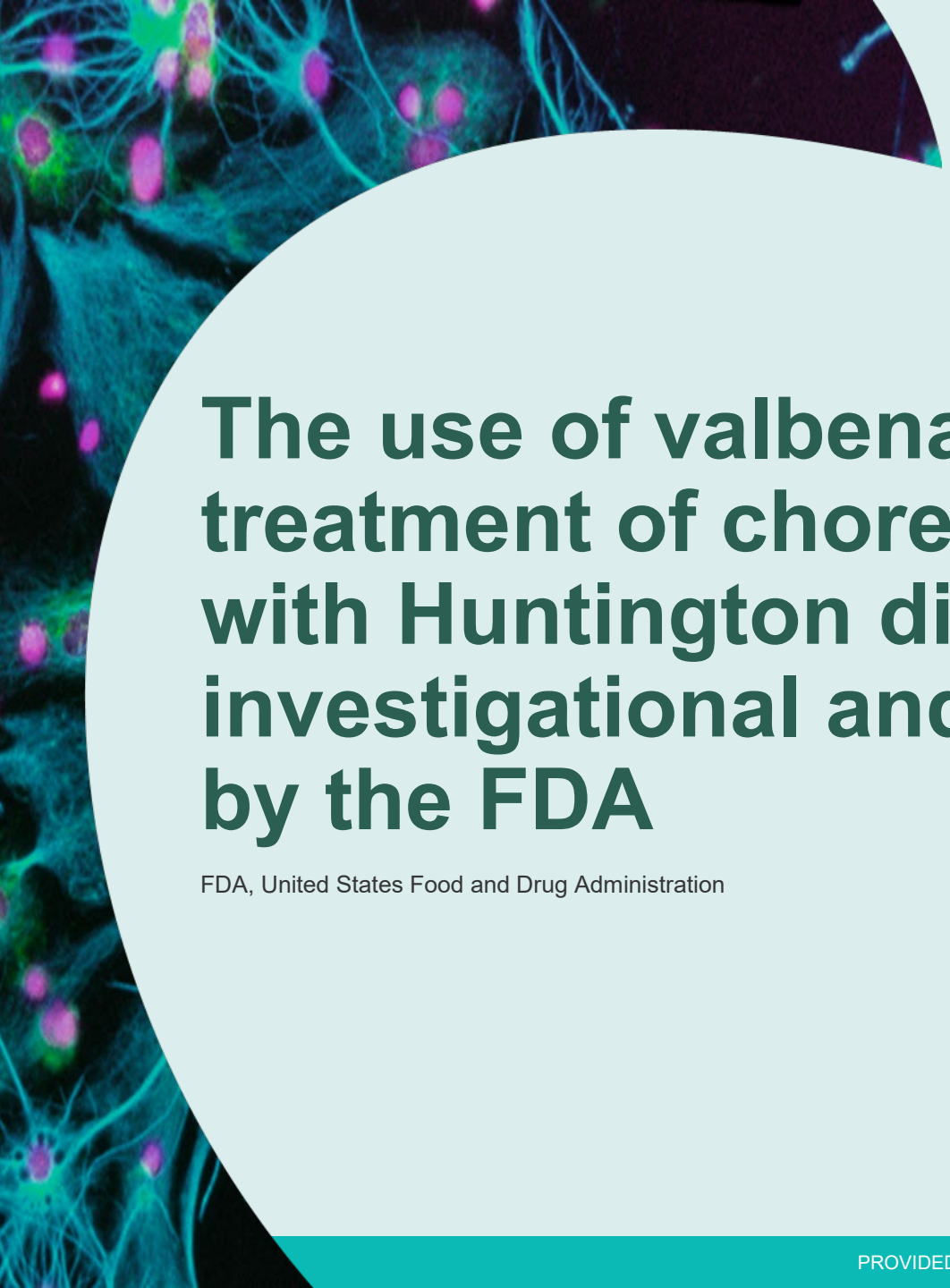
KINECT-HD & KINECT-HD2 Clinical Trial Program

NEUROCRINE® BIOSCIENCES



The use of valbenazine for the treatment of chorea associated with Huntington disease is investigational and not approved by the FDA

FDA, United States Food and Drug Administration

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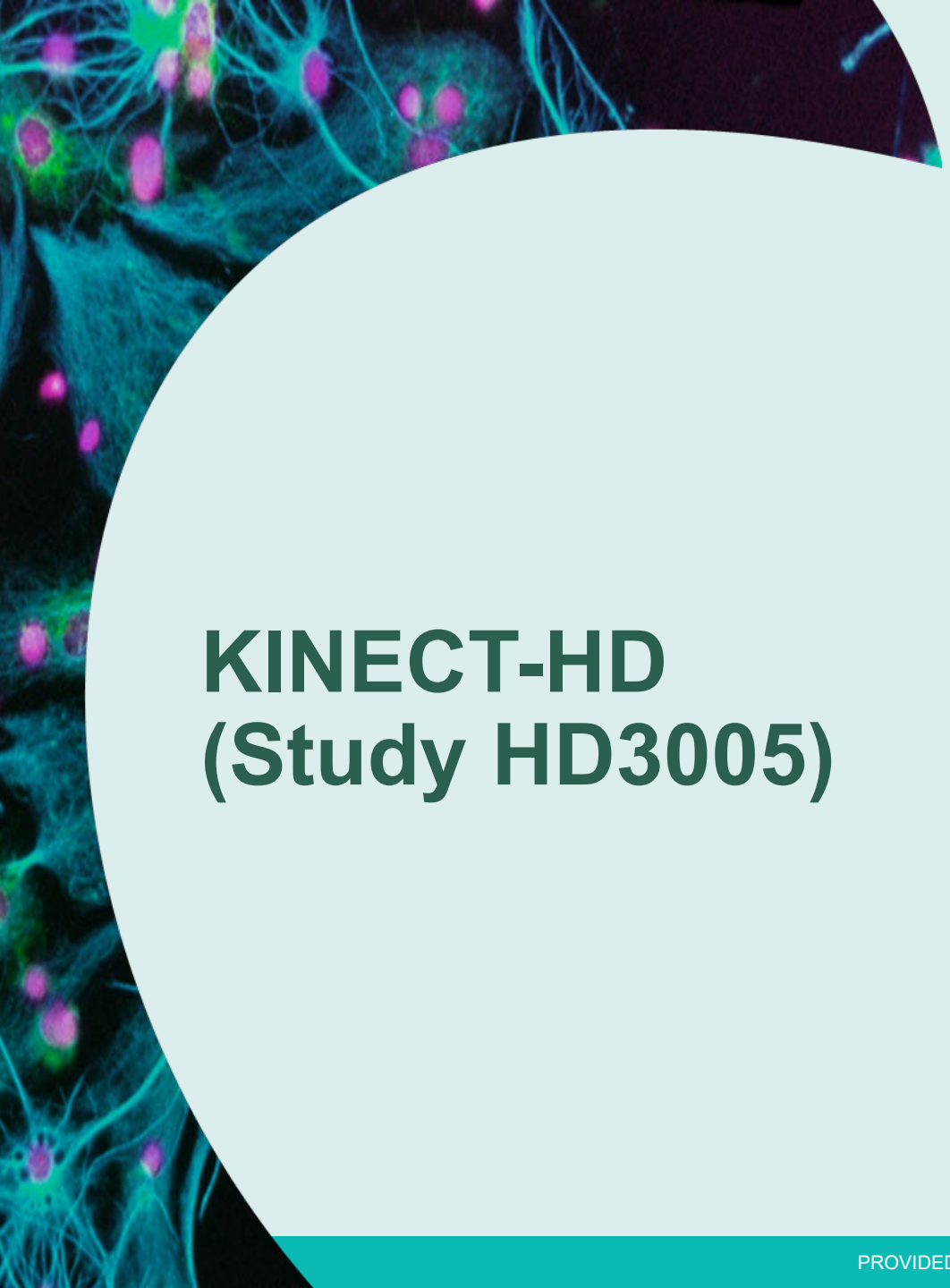


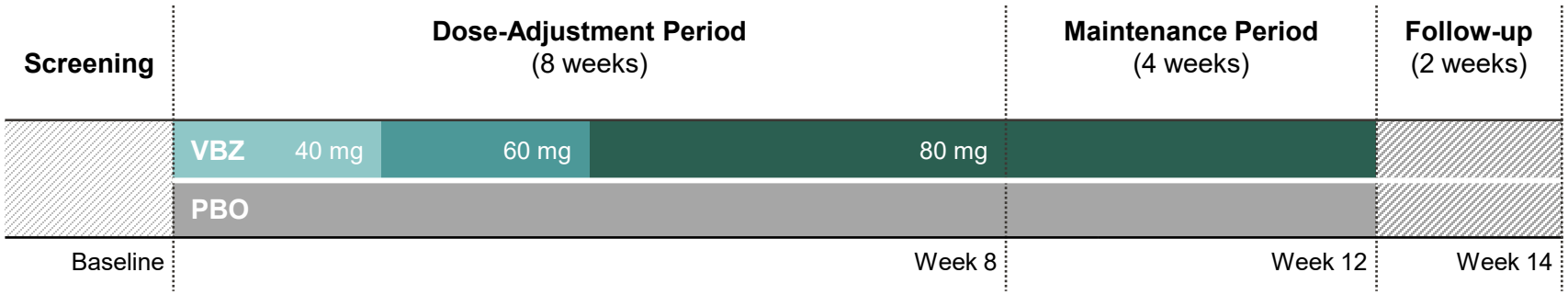
KINECT-HD (Study HD3005)

KINECT-HD: Study Design[1,2]

KINECT-HD is a phase 3, randomized, double-blind, placebo-controlled study to evaluate the efficacy, safety, and tolerability of once-daily valbenazine for the treatment of chorea associated with Huntington disease (HD)

Valbenazine has not been approved by the FDA for the treatment of chorea associated with HD

Study Timeline



Study Details

- 128 adult male and females; randomized 1:1
- The study includes an up to 4-week screening period, a 12-week treatment period (8-week dose-adjustment period and a 4-week maintenance period), and a final study visit 2 weeks following the final dose of study drug (Week 14)
- Conducted in the US and Canada

FDA, US Food and Drug Administration

1. Clinicaltrials.gov. Accessed March 30, 2022. https://clinicaltrials.gov/ct2/show/NCT04102579?cond=NCT04102579&draw=2&rank=1 | 2. Data on File. (VBZ-HD-0001). Neurocrine Biosciences, Inc.

KINECT-HD: Inclusion & Exclusion Criteria[1,2]

Key Inclusion Criteria

- Male or female 18 to 75 years old
- Genetic diagnosis of HD with an expanded CAG repeat (≥37) in huntingtin (HTT) gene and a clinical diagnosis of HD with chorea
- Be able to walk, with or without the assistance of a person or device
- Total Maximal Chorea (TMC) score ≥8 at screening and baseline
- Total Function Capacity (TFC) score ≥5 at screening

Key Exclusion Criteria

- History of prior VMAT2 inhibitor therapy
- History or evidence of long QT syndrome, cardiac tachyarrhythmia, left bundle-branch block, AV block, uncontrolled bradyarrhythmia, or heart failure
- Unstable or serious medical or untreated/undertreated psychiatric illness
- Significant risk of suicidal behavior
- Concurrent substance dependence or abuse

AV, atrioventricular; CAG, cytosine, adenine, and guanine; HD, Huntington disease; VMAT2, vesicular monoamine transporter 2;

1. Clinicaltrials.gov. Accessed March 30, 2022. https://clinicaltrials.gov/ct2/show/NCT04102579?cond=NCT04102579&draw=2&rank=1 | 2. Data on File. (VBZ-HD-0001). Neurocrine Biosciences, Inc.

KINECT-HD3005: Assessments[1,2]

Primary Efficacy Endpoint

- Change from baseline (average of screening and baseline score) to maintenance (average of Week 10 and Week 12) in Unified Huntington's Disease Rating Scale (UHDRS®) Total Maximal Chorea (TMC) score
  - UHDRS® was scored locally by the site investigator or designee

Secondary Objectives

- Clinical Global Impression of Change (CGI-C) and Patient Global Impression of Change (PGI-C) response status* at Week 12
- Change from Baseline to Week 12 in the Quality of Life in Neurological Disorders (Neuro-QoL) Upper and Lower Extremity Function T-score

Safety Endpoints

- AEs, clinical laboratory tests, vital signs, physical examinations, ECG, Columbia-Suicide Severity Rating Scale (C-SSRS), Barnes Akathisia Rating Scale (BARS), Hospital Anxiety and Depression Scale (HADS)

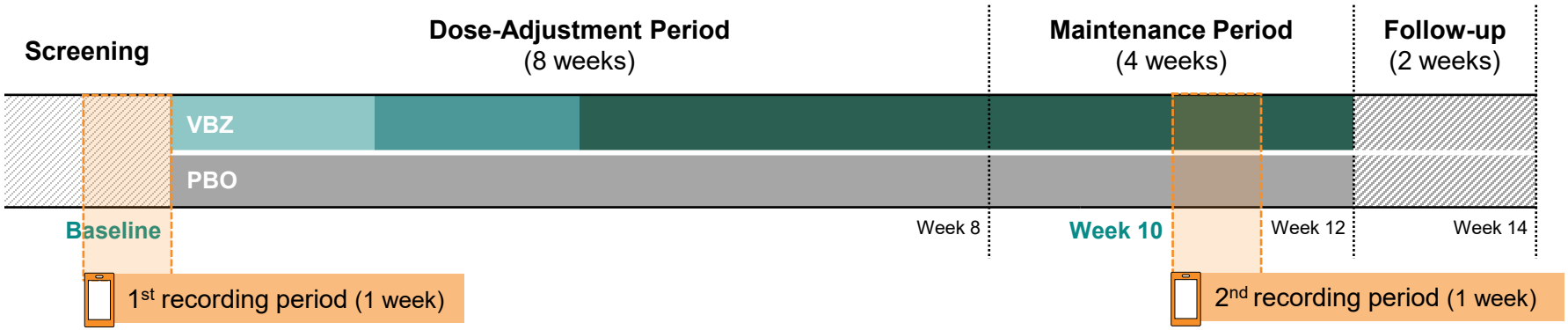
AEs, adverse events; ECG, electrocardiogram. *Participants with CGI-C or PGI-C scores of either a 1 ("very much improved") or a 2 ("much improved") were classified as responders.

1. Clinicaltrials.gov. Accessed March 30, 2022. https://clinicaltrials.gov/ct2/show/NCT04102579?cond=NCT04102579&draw=2&rank=1 | 2. Data on File. (VBZ-HD-0001). Neurocrine Biosciences, Inc.

KINECT-HD: Wearable Movement Sensors Exploratory Sub-Study[1,2]

Exploratory objective: evaluate the ability of wearable movement sensors to detect changes in physical activity

Study Timeline



Sub-Study Details

- Data collected using the Medidata10 BioStamp nPoint System® - a medical device designed to collect biometric and physiological data
  - Data derived from multimodal body-worn sensors to monitor limb or body movements during daily living and sleep
- Two at-home recording periods (after the screening visit and after week 10)
- Available in select sites; optional participation (up to 50 participants)

PBO, placebo; VBZ, valbenazine

1. Clinicaltrials.gov. Accessed March 30, 2022. https://clinicaltrials.gov/ct2/show/NCT04102579?cond=NCT04102579&draw=2&rank=1 | 2. Data on File. (VBZ-HD-0001). Neurocrine Biosciences, Inc.

KINECT-HD: Study Participants

Full Analysis Set[a]

	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 (%)[b]	60 (98.4)	60 (93.8)
Baseline Characteristics		
Body mass index, mean (SD) kg/m^2	27.4 (5.7)	26.6 (5.6)
CAG repeat length, mean (SD)	43.4 (3.0)	43.5 (3.3)
UHDRS® TMC score, mean (SD)[c]	12.1 (2.8)	12.2 (2.3)
CGI-S score ≥4, n (%)[d]	28 (45.9)	33 (51.6)
PGI-S score ≥3, n (%)[e]	25 (41.0)	31 (48.4)

[a] Participants with ≥1 evaluable post-baseline UHDRS® TMC assessment.

[b] Additional self-reported races were as follows: Black/African-American (n=1), Asian (n=1), and other-unspecified (n=3).

[c] For screening period baseline (average of screening and Day -1 assessments).

[d] Investigator rating of "moderately ill" to "among the most extremely ill" for chorea.

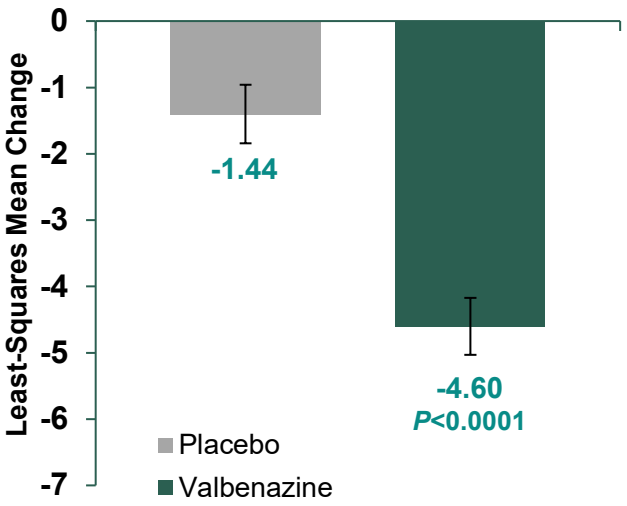
[e] Participant self-rating of "moderate" to "very severe" for chorea.

CGI-C, Clinical Global Impression of Change; PGI-C, Patient Global Impression of Change; TMC, Total Maximal Chorea; UHDRS, Unified Huntington's Disease Rating Scale.

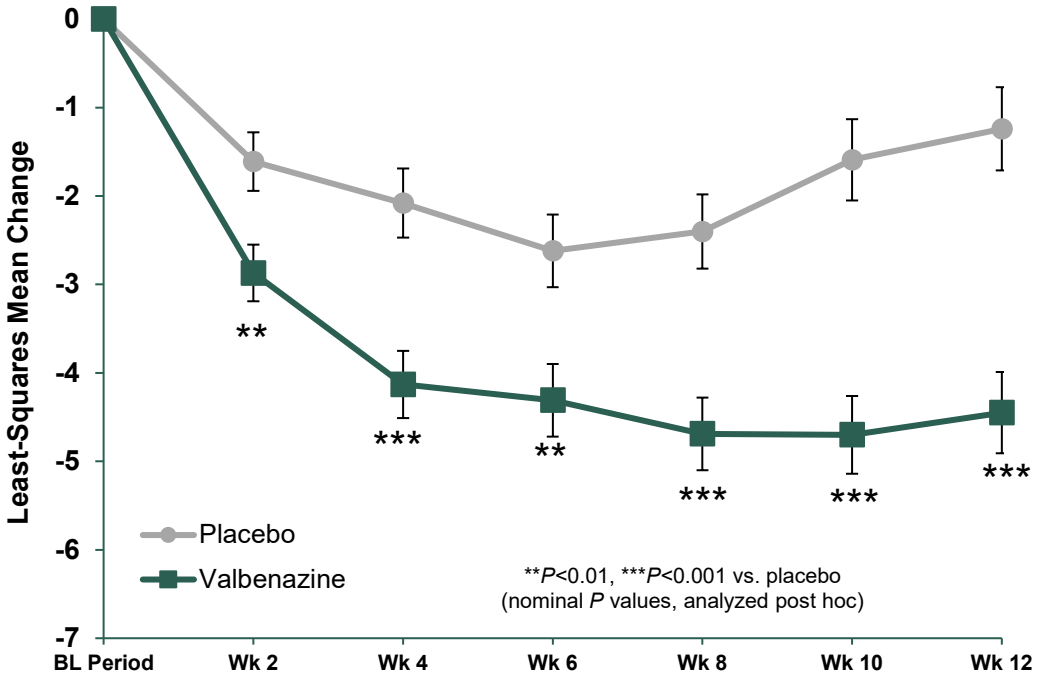
Furr-Stimming E, et al. AAN 2022; Seattle, WA.

KINECT-HD: Mean Changes in UHDRS® Total Maximal Chorea (TMC)

UHDRS® TMC Improvements



Mean Change from Screening Period Baseline by Study Visit



PRIMARY ENDPOINT

Mean improvement in UHDRS® TMC score from screening period baseline (average of screening and Day -1 values) to maintenance period (average of Week 10 and 12 values) was significantly greater with valbenazine versus placebo

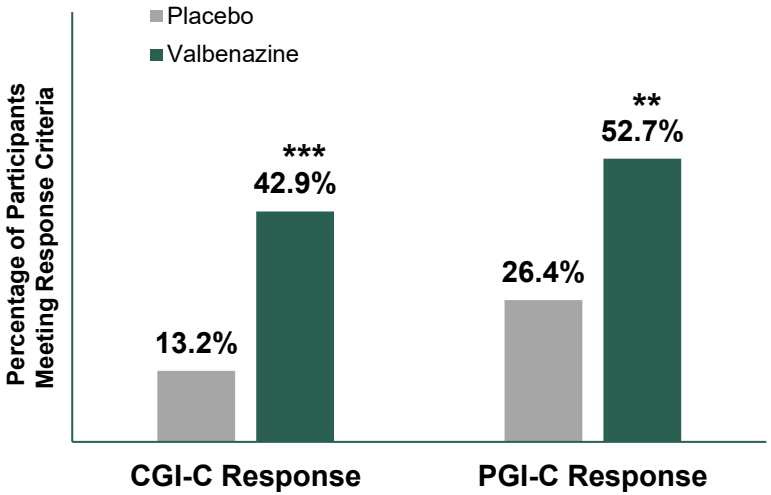
TMC, Total Maximal Chorea; UHDRS, Unified Huntington's Disease Rating Scale.

Furr-Stimming E, et al. AAN 2022; Seattle, WA.

KINECT-HD: Secondary Objectives and Safety Endpoints

Secondary Endpoints

- The proportion of participants with clinician and self-rated global improvements ("much improved" or better) was significantly higher with valbenazine versus placebo at Week 12



**P<0.01, ***P<0.001 vs. placebo

- Mean changes from baseline to Week 12 in Neuro-QoL T-scores were similar for valbenazine versus placebo:
  - Upper Extremity Function: -1.58 vs -3.00 (n.s.)
  - Lower Extremity Function: -0.27 vs 0.61 (n.s.)

Safety Summary

Treatment-Emergent Adverse Events (TEAEs)	Placebo (n=63)	Valbenazine (n=64)
Summary, n (%)		
Overall TEAEs	40 (63.5)	49 (76.6)
Serious TEAEs	2 (3.2)	1 (1.6)
TEAEs resulting in discontinuation	4 (6.3)	5 (7.8)
TEAEs resulting in death[a]	1 (1.6)	0
Common TEAEs,[b] n (%)		
Somnolence	2 (3.2)	10 (15.6)
Fatigue	6 (9.5)	9 (14.1)
Fall	8 (12.7)	8 (12.5)
Urticaria	0	6 (9.4)
Rash	0	5 (7.8)
Akathisia	3 (4.8)	4 (6.3)

[a] Due to colon cancer; judged by investigator as unlikely related to study treatment.
[b] As reported in ≥5% of participants in either treatment group.

- No clinically important differences in vital signs, laboratory results, ECG parameters, and clinical safety scales were observed between treatment groups
- No suicidal behavior or worsening of suicidal ideation was observed in participants treated with valbenazine

CGI-C, Clinical Global Impression of Change; ECG, electrocardiogram; Neuro-QoL, Quality of Life in Neurological Disorders; n.s., not significant; PGI-C, Patient Global Impression of Change; TMC, Total Maximal Chorea; UHDRS, Unified Huntington's Disease Rating Scale. Furr-Stimming E, et al. AAN 2022; Seattle, WA.

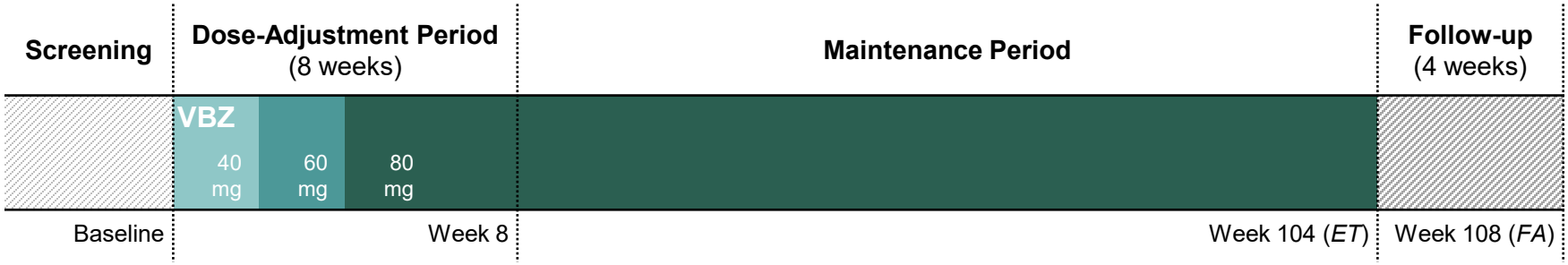
KINECT-HD2 (Study HD3006)

KINECT-HD2: Study Design[1,2]

KINECT-HD2 is a phase 3, open-label, rollover study to evaluate the long-term safety and tolerability of valbenazine

Valbenazine has not been approved by the FDA for the treatment of chorea associated with HD

Study Timeline



Study Details

- Approximately 150 adult male and females will be enrolled
  - Participants who completed KINECT-HD and those who did not participate in KINECT-HD will be enrolled
- The study started in September 2020, and is currently ongoing

Primary Assessment

- Emergence of treatment emergent adverse events (TEAEs)

HD, Huntington Disease; ET, End of Treatment; FA, Final Assessment; FDA, US Food and Drug Administration; TMC, total maximal chorea.

1. Clinicaltrials.gov. Accessed March 30, 2022. https://clinicaltrials.gov/ct2/show/NCT04400331?cond=NCT04400331&draw=2&rank=1 | 2. Data on File. (VBZ-HD-0002). Neurocrine Biosciences, Inc.

KINECT-HD2: Inclusion & Exclusion Criteria[1]

Key Inclusion Criteria[1]

- Have participated in Study HD3005 (KINECT-HD) and
  - Study drug dosing completion of Study HD3005, as demonstrated by completed study drug dosing through the follow-up visit OR
  - Early terminated Study HD3005 for administrative reasons due to COVID-19 (eg, site closure related to COVID-19)
- OR did not participate in KINECT-HD and
  - Meet criteria as set forth in KINECT-HD

Key Exclusion Criteria[1]

- Received an investigational drug within 30 days before the baseline visit or plan to use an investigational drug (other than valbenazine) during the study
- Known history of long QT syndrome, cardiac tachyarrhythmia, left bundle-branch block, atrioventricular (AV) block, uncontrolled bradyarrhythmia, or heart failure
- Unstable or serious medical or psychiatric illness
- Significant risk of suicidal behavior
- Current substance dependence or abuse

AV, atrioventricular; CAG, cytosine, adenine, and guanine; VMAT2, vesicular monoamine transporter 2

1. Clinicaltrials.gov. Accessed March 30, 2022. https://clinicaltrials.gov/ct2/show/NCT04400331?cond=NCT04400331&draw=2&rank=1