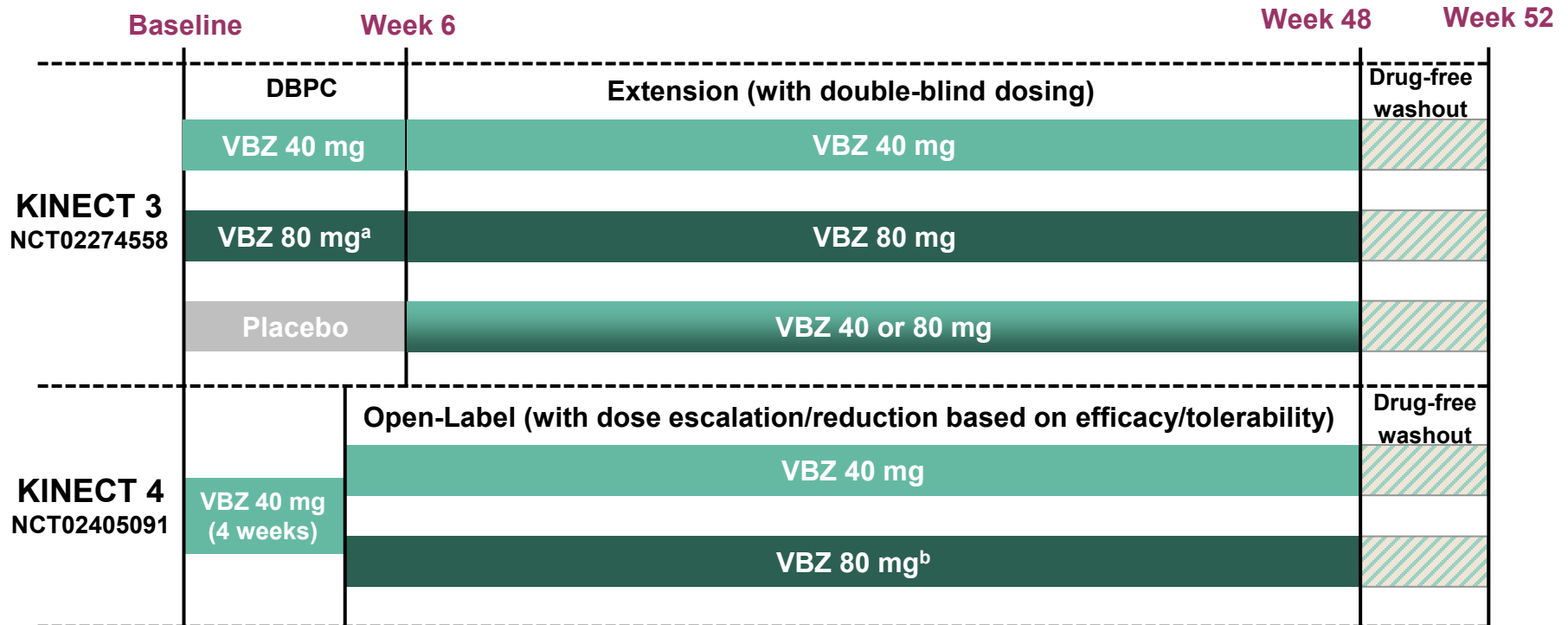


# KINECT 3 & 4 – Mood Disorder Analysis



# KINECT 3 & 4: Study Design



<sup>a</sup>Participants who were randomized to 80 mg were initiated at 40 mg for 1 week.  
<sup>b</sup>Includes participants who had a dose reduction to 40 mg due to tolerability issues.  
 DBPC, double-blind placebo-controlled; VBZ, valbenazine.  
 McIntyre RS, et al. US Psych Congress 2018; Orlando, FL.

# KINECT 3 & 4 – Mood Disorder Analysis: Baseline Characteristics

	Valbenazine 40 mg n=32	Valbenazine 80 mg n=63	All Participants n=95
<b>Age, mean (SD), years</b>	54.9 (9.7)	57.3 (9.6)	56.5 (9.6)
<b>Women, n (%)</b>	20 (62.5)	42 (66.7)	62 (65.3)
<b>White, n (%)</b>	24 (75.0)	48 (76.2)	72 (75.8)
<b>Body mass index, mean (SD), kg/m<sup>2</sup></b>	28.3 (5.6)	29.0 (5.5)	28.8 (5.5)
<b>Mood diagnosis, n (%)</b>			
Bipolar disorder	19 (59.4)	40 (63.5)	59 (62.1)
Depression/major depression	12 (37.5)	20 (31.7)	32 (33.7)
Other	1 (3.1)	3 (4.8)	4 (4.2)
<b>Concomitant medications, n (%)</b>			
Antidepressants	27 (84.4)	53 (84.1)	80 (84.2)
Antipsychotics	28 (87.5)	45 (71.4)	73 (76.8)
Antiepileptics	9 (28.1)	36 (57.1)	45 (47.4)
Anxiolytics	18 (56.3)	19 (30.2)	37 (38.9)
Anticholinergics	6 (18.8)	15 (23.8)	21 (22.1)
<b>Age at TD diagnosis, mean (SD), years</b>	49.8 (10.4)	51.0 (11.9)	50.6 (11.4)
<b>Age at mood disorder diagnosis, mean (SD), years</b>	34.3 (15.3)	35.5 (13.3)	35.1 (13.9)
<b>BPRS total score at screening, mean (SD)</b>	26.5 (5.8)	27.0 (6.0)	26.8 (5.9)
<b>MADRS total score, mean (SD)</b>	6.8 (3.6)	5.4 (3.9)	5.9 (3.9)
<b>YMRS total score, mean (SD)</b>	2.9 (2.7)	2.6 (2.7)	2.7 (2.7)
<b>AIMS total score, mean (SD)</b>	11.8 (4.4)	13.4 (4.4)	12.9 (4.4)

AIMS, Abnormal Involuntary Movement Scale; BPRS, Brief Psychiatric Rating Scale; MADRS, Montgomery-Åsberg Depression Rating Scale; SD, standard deviation; TD, tardive dyskinesia; YMRS, Young Mania Rating Scale  
McIntyre RS, et al. US Psych Congress 2018; Orlando, FL.

## KINECT 3 & 4: Assessment

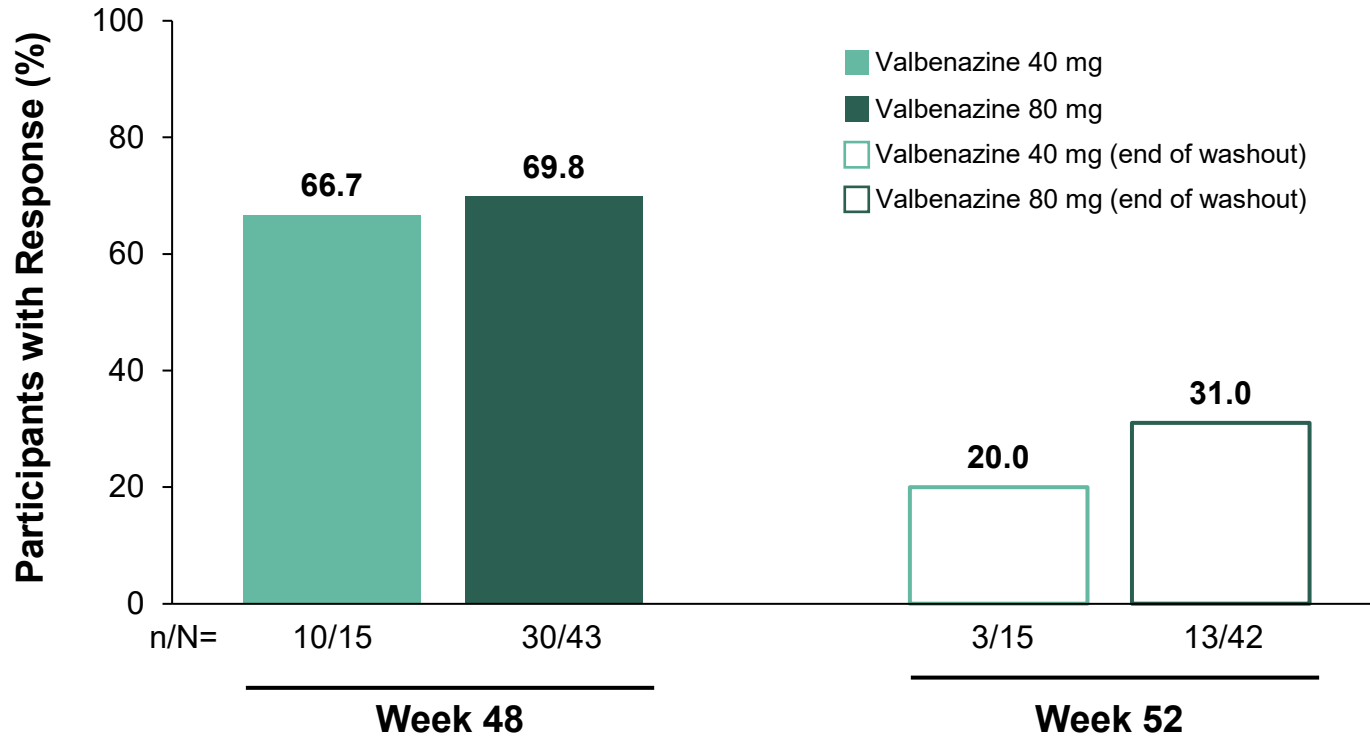
- Analyses were conducted in mood disorder participants who received  $\geq 1$  dose of valbenazine and had any available post-baseline efficacy assessment
- Changes in TD were assessed at Week 48 (after long-term treatment) and Week 52 (after 4-week washout) using the Abnormal Involuntary Movement Scale (AIMS) total score (sum of items 1-7) and Clinical Global Impression of Change-Tardive Dyskinesia (CGI-TD)
- AIMS was scored by blinded central video raters (KINECT 3) or site raters (KINECT 4)
- Analyses included: mean change from baseline in AIMS total score, AIMS response ( $\geq 50\%$  total score improvement from baseline), CGI-TD mean score, and CGI-TD response (score of 1 [“very much improved”] or 2 [“much improved”])
- Changes in mood symptoms were assessed using YMRS and MADRS total scores and individual item scores
- Data were analyzed descriptively, with no statistical testing between dose groups

# KINECT 3 & 4 – Mood Disorder Analysis: Improvements in Tardive Dyskinesia

	Week 48		Week 52	
	Valbenazine 40 mg n=15	Valbenazine 80 mg n=43	Valbenazine 40 mg n=15	Valbenazine 80 mg n=42
<b>AIMS total score, mean change from baseline (SEM)</b>	-7.3 (1.6)	-8.5 (0.9)	-2.1 (1.2)	-3.9 (0.9)
<b>CGI-TD, mean score (SEM)</b>	2.3 (0.3)	1.7 (0.1)	3.3 (0.4)	3.2 (0.3)

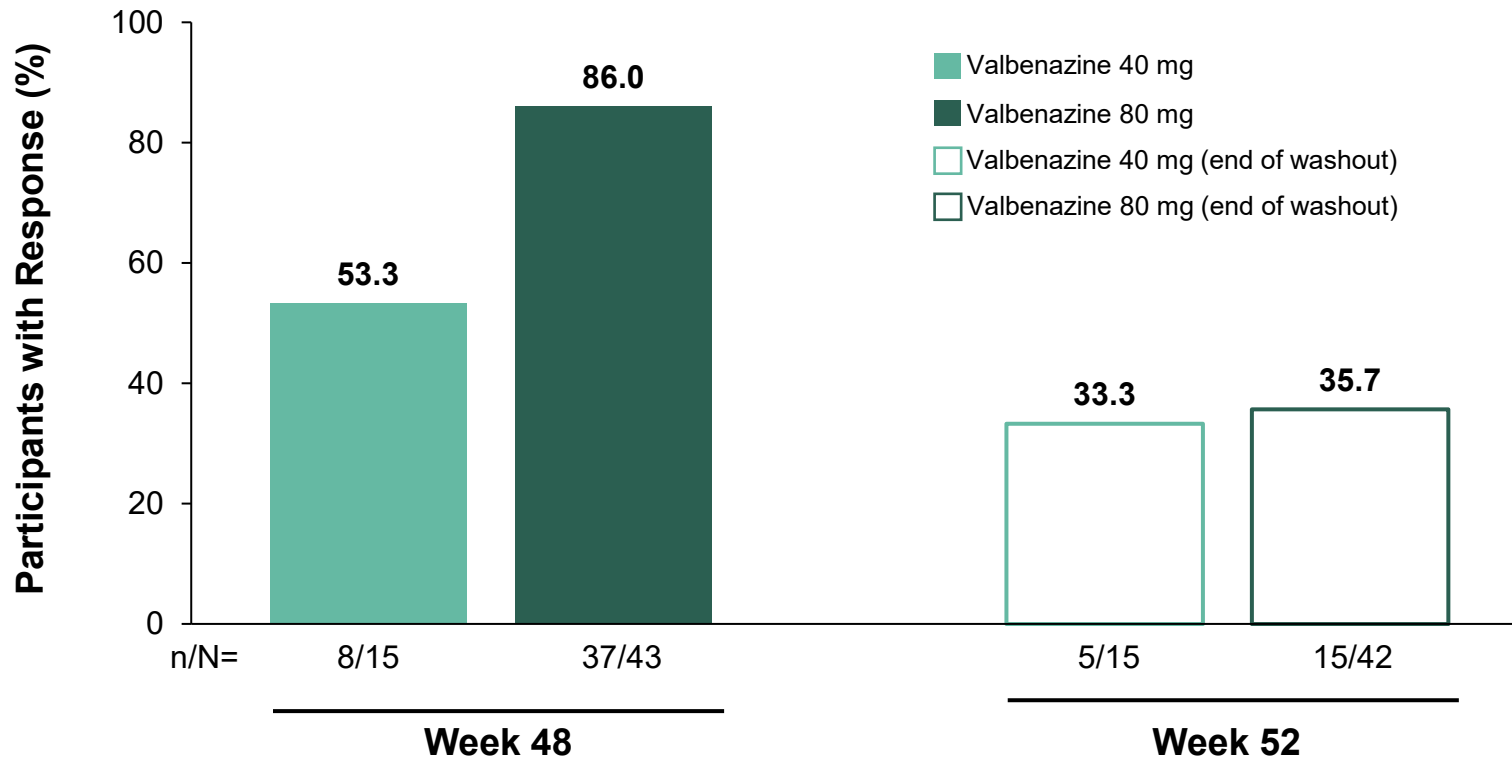
- AIMS was scored by blinded central video raters in KINECT 3 study or site raters in KINECT 4 study
- Based on AIMS and CGI-TD data, mood disorder participants had meaningful and sustained mean TD improvements with valbenazine at Week 48 (end of treatment)
  - There was some return towards baseline levels observed at Week 52 (after 4-week washout)

# KINECT 3 & 4 – Mood Disorder Analysis: Treatment Response (≥50% AIMS Total Score Improvement from Baseline)



- At Week 48, 69% of all mood disorder participants achieved an AIMS response (≥50% total score improvement)

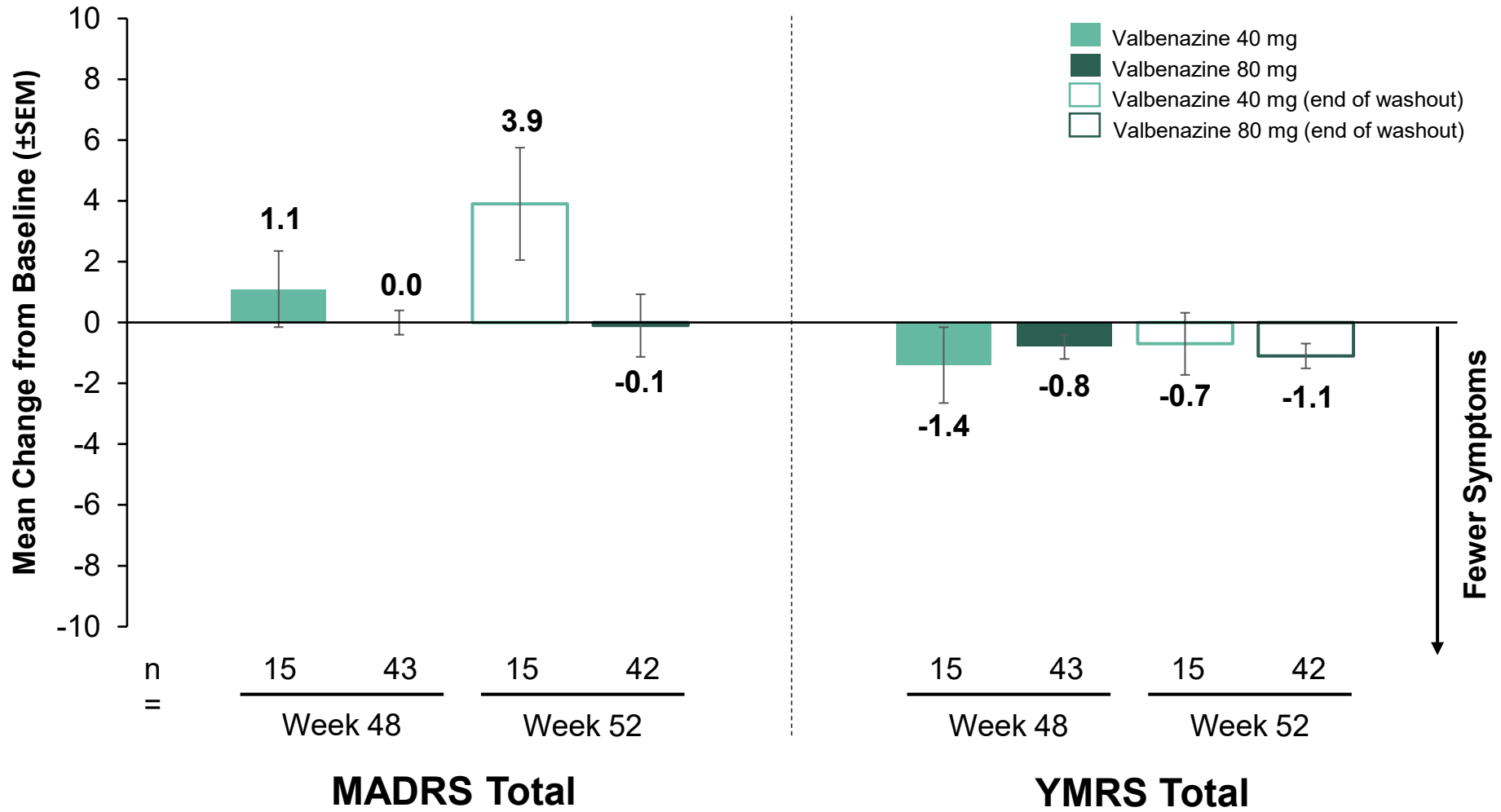
# KINECT 3 & 4 – Mood Disorder Analysis: Treatment Response: CGI-TD (Rating of “Much Improved” or “Very Much Improved”)



- At Week 48, 77.6% achieved a CGI-TD response
  - The percentage of responders decreased after washout

CGI-TD, Clinical Global Impression of Change-Tardive Dyskinesia.  
McIntyre RS, et al. US Psych Congress 2018; Orlando, FL.

# KINECT 3 & 4 – Mood Disorder Analysis: MADRS and YMRS Total Scores Changes from Baseline



MADRS, Montgomery-Åsberg Depression Rating Scale; SEM, standard error of the mean; YMRS, Young Mania Rating Scale.

McIntyre RS, et al. US Psych Congress 2018; Orlando, FL.



# KINECT 3 & 4 – Mood Disorder Analysis: Safety

- Based on available Columbia-Suicide Severity Rating Scale (C-SSRS) data, most mood disorder participants had no suicidal ideation at baseline (97.9% [93/94])
  - Of these participants, 93.5% (87/93) had no emergence of C-SSRS suicidal ideation at any time during the long-term studies
  - In the 1 participant who had suicidal ideation at baseline (“wish to be dead”), no worsening in C-SSRS score was found at any time during the study

# KINECT 3 & 4 – Mood Disorder Analysis: Summary

- As with the overall study population, in participants with a mood disorder, long-term treatment with once-daily valbenazine resulted in sustained and clinically meaningful TD improvements based on the AIMS mean data from baseline to Week 48
  - -7.3 (VBZ 40 mg) and -8.5 (VBZ 80 mg)
- Mean changes in MADRS and YMRS total scores and item scores indicated that psychiatric symptoms generally remained stable throughout the long-term studies (Week 48)
  - MADRS: 1.1 (VBZ 40 mg) and 0.0 (VBZ 80 mg)
  - YMRS: -1.4 (VBZ 40 mg) and -0.8 (VBZ 80 mg)