Once-Daily Valbenazine Improves Chorea Across Body Regions in Adults With Huntington's Disease: Post-Hoc Shift Analyses of KINECT®-HD Data

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ABSTRACT DESCRIPTION

In KINECT®-HD, once-daily valbenazine significantly reduced chorea severity as evaluated using the Unified Huntington's Disease Rating Scale (UHDRS®) Total Maximal Chorea (TMC) score, which comprises seven body regions. In this post-hoc analysis, more participants had potentially meaningful improvements with valbenazine versus placebo in each body region, with statistical significance for the arms and legs.

INTRODUCTION

- Chorea is characterized by irregular, nonrhythmic, and involuntary movements that can affect any part of the body, including the face, buccal-oral-lingual region, trunk, arms, and legs[1]
- Once-daily valbenazine is a highly selective vesicular monoamine transporter 2 (VMAT2) inhibitor that is approved for the treatment of chorea in adults with Huntington's disease (HD) and for tardive dyskinesia[2]
- In a 12-week, phase 3 clinical trial (KINECT-HD: NCT04102579), valbenazine significantly improved HD-associated chorea versus placebo, as assessed using the TMC score[3]
  - Least-squares mean changes from screening/baseline to week 10/12 were –4.6 and –1.4 for valbenazine and placebo, respectively (P<0.0001, primary endpoint)
- The TMC score (range, 0-28) measures chorea in seven body regions, with scores for each region ranging from 0 "absent" to 4 "marked/prolonged"
- Because individuals may experience choreiform movements in different body regions, analyzing these separately provides additional details on treatment effects in the regions where chorea severity is most pronounced

LEARNING OBJECTIVES

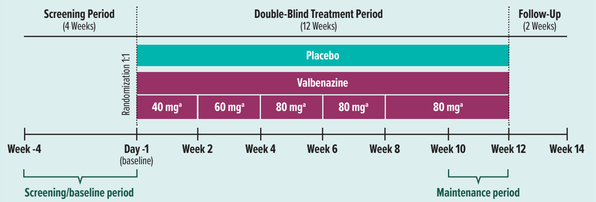
- Recognize that chorea can be more severe in some body regions than in others
- Understand how shift analyses can be used to describe potentially meaningful improvements in chorea (e.g., from moderate or worse to absent or slight/intermittent)
- Describe the effects of valbenazine on chorea by body region in the KINECT-HD clinical trial

METHODS

STUDY DESIGN

- Adults with motor manifest, genetically confirmed HD were randomized 1:1 to once-daily valbenazine or placebo for 12 weeks (**Figure 1**)
  - Valbenazine was initiated at 40 mg and increased to a target dose of 80 mg, as tolerated
  - Participants were required to have a TMC score ≥8 at both screening and baseline

Figure 1. KINECT-HD Study Design



For TMC assessments, **screening/baseline period** scores are based on the average of each participant's scores at baseline and screening; **maintenance period** scores are based on the average of each participant's scores at week 10 and week 12.
[a]Doses represent the maximum daily doses during each treatment period.
TMC, Total Maximal Chorea.

POST-HOC ANALYSES

- Analyses were based on item scores for each TMC body region
  - Seven regions: face, buccal-oral-lingual, trunk, right upper extremity, left upper extremity, right lower extremity, left lower extremity
  - Scoring per region: 0=absent, 1=slight/intermittent, 2=mild/common or moderate/intermittent, 3=moderate/common, 4=marked/prolonged
- Post-hoc analyses were as follows:
  - Distribution of TMC scores by body region at screening/baseline period
  - Category shifts for TMC body region scores, with potentially meaningful improvement defined as a score shift from ≥2 at screening/baseline to ≤1 at maintenance, along with the corresponding relative risks (RRs) and numbers needed to treat (NNTs)
  - Statistical significance for category shifts was analyzed by chi square tests for valbenazine versus placebo
  - Mean TMC body region scores at screening/baseline period and maintenance period
- Because scoring in each period is based on the average of two assessments (screening/baseline, week 10/week 12), scores of 0.5 are possible for TMC body region items

RESULTS

- In the full analysis set (N=125), demographics and baseline TMC scores were generally similar between treatment groups (**Table 1**)
  - A majority of participants in both treatment groups had baseline TMC body region scores ≥2 ("mild/common" or "moderate/intermittent" or worse) for their extremities; fewer than one-third met this threshold for the face or buccal-oral-lingual region

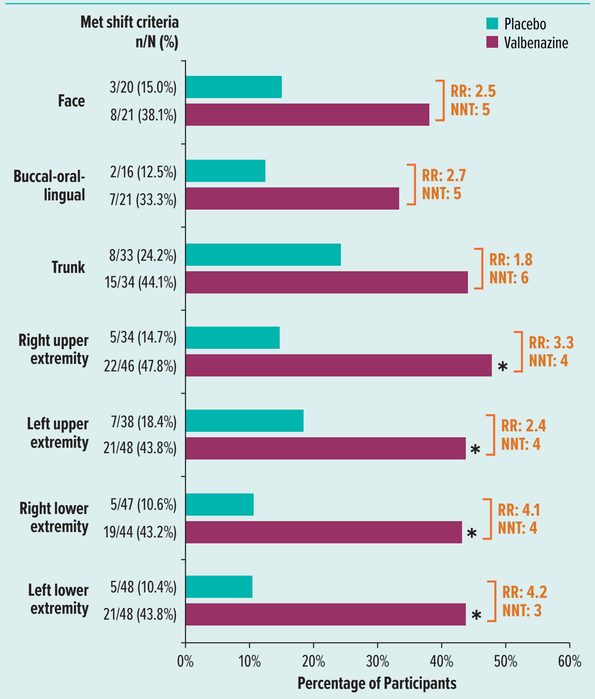
Table 1. Demographics and TMC Scores at Baseline

	Placebo (n=61)	Valbenazine (n=64)
Demographics		
Age, mean (SD), years	53.3 (11.4)	54.1 (10.1)
Female, n (%)	35 (57.4)	33 (51.6)
White, n (%)[a]	60 (98.4)	60 (93.8)
Hispanic or Latino, n (%)	3 (4.9)	5 (7.8)
Body mass index, mean (SD), kg/m^2	27.4 (5.7)	26.6 (5.6)
TMC at baseline[b]		
Mean score (SD)	12.1 (2.8)	12.2 (2.3)
Participants with body region scores ≥2, n (%)		
Face	20 (32.8)	21 (32.8)
Buccal-oral-lingual	16 (26.2)	21 (32.8)
Trunk	33 (54.1)	34 (53.1)
Right upper extremity	34 (55.7)	46 (71.9)
Left upper extremity	38 (62.3)	48 (75.0)
Right lower extremity	47 (77.0)	44 (68.8)
Left lower extremity	48 (78.7)	48 (75.0)

[a]Additional self-reported races were as follows: Black/African American (n=1), Asian (n=1), other/unspecified (n=3).
[b]For screening and baseline period (average of each participant's screening and baseline values), per assessment by study investigator. Score range: 0-28, with higher scores indicating more severe chorea.
SD, standard deviation; TMC, Total Maximal Chorea.

- **Figure 2** shows the proportions of participants with improvements by body region, as indicated by TMC body region scores ≥2 ("mild/common", "moderate/intermittent", "moderate/common", or "marked/prolonged") at screening/baseline and shifts to scores ≤1 ("absent" or "slight/intermittent") at maintenance
  - For all body regions, a numerically greater percentage met these shift criteria with valbenazine versus placebo, with statistical significance for all upper and lower extremities (P<0.05 for each)
  - Robust treatment effects with valbenazine were observed in the upper and lower extremities, as indicated by higher RRs and lower NNTs

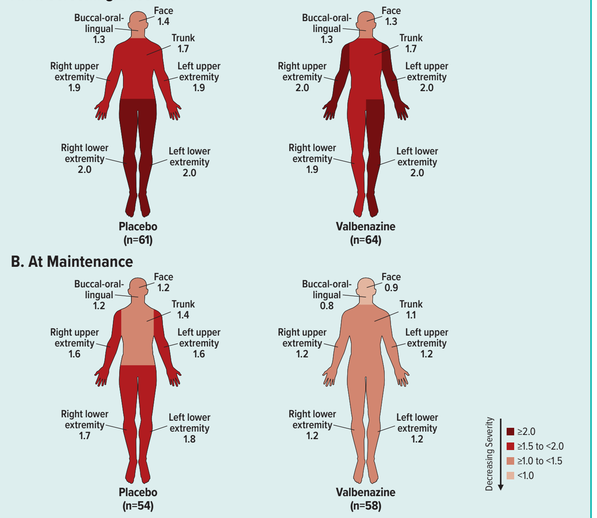
Figure 2. Proportions of Participants With Chorea Improvements by Body Region[a]



*p<0.05 for valbenazine versus placebo.
[a]Defined as a shift from a score ≥2 ("mild/common", "moderate/intermittent", "moderate/common", or "marked/prolonged") at screening/baseline to ≤1 ("absent" or "slight/intermittent") at maintenance for each TMC body region item.
Screening/baseline period scores are based on the average of each participant's scores at baseline and screening; **maintenance period** scores are based on the average of each participant's scores at week 10 and week 12.
n, number of participants who met shift criteria; N, number of participants with screening/baseline body region scores ≥2; NNT, number needed to treat; OR, odds ratio.

- Mean TMC body region scores were generally similar for placebo and valbenazine groups at screening/baseline (**Figure 3A**)
- TMC body region scores improved at maintenance, with numerically greater improvements for all TMC items with valbenazine versus placebo (**Figure 3B**)

Figure 3. Mean TMC Body Region Scores by Treatment Period and Treatment Group



Screening/baseline period scores are based on the average of each participant's scores at baseline and screening; **maintenance period** scores are based on the average of each participant's scores at week 10 and week 12.
TMC, Total Maximal Chorea.

CONCLUSIONS

- In the KINECT-HD population, chorea was present at baseline in all evaluated body regions, with higher chorea severity in the extremities and trunk compared to the face and buccal-oral-lingual region
- A greater percentage of participants achieved potentially meaningful chorea improvements with valbenazine versus placebo in each body region, with significance found for the arms and legs
- These analyses support the primary endpoint of KINECT-HD, which demonstrated a significantly greater TMC reduction with valbenazine versus placebo
- Valbenazine treatment demonstrates a consistent pattern of chorea improvements across body regions

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Please contact medinfo@neurocrine.com with any questions.

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