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Supplementary Material

Article Title: Effects of Valbenazine in Participants With Tardive Dyskinesia: Results of the 1-Year KINECT 3 Extension Study

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List of Supplementary Material for the article

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SUPPLEMENTARY MATERIAL

eAppendix 1. Study Discontinuations Due to Suicidal Ideation, Behavior, or Attempt

Three participants were discontinued from the KINECT 3 extension study due to an adverse event of suicidal ideation: a 62-year-old white woman (80 mg/day) with history of depression with psychotic features, suicidal ideation, and suicidal behavior; a 58-year-old black or African-American man (40 mg/day) with schizophrenia/schizoaffective disorder and comorbid anxiety and depression; and a 61-year-old black or African-American woman (40 mg/day) with a mood disorder and history of suicidal ideation. Two participants were discontinued due to suicidal behavior or aborted suicide attempt: a 36-year-old white man (80 mg/day) with schizophrenia/schizoaffective disorder who overdosed on clonazepam in an attempt to control sexual desires; and a 55-year-old black or African-American woman (80 mg/day) with schizophrenia/schizoaffective disorder and history of intentional overdose who unsuccessfully looked for a bridge to jump from after experiencing visual and auditory hallucinations. All cases were judged by the site investigator as unlikely related or unrelated to valbenazine.

Supplementary eTable 1. C-SSRS Suicidal Ideation Score Shifts from Baseline

Valbenazine Dose Group	Baseline Score[a]	N	Maximum Suicidal Ideation Score[b] During Valbenazine Extension and Washout Periods, n (%)[c]					
			0	1	2	3	4	5
40 mg/day	0	93	87 (93.5)	3 (3.2)	3 (3.2)	0	0	0
	1	2	1 (50.0)	1 (50.0)	0	0	0	0
80 mg/day	0	99	92 (92.9)	2 (2.0)	1 (1.0)	2 (2.0)	1 (1.0)	1 (1.0)
	1	1	1 (100.0)	0	0	0	0	0

[a] No participant had a C-SSRS score of 2 or higher at baseline.

[b] The maximum score on the suicidal ideation scale (0=no suicidal ideation, 1=wish to be dead, 2=nonspecific active suicidal thoughts, 4=active suicidal ideation with some intent to act but without specific plan, 5=active suicidal ideation with specific plan and intent) is reported for each participant with an available assessment.

[c] From post-Week 6 to Week 52. Percentages are calculated as n/N x 100, with N representing the number of participants with a C-SSRS score of 0 or 1 at baseline.

Abbreviation: C-SSRS, Columbia-Suicide Severity Rating Scale.

Supplementary eTable 2. Psychiatric and Movement Scale Mean Scores at Baseline, After Long-Term Treatment (Week 48), and After Treatment Withdrawal (Week 52)

	Baseline				Week 48				Week 52			
	Valbenazine 40 mg/day		Valbenazine 80 mg/day		Valbenazine 40 mg/day		Valbenazine 80 mg/day		Valbenazine 40 mg/day		Valbenazine 80 mg/day	
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)
Psychiatric scales												
PANSS positive symptoms	61	12.6 (3.3)	62	12.9 (3.9)	43	12.2 (4.5)	38	11.7 (3.9)	41	13.0 (5.4)	37	12.3 (4.2)
PANSS negative symptoms	61	15.1 (4.6)	62	14.5 (4.1)	43	15.5 (5.3)	38	13.6 (4.1)	41	14.6 (4.6)	37	13.7 (3.8)
PANSS general psychopathology	61	27.4 (6.0)	62	26.7 (5.6)	43	26.2 (7.8)	38	23.9 (5.2)	41	26.1 (8.1)	37	25.6 (6.0)
CDSS total	61	2.2 (2.2)	62	1.8 (2.1)	43	1.6 (2.7)	38	1.8 (2.8)	42	1.0 (1.8)	37	2.6 (3.5)
YMRS total	33	2.5 (2.7)	36	3.0 (3.1)	18	1.3 (1.4)	25	1.6 (1.9)	18	2.0 (3.3)	24	1.4 (1.8)
MADRS total	33	5.7 (3.4)	36	5.5 (3.9)	18	4.4 (5.1)	25	5.7 (6.5)	18	6.2 (6.5)	24	5.5 (7.6)
Movement scales												
BARS total	94	1.3 (1.8)	98	1.2 (1.8)	61	0.6 (1.4)	63	0.6 (1.2)	60	0.8 (1.4)	61	0.9 (1.7)
SAS global	94	0.2 (0.3)	98	0.3 (0.4)	61	0.1 (0.2)	63	0.2 (0.3)	60	0.2 (0.2)	61	0.2 (0.2)

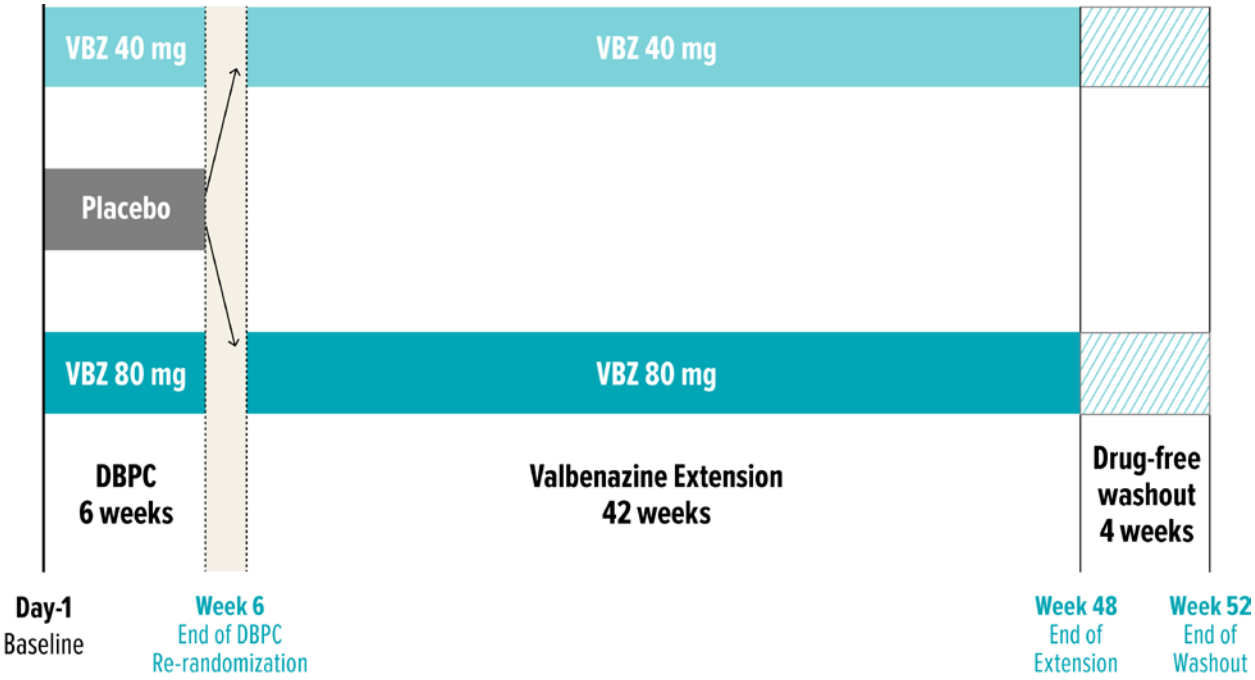
Abbreviations: BARS, Barnes Akathisia Rating Scale; CDSS, Calgary Depression Scale for Schizophrenia; MADRS, Montgomery-Åsberg Depression Rating Scale; PANSS, Positive and Negative Syndrome Scale; SAS, Simpson-Angus Scale; SD, standard deviation; YMRS, Young Mania Rating Scale.

Supplementary eTable 3. Worsening in Tardive Dyskinesia After Long-Term Treatment (Week 48) and Treatment Withdrawal (Week 52)

	Week 48		Week 52	
	Valbenazine 40 mg/day	Valbenazine 80 mg/day	Valbenazine 40 mg/day	Valbenazine 80 mg/day
	n/N (%)	n/N (%)	n/N (%)	n/N (%)
AIMS, ≥50% increase from baseline in total score	4/60 (6.7)	3/63 (4.8)	9/60 (15.0)	7/61 (11.5)
CGI-TD, score ≥6	0/61 (0.0)	1/63 (1.6)	2/60 (3.3)	7/61 (11.5)
PGIC, score ≥6	0/61 (0.0)	0/63 (0.0)	3/59 (5.1)	10/59 (16.9)

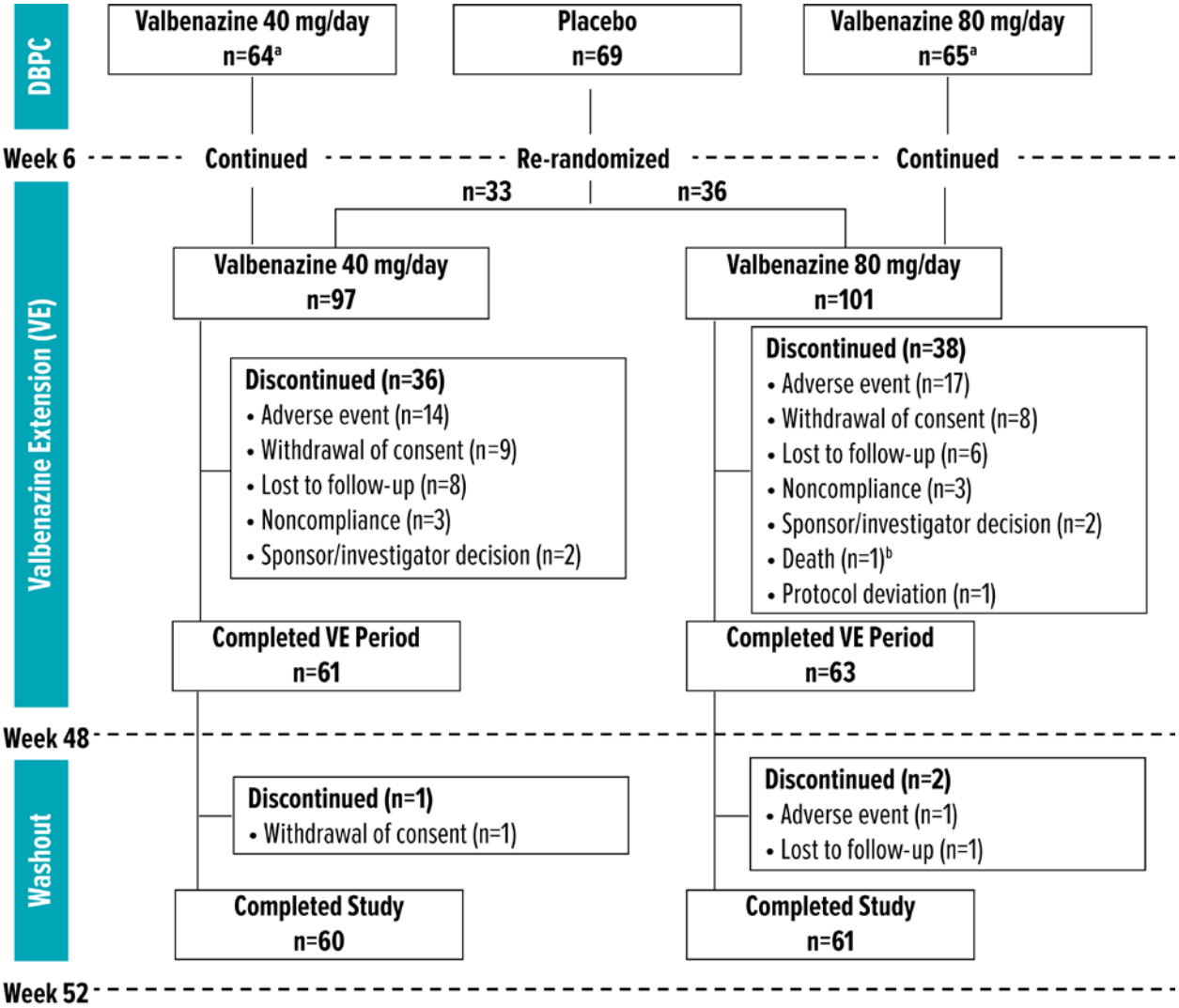
Abbreviations: AIMS, Abnormal Involuntary Movement Scale; CGI-TD, Clinical Global Impression of Change-Tardive Dyskinesia; PGIC, Patient Global Impression of Change.

Supplementary eFigure 1. Study Design



Abbreviations: DBPC, double-blind placebo-controlled; VBZ, valbenazine.

Supplementary eFigure 2. Study Disposition



[a] Three participants initially randomized to valbenazine 80 mg/day had a dose reduction during the 6-week placebo-controlled period and are therefore included in the 40 mg/day group for the valbenazine extension period.

[b] Attributed to multiple organ failure; judged by Investigator as unrelated to study drug.

Abbreviations: DBPC, double-blind placebo-controlled; VE, valbenazine extension.