by blinded central video raters (K3) or site raters (K4)
  - Percentage of participants who had a CGI-TD score of 1 ("very much improved") or 2 ("much improved")
- In addition, the percentage of participants who had a CGIS-TD score of 1 ("normal/not at all ill") or 2 ("borderline ill") was assessed by study visit in the 1506 population

RESULTS

- A majority of participants in the K3/K4 population met the ≥50% AIMS response threshold or had a CGI-TD score ≤2 at Week 48 (**Figure 2**)

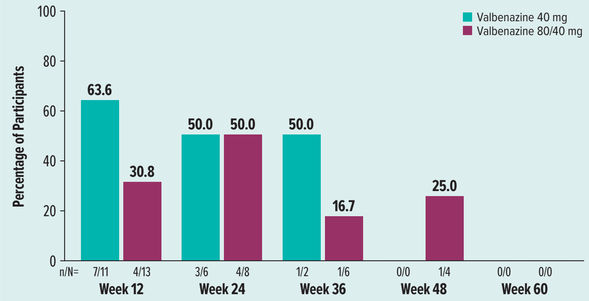
Figure 2. Participants With ≥50% AIMS Response or CGI-TD Score ≤2 ("Very Much Improved" or "Much Improved") at Week 48 (K3/K4 Population)



AIMS, Abnormal Involuntary Movement Scale; CGI-TD, Clinical Global Impression of Change-Tardive Dyskinesia; K3, KINECT 3; K4, KINECT 4.

- In the 1506 population, a majority of participants who had received valbenazine 40 mg throughout their prior study (K3 or K4) and continued to receive valbenazine 40 mg in 1506 had a CGIS-TD score ≤2 during 1506 (**Figure 3**)
  - At time of study termination (due to commercial availability of valbenazine), few participants in the 40 mg group had reached the Week 48 visit and none had reached Week 60

Figure 3. Participants With CGIS-TD Score ≤2 ("Normal/Not at all Ill" or "Borderline Ill") by Study Visit (1506 Population)



CGIS-TD, Clinical Global Impression of Severity-Tardive Dyskinesia.

CONCLUSIONS

- Results from published long-term studies demonstrated clinically meaningful improvements in TD with valbenazine 40 mg
- Dose reductions from 80 to 40 mg did not appear to reduce long-term benefit
- Patients can be educated that valbenazine 40 mg is an effective dose, and reduction to 40 mg can be offered based on clinician judgment

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Disclosures: This study was supported by Neurocrine Biosciences, Inc. (San Diego, CA). Writing and graphical assistance was provided by Prescott Medical Communications Group, a Citrus Health Group, Inc., company (Chicago, IL).
Please contact medinfo@neurocrine.com with any questions.

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