Data supplement for Hauser et al., KINECT 3: A Phase 3 Randomized, Double-Blind, Placebo-Controlled Trial of Valbenazine for Tardive Dyskinesia. Am J Psychiatry (doi: 10.1176/appi.ajp.2017.16091037)

Supplementary Methods

Blinding

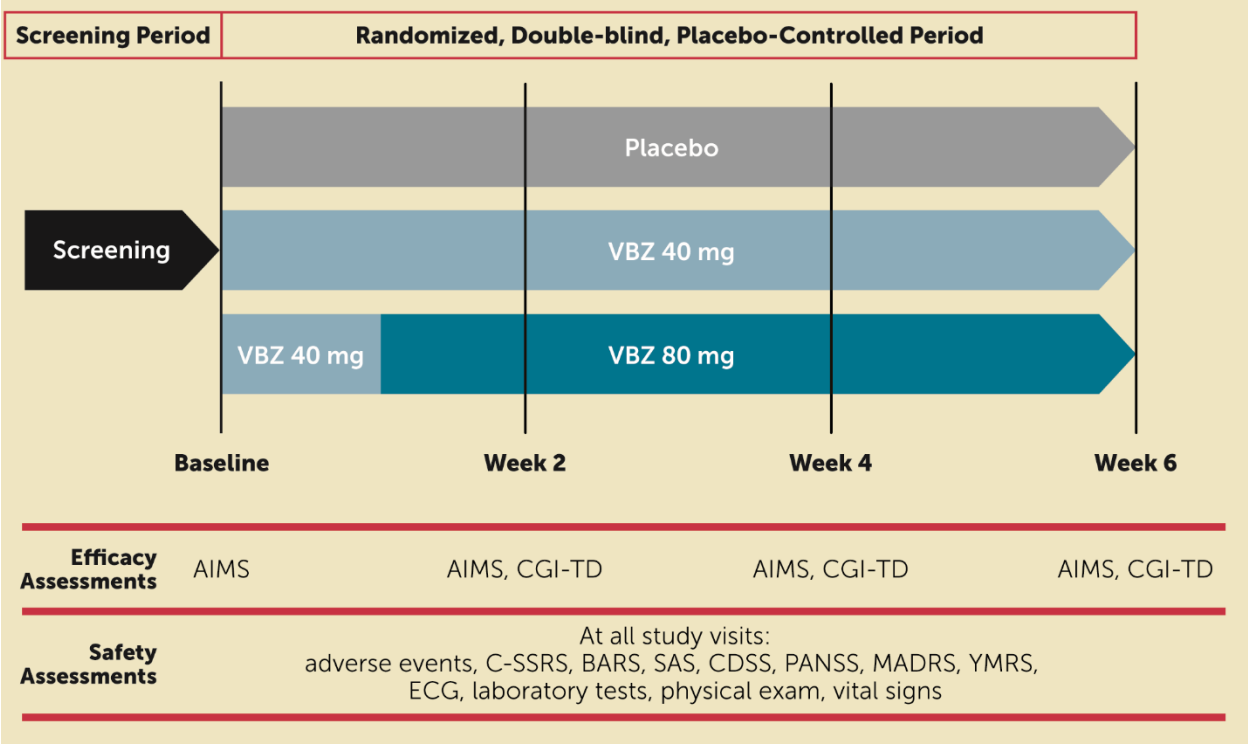
Valbenazine and placebo were identical in appearance and packaging, and subjects were instructed to take the study medication every morning. Placebo was administered as 2 capsules; subjects randomized to valbenazine 40 mg/day received a 40-mg capsule plus matching placebo capsule. Subjects randomized to valbenazine 80 mg/day received 40 mg/day during Week 1 (plus 1 matching placebo capsule) and then 80 mg/day (two 40-mg capsules) at the start of Week 2.

Estimation of sample size

In the prior KINECT 2 study, the least squares mean difference between treatment groups was 2.4 for the AIMS score change from baseline, with a standard deviation of 4.0 (1). Based on this result, along with an assumed discontinuation rate of 12%, it was estimated that 80 subjects would be needed per treatment group in the current study to detect statistically significant differences between valbenazine and placebo at 0.95 power using a standard two-sample t-test with two-sided Type I error of 0.05.

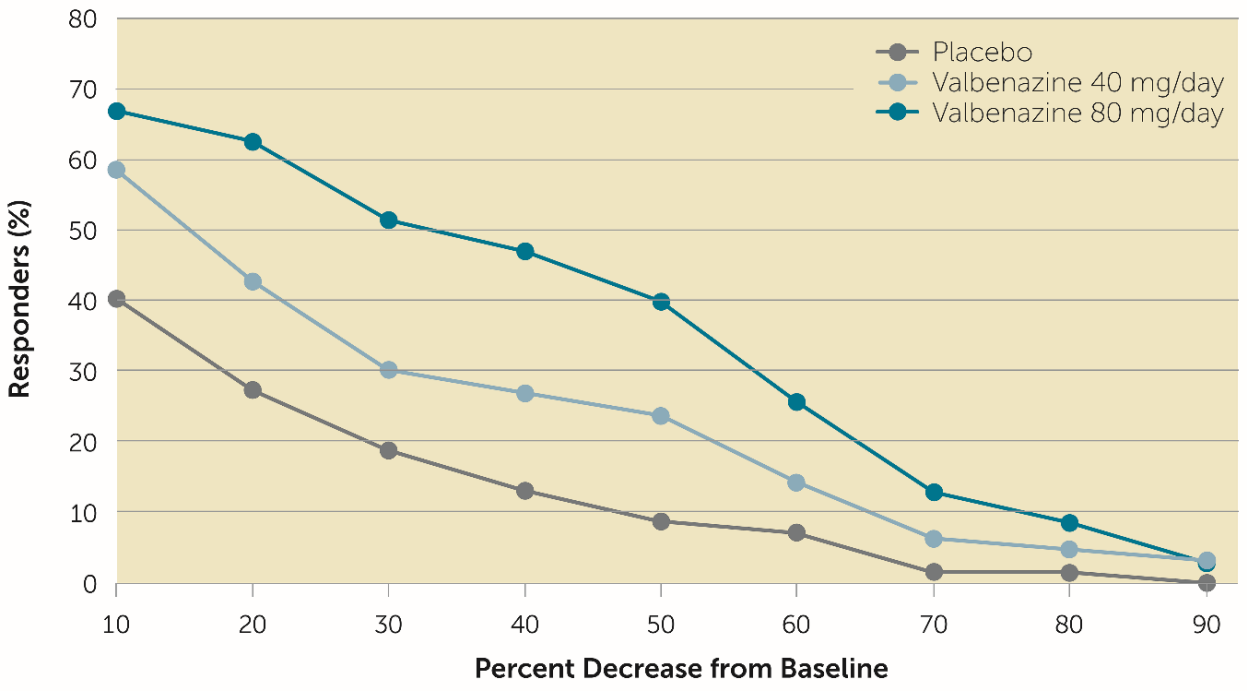
1. O'Brien CF, Jimenez R, Hauser RA, Factor SA, Burke J, Mandri D, Castro-Gayol JC: NBI-98854, a selective monoamine transport inhibitor for the treatment of tardive dyskinesia: a randomized, double-blind, placebo-controlled study. Mov Disord 2015; 30:1681-1687.

FIGURE S1. Study Design and Schedule of Assessments



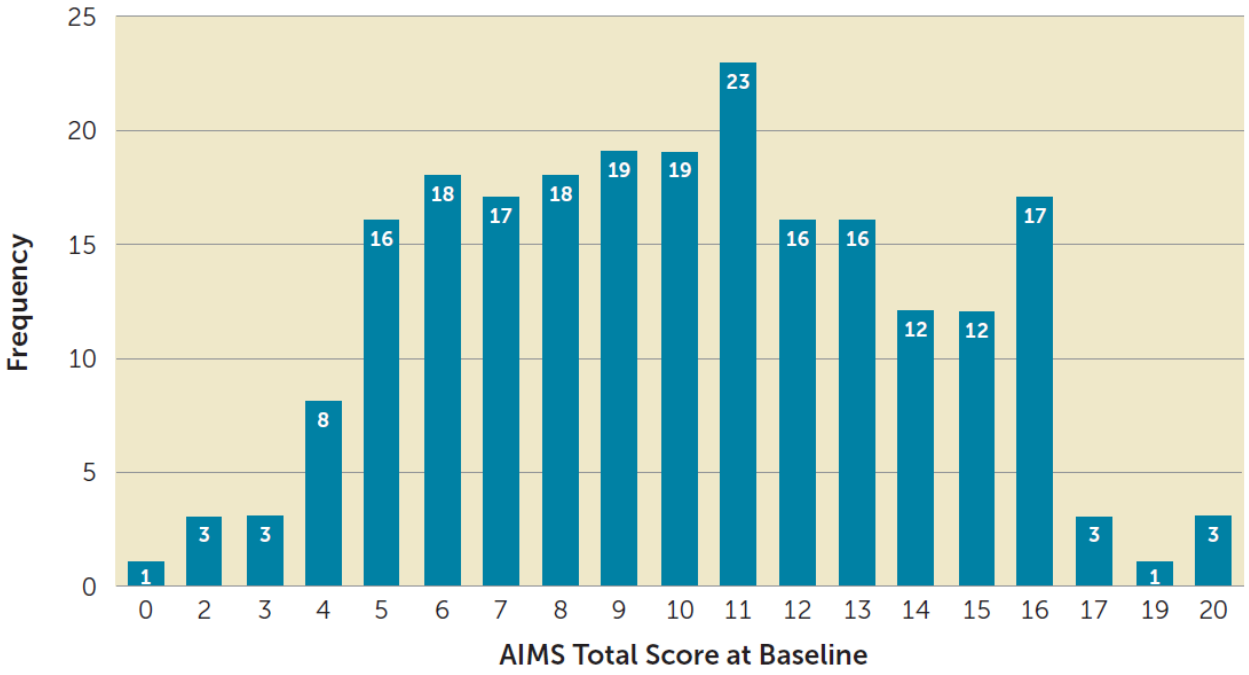
AIMS, Abnormal Involuntary Movement Scale; BARS, Barnes Akathisia Rating Scale; CDSS, Calgary Depression Scale for Schizophrenia; CGI-TD, Clinical Global Impression of Change-Tardive Dyskinesia; C-SSRS, Columbia-Suicide Severity Rating Scale; ECG, electrocardiogram; MADRS, Montgomery-Åsberg Depression Rating Scale; PANSS, Positive and Negative Syndrome Scale; SAS, Simpson-Angus Scale; VBZ, valbenazine; YMRS, Young Mania Rating Scale.

FIGURE S2. Percent Improvement from Baseline in AIMS Total Score



Cumulative proportion of subjects who experienced AIMS improvements (range, 10% to 90% decrease in total score from baseline at Week 6), analyzed descriptively by treatment group.

FIGURE S3. Distribution of AIMS Total Scores at Baseline



AIMS total scores were based on consensus rating of two blinded central video raters. The total score represents the sum of scores from 7 individual AIMS items, with possible ratings ranging from 0 (none) to 4 (severe). The AIMS total score is not a linear scale, and each total score can represent a range of clinical presentations. For example, an AIMS total score=4 may represent a subject who had a score=1 (minimal) on 4 different AIMS items or a score=4 (severe) on just 1 item.

AIMS, Abnormal Involuntary Movement Scale.

TABLE S1. Study Endpoints

Endpoint Classification	Efficacy Endpoint
Primary	AIMS total score mean change from baseline at Week 6
Key Secondary	CGI-TD mean score at Week 6
Secondary	Percentage of subjects classified as AIMS responders at Week 6
	Percentage of subjects classified as CGI-TD responders at Week 6
	PGIC mean score at Week 6
	Percentage of subjects classified as PGIC responders at Week 6
	TDIS total score mean change from baseline at Week 6
Exploratory	AIMS total score mean change from baseline at Weeks 2 and 4
	CGI-TD mean score at Weeks 2 and 4
	Percentage of subjects classified as AIMS responders at Weeks 2 and 4
	Percentage of subjects classified as CGI-TD responders at Weeks 2 and 4
	PGIC mean score at Weeks 2 and 4
	Percentage of subjects classified as PGIC responders at Weeks 2 and 4
	TDIS total score mean change from baseline at Weeks 2 and 4

AIMS, Abnormal Involuntary Movement Scale; CGI-TD, Clinical Global Impression of Change-Tardive Dyskinesia; PGIC, Patient Global Impression of Change; TDIS, Tardive Dyskinesia Impact Scale.

TABLE S2. Psychiatric Status Rating Scale Scores (Safety Population)

	At Baseline						At Week 6					
	Placebo		Valbenazine 40 mg/day		Valbenazine 80 mg/day		Placebo		Valbenazine 40 mg/day		Valbenazine 80 mg/day	
Psychiatric scale	**n**	**Mean Score (SD)**	**n**	**Mean Score (SD)**	**n**	**Mean Score (SD)**	**n**	**Mean Score (SD)**	**n**	**Mean Score (SD)**	**n**	**Mean Score (SD)**
PANSS Negative Symptoms	50	15.4 (4.5)	48	14.9 (4.7)	52	14.3 (3.9)	43	15.0 (4.7)	42	15.1 (4.6)	44	15.2 (4.8)
PANSS Positive Symptoms	50	12.9 (3.3)	48	12.8 (3.7)	52	13.0 (4.2)	43	12.7 (4.1)	42	12.0 (3.6)	44	12.8 (4.0)
PANSS General Psychopathology	50	27.5 (5.3)	48	27.2 (6.5)	52	26.8 (5.5)	43	26.6 (6.3)	42	25.9 (5.5)	44	26.2 (6.0)
Calgary Depression Scale for Schizophrenia	50	2.0 (2.2)	48	2.0 (2.1)	52	1.9 (2.2)	43	1.9 (2.4)	42	1.4 (2.4)	44	1.6 (2.1)
Montgomery-Åsberg Depression Rating Scale	26	5.2 (2.9)	24	7.1 (3.8)	27	5.4 (4.0)	26	6.5 (6.4)	21	6.9 (4.7)	26	3.9 (4.1)
Young Mania Rating Scale	26	1.8 (2.3)	24	3.0 (3.0)	27	3.3 (3.2)	26	2.3 (3.3)	21	2.6 (2.6)	26	2.0 (2.2)

PANSS, Positive and Negative Syndrome Scale; SD, standard deviation.