Valbenazine Safety: Chorea in Huntington's Disease

NEUROCRINE® BIOSCIENCES

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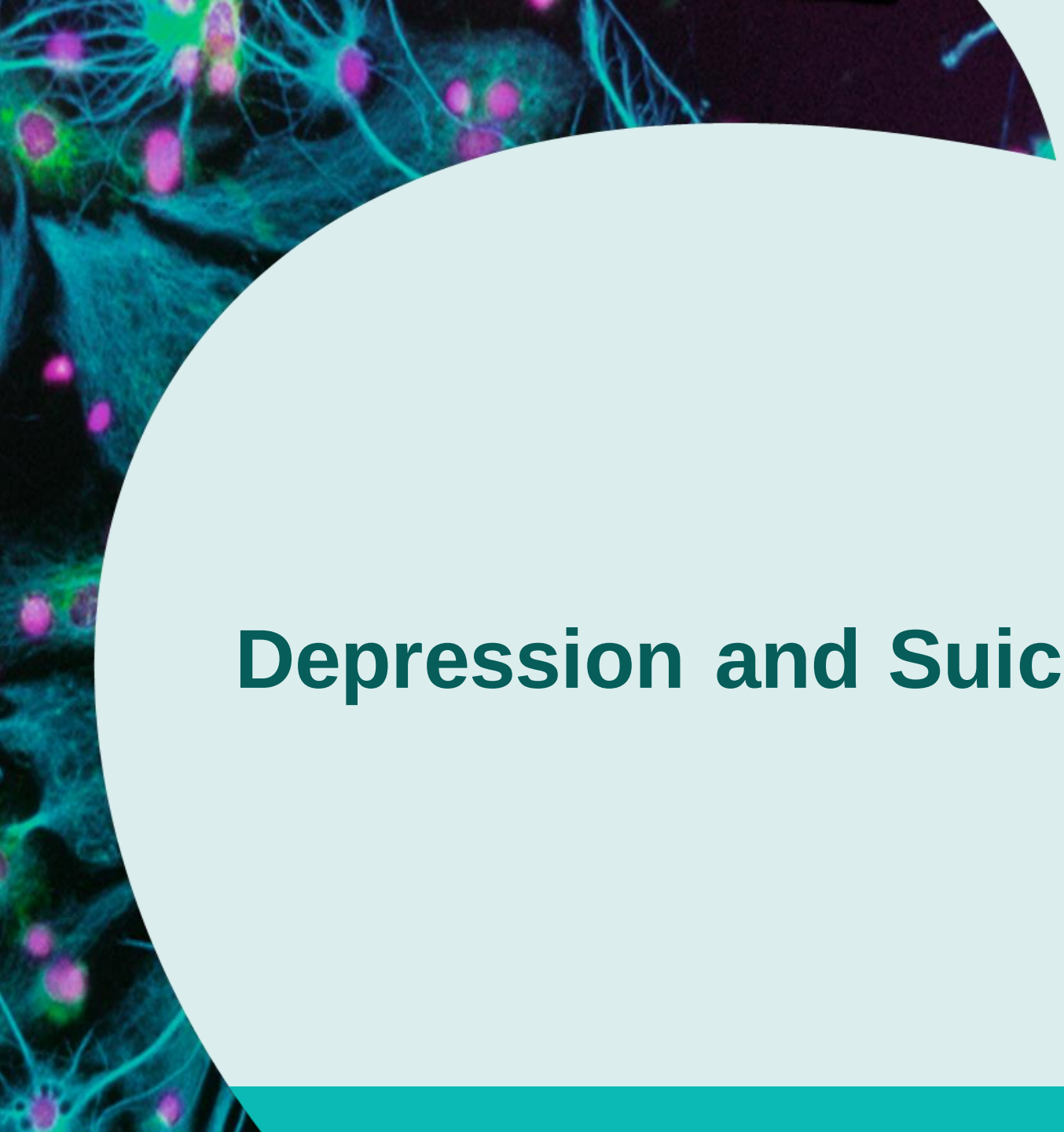


Depression and Suicidality

Valbenazine Important Safety Information

WARNING: DEPRESSION AND SUICIDAL IDEATION AND BEHAVIOR IN PATIENTS WITH HUNTINGTON'S DISEASE

VMAT2 inhibitors, including INGREZZA, can increase the risk of depression and suicidal thoughts and behavior in patients with Huntington's disease. Anyone considering the use of INGREZZA must balance the risks of depression and suicidal ideation and behavior with the clinical need for treatment of chorea. Closely monitor patients for the emergence or worsening of depression, suicidal ideation, or unusual changes in behavior. Inform patients, their caregivers, and families of the risk of depression and suicidal ideation and behavior and instruct them to report behaviors of concern promptly to the treating physician.

Particular caution should be exercised in treating patients with a history of depression or prior suicide attempts or ideation, which are increased in frequency in patients with Huntington's disease.

Valbenazine is not contraindicated in patients with depression or suicidality, but the risk of suicidal ideation and behaviors must be balanced against the need for treatment of chorea

Prescribing Information

VMAT2, vesicular monoamine transporter 2

INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.

Depression & Suicidality in HD and KINECT®-HD Studies

Depression estimates in people with HD can vary greatly in the literature but has been reported to affect approximately 40% to 50% of those with HD[1,2]

Suicide has been reported as the second most common cause of death in people with HD following pneumonia[3,4]

In both valbenazine HD studies the baseline prevalence of medical history of depression and suicidality was consistent with depression and suicidality estimates in the literature[5]

Prevalence Rates of Medical History of Depression and Suicidality in Patients with Huntington's Disease

	Prevalence Estimates in HD Patients	KINECT-HD Population at baseline[5,¶]	Interim KINECT-HD2 Population at baseline[5,¶]
Depression			
	40% to 50%[2,†]	47%	48%
Suicidal ideation			
	20% to 30%[6,‡]	21%	20%
Suicidal behavior			
	7% to 10%[6,§]	5%	5%

†Based on a review of 8 observational and 6 retrospective studies comprising 11,782 and 2,027 patients, respectively. Depression prevalence estimates vary greatly in the literature.
‡Based on a review of 7 observational studies comprising 14,406 patients.
§Based on a review of 4 observational studies comprising 6,358 patients.
¶Based on medical history. Patients with significant risk of suicidal behavior or unstable/serious medical or psychiatric illness were excluded from both studies.

HD, Huntington's disease.
KINECT-HD is the 12-week, Phase 3, randomized, double-blind placebo-controlled study to evaluate the safety and efficacy of valbenazine for the treatment of chorea associated with Huntington's disease (HD).
KINECT-HD2 is the Phase 3, open-label rollover study to evaluate the long-term safety and tolerability of valbenazine for the treatment of chorea associated with HD.

1. van Duijn E, et al. J Neurol Neurosurg Psychiatry. 2014 Dec;85(12):1411-8. 2. Paoli RA, et al. Brain Sci. 2017 Jun 16;7(6):67. 3. Nance M, et al. Huntington's Disease Society of America. 2011.4. Roos RAC. Orphanet Journal of Rare Diseases. 2010;5(40). 5. Neurocrine Biosciences. VBZ-HD-0006. Data on file. 6. Kachian ZR, et al. J Affect Disord. 2019 May 1;250:319-329.

Safety Results: KINECT-HD

In KINECT-HD, depression or depressed mood was collectively reported in 4.7% of patients taking valbenazine (VBZ), compared to 1.6% in placebo (PBO)[1]

- In patients taking VBZ, there were no reports of suicidal ideation or suicide attempts
- One patient (1.6%) on PBO reported suicidal ideation
- During the 12-week study, no participants reported an increase in suicidal ideation on the Columbia-Suicide Severity Rating Scale (C-SSRS)[2]

Adverse Events in KINECT-HD (Safety Analysis Set)

Depression and suicidality category[1,3],‡	**Placebo** (N=63) n (%)	**Valbenazine** (N=64) n (%)
Depression	1 (1.6)	2 (3.1)
Depressed mood	0	1 (1.6)
Adjustment disorder with depressed mood	0	0
Major depression	0	0
Suicidal ideation	1 (1.6)	0
Suicide attempt	0	0

‡By standardized MedDRA query of depression and suicide/self-injury.
Patients in KINECT-HD with significant risk for suicidal behavior or with unstable psychiatric symptoms were excluded from the study.

KINECT-HD is the 12-week, Phase 3, randomized, double-blind placebo-controlled study to evaluate the safety and efficacy of valbenazine for the treatment of chorea associated with Huntington's disease (HD).
The C-SSRS was administered and scored by the investigator at screening, baseline and Weeks 2, 4, 6, 8, 10, 12 (or early termination), and 14.
C-SSRS, Columbia-Suicide Severity Rating Scale; PBO, placebo; VBZ, valbenazine.

1. INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc. 2. Furr Stimming E, et al. Lancet Neurol. 2023;22(6):494-504. 3. Neurocrine Biosciences. VBZ-HD-0003. Data on file.

Safety Results: Interim Analysis of KINECT-HD2

In the interim analysis of KINECT-HD2[3]

- Depression, depressed mood, and major depression were collectively reported in 15.2% of patients on valbenazine[1]
- 9 patients (7.2%) reported suicidal ideation
- 3 patients (2.4%) reported suicide attempts

KINECT-HD2 is an ongoing study. Full results and analysis are expected in 2024.

Adverse Events in the Interim Analysis of KINECT-HD2† (Safety Analysis Set)

Depression and suicidality category [1,‡]	All Patients Valbenazine (N=125) n (%)
Depression	14 (11.2)
Depressed mood	3 (2.4)
Adjustment disorder with depressed mood	1 (0.8)
Major depression	1 (0.8)
Suicidal ideation	9 (7.2)
Suicide attempt	3 (2.4)

†Data included in this 120-day safety update reflects increased duration of exposure to VBZ from the ongoing long-term open-label KINECT-HD2 study. At the time of the 120-day safety update, a total of 142 patients had been exposed to VBZ at any dose for a median duration of 373 days. There were 111 patients (78.2%) with at least 6 months of VBZ exposure, and 81 patients (57.0%) with at least 12 months.
‡By standardized MedDRA query of depression and suicide/self-injury
Patients in KINECT-HD2 with significant risk for suicidal behavior or with unstable psychiatric symptoms were excluded from the study.

KINECT-HD2 is the Phase 3, open-label rollover study to evaluate the long-term safety and tolerability of valbenazine for the treatment of chorea associated with HD. The study duration was up to 156 weeks.

1. Neurocrine Biosciences. VBZ-HD-0008. Data on file. 2. Neurocrine Biosciences. VBZ-HD-0006. Data on file. 3. INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.

Depression & Suicidality Summary

Depression:

- Depression AEs occurred in 4.7% of patients on VBZ in KINECT-HD and 15.2% of patients in the interim analysis of KINECT-HD2
  - Most patients had a prior history of depression or related psychiatric conditions
- Most patients with depression AEs* continued valbenazine treatment without dose reduction or discontinuation
  - KINECT-HD: no dose changes (100%)
  - Interim analysis of KINECT-HD2: 13 (76.5%) no dose changes, 3 (17.6%) dose reduction, 1 (5.9%) discontinued treatment

Suicidality:

- In VBZ-treated patients in the 12-week KINECT-HD study, no AEs of suicidality were reported. In the interim analysis of KINECT-HD2, 9 patients (7.2%) reported suicidal ideation and 3 patients (2.4%) reported suicide attempts
- All AEs of suicidality in the interim analysis of KINECT-HD2 occurred in patients with a medical history of suicidality or other psychiatric conditions that are associated with a higher risk of suicidal thoughts or behaviors

Given the risk for suicidal ideation and suicide attempts among individuals with Huntington's disease, all patients taking a VMAT2 inhibitor or other medication for chorea should be monitored regularly for suicidal thoughts and behaviors

KINECT-HD2 is an ongoing study. Full results and analysis are expected in 2024.

*Includes adverse events of depression, depressed mood, and adjustment disorder with depressed mood. Percentages are based on the number of patients with an adverse event in the category. AE, adverse event; C-SSRS, Columbia-Suicide Severity Rating Scale; VBZ, valbenazine. Neurocrine Biosciences. VBZ-HD-0006. Data on file.

Hypersensitivity

Hypersensitivity in KINECT®-HD Studies

INGREZZA is contraindicated in patients with a history of hypersensitivity to valbenazine or any components of INGREZZA. Rash, urticaria, and reactions consistent with angioedema (e.g., swelling of the face, lips, and mouth) have been reported.[1]

Hypersensitivity reactions, including cases of angioedema involving the larynx, glottis, lips, and eyelids, have been reported in the post-marketing setting in patients after taking the first or subsequent doses of INGREZZA. A case of angioedema involving the lips and face, with rash and shortness of breath was reported in a patient with Huntington's disease taking INGREZZA during a clinical study.[1,*]

Angioedema associated with laryngeal edema can be fatal. If any of these reactions occur, discontinue INGREZZA.[1]

In KINECT-HD, AEs of urticaria, rash, angioedema, and pruritus occurred in the VBZ group and pruritus in the PBO group[2]

- One serious adverse event of angioedema in the VBZ group was considered unlikely related to study treatment (likely cause, shellfish allergy) and resolved within 1 day
- The patient continued treatment and completed the study on 80 mg

KINECT-HD Treatment Emergent Adverse Events

	Placebo (N=63) n (%)	Valbenazine (N=64) n (%)
Urticaria	0	6 (9.4)
Rash	0	5 (7.8)
Angioedema	0	1 (1.6)
Pruritus	1 (1.6)	1 (1.6)

*Case from the interim analysis of KINECT-HD2 and "possibly related" to study drug. Serious adverse event of angioedema that led to treatment discontinuation and withdrawal from the study. Symptoms: hives, swelling of the lips and face, mild shortness of breath and nausea. Significant improvement was seen after 1 day, resolution of the rash and itching after 4 days.[3] AE, adverse event; PBO, placebo; VBZ, valbenazine. 1. INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc. 2. Neurocrine Biosciences. VBZ-HD-0003. Data on file. 3. Neurocrine Biosciences. VBZ-HD-0005. Data on file.

Somnolence & Sedation

Somnolence and Sedation in KINECT®-HD

Somnolence is a known adverse event of valbenazine[1]

In KINECT-HD, the most common treatment emergent adverse event (TEAE) with valbenazine was somnolence[1,2]

All AEs similar to somnolence were[3]

- Mild or moderate
- Nonserious
- Generally managed with dose reductions with most patients (>90%) on VBZ staying on treatment[4]
  - 7 (10.9%) dose reduced
  - 1 (1.6%) discontinued study

KINECT-HD Treatment Emergent Adverse Events Related to Somnolence[2,3]

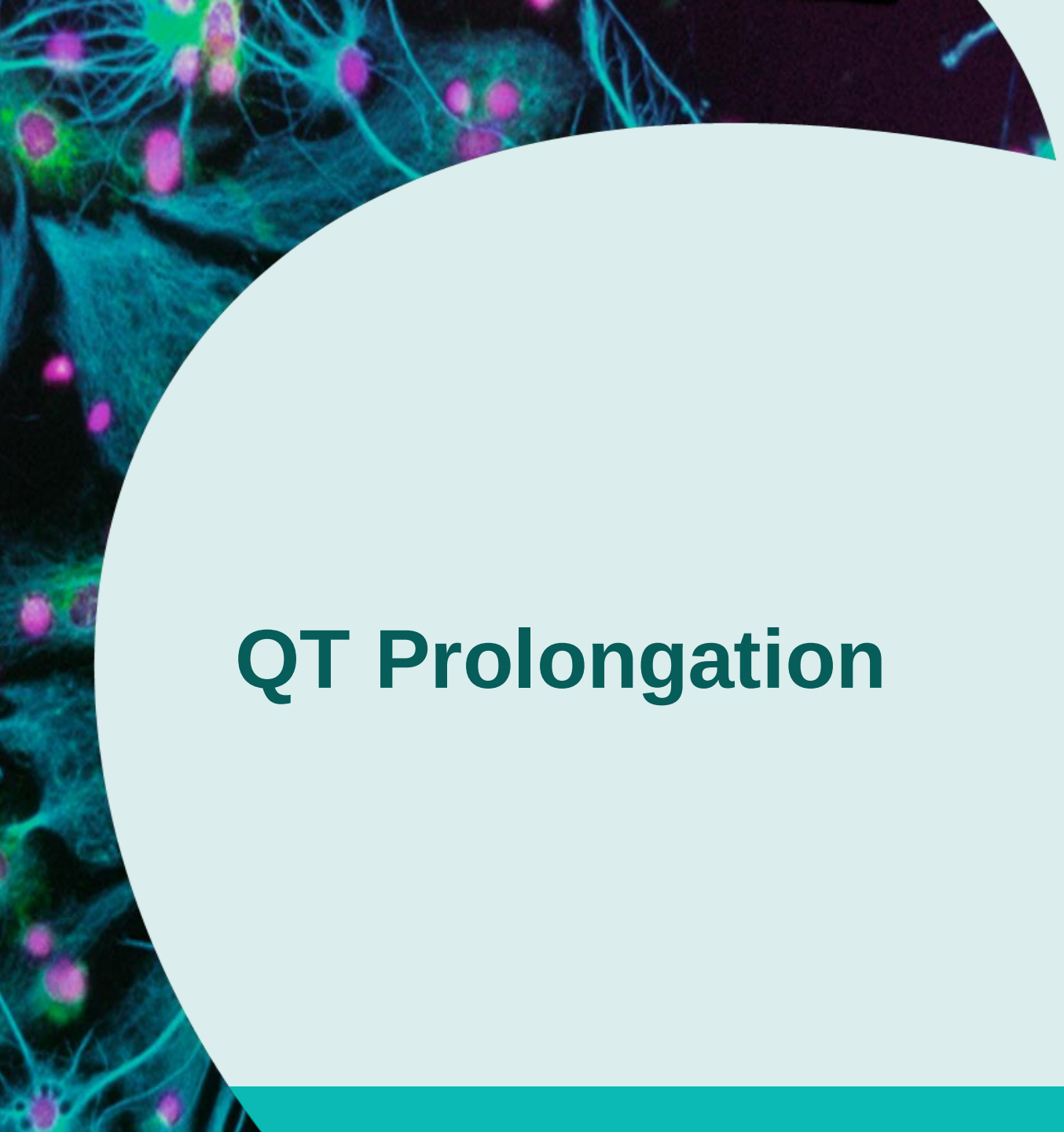
	Placebo (N=63) n (%)	Valbenazine (N=64) n (%)
Somnolence	2 (3.2%)	10 (15.6)
Fatigue	6 (9.5%)	9 (14.1%)
Lethargy	0	1 (1.6%)
Sedation	0	1 (1.6%)

Patients should not perform activities requiring mental alertness such as operating a motor vehicle or operating hazardous machinery until they know how they will be affected by valbenazine[1]

Prescribing Information

AE, adverse event; TEAE, treatment emergent adverse event; VBZ, valbenazine.

1. INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc. 2. Furr Stimming E, et al. Lancet Neurol. 2023;22(6):494-504. 3. Neurocrine Biosciences. VBZ-HD-0006. Data on file. . 3. Neurocrine Biosciences. VBZ-HD-0003. Data on file.



QT Prolongation

QT Prolongation in KINECT®-HD

In KINECT-HD, mean baseline ECG parameters including QTcF were similar between treatment groups[1]

Twelve patients had QTcF >450 msec[1]
- 7 patients (10.9%) in the VBZ
- 5 patients (8.2%) in the PBO

One patient in the VBZ group and none in the PBO group had QTcF >480 msec[1]

Mean QTcF change from baseline:[1]
- >30 msec: 4 patients in VBZ and 2 patients with PBO

Patients with a history or evidence of long QT syndrome or QTcF >450 msec (males) or >470 msec (females) were excluded from the study[2]

QTcF Maximum Observed and Change from Baseline Categories (Safety Analysis Set)[1,a]

	Placebo (N=63) n (%)	Valbenazine (N=64) n (%)
QTcF Interval		
>450 msec	5 (8.2)	7 (10.9)
>480 msec	0	1 (1.6)
>500 msec	0	0
QTcF Interval Change from Baseline		
>30 msec	2 (3.3)	4 (6.3)
>60 msec	0	0

Prescribing Information

[a]Includes each patient's highest reported postbaseline value, using the averages of the triplicate values. ECG, electrocardiogram; PBO, placebo; QTcF, corrected QT interval using Fridericia's formula; VBZ, valbenazine.

1. Neurocrine Biosciences. VBZ-HD-0006. Data on file. 2. Furr Stimming E, et al. Lancet Neurol. 2023;22(6):494-504.

Neuroleptic Malignant Syndrome (NMS)

NMS Background

Neuroleptic malignant syndrome (NMS) is a life-threatening syndrome associated with the use of dopamine-receptor antagonist medications or with rapid withdrawal of dopaminergic medications[1]

NMS is listed as a warning and potential adverse reaction for most neuroleptic medications and all VMAT2 inhibitors including valbenazine[2-4]

The incidence of NMS has been reported in 0.02% of patients who are treated with antipsychotics[1]

The pathophysiology of NMS is not completely understood, but sudden reduction in central dopaminergic activity due to a D2 receptor blockade or abrupt withdrawal of D2 receptor stimulation may account for the symptoms including:[1]


Fever


Muscle rigidity


Altered mental status


Diaphoresis


Irregular pulse/blood pressure & Tachycardia

VMAT2, vesicular monoamine transporter 2

1. Simon LS, et al. Neuroleptic Malignant Syndrome. [Updated 2023 Apr 24]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan 2. INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc. 3. AUSTEDO [package Insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc. 4. XENAZINE [package Insert]. Deerfield, IL: Lundbeck Pharmaceuticals, LLC.

NMS Results in KINECT®-HD Studies and Literature Reports

In both HD studies, KINECT-HD and the interim analysis of KINECT-HD2, and the double-blind, placebo-controlled study of TD (KINECT 3), patients with a history of NMS were excluded[1,2]

- NMS was not reported as an adverse event in the studies/interim data[4]
- NMS has been reported in post-marketing reports of patients taking VMAT2 inhibitors, including VBZ[3]

In 2020, a literature review was published describing 13 cases of possible NMS episodes in patients on VMAT2 inhibitors[5]

Tetrabenazine	Reserpine	Valbenazine
10 cases	2 cases	1 case

A separate case report in 2022 described a 58-year-old woman on valbenazine and fluphenazine who presented with possible atypical NMS[6]

If treatment with valbenazine is needed after recovery from NMS, patients should be monitored for signs of recurrence[3]

Prescribing Information

KINECT-HD, the 12-week, Phase 3, randomized, double-blind placebo-controlled study to evaluate the safety and efficacy of valbenazine for the treatment of chorea associated with Huntington's Disease (HD). KINECT-HD2, the Phase 3, open-label rollover study to evaluate the long-term safety and tolerability of valbenazine for the treatment of chorea associated with HD. NMS, neuroleptic malignant syndrome; VBZ, valbenazine; VMAT2, vesicular monoamine transporter

1. Furr Stimming E, et al. Lancet Neurol. 2023;22(6):494-504 2. Hauser RA, et al. Am J Psychiatry. 2017;174(5):476-484.3. INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc. 4. Neurocrine Biosciences. VBZ-HD-0006. Data on file. 5. Caroff SN. Clin Psychopharmacol Neurosci. 2020;18(2):322-326. 6. Vellanki KD, et al. J Clin Psychopharmacol. 2022;42(4):421-422.

Parkinsonism

Parkinsonism in KINECT®-HD

Parkinsonism (motor symptoms such as bradykinesia, rigidity, and postural instability) can manifest in early and later stages of HD and is often associated with falls and injuries[1]

In KINECT-HD, Parkinson-like adverse events occurred in 3 (4.7%) patients treated with valbenazine (2 patients tremor, 1 patient drooling) and 0% of placebo-treated patients[2,3]

Parkinsonism was evaluated in KINECT-HD using the Unified Huntington's Disease Rating Scale (UHDRS®) motor assessment items for parkinsonsim[4,*]

- No worsening in the mean parkinsonism score from baseline was noted in either treatment group up to 12 weeks in KINECT-HD

KINECT-HD UHDRS Parkinsonism[4]

Key Safety Measure	Placebo			Valbenazine		
	Baseline*	Week 12*	Change from baseline‡	Baseline*	Week 12*	Change from baseline‡
UHDRS parkinsonism	7.5 (3.7)	6.4 (3.9)	-1.0 (NA)	8.6 (4.4)	8.2 (4.5)	-0.3 (NA)

Data are n (%), mean (SEM), or mean change (95% CI). NA=not applicable, UHDRS=Unified Huntington's Disease Rating Scale. *Mean (SD) at study baseline (day –1) and week 12. ‡Mean changes are presented for UHDRS parkinsonism. A negative change from baseline indicates a favorable effect.

Reduce the dose or discontinue valbenazine treatment in patients who develop clinically significant parkinson-like signs or symptoms[2]

Prescribing Information

*Includes retropulsion pull test, finger taps, pronation/supination of hands, arm rigidity, and body bradykinesia

1.Reilmann R. Parkinsonism in Huntington's disease. Int Rev Neurobiol. 2019;149:299-306. 2. NGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc. 3. Neurocrine Biosciences. VBZ-HD-0006. Data on file. 4. Furr Stimming E, et al. Lancet Neurol. 2023;22(6):494-504.

Appendix

Valbenazine Full Prescribing Information: Depression and Suicidal Ideation and Behavior in Patients with Huntington's Disease

Patients with Huntington's disease are at increased risk for depression, and suicidal ideation or behaviors. VMAT2 inhibitors, including INGREZZA, can increase the risk for suicidal ideation and behaviors in patients with Huntington's disease.

In a 14-week, double-blind, placebo-controlled trial, depression or depressed mood was reported in 4.7% of patients taking INGREZZA compared to 1.6% of patients who received placebo, and no patients taking INGREZZA reported suicidal ideation or behavior compared to 1 patient (1.6%) who received placebo. Patients with significant risk for suicidal behavior or with unstable psychiatric symptoms were excluded from this trial. Suicidal ideation (9 subjects; 7.2%) and suicide attempts (3 subjects; 2.4%) were reported in the longer open-label extension trial (N = 125).

When considering the use of INGREZZA, the risk of suicidal ideation and behaviors must be balanced against the need for treatment of chorea. All patients treated with INGREZZA should be observed for new or worsening depression, suicidal ideation or behaviors. If any of these reactions occur and do not resolve, consider discontinuing treatment with INGREZZA.

INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.

Valbenazine Full Prescribing Information: Somnolence and Sedation

INGREZZA can cause somnolence and sedation, which was the most common adverse reaction in placebo-controlled trials.

Patients should not perform activities requiring mental alertness such as operating a motor vehicle or operating hazardous machinery until they know how they will be affected by INGREZZA.

INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.

Valbenazine Full Prescribing Information: QT Prolongation

INGREZZA may prolong the QT interval, although the degree of QT prolongation is not clinically significant at concentrations expected with recommended dosing.

In patients taking a strong CYP2D6 or CYP3A4 inhibitor, or who are CYP2D6 poor metabolizers, INGREZZA concentrations may be higher and QT prolongation clinically significant.

For patients who are CYP2D6 poor metabolizers or are taking a strong CYP2D6 inhibitor, dose reduction may be necessary.

For patients taking a strong CYP3A4 inhibitor, reduce the dose of INGREZZA to 40 mg once daily .

INGREZZA should be avoided in patients with congenital long QT syndrome or with arrhythmias associated with a prolonged QT interval. For patients at increased risk of a prolonged QT interval, assess the QT interval before increasing the dosage.

INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.

Valbenazine Full Prescribing Information: NMS

A potentially fatal symptom complex referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with drugs that reduce dopaminergic transmission. In the post-marketing setting, NMS has been reported in patients taking VMAT2 inhibitors, including INGREZZA. Clinicians should be alerted to the signs and symptoms associated with NMS. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatine phosphokinase, myoglobinuria, rhabdomyolysis, and acute renal failure. The diagnosis of NMS can be complicated; other serious medical illness (e.g., pneumonia, systemic infection) and untreated or inadequately treated extrapyramidal disorders can present with similar signs and symptoms. Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever, and primary central nervous system pathology.

The management of NMS should include (1) immediate discontinuation of INGREZZA; (2) intensive symptomatic treatment and medical monitoring; and (3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for NMS.

Recurrence of NMS has been reported with resumption of drug therapy. If treatment with INGREZZA is needed after recovery from NMS, patients should be monitored for signs of recurrence.

INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.

Valbenazine Full Prescribing Information: Parkinsonism

INGREZZA may cause parkinsonism. Parkinsonism has also been observed with other VMAT2 inhibitors. In the 3 placebo-controlled clinical studies in patients with tardive dyskinesia, the incidence of parkinson-like adverse events was 3% of patients treated with INGREZZA and <1% of placebo-treated patients.

In a placebo-controlled clinical study in patients with chorea associated with Huntington's disease, the incidence of parkinson-like adverse events was 4.7% in patients treated with INGREZZA and 0% in placebo-treated patients. Because rigidity can develop as part of the underlying disease process in Huntington's disease, it may be difficult to distinguish between potential drug-induced parkinsonism and progression of underlying Huntington's disease. Drug-induced parkinsonism has the potential to cause more functional disability than untreated chorea for some patients with Huntington's disease.

Postmarketing safety reports have described parkinson-like symptoms in patients taking INGREZZA for tardive dyskinesia, some of which were severe and required hospitalization. In most cases, severe parkinsonism occurred within the first two weeks after starting or increasing the dose of INGREZZA. Associated symptoms have included falls, gait disturbances, tremor, drooling and hypokinesia. In cases in which follow-up clinical information was available, parkinson-like symptoms were reported to resolve following discontinuation of INGREZZA therapy.

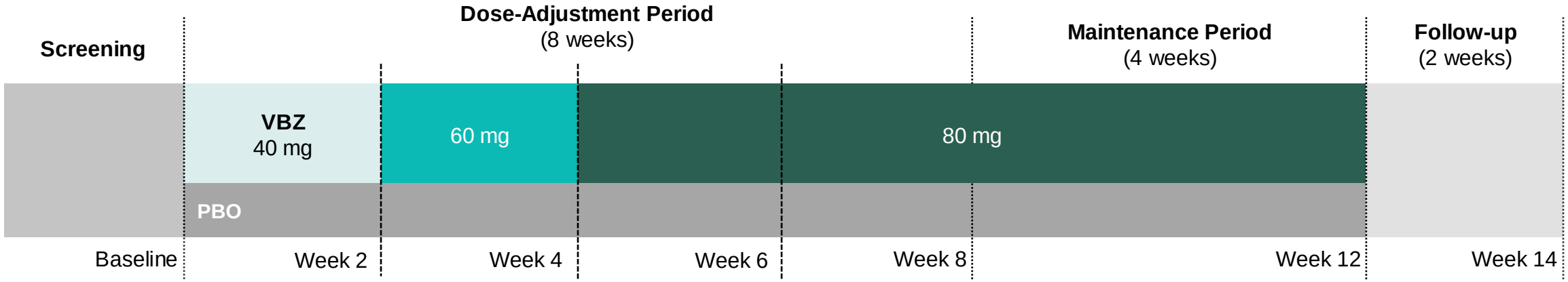
Reduce the dose or discontinue INGREZZA treatment in patients who develop clinically significant parkinson-like signs or symptoms.

INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.

Backup

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 HD



- **4-week** screening period
- **12-week** treatment period
- Final study visit after a 2-week washout

In the dose adjustment period, VBZ dosing started at **40 mg once daily**, with 20-mg increases allowed as tolerated at the end of Weeks 2, 4, and 6 to a target dose of **80 mg once daily**; dose reductions were allowed

- **128 adult male and females**
- Randomized 1:1
- United States/Canada

ClinicalTrials.gov Identifier: NCT04102579

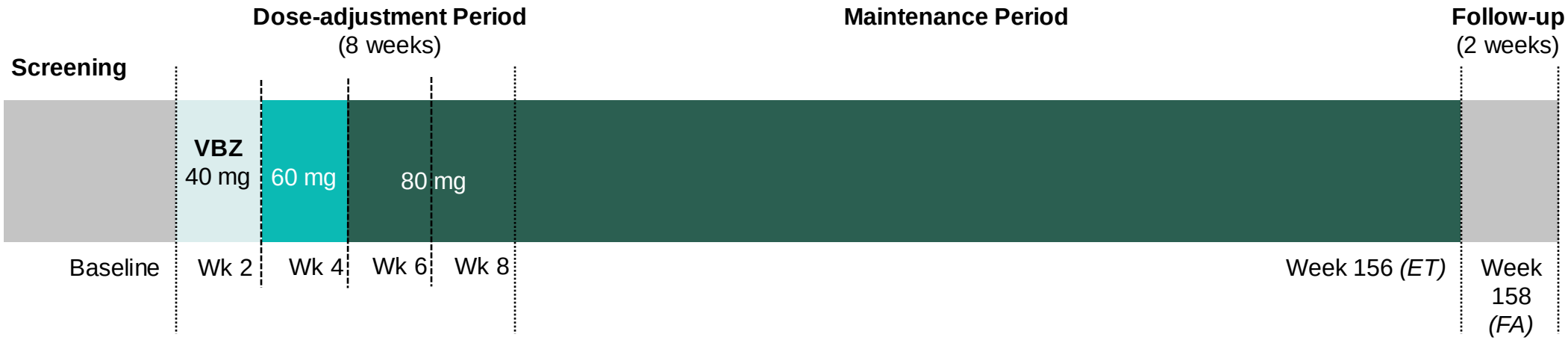
FDA, US Food and Drug Administration; HD, Huntington's disease; PBO, placebo; UHDRS, Unified Huntington's Disease Rating Scale; TMC, total maximal chorea; VBZ, valbenazine.

1. Furr Stimming E, et al. *Lancet Neurol*. 2023;22(6):494-504. 2. Clinicaltrials.gov. Accessed October 16, 2023. https://clinicaltrials.gov/study/NCT04102579.

KINECT®-HD2 Study Design

Phase 3, open-label study to evaluate the long-term safety and tolerability of valbenazine for the treatment of chorea associated with HD[1,2]

- Concomitant use of antipsychotic therapy (at a stable dose for 30 days before baseline) is permitted at study entry



Primary assessment: Emergence of TEAEs

Approximately **150 adult males and females** will be enrolled

ET, end of treatment; FA, final assessment; HD, FDA, US Food and Drug Administration; HD, Huntington's disease; TEAE, treatment-emergent adverse event; VBZ, Valbenazine; Wk, week.

1. ClinicalTrials.gov Identifier: NCT04400331. 2. Neurocrine Biosciences. VBZ-HD-0001. Data on file.