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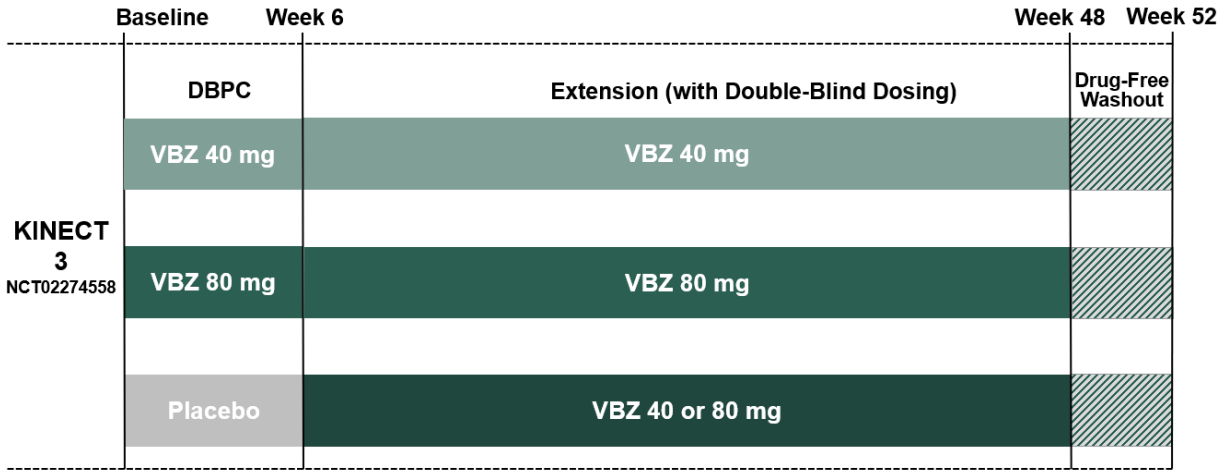
Long-Term Outcomes in Participants with Tardive Dyskinesia Who Achieved Early Improvement with INGREZZA® (valbenazine) Capsules and INGREZZA® SPRINKLE (valbenazine) Capsules

Thank you for contacting Neurocrine Biosciences with your unsolicited Medical Information request regarding long-term outcomes of adult participants with tardive dyskinesia (TD) who achieved early improvement with INGREZZA and INGREZZA SPRINKLE.

INGREZZA and INGREZZA SPRINKLE are vesicular monoamine transporter 2 (VMAT2) inhibitors indicated for the treatment of adults with tardive dyskinesia.[1]

KINECT® 3, a randomized, double-blind, placebo-controlled (DBPC) Phase 3 study, was designed to assess the efficacy, safety, and tolerability of valbenazine 40 mg and 80 mg in the treatment of adults with TD. Participants who completed the DBPC period continued with a 42-week double-blind valbenazine extension (VE) period (Week 48) and a 4-week drug-free follow-up period (Week 52) (**Figure 1**).[2]

Figure 1. KINECT 3 Study Design[2]



Participants who were randomized or re-randomized to valbenazine 80 mg were initiated at 40 mg for 1 week; DBPC, double-blind, placebo-controlled; VBZ, valbenazine

Data from the KINECT 3 study were analyzed post hoc to assess the long-term outcomes (as measured by the Abnormal Involuntary Movement Scale, AIMS) of once-daily valbenazine in adult participants with TD who achieved early improvement, based on self-report (Patient Global Impression of Change, PGIC) or clinician judgment (Clinical Global Impression of Change-Tardive Dyskinesia, CGI-TD). Early improvement was defined as those who had a PGIC or CGI-TD score of 1 (“very much improved”), 2 (“much improved”), or 3 (“minimally improved”) at their first post-baseline visit (Week 2) of the DBPC period. Data were analyzed from participants who were initially randomized to valbneazine (40 or 80 mg) and continued receiving valbenazine during the extension phase. Participants who were originally randomized to placebo were not included in this analysis. Long-term outcomes were assessed by a mean change from baseline in the AIMS total score (sum of items 1-7) and an AIMS response (≥50% total score improvement from baseline) at Week 48, based on scoring by blinded central video raters.[3]

Among participants who received valbenazine (40 or 80 mg) during the KINECT 3 study, 72/143 (50%) achieved early PGIC improvement (score ≤3 at Week 2), and 61/142 (43%) achieved early CGI-TD improvement (score ≤3 at Week 2). Baseline demographics and disease characteristics were generally similar between participants who achieved early PGIC or CGI-TD improvement and those who did not.[3]

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After 48 weeks of treatment with valbenazine, mean AIMS total score changes from baseline in participants with early PGIC and CGI-TD improvement were similar to those who did not reach the early improvement thresholds (**Table 1**). Further, AIMS response (≥50% total score improvement from baseline) at Week 48 were similar in those who achieved early PGIC improvement (all valbenazine [n=14/35], 40%) or CGI-TD improvement (all valbenazine [n=13/31], 42%) compared to those who did not achieve early PGIC improvement (all valbenazine [n=16/41], 39%) or CGI-TD improvement (all valbenazine [n=17/45], 38%).[3]

Table 1. AIMS Total Score Mean Change from Baseline to Week 48[3]

Global Improvement at Week 2	Valbenazine 40 mg		Valbenazine 80 mg[a]		All Valbenazine[b]	
	n	Mean Change (SE)	n	Mean Change (SE)	n	Mean Change (SE)
PGIC ≤3	15	-3.7 (1.1)	19	-4.5 (1.1)	35	-4.1 (0.8)
PGIC ≥4	19	-2.5 (1.0)	19	-4.5 (1.0)	41	-3.5 (0.7)
CGI-TD ≤3	13	-4.3 (1.2)	16	-4.3 (1.3)	31	-4.2 (0.8)
CGI-TD ≥4	21	-2.2 (0.9)	22	-4.6 (0.9)	45	-3.5 (0.6)

[a]Includes participants who remained at 80 mg with no dose reductions; [b]Includes participants who had a dose reduction from 80 mg to 40 mg after Week 4; PGIC ≤3: "Minimally improved" or better (patient-reported); PGIC ≥4: "No change" or worse (patient-reported); CGI-TD ≤3: "Minimally improved" or better (clinician-reported); CGI-TD ≥4: "No change" or worse (clinician-reported); AIMS, Abnormal Involuntary Movement Scale; CGI-TD, Clinical Global Impression of Change-Tardive Dyskinesia; PGIC, Patient Global Impression of Change; SE, standard error.

In the KINECT 3 study, the safety analysis included 227 participants from the three treatment groups, 76 from placebo, 72 from valbenazine 40mg, and 79 from valbenazine 80mg. The most commonly reported adverse events (≥3% of participants in either valbenazine group at an incidence greater than placebo) for the valbenazine 40 mg, 80 mg, and placebo groups, respectively, were dry mouth (1.3% vs. 6.9% vs. 0%), somnolence (3.9% vs. 5.6% vs. 5.1%), akathisia (1.3% vs. 4.2% vs. 2.5%), urinary tract infection (3.9% vs. 4.2% vs. 0%), arthralgia (1.3% vs. 1.4% vs. 3.8%), vomiting (0% vs. 0% vs. 3.8%), and dyskinesia (0% vs. 0% vs. 3.8%). There were no treatment-related serious adverse events and no safety signals observed from clinical hematology, chemistry, or ECG readings.[2]

This letter and the enclosed material are provided in response to your unsolicited medical information inquiry. Please feel free to contact Neurocrine Medical Information at (877) 641-3461 or medinfo@neurocrine.com if you would like to request additional information.

References:

1. INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.
2. Hauser RA, et al. KINECT 3: a phase 3 randomized, double-blind, placebo-controlled trial of valbenazine for tardive dyskinesia. American Journal of Psychiatry. 2017; 174:5,476-484.
3. Factor SA, et al. Long-term outcomes in patients with tardive dyskinesia who were early responders with valbenazine. Poster presented at the International Congress of Parkinson's Disease and Movement Disorders; September 22-26, 2019; Nice, France.

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Enclosure:

A. INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.
B. INGREZZA [Important Safety Information]. San Diego, CA: Neurocrine Biosciences, Inc.
C. Factor SA, et al. Long-term outcomes in patients with tardive dyskinesia who were early responders with valbenazine. Poster presented at the International Congress of Parkinson's Disease and Movement Disorders; September 22-26, 2019; Nice, France.