KINECT® 4 – Full Data Set, Subgroup Analyses, & Post Hoc Analyses

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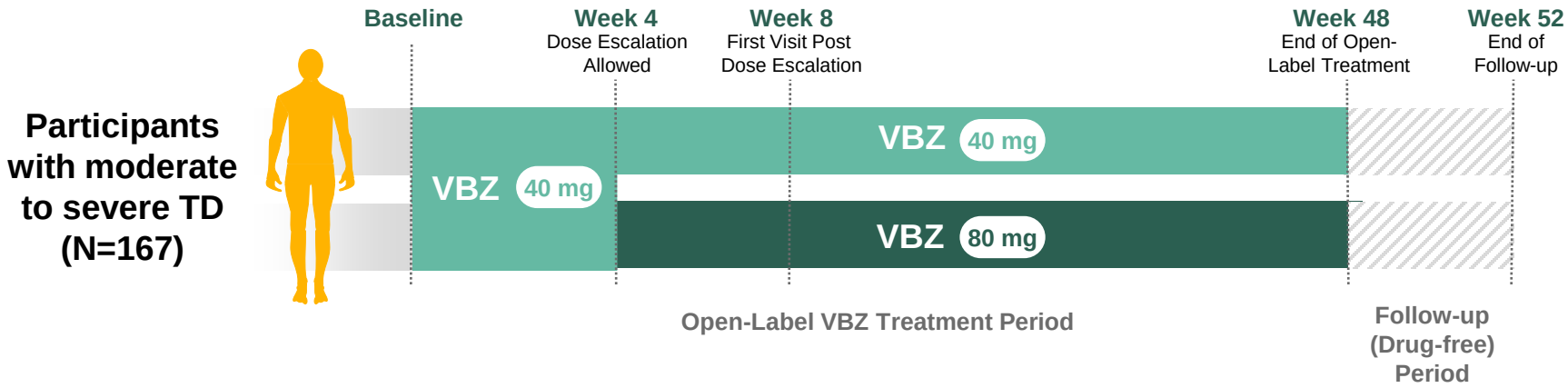
KINECT® 4 – Full Dataset Analysis

KINECT 4: Study Design



Post-baseline study visits during open-label treatment were at Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, and 48.
VBZ, valbenazine

- Open-label study to evaluate safety and tolerability of once-daily valbenazine with an escalation from 40 to 80 mg in participants on drug for up to 48 weeks
  - Included a 4-week drug-free follow-up period (total of 52 weeks)
- All participants received valbenazine 40 mg/day for 4 weeks
- Participants could be escalated to 80 mg/day at the end of Week 4 if:
  - Clinical Global Impression-Tardive Dyskinesia (CGI-TD) was ≥3
  - If they tolerated 40 mg/day during the duration of treatment
- Participants unable to tolerate 80 mg/day were allowed a dose reduction to 40 mg/day between Weeks 4-48
- Participants unable to tolerate 40 mg/day were discontinued from the study

*Including CGI-TD scores ranging from 3 (“minimally improved”) to 7 (“very much worse”)

Patients who received 80 mg in the KINECT 4 study followed a different dosing schedule than those in the KINECT 3 pivotal study. In KINECT 3, patients had a dose increase from 40 mg to 80 mg after Week 1. In KINECT 4, patients had a dose increase from 40 mg to 80 mg after Week 4. The impact of this on long-term effectiveness is not known.

Marder SR, et al. J Clin Psychopharmacology. 2019;39(6):620-627

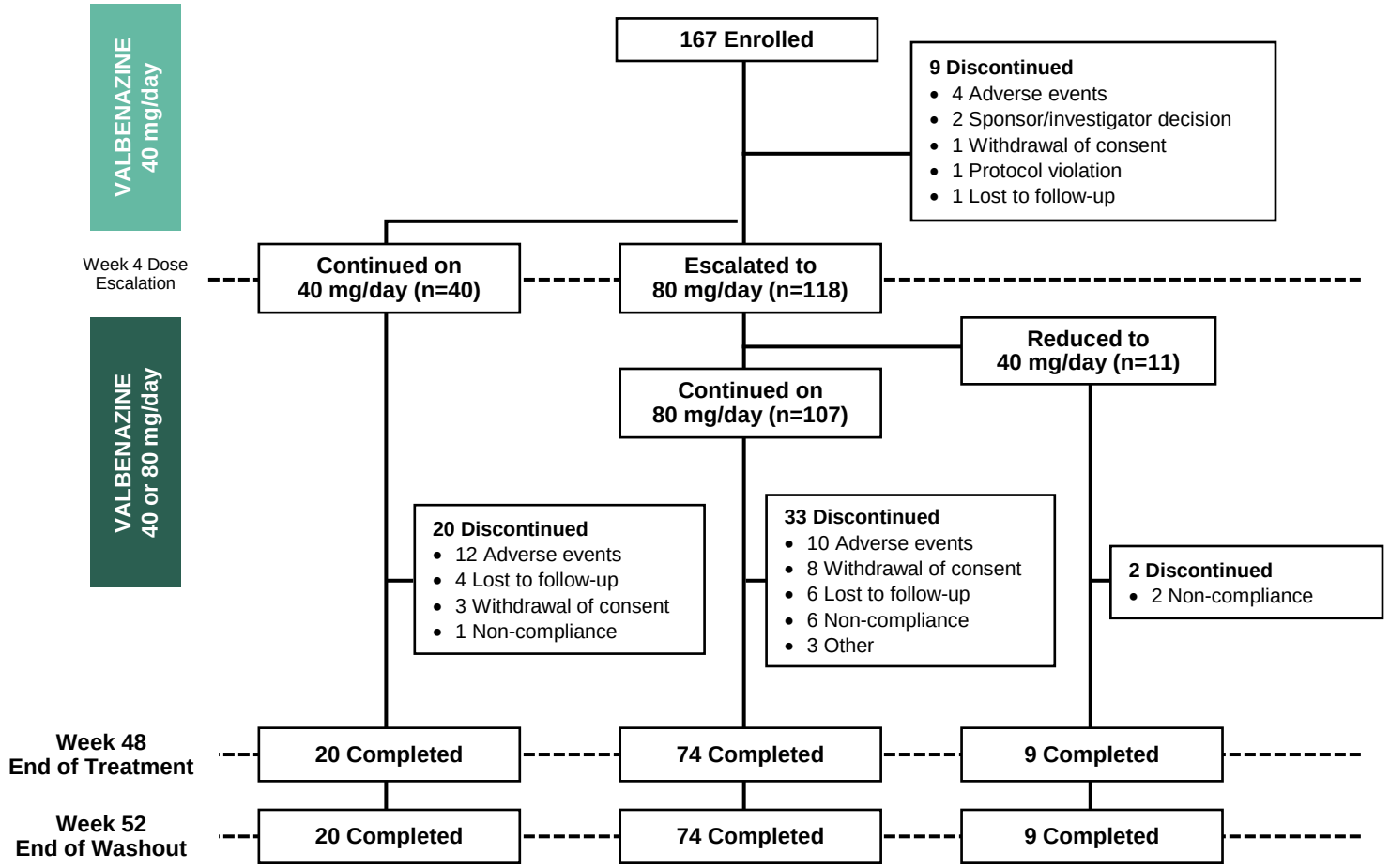
KINECT 4 – Full Dataset Analysis: Assessments

- Safety was the primary objective of the study but effectiveness of valbenazine treatment was also evaluated
- Safety:
  - Treatment-emergent adverse events (TEAE), lab tests, and vital sign measurements
  - Psychiatric scales:
    - PANSS, CDSS, YMRS and MADRS
  - The BARS and SAS were administered to evaluate the presence and severity of drug-induced akathisia and parkinsonism
- Effectiveness:
  - Abnormal Involuntary Movement Scale (AIMS) total score (sum of items 1-7) by blinded central video raters (scored at baseline, Weeks 8 and 52)
  - AIMS total score by site investigators (scored at baseline, Weeks 4, 8, 12, 24, 36, 48, and 52)
  - AIMS response by study visit, defined as ≥50% total score (sum of items 1-7) improvement from baseline (site and central raters)
  - Mean scores for AIMS item 8 (severity of abnormal movements overall), item 9 (incapacitation due to abnormal movements), and item 10 (participant's awareness of abnormal movements and distress level) (AIMS items 8-10, site raters only)
  - Clinical Global Impression of Change-Tardive Dyskinesia (CGI-TD)
  - Patient Global Impression of Change (PGIC)

CDSS, Calgary Depression Scale for Schizophrenia; MADRS, Montgomery-Åsberg Depression Rating Scale; PANSS, Positive and Negative Syndrome Scale; YMRS, Young Mania Rating Scale

Marder SR, et al. *J Clin Psychopharmacology.* 2019;39(6):620-627.

KINECT 4 – Full Dataset Analysis: Participant Enrollment & Disposition



Marder SR, et al. *J Clin Psychopharmacology.* 2019;39(6):620-627.

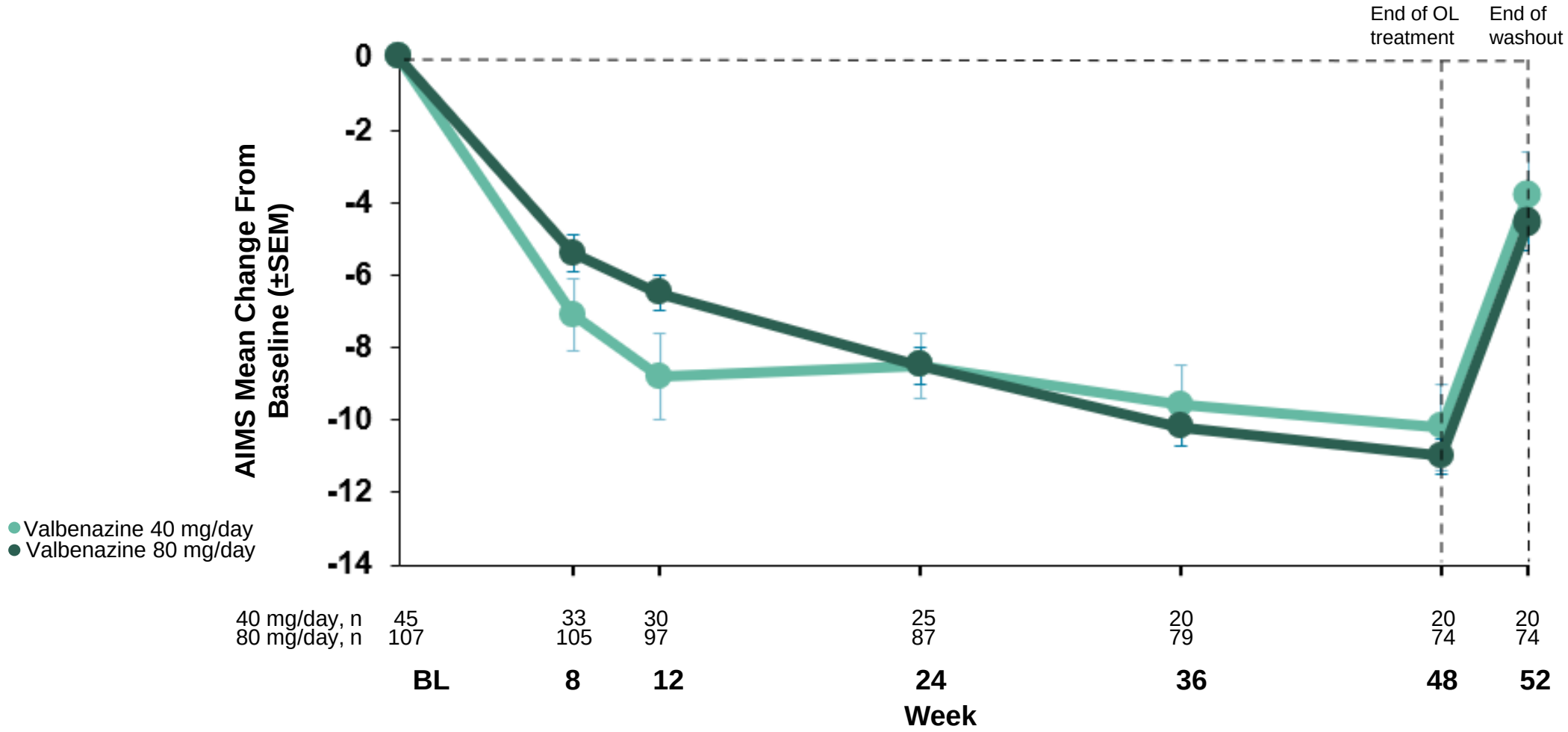
KINECT 4 – Full Dataset Analysis: Baseline Characteristics

Characteristic	40 mg/day (n=45)	80 mg/day (n=107)	All Participants[a] (n=163)
Age, mean (SD), years	56.8 (11.2)	57.8 (9.0)	57.4 (9.6)
Male, n (%)	21 (46.7)	59 (55.1)	86 (52.8)
Race, n (%)			
White/Caucasian	26 (57.8)	74 (69.2)	110 (67.5)
Black/African American	16 (35.6)	31 (29.0)	48 (29.4)
Other	3 (6.7)	2 (1.9)	5 (3.1)
BMI, mean (SD), kg/m^2	27.8 (6.0)	29.0 (5.4)	28.5 (5.5)
Age at TD diagnosis, mean (SD), years	47.8 (11.9)	49.2 (11.4)	48.4 (11.9)
Primary psychiatric diagnosis, n (%)			
Schizophrenia/schizoaffective disorder	37 (82.2)	76 (71.0)	119 (73.0)
Mood disorder	8 (17.8)	31 (29.0)	44 (27.0)
Lifetime suicidal ideation or behavior, n (%)[b]	17 (37.8)	48 (44.9)	69 (42.3)
AIMS scores, mean (SD)			
Total score by central raters[c]	10.2 (3.9)	10.0 (3.9)	10.0 (3.8)
Total score by site raters[c]	14.2 (5.5)	15.0 (4.5)	14.6 (4.8)
Item 8 score (severity of abnormal movements overall) by site raters[d]	3.1 (0.5)	3.2 (0.5)	3.2 (0.6)
Item 9 score (incapacitation due to abnormal movements) by site raters[d]	2.4 (0.9)	2.6 (0.8)	2.5 (0.9)
Item 10 (participant's awareness of abnormal movements) score by site raters[d]	2.8 (0.9)	2.7 (0.7)	2.7 (0.8)

[a]Includes 11 participants who had a dose reduction from 80 mg/day to 40 mg/day after Week 4. [b]Based on the Columbia-Suicide Severity Rating Scale.
[c]Sum of AIMS items 1-7. [d]AIMS items were scored on a scale from 0 ("none") to 4 ("severe").
AIMS, Abnormal Involuntary Movement Scale; BMI, body mass index; SD, standard deviation; TD, tardive dyskinesia.

Marder SR, et al. *J Clin Psychopharmacology.* 2019;39(6):620-627.

KINECT 4 – Full Dataset Analysis: AIMS Mean Score Change from Baseline (Site Raters)

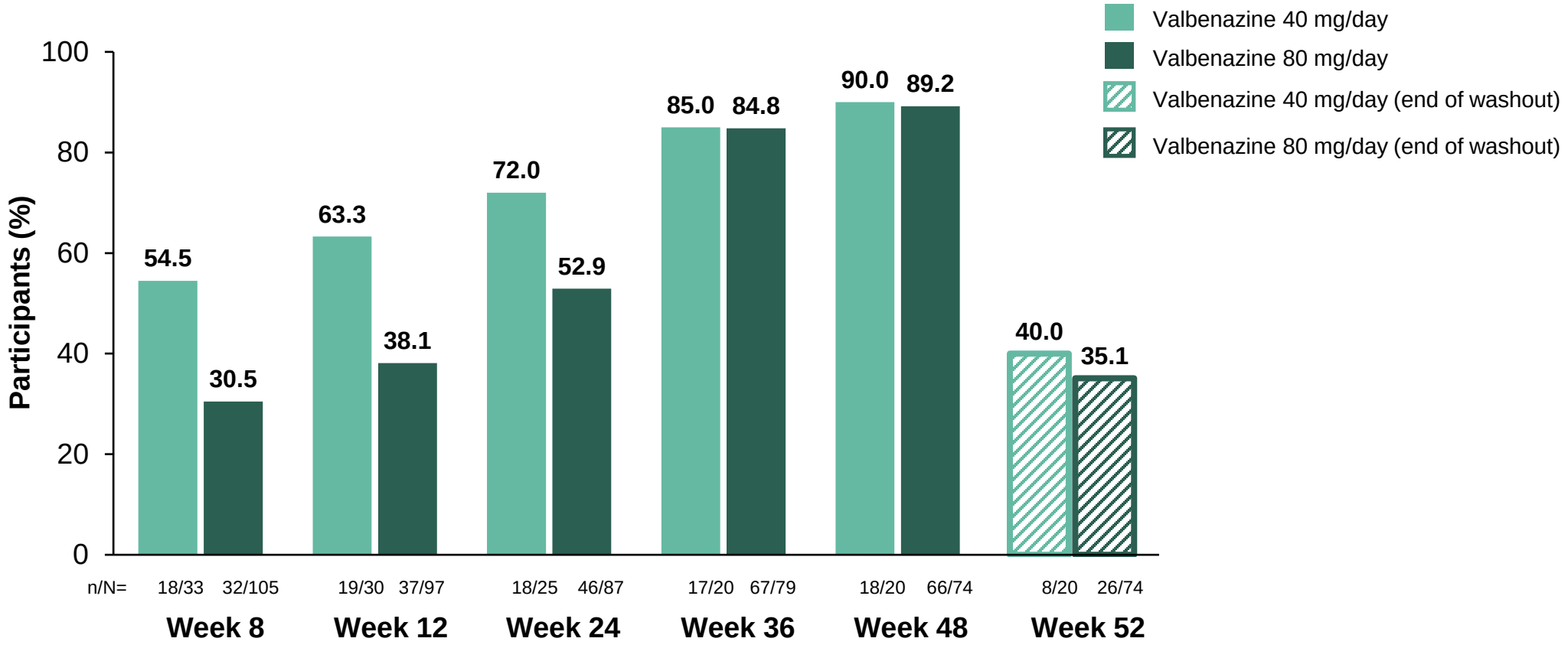


AIMS total score was defined as the sum of items 1-7. Analyses were based on observed cases, with no imputation of missing data. Data are not shown for 11 participants who had a dose reduction from 80 mg/day to 40 mg/day after Week 4. AIMS, Abnormal Involuntary Movement Scale; BL, baseline; OL, open-label; SEM, standard error of the mean.

Patients who received 80 mg in the KINECT 4 study followed a different dosing schedule than those in the KINECT 3 pivotal study. In KINECT 3, patients had a dose increase from 40 mg to 80 mg after Week 1. In KINECT 4, patients had a dose increase from 40 mg to 80 mg after Week 4. The impact of this on long-term effectiveness is not known.

Marder SR, et al. *J Clin Psychopharmacology.* 2019;39(6):620-627.

KINECT 4 – Full Dataset Analysis: AIMS Response by Site Raters (≥50% Total Score Improvement from Baseline)

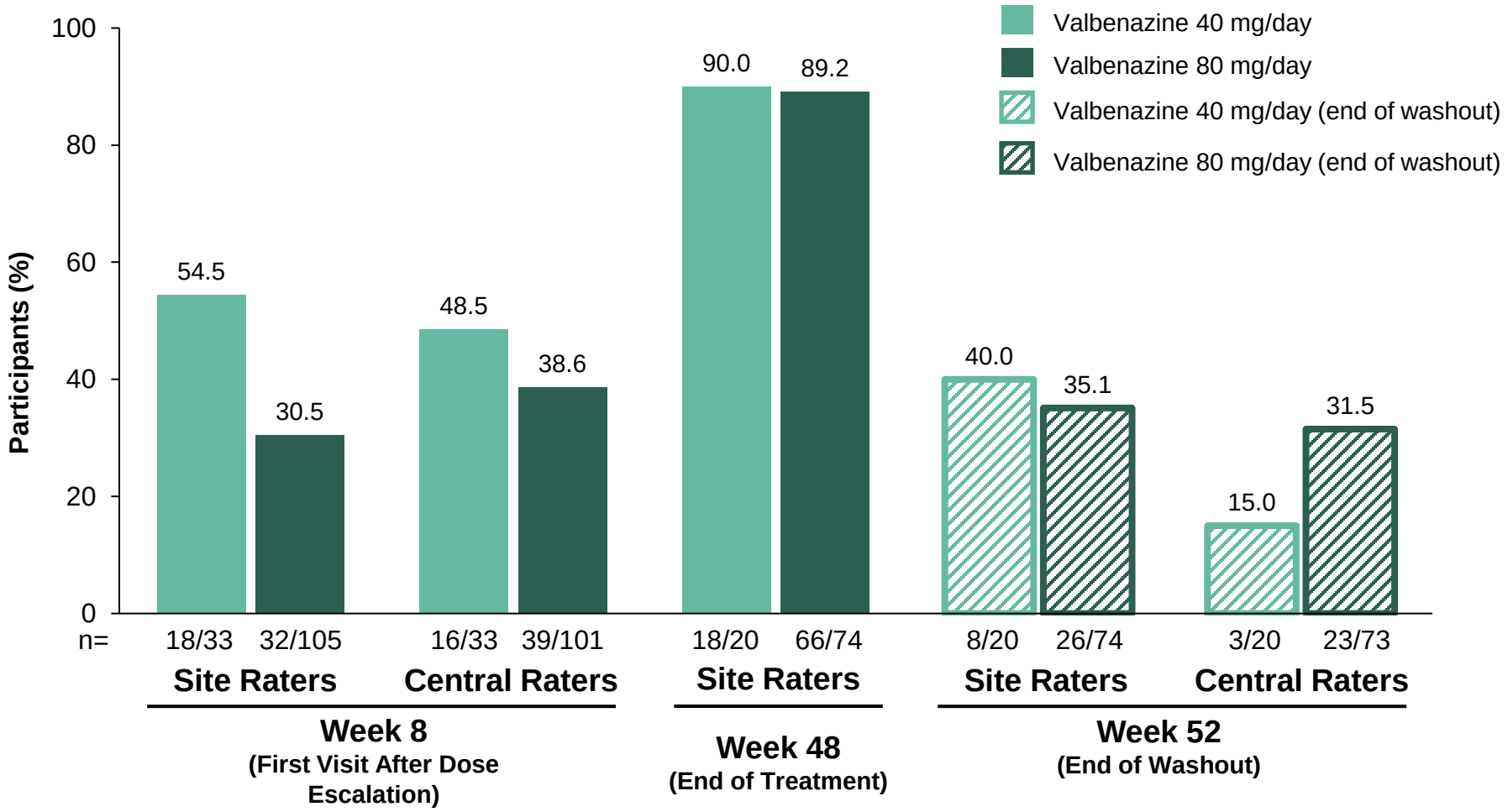


AIMS responses were based on scoring by site raters. Week 8 was the first study visit after dose escalation; Week 52 was the end of washout.
Data are not shown for 11 participants who had a dose reduction from 80 mg/day to 40 mg/day after Week 4.
AIMS, Abnormal Involuntary Movement Scale.

Marder SR, et al. *J Clin Psychopharmacology*. 2019;39(6):620-627.

KINECT 4 – Full Dataset Analysis: AIMS Response* Rates by Central and Site Raters

*≥50% AIMS Total Score Improvement from Baseline



Per study protocol, Week 48 AIMS was not evaluated by central AIMS video raters.
Data are not shown for 11 participants who had a dose reduction from 80 mg/day to 40 mg/day after Week 4.
AIMS response defined as ≥50% improvement from baseline in the total score (sum of items 1-7).
AIMS, Abnormal Involuntary Movement Scale.

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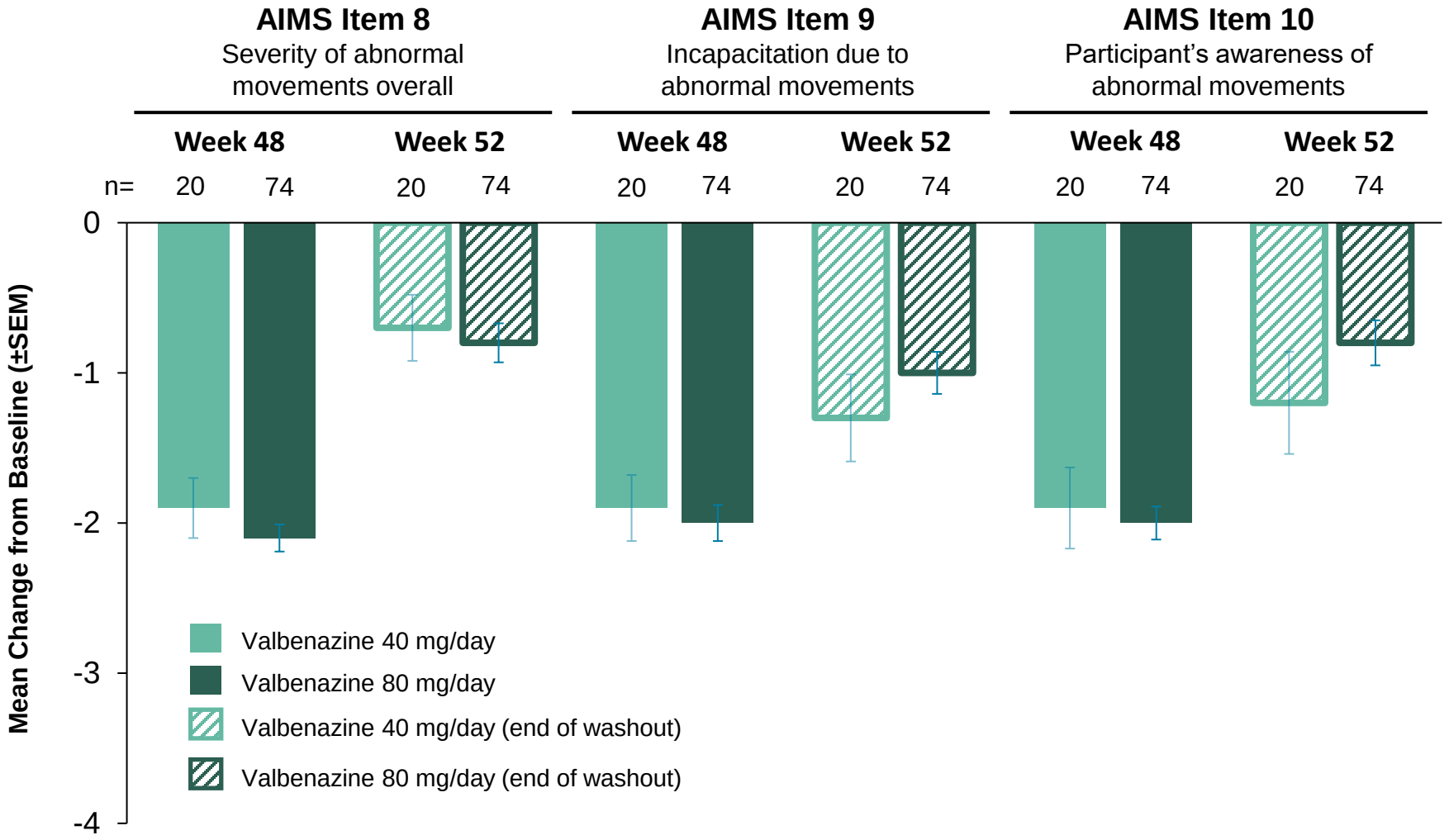
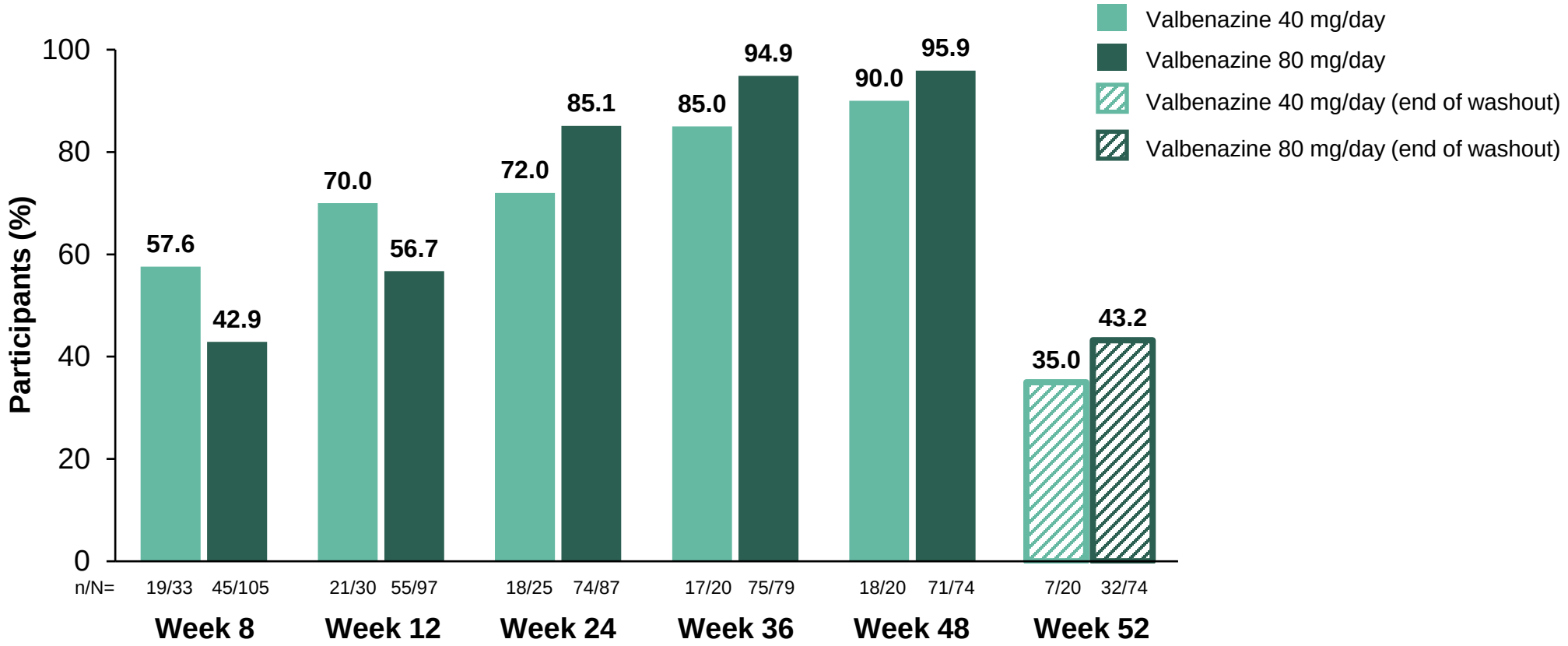
KINECT 4 – Full Dataset Analysis: AIMS Items 8, 9, and 10 Mean Score Changes from Baseline (Site Raters)



Week 48 was the end of open-label treatment; Week 52 was the end of washout.
Data are not shown for 11 participants who had a dose reduction from 80 mg/day to 40 mg/day after Week 4.
AIMS, Abnormal Involuntary Movement Scale; SEM, standard error of the mean.

Marder SR, et al. *J Clin Psychopharmacology.* 2019;39(6):620-627.

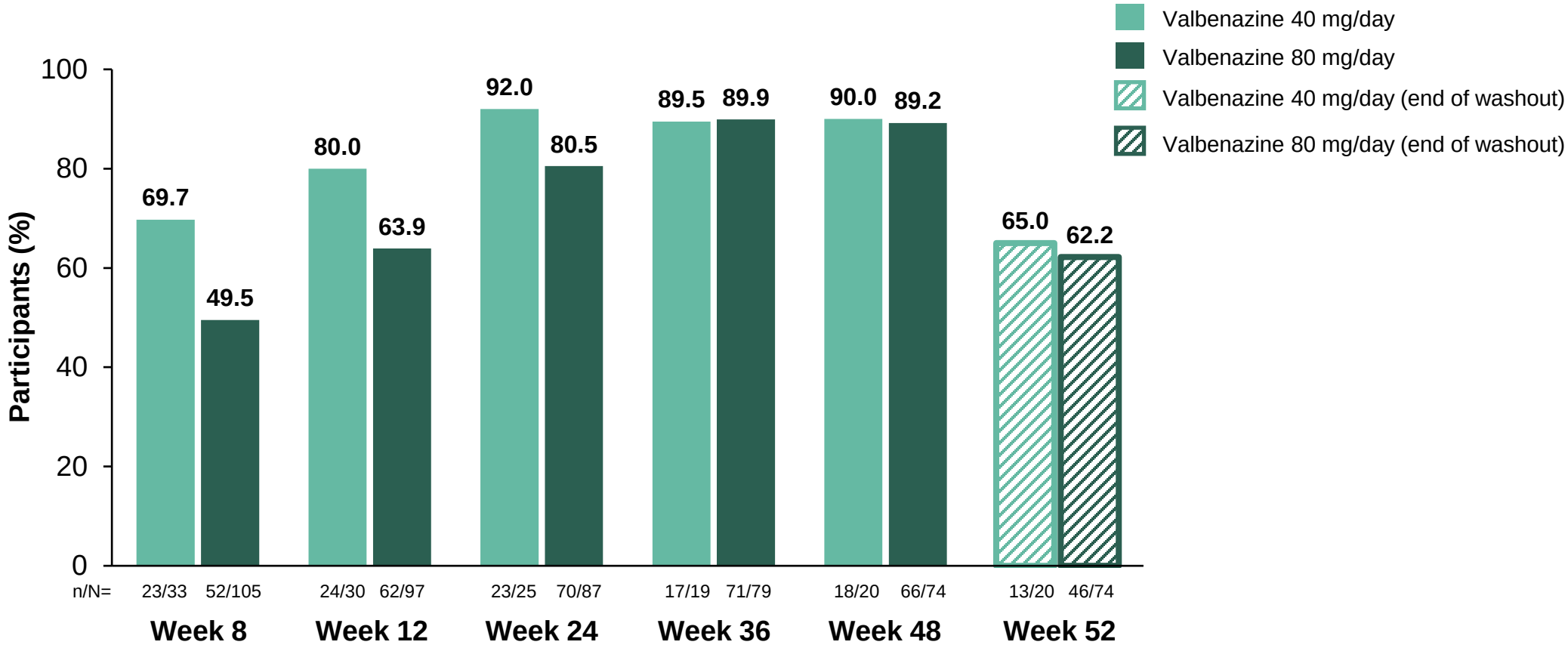
KINECT 4 – Full Dataset Analysis: CGI-TD Response by Site Raters (Rating of "Very Much Improved" or "Much Improved")



CGI-TD responses were based on scoring by site raters. Week 8 was the first study visit after dose escalation; Week 52 was the end of washout.
Data are not shown for 11 participants who had a dose reduction from 80 mg/day to 40 mg/day after Week 4.
CGI-TD, Clinical Global Impression of Change-Tardive Dyskinesia.

Marder SR, et al. *J Clin Psychopharmacology*. 2019;39(6):620-627.

KINECT 4 – Full Dataset Analysis: PGIC Response (Rating of “Very Much Improved” or “Much Improved”)



Week 8 was the first study visit after dose escalation; Week 52 was the end of washout.
Data are not shown for 11 participants who had a dose reduction from 80 mg/day to 40 mg/day after Week 4.
PGIC, Patient Global Impression of Change.

Marder SR, et al. *J Clin Psychopharmacology*. 2019;39(6):620-627.

KINECT 4 – Full Dataset Analysis: Psychiatric and Movement Scales Mean Score Change from Baseline

	Week 48						Week 52					
	40 mg/day		80 mg/day		All Participants[a]		40 mg/day		80 mg/day		All Participants[a]	
	n	Mean Change (SD)	n	Mean Change (SD)	n	Mean Change (SD)	n	Mean Change (SD)	n	Mean Change (SD)	n	Mean Change (SD)
Psychiatric scales												
PANSS positive[b]	14	-1.9 (2.4)	52	-0.6 (2.1)	71	-0.7 (2.5)	14	-1.5 (2.9)	52	-0.5 (2.1)	71	-0.6 (2.3)
PANSS negative[b]	14	-1.5 (4.8)	52	-0.6 (2.9)	71	-0.6 (3.3)	14	-0.2 (5.9)	52	0.0 (3.1)	71	0.0 (3.7)
PANSS general psychopathology[b]	14	-2.9 (5.6)	52	-1.8 (3.7)	71	-2.0 (4.5)	14	-1.7 (6.9)	52	-0.7 (4.5)	71	-1.0 (5.0)
CDSS total[b]	14	-0.2 (2.8)	52	-0.9 (2.2)	71	-0.7 (2.3)	14	-0.2 (3.2)	52	-0.6 (2.6)	71	-0.5 (2.6)
YMRS total[c]	6	-0.8 (2.3)	22	-0.2 (1.8)	32	-0.3 (1.7)	6	-1.2 (2.1)	22	-0.8 (1.4)	32	-0.8 (1.5)
MADRS total[c]	6	1.7 (3.9)	22	-0.4 (4.9)	32	-0.3 (5.0)	6	4.0 (8.1)	22	-0.4 (6.4)	32	0.0 (6.8)
Movement scales												
BARS total	20	-1.1 (2.2)	74	-1.0 (1.5)	103	-1.0 (1.7)	20	-1.0 (2.0)	74	-0.4 (1.6)	103	-0.5 (1.8)
SAS global	20	-0.1 (0.1)	74	-0.1 (0.2)	103	-0.1 (0.2)	20	-0.0 (0.2)	74	-0.1 (0.2)	103	-0.1 (0.2)

Week 48 was the end of open-label treatment; Week 52 was the end of washout. Lower scores indicate less severity.
[a]Includes participants who had a dose reduction from 80 mg/day to 40 mg/day after Week 4.
[b]PANSS and CDSS administered to participants with schizophrenia/schizoaffective disorder.
[c]YMRS and MADRS administered to participants with a mood disorder.
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.

Marder SR, et al. *J Clin Psychopharmacology.* 2019;39(6):620-627.

KINECT 4 – Full Dataset Analysis: TEAEs

Participants, n (%)	Baseline to Week 4	Week 4 to Week 48		
	40 mg/day (n=163)	40 mg/day (n=35)	80 mg/day (n=107)	All Participants[a] (n=153)
Any TEAE	36 (22.1)	22 (62.9)	66 (61.7)	99 (64.7)
Any serious TEAE	0	3 (8.6)	17 (15.9)	21 (13.7)
Any TEAE leading to discontinuation	6 (3.7)	7 (20.0)	11 (10.3)	18 (11.8)
Death	0	0	1 (0.9)[b]	1 (0.7)
TEAEs by preferred term[c]				
Urinary tract infection	2 (1.2)	3 (8.6)	9 (8.4)	13 (8.5)
Headache	7 (4.3)	2 (5.7)	6 (5.6)	8 (5.2)
Nasopharyngitis	2 (1.2)	1 (2.9)	4 (3.7)	7 (4.6)
Suicidal ideation	1 (0.6)	3 (8.6)	4 (3.7)	7 (4.6)
Constipation	1 (0.6)	2 (5.7)	2 (1.9)	6 (3.9)
Fall	0	1 (2.9)	3 (2.8)	6 (3.9)
Fatigue	6 (3.7)	3 (8.6)	3 (2.8)	6 (3.9)
Hypertension	0	0	4 (3.7)	6 (3.9)
Somnolence	6 (3.7)	0	4 (3.7)	6 (3.9)
Back pain	1 (0.6)	1 (2.9)	3 (2.8)	5 (3.3)
Dizziness	1 (0.6)	0	5 (4.7)	5 (3.3)

Week 4 was the end of treatment initiation with 40 mg/day; Week 48 was the end of open-label treatment.
[a]Includes 11 participants who had a dose reduction from 80 mg/day to 40 mg/day after Week 4.
[b]Due to breast cancer and judged by the investigator as not related to valbenazine.
[c]Reported in ≥3% of all participants during treatment initiation (baseline to Week 4) or after dose escalation (Week 4 to 48).
TEAE, treatment-emergent adverse event.

Marder SR, et al. *J Clin Psychopharmacology.* 2019;39(6):620-627.

KINECT 4 – Full Dataset Analysis: Summary

- Sustained improvements were found in adults with tardive dyskinesia who received once-daily valbenazine for up to 48 weeks, based on clinician- and patient-rated measures
- After stopping valbenazine, scores indicated a return toward baseline, suggesting that patients may require ongoing therapy with valbenazine to maintain effect
- 64.7% of all participants had ≥1 treatment-emergent adverse event after Week 4 through Week 48

Marder SR, et al. *J Clin Psychopharmacology*. 2019;39(6):620-627.

KINECT 4
Post Hoc Analysis of Treatment Completers

KINECT 4 Post Hoc Analysis of Treatment Completers

Objectives

- Evaluation of KINECT 4[a] participants who completed 48 weeks of open-label valbenazine (VBZ) (40 or 80 mg) treatment: **"treatment completers"**
- To evaluate the therapeutic effects of VBZ during long-term treatment in treatment completers
- Determine when treatment completers on long-term VBZ first experience clinically meaningful improvements in TD

Methodology

- **167** participants entered KINECT 4 and **103** (62%) participants completed 48 weeks of open-label, once daily treatment of VBZ (40 or 80 mg) – **"treatment completers"**
- Of the **103 treatment completers**:
  - 20 continued VBZ 40 mg after the initial 40-mg dose period
  - 74 increased dose to 80 mg and continued on 80 mg
  - 9 had a decrease from 80 mg to 40 mg
- Assessments
  - AIMS total score, AIMS items 1-7, Global response to CGI-TD, PGIC, and AIMS items 8, 9, and 10

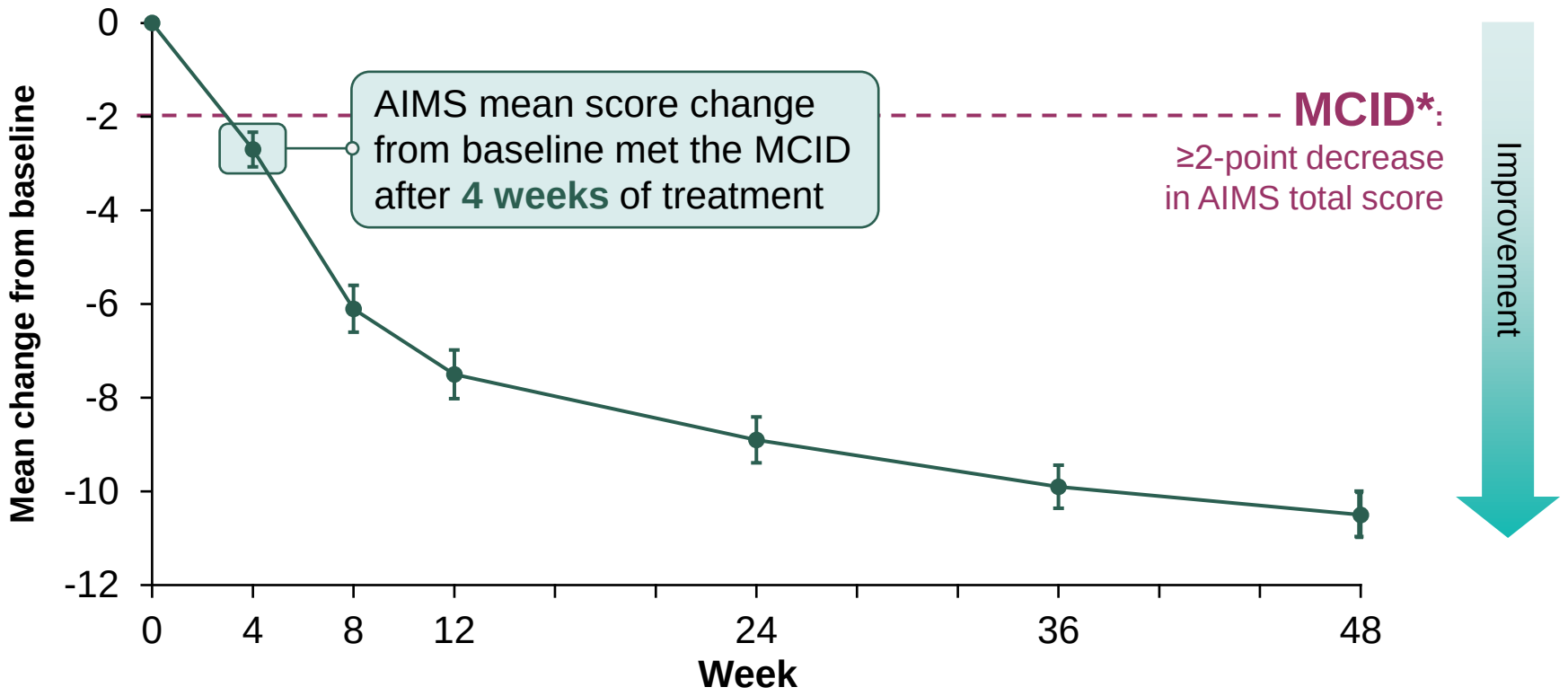
TD, tardive dyskinesia; VBZ, valbenazine.

[a]Patients who received 80 mg in the KINECT 4 study followed a different dosing schedule than those in the KINECT 3 pivotal study. In KINECT 3, patients had a dose increase from 40 mg to 80 mg after Week 1. In KINECT 4, patients had a dose increase from 40 mg to 80 mg after Week 4.

Correll CU, et al. *J Clin Psychopharmacol*. 2024;44(4):353-361.

Early and Sustained Clinically Meaningful Improvements in TD Were Seen With Long-term VBZ Treatment[1]

Mean Change From Baseline in AIMS Total Score[a] Over Time in Treatment Completers (n=103[b])



The mean AIMS total score at **baseline** was

14.8

AIMS mean total score change from baseline to **Week 48** was

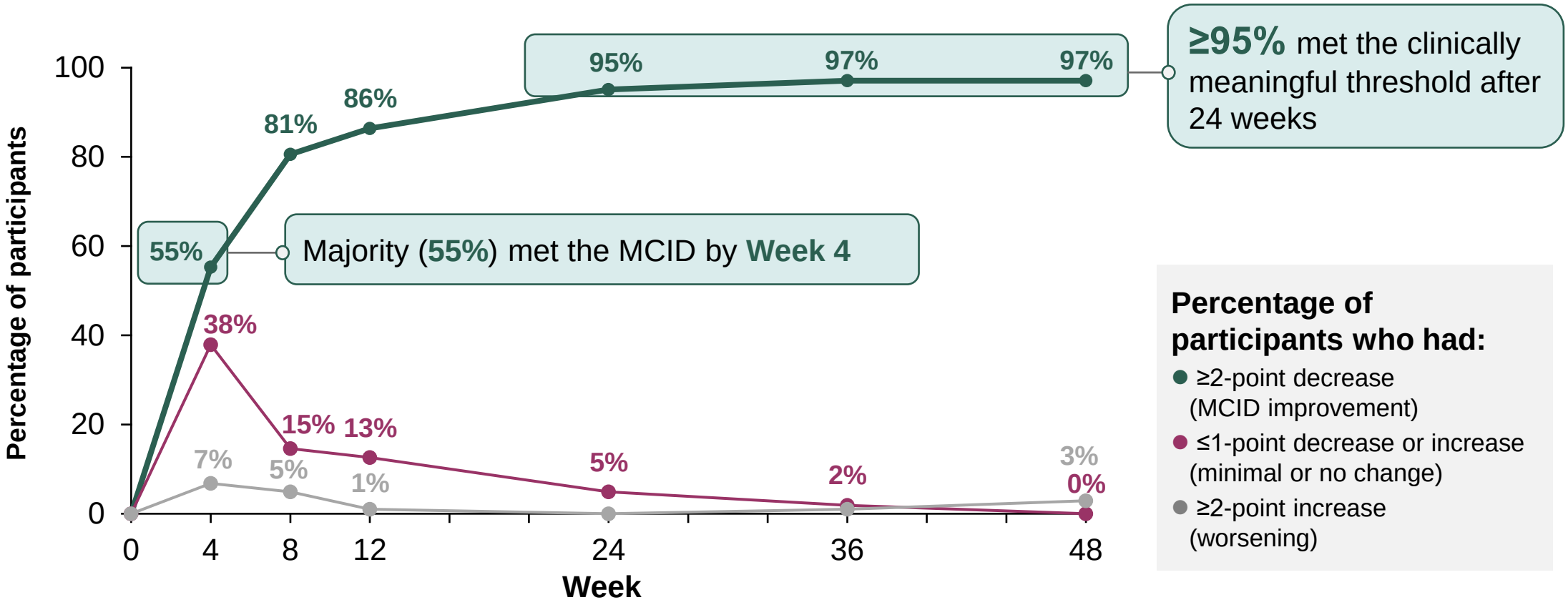
-10.5

(Site Raters)

AIMS, Abnormal Involuntary Movement Scale; MCID, minimal clinically important difference; TD, tardive dyskinesia; VBZ, valbenazine.
*A threshold that helps determine whether a treatment effect is clinically meaningful and can serve as a benchmark for interpreting the clinical relevancy of trial results.[2]
[a]Based on AIMS score by site raters. [b]Total number of participants who completed 48 weeks of open-label, once-daily treatment with VBZ (40 or 80 mg) of the 167 participants who entered the study.
1. Correll CU, et al. *J Clin Psychopharmacol*. 2024;44(4):353-361. 2. Stacy M, et al. Mov Disord. 2019;34(8):1203-1209.

Early and Sustained Clinically Meaningful Improvements in TD Were Seen With Long-term VBZ Treatment (cont.)

MCID Changes in AIMS Total Score[a] Over Time in Treatment Completers (n=103[b]/167)

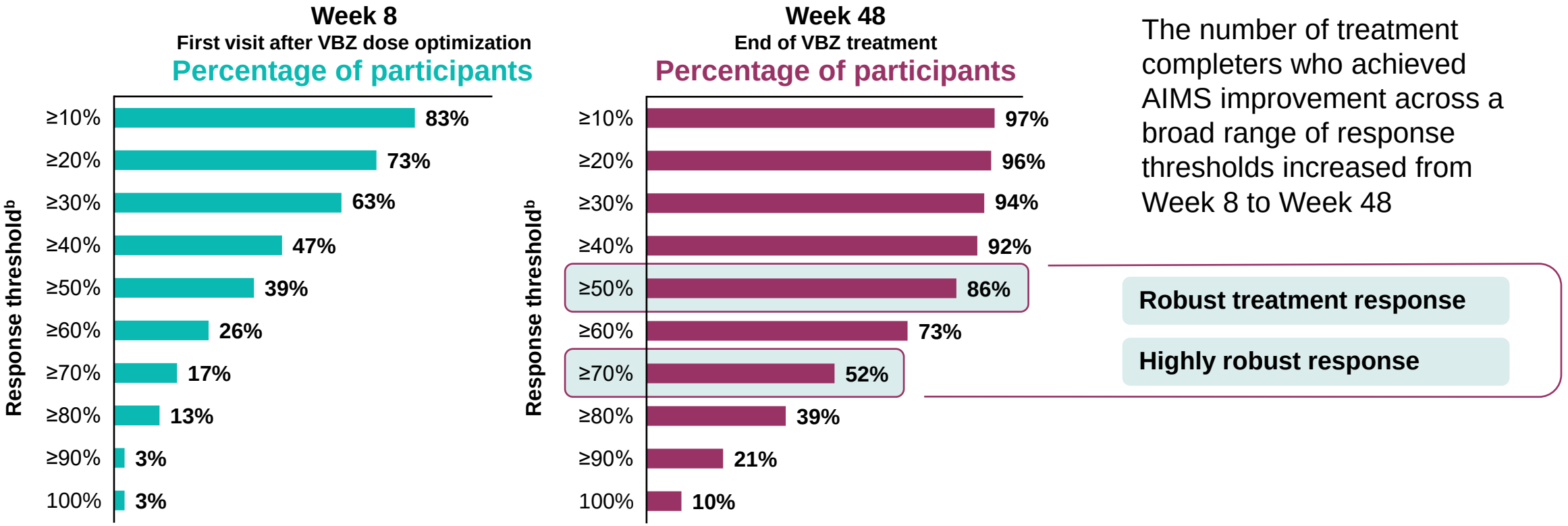


AIMS, Abnormal Involuntary Movement Scale; MCID, minimal clinically important difference; TD, tardive dyskinesia; VBZ, valbenazine.
[a]Based on AIMS score by site raters. [b]Total number of participants who completed 48 weeks of open-label, once-daily treatment with VBZ (40 or 80 mg), of the 167 participants who entered the study. Including 9 participants who had a dose reduction from 80 to 40 mg

Correll CU, et al. *J Clin Psychopharmacol*. 2024;44(4):353-361.

The Majority of Treatment Completers on VBZ therapy Experienced a Robust Treatment Response After Week 48

Range of AIMS Total Score Response Thresholds at Weeks 8 and 48 (n=103[a])



The number of treatment completers who achieved AIMS improvement across a broad range of response thresholds increased from Week 8 to Week 48

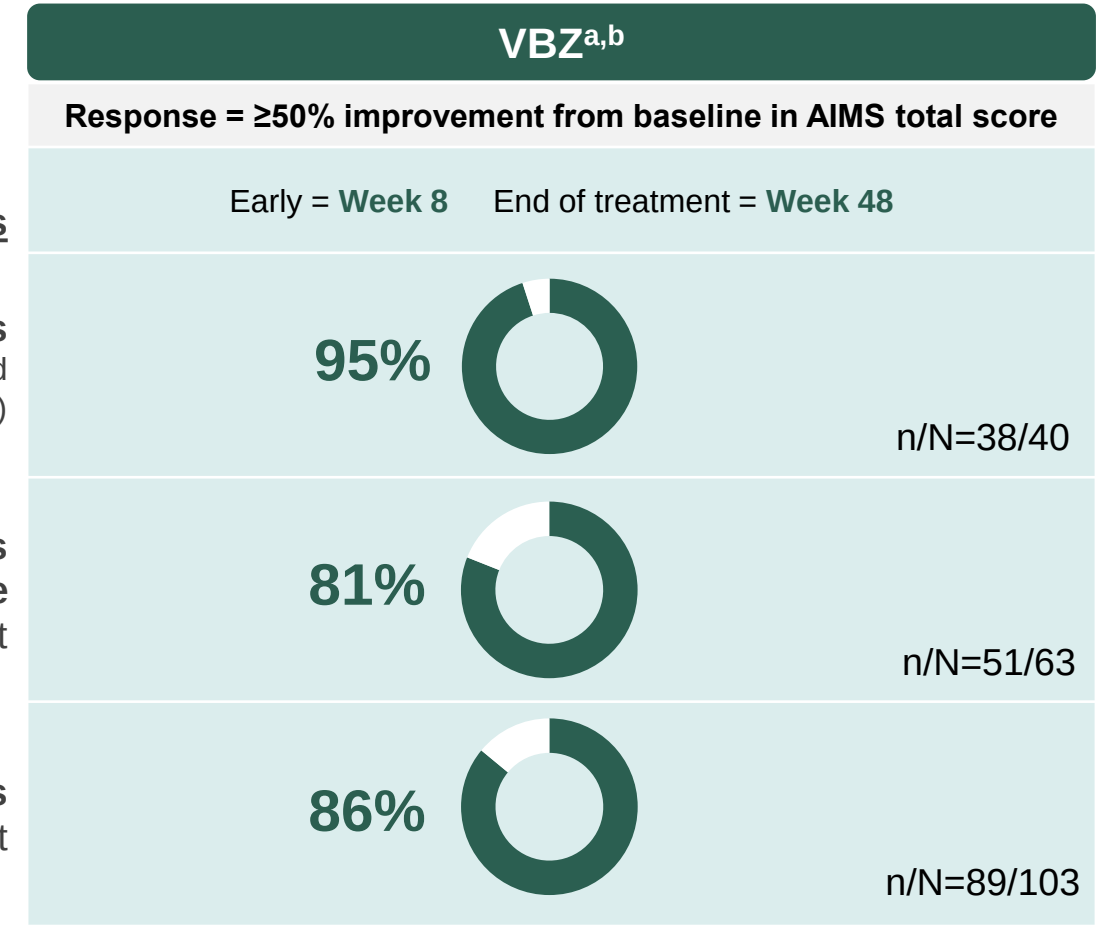
Robust treatment response

Highly robust response

AIMS, Abnormal Involuntary Movement Scale; VBZ, valbenazine.
[a]Total number of participants who completed 48 weeks of open-label, once-daily treatment with VBZ (40 or 80 mg), of the 167 participants who entered the study. [b]Response threshold was defined as the minimum percent change in AIMS total score (based on site-rater score) from baseline to Week 8 (panel A) and Week 48 (panel B).

Correll CU, et al. *J Clin Psychopharmacol*. 2024;44(4):353-361.

Long-term VBZ Use Resulted in AIMS Improvement, Regardless of When Participants First Achieved Response



While many patients may experience substantial improvement in TD early in their treatment course, some may require longer treatment but generally do reach full benefit

AIMS, Abnormal Involuntary Movement Scale; VBZ, valbenazine.
[a]Total number of participants who completed 48 weeks of open-label, once-daily treatment with VBZ (40 or 80 mg), of the 167 participants who entered the study. [b]Based on AIMS score by site raters.
Correll CU, et al. *J Clin Psychopharmacol*. 2024;44(4):353-361.

AIMS Improvement From Baseline Within Each Body Region Was Observed With Long-term VBZ Treatment (n=103[a])

AIMS Item	Participants With AIMS Item Shifts (Score ≥3 to ≤2[b]), % (n/N)
1. Face	98 (40/41)
2. Lips	100 (63/63)
3. Jaw	98 (50/51)
4. Tongue	98 (58/59)
5. Upper extremities	100 (50/50)
6. Lower extremities	100 (29/29)
7. Trunk	89 (23/26)
8. Global (site-rater judgment)[c]	96 (94/98)
8. Global (highest score from items 1-7)[d]	94 (93/99)

At Week 48, **≥98%** of completers with "moderate" or "severe" abnormal movements at baseline **shifted to "none," "minimum," or "mild"** in all body regions except for the trunk

AIMS, Abnormal Involuntary Movement Scale; n, number of participants with item score ≤2 at Week 48; N, number of participants with item score ≥3 at baseline; VBZ, valbenazine.
[a]Total number of participants who completed 48 weeks of open-label, once-daily treatment with VBZ (40 or 80 mg), of the 167 participants who entered the study. [b]Shift from “moderate” or “severe” to “mild” or better (based on AIMS score by site raters). [c]Based on site rater’s score on item 8 (based on clinical judgment regarding the entire examination as a whole). [d]Based on site rater’s highest single score from items 1 to 7 (ie, determined algorithmically from the site rater’s individual ratings).
Correll CU, et al. *J Clin Psychopharmacol*. 2024;44(4):353-361.

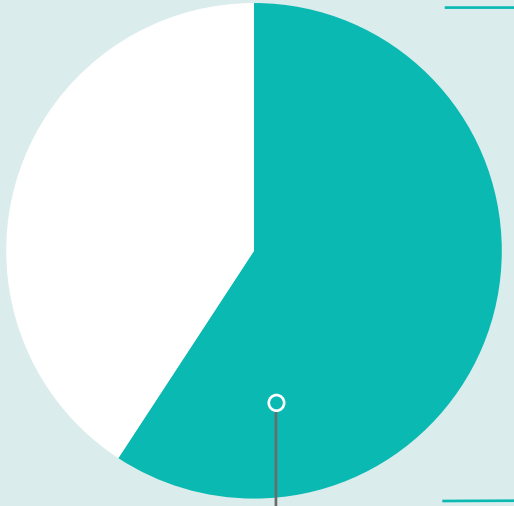
Over Half of the Participants Treated With VBZ Reached the Remission Threshold in TD After 48 Weeks of Treatment

Proportion of Participants With Response on AIMS Item Scores at Week 48 (n=103[a])

AIMS Item	Item Score ≤1, n (%)[b]
1. Face	95 (92)
2. Lips	90 (87)
3. Jaw	85 (83)
4. Tongue	82 (80)
5. Upper extremities	96 (93)
6. Lower extremities	93 (90)
7. Trunk	95 (92)
8. Global (site-rater judgment)[c]	68 (66)
8. Global (highest score from items 1-7)[d]	61 (59)

Remission in TD*

Defined as an AIMS score of 0 (“none”) or 1 (“minimal”) in each of the AIMS items 1-7 at Week 48



59%

(61/103)

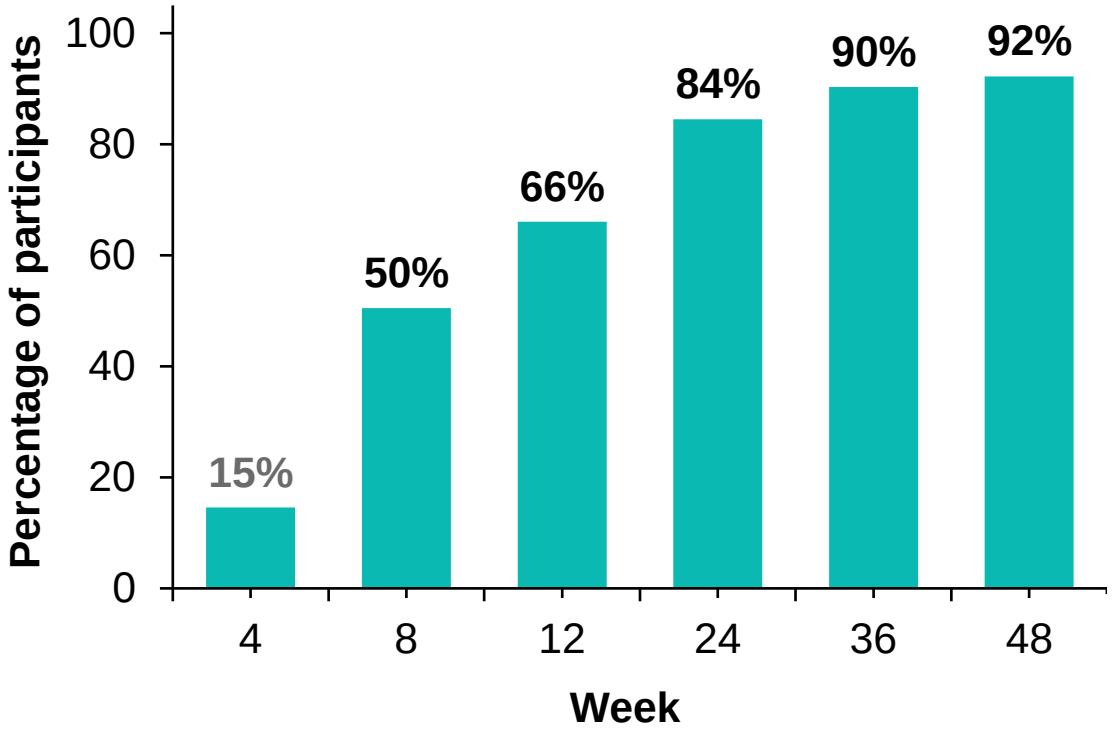
of VBZ-treated patients met the criteria for remission by Week 48

AIMS, Abnormal Involuntary Movement Scale; VBZ, valbenazine.
*Remission defined as “complete response” by study authors.
[a]Total number of participants who completed 48 weeks of open-label, once-daily treatment with VBZ (40 or 80 mg), of the 167 participants who entered the study. [b]Response was defined as item score ≤1 (“none” or “minimal”) based on AIMS score by site raters. [c]Based on site rater’s rating on item 8 (based on clinical judgment regarding the entire examination as a whole). [d]Based on site rater’s highest single score from items 1 to 7 (ie, determined algorithmically from the site rater’s individual ratings).

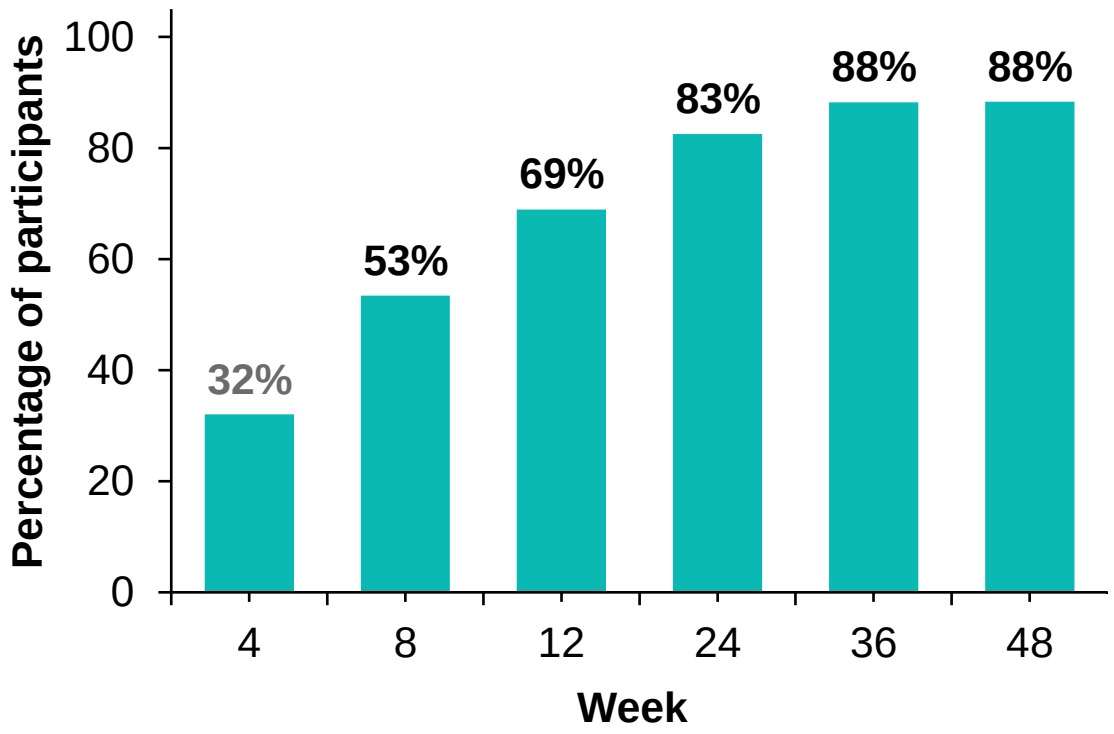
Correll CU, et al. *J Clin Psychopharmacol*. 2024;44(4):353-361.

Clinician and Patient Global Improvements Increased Over Time With Long-term VBZ Therapy in Treatment Completers

CGI-TD[a] (n=103[b])



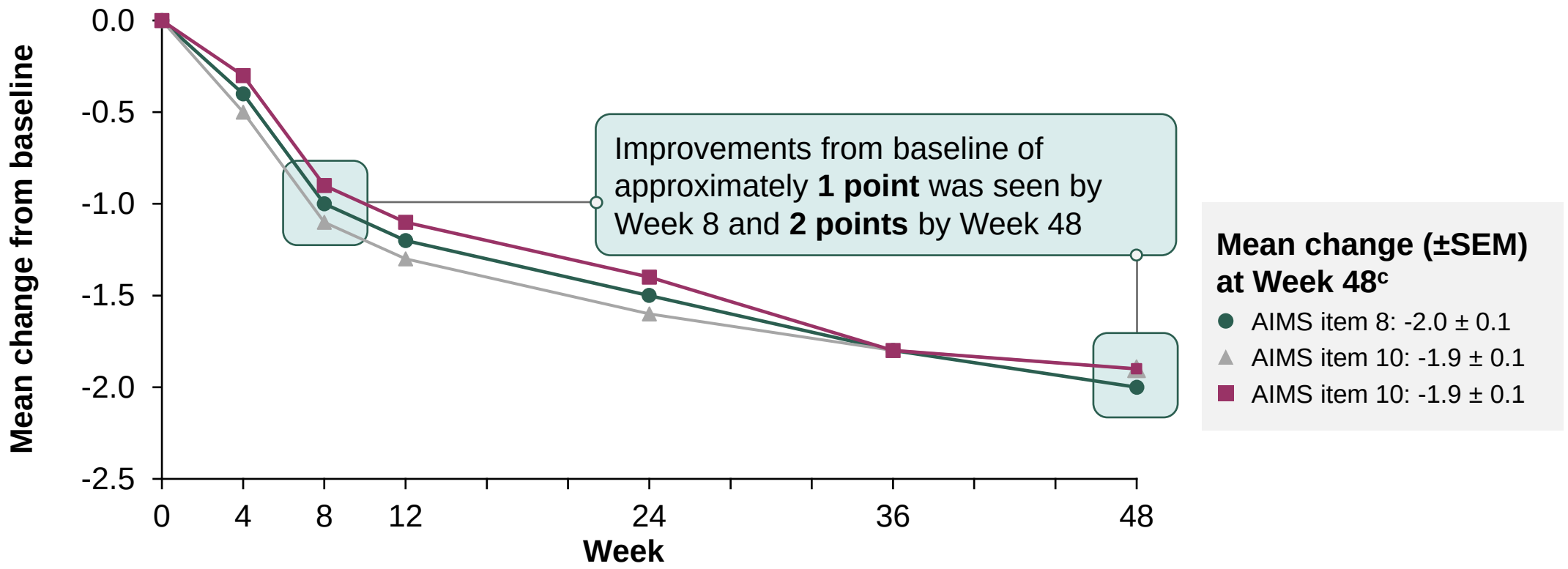
PGIC[a] (n=103[b])



CGI-TD, Clinical Global Impression of Tardive Dyskinesia; PGIC, Patient Global Impression of Change; VBZ, valbenazine.
[a]Response was defined as "much improved" or "very much improved" (score ≤2). [b]Total number of participants who completed 48 weeks of open-label, once-daily treatment with VBZ (40 or 80 mg), of the 167 participants who entered the study.
Correll CU, et al. *J Clin Psychopharmacol*. 2024;44(4):353-361.

Early and Sustained Improvements With Long-Term VBZ Treatment Were Observed in AIMS Items 8, 9, and 10

Mean Change From Baseline in AIMS Items 8, 9, and 10[a] (n=103[b])



AIMS, Abnormal Involuntary Movement Scale; SEM, standard error of the mean; VBZ, valbenazine.
[a]Based on AIMS score by site raters. [b]Total number of participants who completed 48 weeks of open-label, once-daily treatment with VBZ (40 or 80 mg), of the 167 participants who entered the study. [c]AIMS items 8 to 10 represent clinical-rated assessment of the overall severity of abnormal movements (item 8), incapacitation due to abnormal movements (item 9), and participant's awareness of abnormal movements and distress level (item 10).
Correll CU, et al. *J Clin Psychopharmacol*. 2024;44(4):353-361.

KINECT 4 – Full Dataset Analysis: TEAEs

Participants, n (%)	Baseline to Week 4	Week 4 to Week 48		
	40 mg/day (n=163)	40 mg/day (n=35)	80 mg/day (n=107)	All participants[a] (n=153)
Any TEAE	36 (22.1)	22 (62.9)	66 (61.7)	99 (64.7)
Any serious TEAE	0	3 (8.6)	17 (15.9)	21 (13.7)
Any TEAE leading to discontinuation	6 (3.7)	7 (20.0)	11 (10.3)	18 (11.8)
Death	0	0	1 (0.9)[b]	1 (0.7)
TEAEs by preferred term[c]				
Urinary tract infection	2 (1.2)	3 (8.6)	9 (8.4)	13 (8.5)
Headache	7 (4.3)	2 (5.7)	6 (5.6)	8 (5.2)
Nasopharyngitis	2 (1.2)	1 (2.9)	4 (3.7)	7 (4.6)
Suicidal ideation	1 (0.6)	3 (8.6)	4 (3.7)	7 (4.6)
Constipation	1 (0.6)	2 (5.7)	2 (1.9)	6 (3.9)
Fall	0	1 (2.9)	3 (2.8)	6 (3.9)
Fatigue	6 (3.7)	3 (8.6)	3 (2.8)	6 (3.9)
Hypertension	0	0	4 (3.7)	6 (3.9)
Somnolence	6 (3.7)	0	4 (3.7)	6 (3.9)
Back pain	1 (0.6)	1 (2.9)	3 (2.8)	5 (3.3)
Dizziness	1 (0.6)	0	5 (4.7)	5 (3.3)

TEAE, treatment-emergent adverse event.
Week 4 was the end of treatment initiation with 40 mg/day; Week 48 was the end of open-label treatment.
[a]Includes 11 participants who had a dose reduction from 80 mg/day to 40 mg/day after Week 4. [b]Due to breast cancer and judged by the investigator as not related to valbenazine. [c]Reported in ≥3% of all participants during treatment initiation (baseline to Week 4) or after dose escalation (Week 4 to 48).
Marder SR, et al. *J Clin Psychopharmacology.* 2019;39(6):620-627.

KINECT 4 – Full Dataset Analysis: Psychiatric and Movement Scales Mean Score Change From Baseline

	Week 48						Week 52					
	40 mg/day		80 mg/day		All participants[a]		40 mg/day		80 mg/day		All participants[a]	
	n	Mean change (SD)	n	Mean change (SD)	n	Mean change (SD)	n	Mean change (SD)	n	Mean change (SD)	n	Mean change (SD)
Psychiatric scales												
PANSS positive[b]	14	-1.9 (2.4)	52	-0.6 (2.1)	71	-0.7 (2.5)	14	-1.5 (2.9)	52	-0.5 (2.1)	71	-0.6 (2.3)
PANSS negative[b]	14	-1.5 (4.8)	52	-0.6 (2.9)	71	-0.6 (3.3)	14	-0.2 (5.9)	52	0.0 (3.1)	71	0.0 (3.7)
PANSS general psychopathology[b]	14	-2.9 (5.6)	52	-1.8 (3.7)	71	-2.0 (4.5)	14	-1.7 (6.9)	52	-0.7 (4.5)	71	-1.0 (5.0)
CDSS total[b]	14	-0.2 (2.8)	52	-0.9 (2.2)	71	-0.7 (2.3)	14	-0.2 (3.2)	52	-0.6 (2.6)	71	-0.5 (2.6)
YMRS total[c]	6	-0.8 (2.3)	22	-0.2 (1.8)	32	-0.3 (1.7)	6	-1.2 (2.1)	22	-0.8 (1.4)	32	-0.8 (1.5)
MADRS total[c]	6	1.7 (3.9)	22	-0.4 (4.9)	32	-0.3 (5.0)	6	4.0 (8.1)	22	-0.4 (6.4)	32	0.0 (6.8)
Movement scales												
BARS total	20	-1.1 (2.2)	74	-1.0 (1.5)	103	-1.0 (1.7)	20	-1.0 (2.0)	74	-0.4 (1.6)	103	-0.5 (1.8)
SAS global	20	-0.1 (0.1)	74	-0.1 (0.2)	103	-0.1 (0.2)	20	-0.0 (0.2)	74	-0.1 (0.2)	103	-0.1 (0.2)

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.
Week 48 was the end of open-label treatment; Week 52 was the end of washout. Lower scores indicate less severity.
[a]Includes participants who had a dose reduction from 80 mg/day to 40 mg/day after Week 4. [b]PANSS and CDSS were administered to participants with schizophrenia/schizoaffective disorder. [c]YMRS and MADRS were administered to participants with a mood disorder.
Marder SR, et al. *J Clin Psychopharmacology.* 2019;39(6):620-627.

Summary

- Early and sustained clinically meaningful improvements in TD, as measured by AIMS and clinician- and participant-rated assessments, were seen with treatment completers on long-term VBZ for 48 weeks[1]
- Over half of the treatment completers reached the remission threshold* in TD after 48 weeks, defined as an AIMS score of 0 (“none”) or 1 (“minimal”) in each of the AIMS items 1-7 at Week 48.
- VBZ was generally well tolerated, with most TEAEs considered mild or moderate in intensity and without notable worsening in psychiatric symptoms or induction or worsening of akathisia or parkinsonism[2]

AIMS, Abnormal Involuntary Movement Scale; TD, tardive dyskinesia; TEAE, treatment-emergent adverse event; VBZ, valbenazine.
*Remission defined as “complete response” by study authors..
1. Correll CU, et al. *J Clin Psychopharmacol*. 2024;44(4):353-361. 2. Marder SR, et al. *J Clin Psychopharmacology*. 2019;39(6):620-627.

KINECT® 4 – Underlying Disease Diagnosis Analysis

KINECT 4 – Underlying Disease Diagnosis Analysis: Assessments

- All analyses were conducted in participants who received ≥1 dose of valbenazine and had any available post-baseline data
- All outcomes were analyzed descriptively with no statistical testing between diagnosis subgroups (schizophrenia/schizoaffective disorder, mood disorder)
- Effectiveness measures at Weeks 48 and 52 included:
  - Mean change from baseline in the Abnormal Involuntary Movement Scale (AIMS) total score (sum of items 1-7), scored by site raters
  - AIMS response, defined as ≥50% total score improvement from baseline
  - CGI-TD (assessed by site raters) and Patient Global Impression of Change (PGIC) mean scores (range from 1 “very much improved” to 7 “very much worse”) and PGIC response, defined as a score of 1 (“very much improved”) or 2 (“much improved”)
- Safety assessments included:
  - Treatment-emergent adverse events (TEAEs)
  - Psychiatric scales: Positive and Negative Syndrome Scale (PANSS) and Calgary Depression Scale for Schizophrenia (CDSS) in the schizophrenia/schizoaffective disorder subgroup; Young Mania Rating Scale (YMRS) and the Montgomery-Åsberg Depression Rating Scale (MADRS) in the mood disorder subgroup; Columbia-Suicide Severity Rating Scale (C-SSRS) in all participants
  - Clinical laboratory tests, vital signs, and electrocardiograms (ECGs)

Lindenmayer JP, et al. APA 2018; New York, NY.

KINECT 4 – Underlying Disease Diagnosis Analysis: Baseline Characteristics

- Of 167 enrolled participants, 163 had available post-baseline data and 103 completed the study; the most common reason for discontinuation was adverse events (n=26)
- Within each disorder subgroup, baseline characteristics were generally similar across treatment arms

	Schizophrenia/Schizoaffective Disorder (n=119)			Mood Disorder (n=44)		
	40 mg (n=37)	80 mg (n=76)	All[a] (n=119)	40 mg (n=8)	80 mg (n=31)	All[a] (n=44)
Age, mean (SD), years	57.1 (11.3)	57.3 (9.4)	56.9 (9.9)	55.8 (11.8)	59.2 (8.0)	58.8 (8.6)
Age at psychiatric diagnosis	30.9 (12.2)	28.0 (12.0)	28.8 (12.0)	40.6 (6.7)	36.9 (12.5)	36.8 (12.9)
Age at TD diagnosis	46.6 (11.5)	47.0 (10.8)	46.4 (11.3)	52.3 (12.9)	54.3 (11.2)	53.2 (12.4)
Male, n (%)	20 (54.1)	51 (67.1)	74 (62.2)	1 (12.5)	8 (25.8)	12 (27.3)
White, n (%)	20 (54.1)	48 (63.2)	73 (61.3)	6 (75.0)	26 (83.9)	37 (84.1)
BMI, mean (SD), kg/m^2	28.1 (6.0)	28.8 (5.5)	28.5 (5.6)	26.6 (6.0)	29.4 (5.3)	28.7 (5.2)
C-SSRS lifetime history, n (%)						
Suicidal ideation	14 (37.8)	21 (27.6)	37 (31.1)	3 (37.5)	15 (48.4)	20 (45.5)
Suicidal behavior	10 (27.0)	22 (28.9)	34 (28.6)	2 (25.0)	9 (29.0)	12 (27.3)
BPRS total score at screening, mean (SD)	29.9 (6.8)	27.3 (6.8)	28.2 (7.0)	26.0 (6.3)	27.3 (6.0)	27.1 (6.0)
AIMS total score by site raters, mean (SD)	14.4 (5.3)	14.7 (4.7)	14.5 (4.9)	13.1 (6.5)	15.7 (3.8)	14.9 (4.5)

[a]Includes 11 participants (schizophrenia/schizoaffective disorder, n=6; mood disorder, n=5) who had a dose reduction from 80 to 40 mg after Week 4.
AIMS, Abnormal Involuntary Movement Scale; BMI, body mass index; BPRS, Brief Psychiatric Rating Scale, C-SSRS, Columbia-Suicide Severity Scale; SD, standard deviation; TD, tardive dyskinesia.

Lindenmayer JP, et al. APA 2018; New York, NY.

KINECT 4 – Underlying Disease Diagnosis Analysis: Mean AIMS, CGI-TD and PGIC Scores

- Mean improvements in AIMS total score change from baseline to Week 48 were observed with valbenazine 40 and 80 mg in both diagnosis subgroups, with some loss of effect at Week 52 (after 4-week washout)
- CGI-TD and PGIC scores at Week 48 indicated TD improvement, with similar mean scores in both diagnosis subgroups

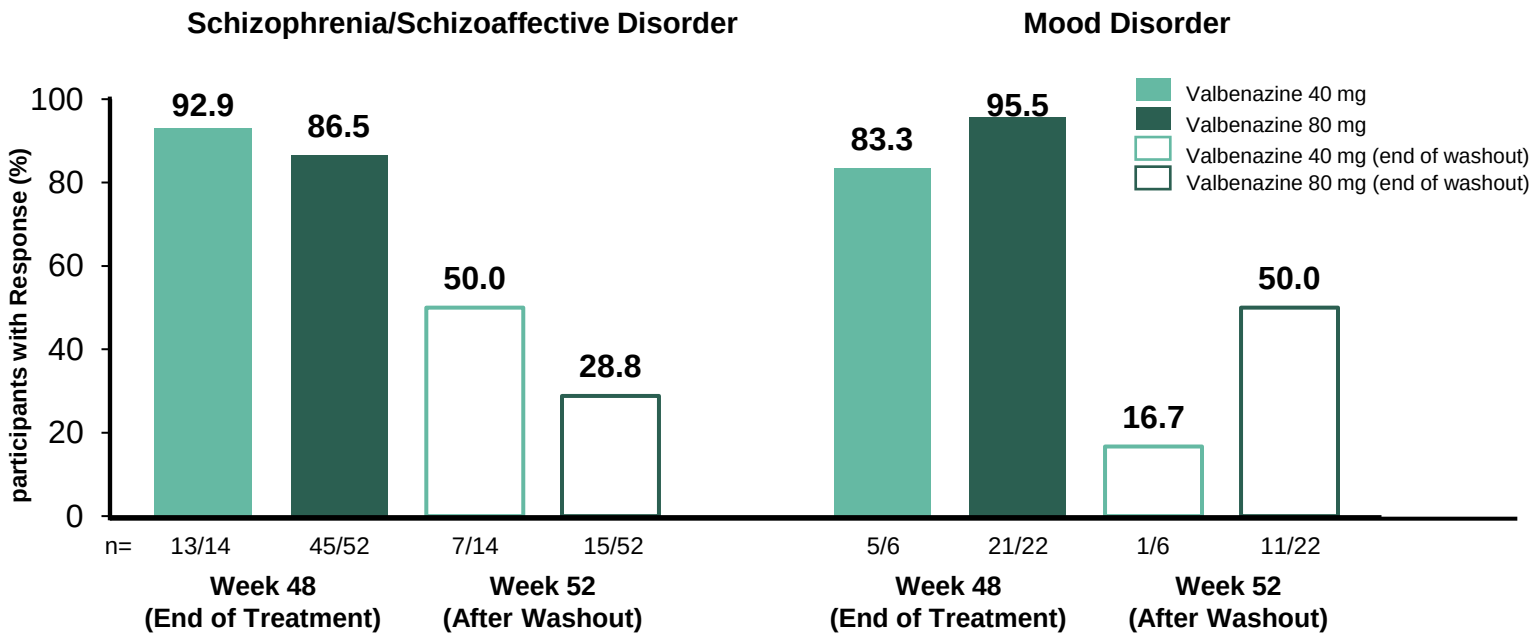
	Schizophrenia/Schizoaffective Disorder (n=66)		Mood Disorder (n=28)	
	40 mg (n=14)	80 mg (n=52)	40 mg (n=6)	80 mg (n=22)
AIMS score change from baseline by site raters, mean (SD)				
At Week 48	-10.1 (4.2)	-10.7 (4.4)	-10.2 (8.1)	-11.6 (4.2)
At Week 52	-5.1 (5.0)	-3.8 (5.6)	-0.7 (4.8)	-6.6 (6.1)
CGI-TD score by site raters, mean (SD)				
At Week 48	1.5 (0.5)	1.7 (0.6)	2.0 (0.9)	1.4 (0.5)
At Week 52	3.4 (1.9)	3.0 (1.6)	4.0 (1.8)	2.7 (1.7)
PGIC score, mean (SD)				
At Week 48	1.6 (0.7)	1.8 (0.9)	1.3 (0.5)	1.5 (0.6)
At Week 52	2.8 (1.9)	2.6 (1.6)	2.2 (2.4)	2.0 (1.6)

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

Lindenmayer JP, et al. APA 2018; New York, NY.

KINECT 4 – Underlying Disease Diagnosis Analysis: AIMS Response (≥50% Total Score Improvement from Baseline)

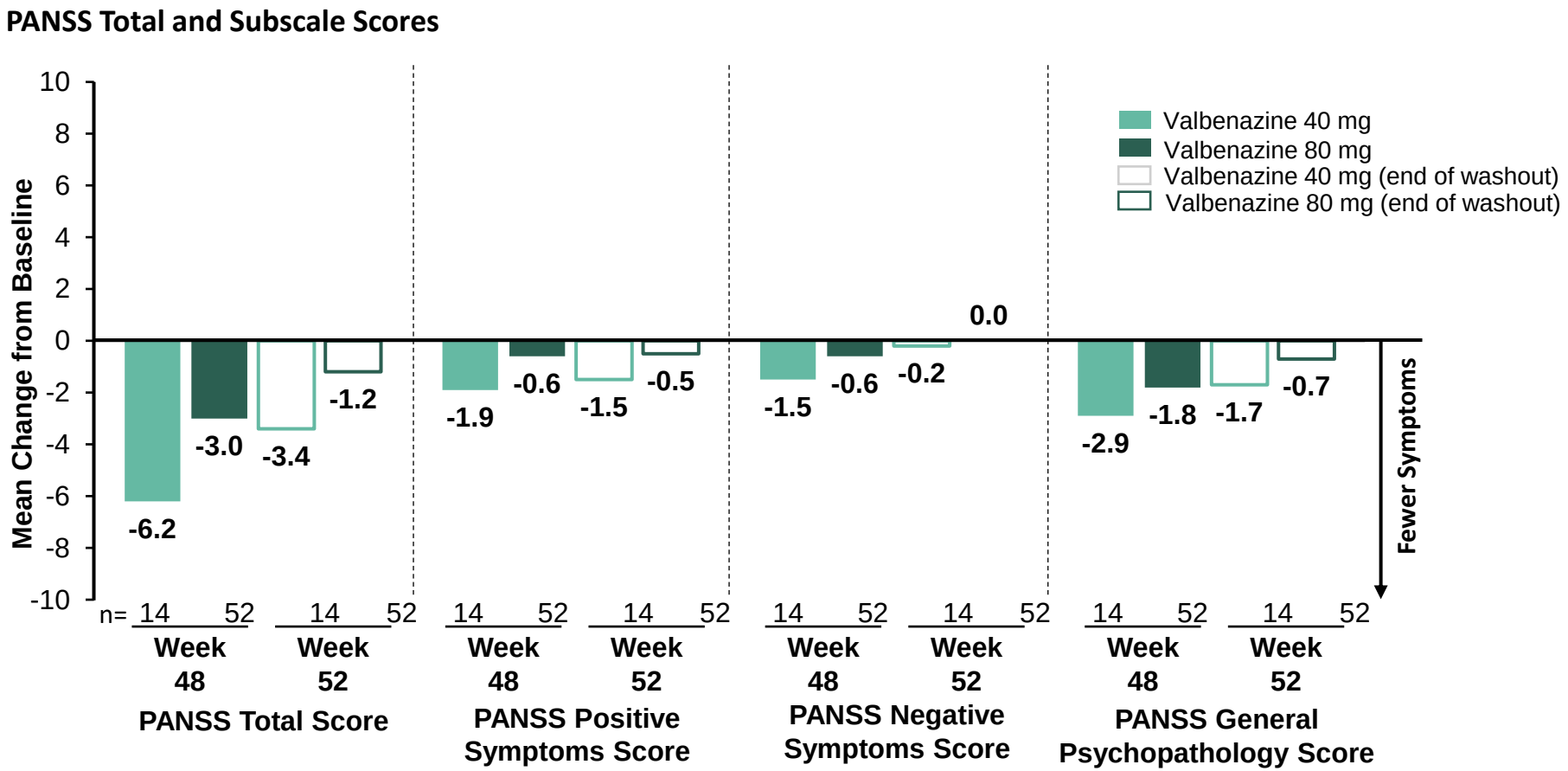
- At Week 48 in both diagnosis subgroups, >80% of participants receiving valbenazine achieved an AIMS response (≥50% total score improvement from baseline), with up to 50% of participants maintaining this response after washout



AIMS, Abnormal Involuntary Movement Scale (site raters).

Lindenmayer JP, et al. APA 2018; New York, NY.

KINECT 4 – Underlying Disease Diagnosis Analysis: Psychiatric Scale Mean Score Changes from Baseline

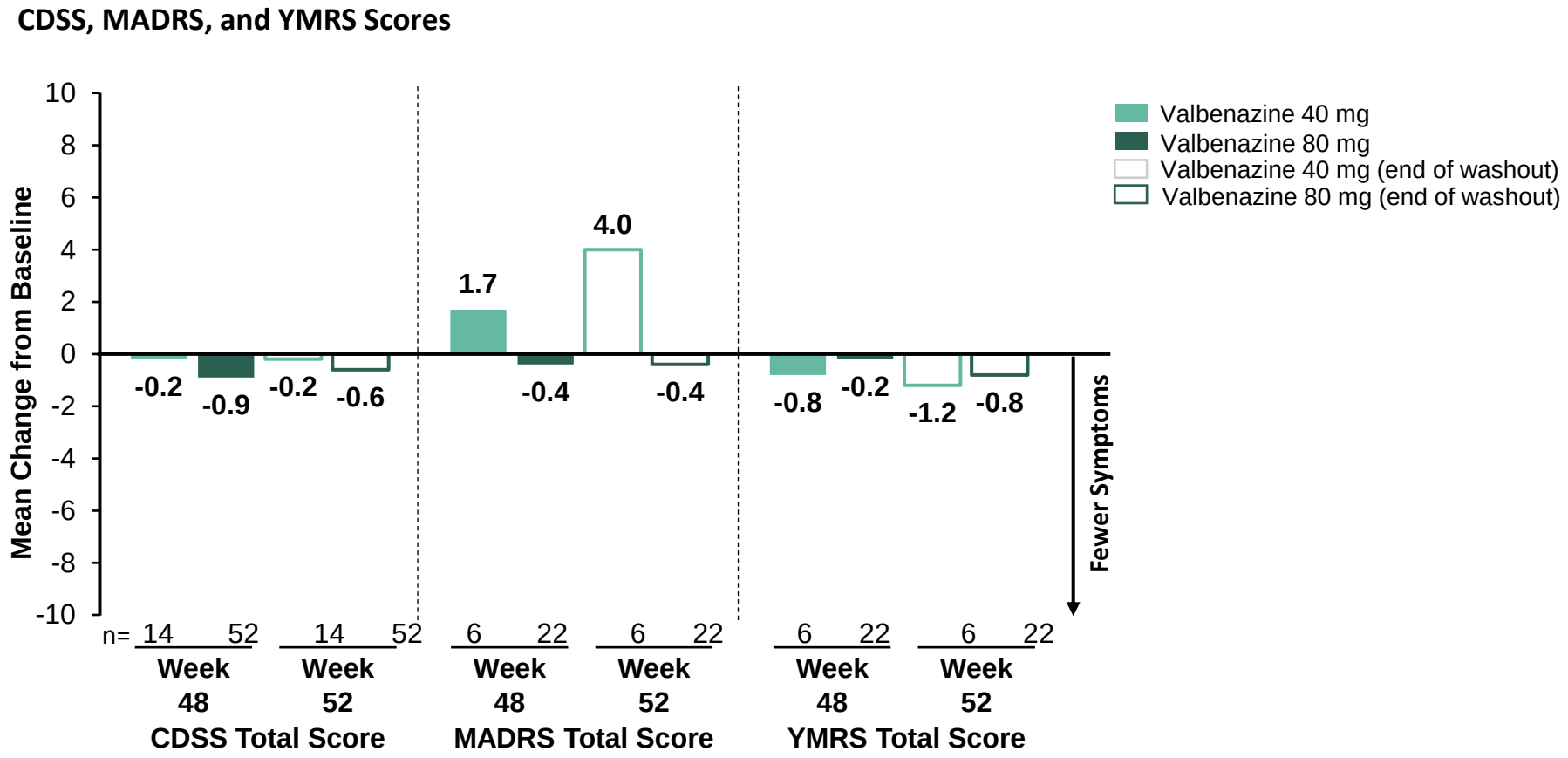


- Mean psychiatric scale scores generally remained stable during the study

[a]PANSS and CDSS administered to patients with schizophrenia/schizoaffective disorder
PANSS, Positive and Negative Syndrome Scale

Lindenmayer JP, et al. APA 2018; New York, NY.

KINECT 4 – Underlying Disease Diagnosis Analysis: Psychiatric Scale Mean Score Changes from Baseline



- Mean psychiatric scale scores generally remained stable during the study

[a]MADRS and YMRS administered to patients with a mood disorder
CDSS, Calgary Depression Scale for Schizophrenia; MADRS, Montgomery-Åsberg Depression Rating Scale; PANSS, Positive and Negative Syndrome Scale; YMRS, Young Mania Rating Scale

Lindenmayer JP, et al. APA 2018; New York, NY.

KINECT 4 – Underlying Disease Diagnosis Analysis: Safety Results

- TEAEs were reported more frequently in the mood disorder subgroup than in the schizophrenia/schizoaffective disorder subgroup
  - TEAEs reported in ≥10% of participants in the mood disorder subgroup were urinary tract infection (18.2%) and headache (15.9%)
  - No TEAEs were reported in ≥10% of participants with schizophrenia/schizoaffective disorder
  - No serious TEAEs were reported in >1 participant, except for diverticulitis, schizophrenia, and suicidal ideation (all n=2); all of these events resolved
- In participants with no suicidal ideation at baseline (C-SSRS score=0), >90% continued to have no suicidal ideation throughout the study (baseline to Week 52): schizophrenia/schizoaffective disorder, 95.7% (110/115); mood disorder, 93.0% (40/43)
  - Of the 5 participants who had suicidal ideation at baseline (C-SSRS score=1 to 3), none had any worsening during the study
  - No participants had a C-SSRS score of 4 or 5 at baseline
- Changes from baseline in movement scale scores, vital signs, ECG parameters, and laboratory test values were generally small and not clinically meaningful; values were similar in diagnosis subgroups

Lindenmayer JP, et al. APA 2018; New York, NY.

KINECT 4 – Underlying Disease Diagnosis Analysis: Treatment-Emergent Adverse Events

	Schizophrenia/Schizoaffective Disorder			Mood Disorder		
	40 mg (n=37)	80 mg (n=76)	All[a] (n=119)	40 mg (n=8)	80 mg (n=31)	All[a] (n=44)
Summary, n (%)						
Any TEAE	24 (64.9)	43 (56.6)	73 (61.3)	8 (100.0)	24 (77.4)	37 (84.1)
Serious TEAE	3 (8.1)	12 (15.8)	16 (13.4)	0	5 (16.1)	5 (11.4)
TEAE leading to study discontinuation	12 (32.4)	9 (11.8)	21 (17.6)	1 (12.5)	2 (6.5)	3 (6.8)
Death	0	1 (1.3)[b]	1 (0.8)[b]	0	0	0
Common TEAEs, n (%)[c]						
Arthralgia	0	1 (1.3)	1 (0.8)	0	2 (6.5)	3 (6.8)
Back pain	0	2 (2.6)	2 (1.7)	1 (12.5)	1 (3.2)	3 (6.8)
Bronchitis	0	0	0	0	3 (9.7)	4 (9.1)
Chronic obstructive pulmonary disease	0	0	0	0	3 (9.7)	3 (6.8)
Constipation	1 (2.7)	1 (1.3)	4 (3.4)	1 (12.5)	1 (3.2)	3 (6.8)
Dizziness	0	2 (2.6)	2 (1.7)	0	4 (12.9)	4 (9.1)
Fatigue	4 (10.8)	3 (3.9)	7 (5.9)	3 (37.5)	1 (3.2)	4 (9.1)
Headache	2 (5.4)	6 (7.9)	8 (6.7)	3 (37.5)	3 (9.7)	7 (15.9)
Hypertension	0	3 (3.9)	3 (2.5)	0	1 (3.2)	3 (6.8)
Insomnia	2 (5.4)	1 (1.3)	3 (2.5)	1 (12.5)	1 (3.2)	3 (6.8)
Nasopharyngitis	1 (2.7)	5 (6.6)	7 (5.9)	0	1 (3.2)	2 (4.5)
Somnolence	4 (10.8)	3 (3.9)	8 (6.7)	1 (12.5)	1 (3.2)	4 (9.1)
Suicidal ideation	2 (5.4)	3 (3.9)	5 (4.2)	1 (12.5)	2 (6.5)	3 (6.8)
Urinary tract infection	2 (5.4)	3 (3.9)	6 (5.0)	1 (12.5)	7 (22.6)	8 (18.2)

[a]Includes 11 participants (schizophrenia/schizoaffective disorder, n=6; mood disorder, n=5) who had a dose reduction from 80 mg to 40 mg after Week 4; [b]Due to breast cancer and judged by the investigator as not related to valbenazine; [c]MedDRA preferred terms reported in ≥5% of all participants in either diagnosis subgroup; MedDRA, Medical Dictionary for Regulatory Activities; TEAE, treatment-emergent adverse event

Lindenmayer JP, et al. APA 2018; New York, NY.

KINECT 4 – Underlying Disease Diagnosis Analysis: Summary

- Sustained tardive dyskinesia improvements were observed in participants with schizophrenia/schizoaffective disorder or mood disorder who received up to 48 weeks of open-label treatment with once-daily valbenazine
- Loss of improvement was observed in both diagnosis subgroups after 4-week washout, suggesting that patients may require ongoing therapy with valbenazine to maintain effect
- Treatment-emergent adverse events were reported more frequently in the mood disorder subgroup than in the schizophrenia/schizoaffective disorder subgroup
- Psychiatric scale mean scores generally remained stable
- In participants with no suicidal ideation at baseline (C-SSRS score=0), >90% continued to have no suicidal ideation throughout the study (baseline to Week 52):
  - Schizophrenia/schizoaffective disorder: 95.7% (110/115)
  - Mood disorder: 93.0% (40/43)

Lindenmayer JP, et al. APA 2018; New York, NY.

KINECT ® 4 – Age Analysis

KINECT 4 – Age Analysis: Assessments

- All analyses were conducted in younger (18 to <55 years) and older (≥55 to 85 years) participants who received ≥1 dose of valbenazine and had any available post-baseline data
- The effects of valbenazine on TD were evaluated at Week 48 (end of treatment) and Week 52 (end of 4-week washout) using the following measures:
  - Abnormal Involuntary Movement Scale (AIMS) total score (sum of items 1-7; scored by site raters): mean change from baseline and response (≥50% total score improvement from baseline)
  - CGI-TD (scored by site raters): mean scores and response (score ≤2 [“much improved” or “very much improved”])
- Differences between age subgroups were analyzed descriptively

Johnson J, et al. GAPNA 2018; Washington, DC.

KINECT 4 – Age Analysis: Baseline Characteristics

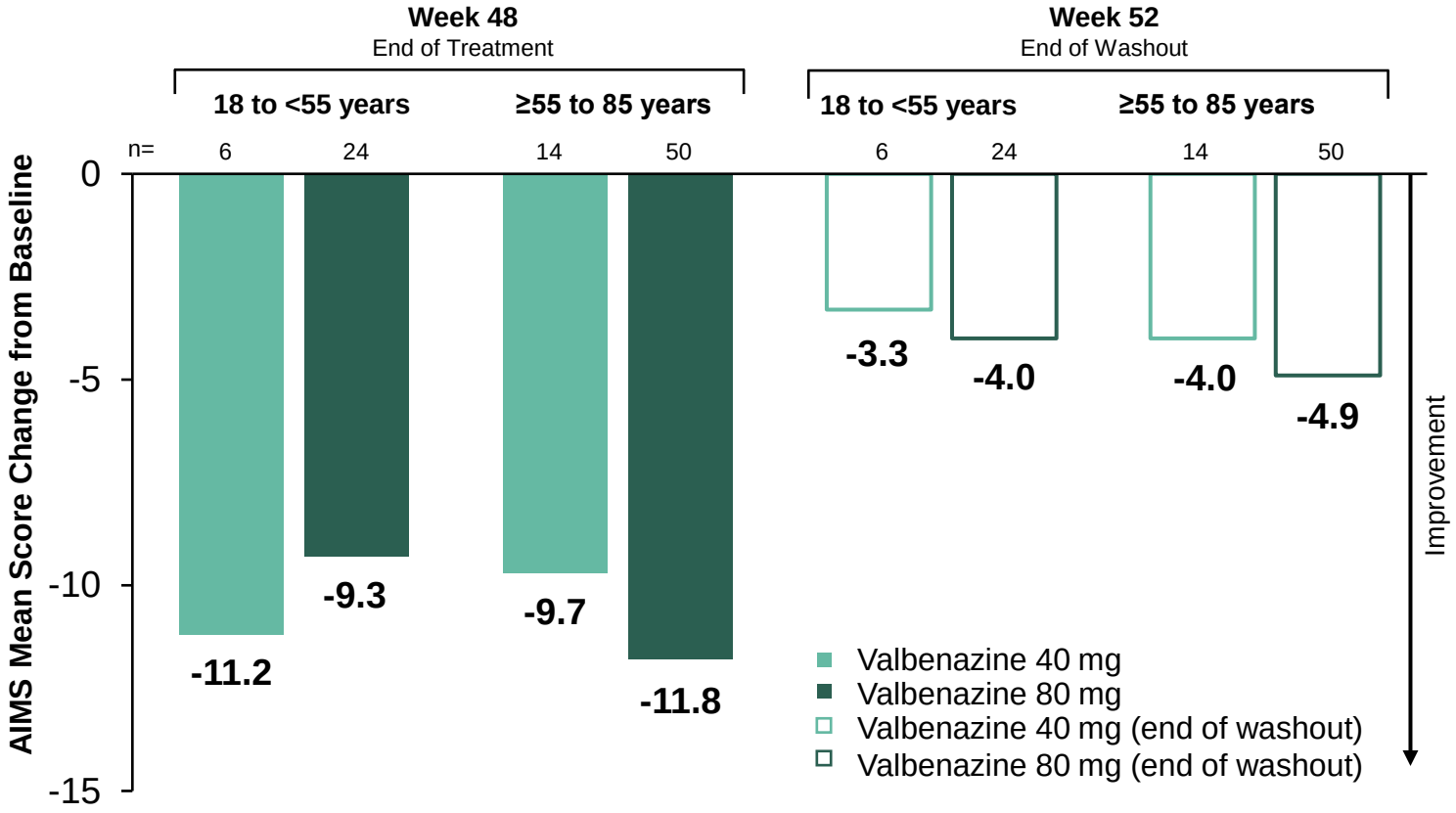
	18 to <55 Years			≥55 to 85 Years		
	40 mg (n=16)	80 mg (n=37)	All[a] (n=58)	40 mg (n=29)	80 mg (n=70)	All[b] (n=105)
Age, mean (SD), years	45.1 (7.6)	48.5 (6.3)	47.6 (6.7)	63.3 (6.7)	62.8 (5.7)	62.9 (5.9)
Age, median (min, max), years	45.5 (30, 54)	51 (32, 54)	49.5 (30, 54)	61 (55, 80)	61.5 (55, 82)	61 (55, 82)
Male, n (%)	5 (31.3)	18 (48.6)	26 (44.8)	16 (55.2)	41 (58.6)	60 (57.1)
White, n (%)	6 (37.5)	19 (51.4)	29 (50.0)	20 (69.0)	55 (78.6)	81 (77.1)
BMI, mean (SD), kg/m^2	27.5 (7.3)	29.7 (5.3)	28.8 (5.9)	28.0 (5.2)	28.6 (5.5)	28.4 (5.2)
Schizophrenia/schizoaffective disorder, n (%)	13 (81.3)	28 (75.7)	45 (77.6)	24 (82.8)	48 (68.6)	74 (70.5)
BPRS total score at screening, mean (SD)	30.0 (6.7)	27.4 (6.6)	28.4 (6.8)	28.8 (6.9)	27.3 (6.6)	27.6 (6.6)
AIMS total score at baseline (site raters), mean (SD)	14.3 (5.7)	14.5 (4.4)	14.2 (4.8)	14.1 (5.4)	15.3 (4.5)	14.9 (4.8)

[a]Includes 5 participants who had a dose reduction from 80 to 40 mg after Week 4
[b]Includes 6 participants who had a dose reduction from 80 to 40 mg after Week 4
AIMS, Abnormal Involuntary Movement Scale; BMI, body mass index; BPRS, Brief Psychiatric Rating Scale; SD, standard deviation

- Baseline characteristics were generally similar across treatment groups and age subgroups

Johnson J, et al. GAPNA 2018; Washington, DC.

KINECT 4 – Age Analysis: AIMS Mean Score Change from Baseline (Site Raters)

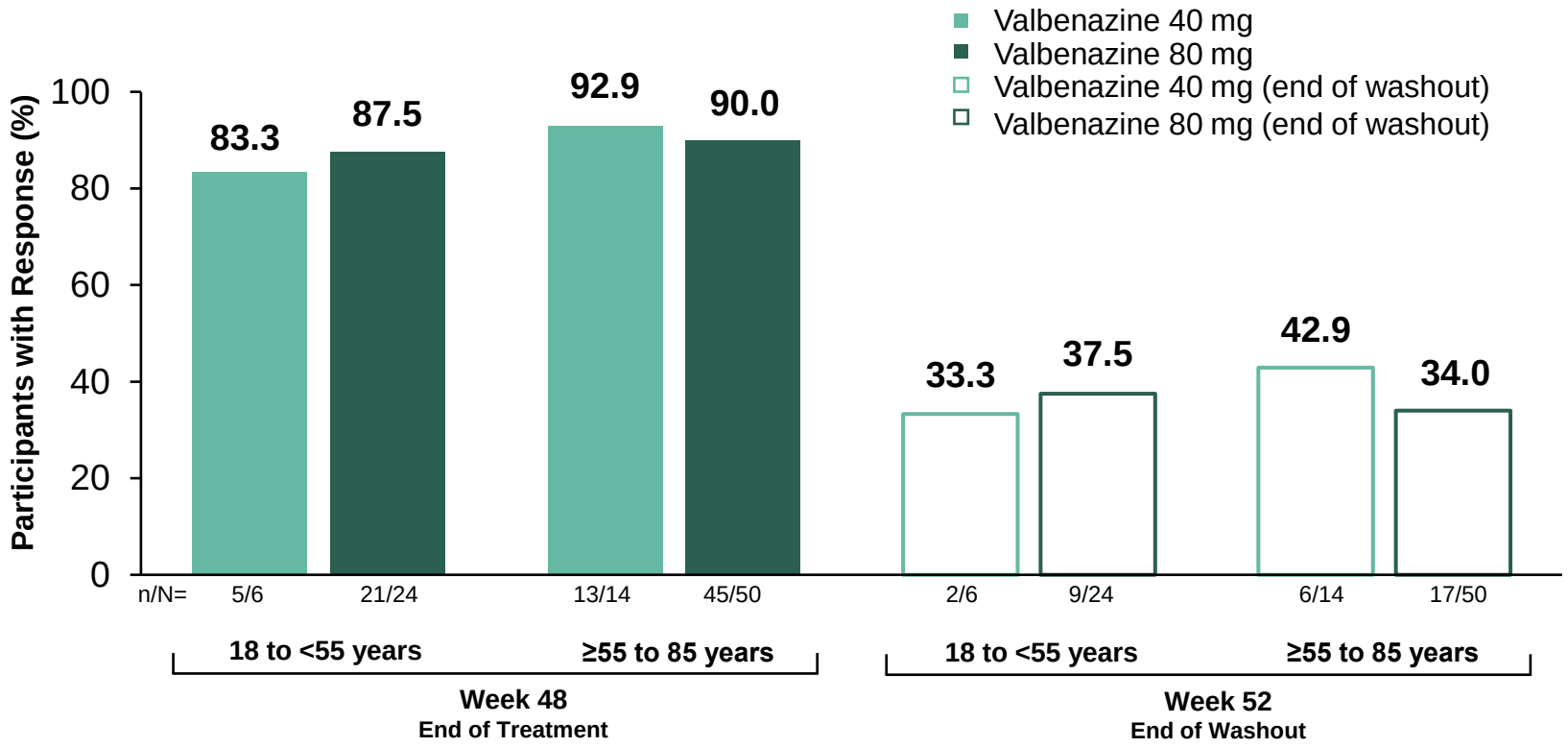


- At Week 48 (end of treatment), mean improvements from baseline in AIMS total score were observed in both younger and older participants
  - A return towards baseline levels was observed at Week 52 (end of washout) in both age subgroups

AIMS, Abnormal Involuntary Movement Scale.

Johnson J, et al. GAPNA 2018; Washington, DC.

KINECT 4 – Age Analysis: AIMS Response (≥ 50% Improvement from Baseline)

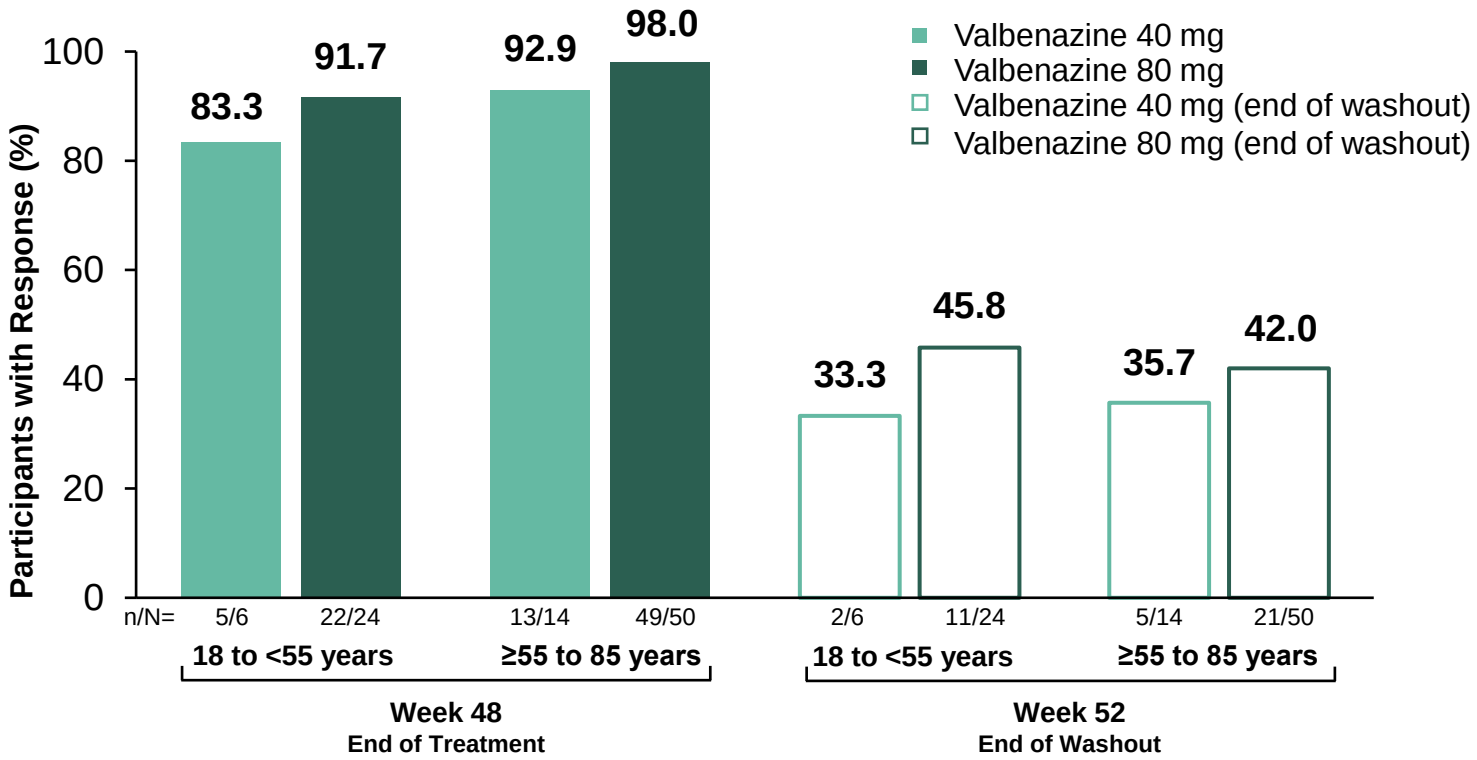


- At Week 48, >80% of participants in both age subgroups had an AIMS response (≥50% total score improvement from baseline)
  - The percentage of participants with an AIMS response decreased at Week 52 (after washout) in both subgroups

AIMS, Abnormal Involuntary Movement Scale.

Johnson J, et al. GAPNA 2018; Washington, DC.

KINECT 4 – Age Analysis: CGI-TD Response (Score ≤2)



- At Week 48, >80% of participants in both age subgroups had a CGI-TD response (rating of "much improved" or "very much improved")
  - The percentage of participants with a CGI-TD response decreased at Week 52 (after washout) in both subgroups

CGI-TD, Clinical Global Impression of Change-Tardive Dyskinesia

Johnson J, et al. GAPNA 2018; Washington, DC.

KINECT 4 – Age Analysis: Summary

- Consistent and clinically meaningful tardive dyskinesia improvements were found in both younger and older adults (18 to <55 and ≥55 to 85 years) who received up to 48 weeks of treatment with once-daily valbenazine[1]
- More than 80% of younger and 90% of older adults achieved an AIMS or CGI-TD response after long-term treatment (Week 48)[1]
- A loss of effect was generally found in both age subgroups after a 4-week washout, suggesting that patients may require ongoing therapy with valbenazine to maintain TD improvements[1]
- 64.7% of all participants had ≥1 treatment-emergent adverse event after Week 4 through Week 48 in the KINECT 4 study[2]

1. Johnson J, et al. GAPNA 2018; Washington, DC. 2. Marder SR, et al. ACNP 2017; Palm Springs, CA.

KINECT® 4 – AIMS Response and Shift Analyses by Age

KINECT 4 – AIMS Response and Shift Analyses by Age: Assessments

- Three sets of outcomes were analyzed post hoc based on AIMS total score (sum of items 1–7) or AIMS items (representing 7 different body regions), as rated by site investigators:
  - AIMS total score response: ≥10% to 100% improvement from baseline at Week 48 (end of treatment), with certain thresholds defined descriptively:
    - Minimal response: ≥10% improvement
    - Clinically meaningful response: ≥30% improvement
    - Robust response: ≥50% improvement
    - Maximal response: 80–100% improvement
  - AIMS item response: score ≤2 (“none” to “mild”) or score ≤1 (“none” to “minimal”) at Week 48
  - AIMS item shift: score ≥3 (“moderate” or “severe”) at baseline and score ≤2 at Week 48
- Safety assessments included treatment-emergent adverse events (TEAEs)
- All outcomes were analyzed for comparison between younger (18 to <55 years) and older (≥55 to 85 years) participants across both valbenazine doses

Sajatovic M, et al. Poster intended for presentation at AAGP 2020; San Antonio, TX.

KINECT 4 – AIMS Response and Shift Analyses by Age: Baseline Characteristics

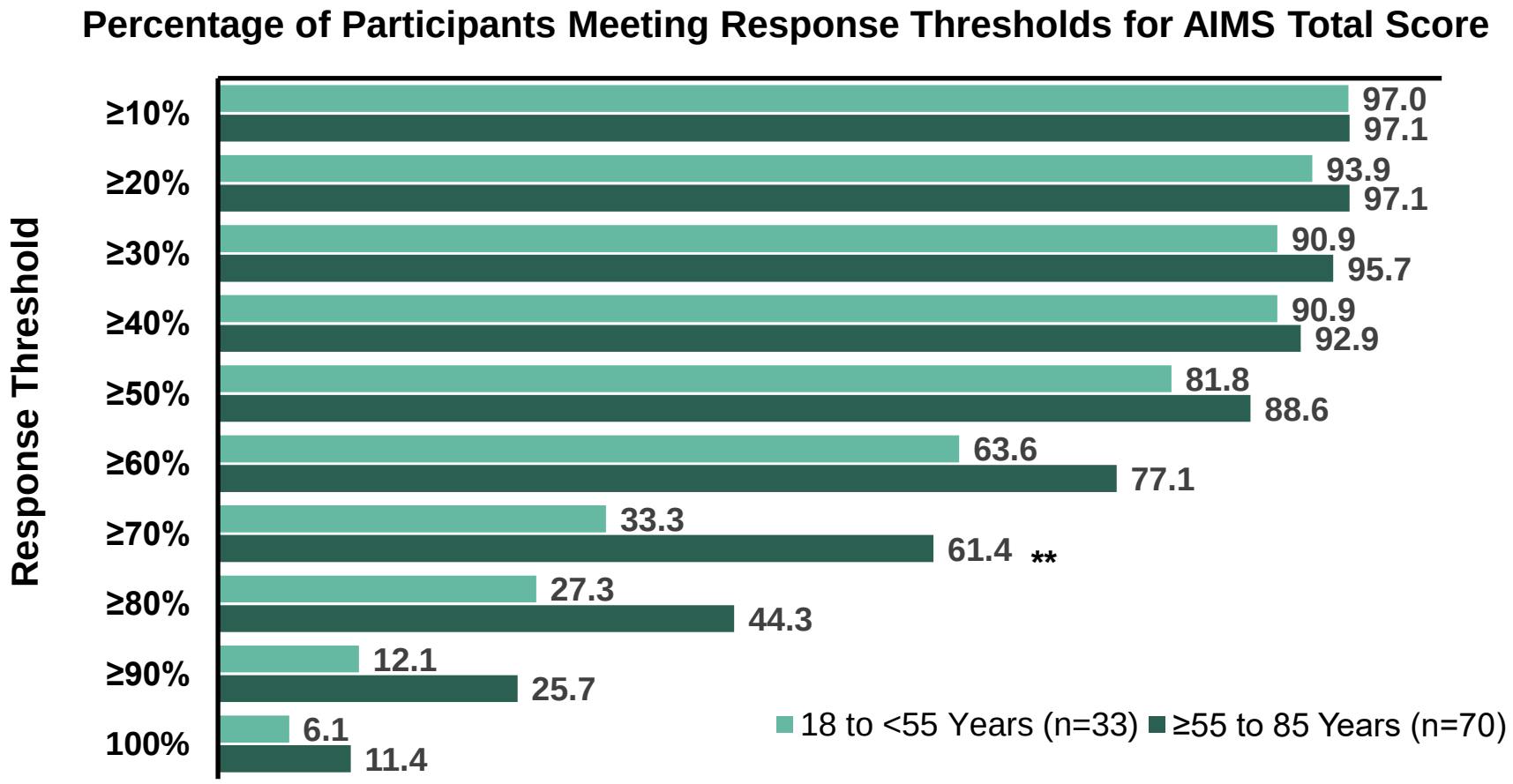
	18 to <55 Years (n=33)	≥55 to 85 Years (n=70)
Age, mean (SD), years	48.5 (5.8)	62.7 (6.0)
Age, median (min, max), years	51.0 (33, 54)	61.0 (55, 82)
Male, n (%)	14 (42.4)	35 (50.0)
White, n (%)	21 (63.6)	57 (81.4)
BMI, mean (SD), kg/m^2	30.0 (4.9)	28.1 (5.3)
Schizophrenia/schizoaffective disorder, n (%)	26 (78.8)	45 (64.3)
BPRS total score, mean (SD)	26.6 (5.3)	26.6 (6.3)
AIMS total score, mean (SD)	14.2 (4.4)	15.2 (4.9)

AIMS, Abnormal Involuntary Movement Scale; BMI, body mass index; BPRS, Brief Psychiatric Rating Scale; SD, standard deviation.

- Mean ages in the younger and older subgroups were 48.5 and 62.7 years, respectively
- Other baseline characteristics were generally similar between age subgroups

Sajatovic M, et al. Poster intended for presentation at AAGP 2020; San Antonio, TX.

KINECT 4 – AIMS Response and Shift Analyses by Age: Response Thresholds



**P<0.01 for 18 to <55 years versus ≥55 to 85 years; AIMS, Abnormal Involuntary Movement Scale.

Sajatovic M, et al. Poster intended for presentation at AAGP 2020; San Antonio, TX.

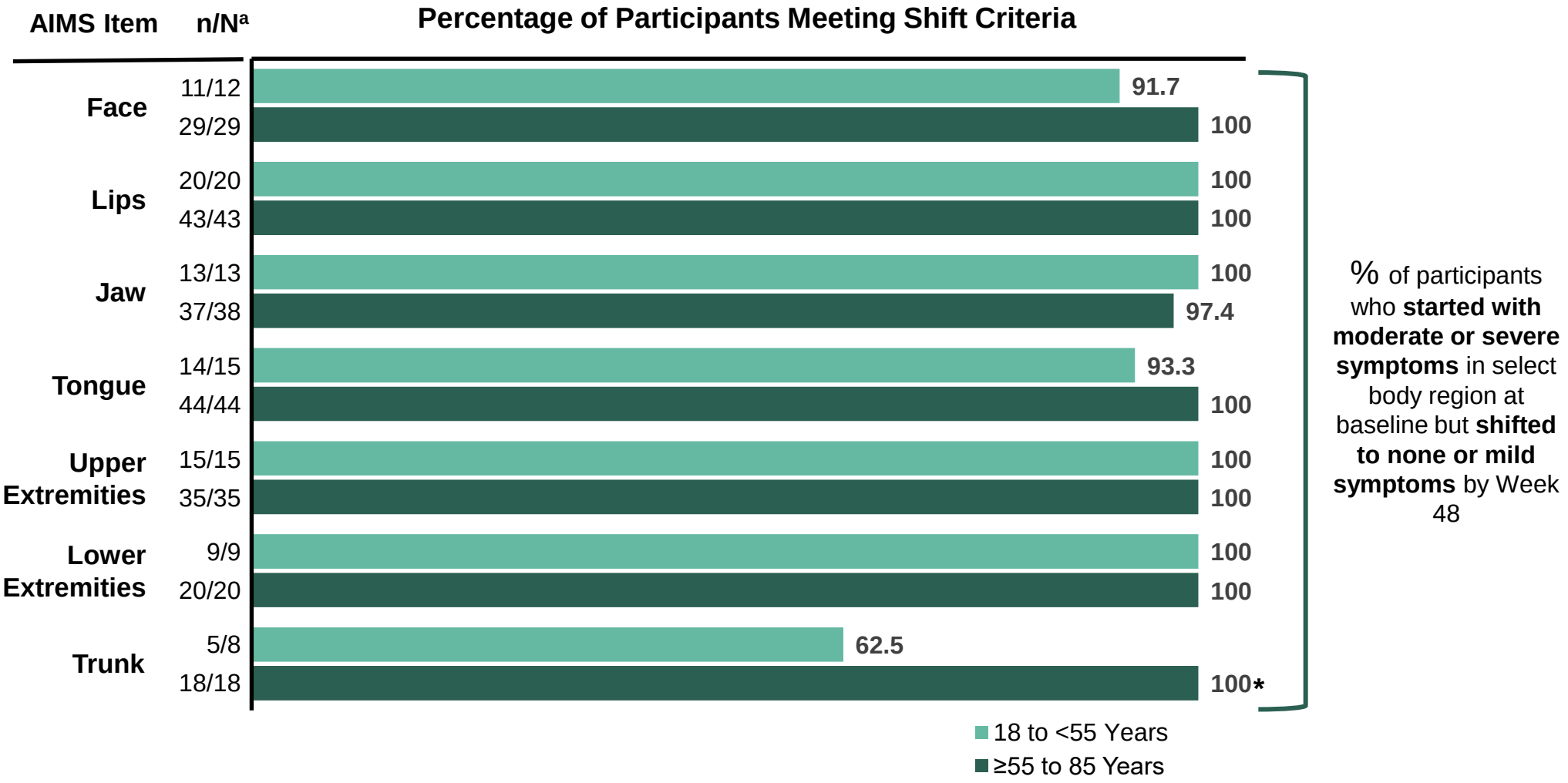
KINECT 4 – AIMS Response and Shift Analyses by Age: Response Thresholds for AIMS Item Score

AIMS Item, n (%)	Score ≤2 at Week 48: "None" to "Mild"		Score ≤1 at Week 48: "None" or "Minimal"	
	18 to <55 Years (n=33)	≥55 to 85 Years (n=70)	18 to <55 Years (n=33)	≥55 to 85 Years (n=70)
Face	31 (93.9)	70 (100)	30 (90.9)	65 (92.9)
Lips	33 (100)	70 (100)	29 (87.9)	61 (87.1)
Jaw	33 (100)	69 (98.6)	23 (69.7)	62 (88.6)*
Tongue	32 (97.0)	69 (98.6)	27 (81.8)	55 (78.6)
Upper Extremities	33 (100)	70 (100)	30 (90.9)	66 (94.3)
Lower Extremities	33 (100)	69 (98.6)	27 (81.8)	66 (94.3)
Trunk	30 (90.9)	70 (100)*	28 (84.8)	67 (95.7)

*P<0.05 for 18 to <55 years versus ≥55 to 85 years; AIMS, Abnormal Involuntary Movement Scale.

Sajatovic M, et al. Poster intended for presentation at AAGP 2020; San Antonio, TX.

KINECT 4 – AIMS Response and Shift Analyses by Age: AIMS Item Shifts



% of participants who **started with moderate or severe symptoms** in select body region at baseline but **shifted to none or mild symptoms** by Week 48

*P<0.05 for 18 to <55 years versus ≥55 to 85 years; [a]N represents the number of participants who had a score ≥3 (“moderate” or “severe”) at baseline; n represents the number of those participants who shifted to a score ≤2 (“none” to “mild”) at Week 48.
AIMS, Abnormal Involuntary Movement Scale.

Sajatovic M, et al. Poster intended for presentation at AAGP 2020; San Antonio, TX.

KINECT 4 – AIMS Response and Shift Analyses by Age: TEAEs

	18 to <55 Years (n=33)	≥55 to 85 Years (n=70)
Summary, n (%)		
Any TEAE[a]	18 (54.5)	49 (70.0)
Any TEAE leading to discontinuation[a]	0	0
Any serious TEAE[a]	0	9 (12.9)
Death[a]	0	0
Common TEAEs[b], n (%)		
Headache	2 (6.1)	8 (11.4)
Somnolence	1 (3.0)	7 (10.0)
Nasopharyngitis	1 (3.0)	6 (8.6)
Urinary tract infection	4 (12.1)	5 (7.1)
Constipation	1 (3.0)	4 (5.7)
Dizziness	0	4 (5.7)
Hypertension	1 (3.0)	4 (5.7)
Salivary hypersecretion	0	4 (5.7)
Fatigue	2 (6.1)	3 (4.3)
Neutropenia	2 (6.1)	0

[a]Not significant for 18 to <55 years versus ≥55 to 85 years; [b]Reported in ≥5% of participants in either age subgroup. Statistics were not conducted for individual common TEAEs.
TEAE, treatment-emergent adverse event.

Sajatovic M, et al. Poster intended for presentation at AAGP 2020; San Antonio, TX.

KINECT 4 – AIMS Response and Shift Analyses by Age: Summary

- The percentages of participants who met response thresholds for AIMS total score at Week 48 were generally similar between the younger (18 to <55 years) and older (≥55 to 85 years) subgroups, with no statistically significant differences for most outcomes (all P>0.05 except for ≥70% threshold)
  - >90% of participants in both subgroups met the threshold for minimal response (≥10% AIMS total score improvement) and clinically meaningful response (≥30% improvement)
  - >80% met the threshold for a robust response (≥50% improvement)
  - Maximal response (80–100% improvement) was reached in 27.3% and 44.3% of younger and older participants, respectively
- Headache, somnolence, and urinary tract infection were the only TEAEs to occur in ≥10% of participants in either age subgroup
  - Younger: 6.1%, 3.0%, 12.1%, respectively
  - Older: 11.4%, 10.0%, 7.1%, respectively

Sajatovic M, et al. Poster intended for presentation at AAGP 2020; San Antonio, TX.

KINECT® 4 – AIMS Shift Analysis

KINECT 4 – AIMS Shift Analysis: Assessments

- AIMS was scored at baseline, Week 48 (end of treatment), and Week 52 (after 4-week washout) by site raters (i.e., investigators or other trained and qualified individuals)
- Shift analyses were based on AIMS items 1-7, with each item scored on a 0 to 4 scale
  - 0=no dyskinesia
  - 1=minimal or slight dyskinesia: low amplitude present during some but not most of the exam
  - 2=mild dyskinesia: low amplitude and present during most of the exam (or moderate amplitude and present during some of the exam)
  - 3=moderate dyskinesia: moderate amplitude and present during most of the exam
  - 4=severe dyskinesia: maximal amplitude and present during most of the exam
- Category shifts for AIMS items 1-7 defined as an improvement from score ≥3 (moderate/severe) at baseline to score ≤2 (mild/minimal/none) at Week 48 and Week 52

Comella CL, et al. MDS 2018; Hong Kong, China.

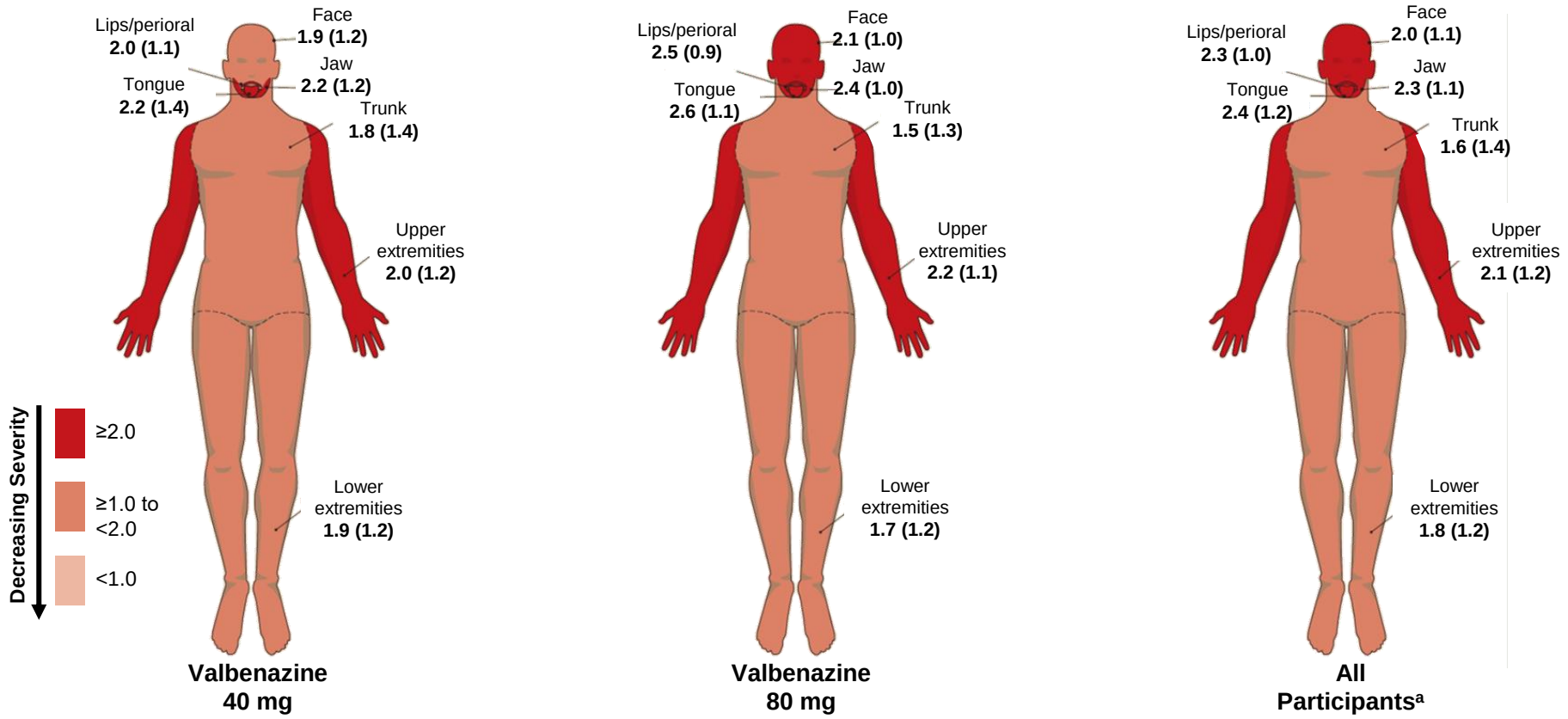
KINECT 4 – AIMS Shift Analysis: Baseline Characteristics

	Valbenazine 40 mg (n=45)	Valbenazine 80 mg (n=107)	All Participants[a] (n=163)
Age, mean (SD), years			
Mean (SD)	56.8 (11.2)	57.8 (9.0)	57.4 (9.6)
Median (min, max)	58 (30, 80)	59 (32, 82)	58 (30, 82)
Male, n (%)	21 (46.7)	59 (55.1)	86 (52.8)
Race, n (%)			
White/Caucasian	26 (57.8)	74 (69.2)	110 (67.5)
Black/African-American	16 (35.6)	31 (29.0)	48 (29.4)
Other	3 (6.7)	2 (1.9)	5 (3.1)
Body mass index, mean (SD), kg/m^2	27.8 (6.0)	29.0 (5.4)	28.5 (5.5)

[a]Includes 11 participants who had a dose reduction from 80 to 40 mg after Week 4
SD, standard deviation

Comella CL, et al. MDS 2018; Hong Kong, China.

KINECT 4 – AIMS Shift Analysis: Mean (SD) AIMS Item Scores at Baseline

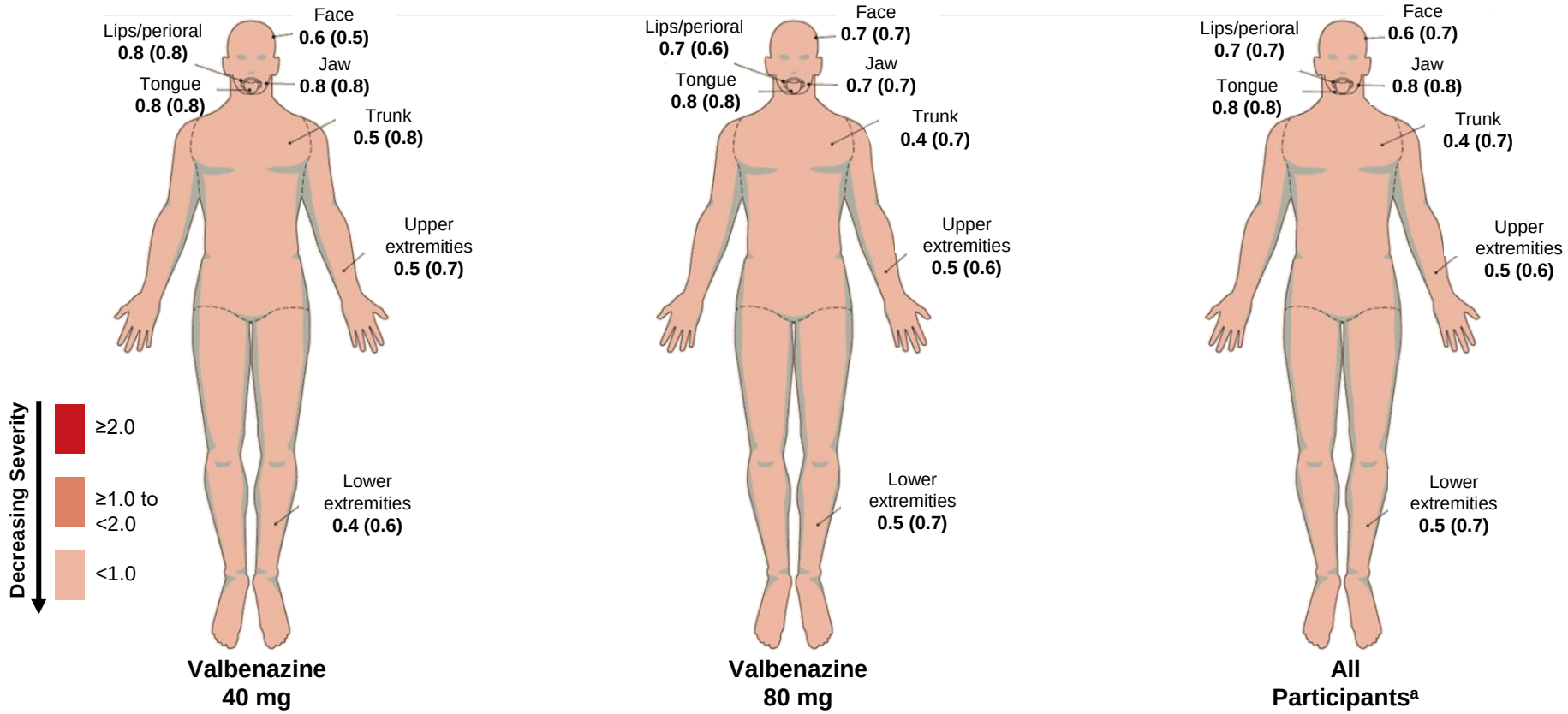


No AIMS item had a mean score >3.0 at baseline, Week 48, or Week 52
[a]Includes the 11 participants who had a dose reduction from 80 to 40 mg after Week 4
AIMS, Abnormal Involuntary Movement Scale; SD, standard deviation

- At baseline in all participants (combined 40 mg and 80 mg), mean AIMS item scores at baseline ranged from >2.0 to 3.0 (mild to moderate) in all regions except the trunk and lower extremities

Comella CL, et al. MDS 2018; Hong Kong, China.

KINECT 4 – AIMS Shift Analysis: Mean (SD) AIMS Item Scores at Week 48

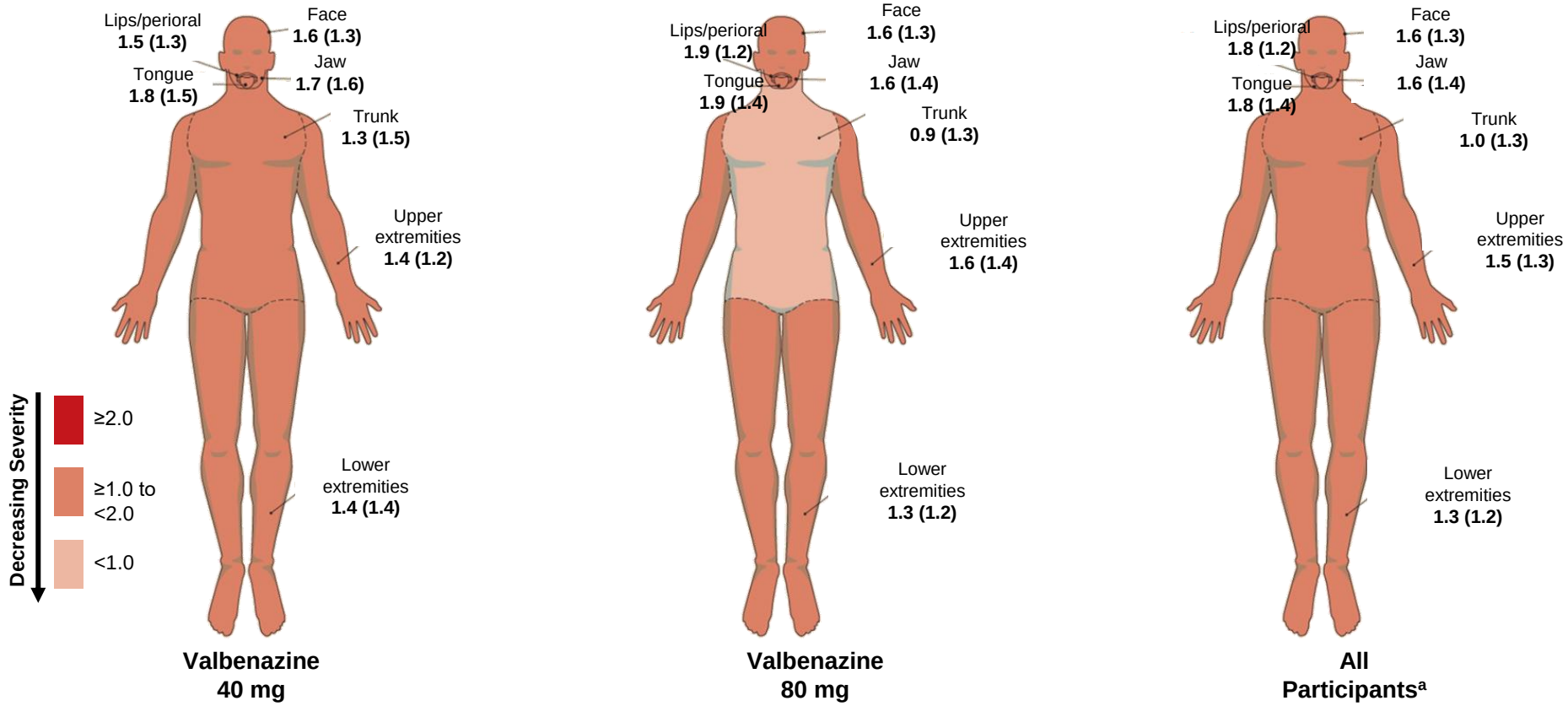


No AIMS item had a mean score >3.0 at baseline, Week 48, or Week 52
[a]Includes the 11 participants who had a dose reduction from 80 to 40 mg after Week 4
AIMS, Abnormal Involuntary Movement Scale; SD, standard deviation

- At Week 48, mean AIMS item scores ≤1 (none to minimal) were observed in all participants in all body regions
  - From baseline to Week 48, mean AIMS item scores improved by >50% in all body regions; regions with ≥70% mean improvement were face (70%), lips (70%), upper extremities (76%), lower extremities (72%), and trunk (75%)

Comella CL, et al. MDS 2018; Hong Kong, China.

KINECT 4 – AIMS Shift Analysis: Mean (SD) AIMS Item Scores at Week 52



No AIMS item had a mean score >3.0 at baseline, Week 48, or Week 52
[a]Includes the 11 participants who had a dose reduction from 80 to 40 mg after Week 4
AIMS, Abnormal Involuntary Movement Scale; SD, standard deviation

- At Week 52 (after 4-week washout), mean AIMS item scores reverted towards baseline levels

Comella CL, et al. MDS 2018; Hong Kong, China.

KINECT 4 – AIMS Shift Analysis: Participants with Shift Criteria at Week 48 & Week 52

Shift, n/N (%)	Body Region (AIMS Items 1-7)						
	Face	Lips	Jaw	Tongue	Upper Extremities	Lower Extremities	Trunk
At Week 48							
Valbenazine 40 mg	9/9 (100)	6/6 (100)	10/10 (100)	11/11 (100)	8/8 (100)	5/5 (100)	7/8 (88)
Valbenazine 80 mg	28/29 (97)	53/53 (100)	38/38 (100)	44/45 (98)	40/40 (100)	22/22 (100)	16/18 (89)
All Participants[a]	40/41 (98)	63/63 (100)	50/51 (98)	58/59 (98)	50/50 (100)	29/29 (100)	23/26 (89)
At Week 52[b]							
Valbenazine 40 mg	5/9 (56)	2/6 (33)	5/10 (50)	3/11 (27)	5/8 (63)	1/5 (20)	4/8 (50)
Valbenazine 80 mg	17/29 (59)	32/53 (60)	21/38 (55)	20/45 (44)	20/40 (50)	14/22 (64)	10/18 (56)
All Participants[a]	23/41 (56)	36/63 (57)	26/51 (51)	26/59 (44)	27/50 (54)	17/29 (59)	14/26 (54)

[a]Includes the 11 participants who had a dose reduction from 80 to 40 mg after Week 4
[b]After a 4-week washout

- At Week 48 (end of treatment):
  - 100% of all participants shifted from a score ≥3 to ≤2 for lips, upper extremities, and lower extremities
  - 98% shifted to score ≤2 for face, jaw, and tongue
- At Week 52 (after washout), shift rates decreased across all items
  - ≥50% of all participants had an item score ≤2 in the face, lips, jaw, upper extremities, lower extremities, and trunk

Comella CL, et al. MDS 2018; Hong Kong, China.

KINECT 4 – AIMS Shift Analysis: Summary

- At Week 48, mean AIMS item scores ≤1 (none to minimal) were observed in all participants in all body regions
  - From baseline to Week 48, mean AIMS item scores improved by >50% in all body regions
  - Regions with ≥70% mean improvement were face (70%), lips (70%), upper extremities (76%), lower extremities (72%), and trunk (75%)
- At Week 52 (after 4-week washout), mean AIMS item scores reverted towards baseline levels

Comella CL, et al. MDS 2018; Hong Kong, China.

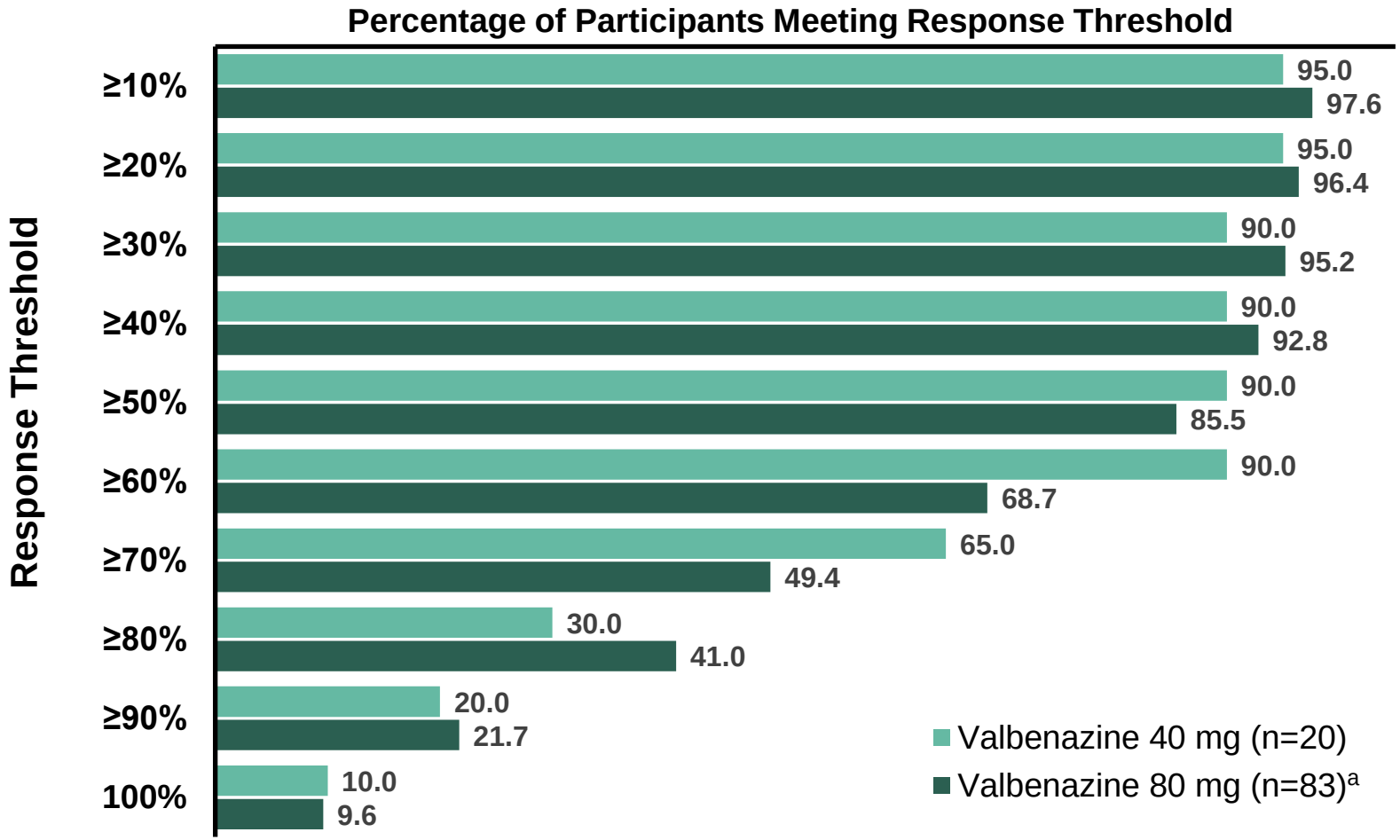
KINECT® 4 – Response and Shift Analyses

KINECT 4 – Response and Shift Analyses: Assessments

- KINECT 4 post-hoc analysis to evaluate treatment responses and clinically meaningful severity shifts in patients who received valbenazine (40 or 80 mg) for 48 weeks[1,2]
- Three sets of outcomes were analyzed descriptively based on AIMS total score (sum of items 1-7) or AIMS items
  - AIMS total score response: ≥10% to 100% improvement from baseline at Week 48 (end of treatment)[1,2]
  - AIMS item response: score ≤2 (“none” to “mild”) or score ≤1 (“none” to “minimal”) at Week 48[1,2]
  - AIMS item shift: score ≥3 (“moderate” or “severe”) at baseline and score ≤2 at Week 48[1]
  - CGI-TD or Patient Global Impression of Change (PGIC) response: score of ≤2 (“much improved” or better) or ≤3 (“minimally improved” or better)[2]
- Post-hoc analyses reflect ratings by site investigators (AIMS and CGI-TD) and patients (PGIC)[1,2]
- All analyses were based on the number of participants with available data[1,2]

1. Marder SR, et al. NEI 2019; CO Springs, CO. 2. Singer C, et al. MDS-PAS 2020; Miami, FL.

KINECT 4 – Response and Shift Analyses: Response Thresholds for AIMS Total Score



[a]Includes 9 participants with available data who had a dose reduction from 80 mg to 40 mg.

AIMS, Abnormal Involuntary Movement Scale.

Marder SR, et al. NEI 2019; CO Springs, CO.

KINECT 4 – Response and Shift Analyses: Response Thresholds for AIMS Item Scores

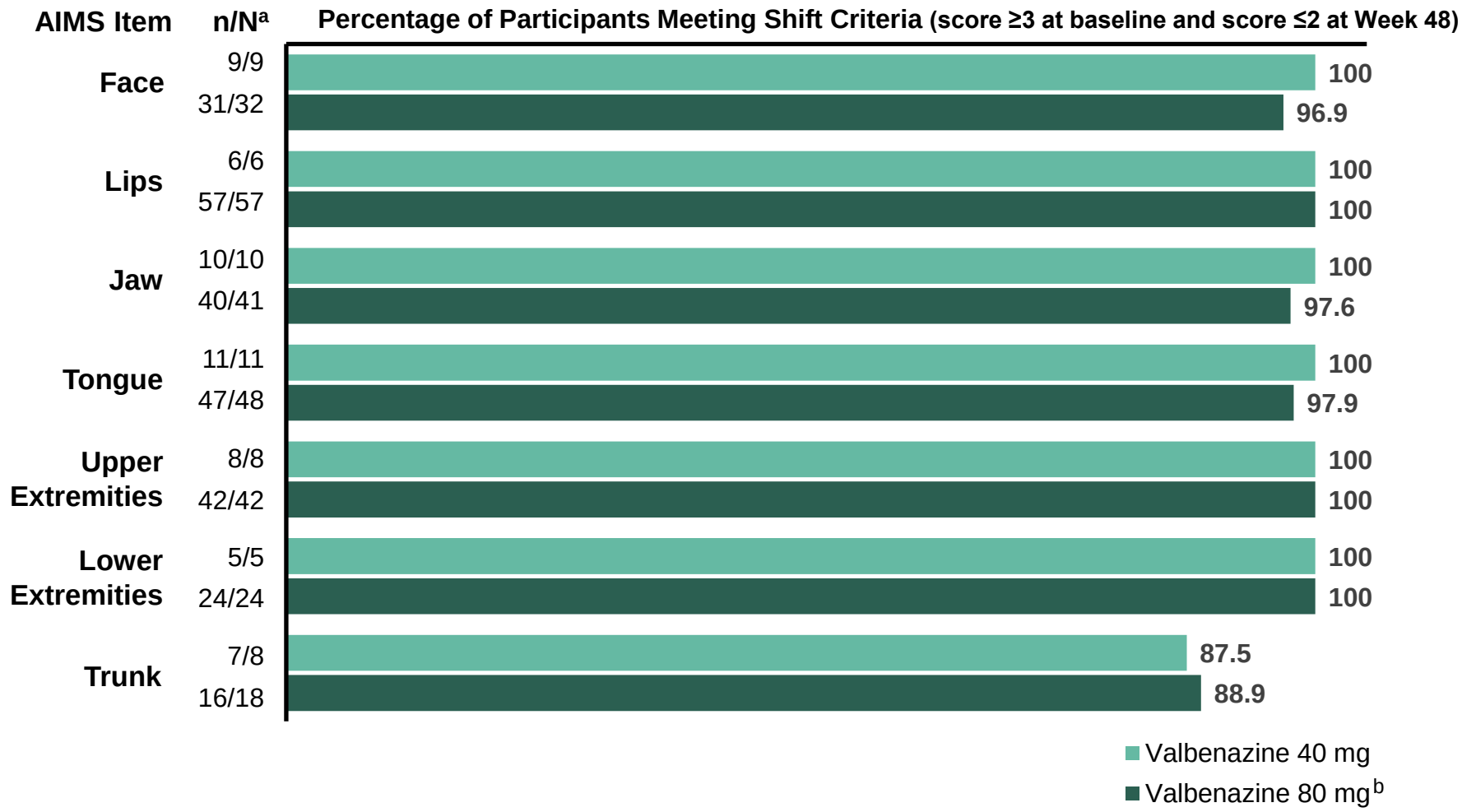
AIMS Item, n (%)	Score ≤2 at Week 48: "None" to "Mild"		Score ≤1 at Week 48: "None" or "Minimal"	
	40 mg (n=20)	80 mg (n=83)[a]	40 mg (n=20)	80 mg (n=83)[a]
Face	20 (100)	81 (97.6)	20 (100)	75 (90.4)
Lips	20 (100)	83 (100)	16 (80.0)	74 (89.2)
Jaw	20 (100)	82 (98.8)	16 (80.0)	69 (83.1)
Tongue	20 (100)	81 (97.6)	15 (75.0)	67 (80.7)
Upper Extremities	20 (100)	83 (100)	18 (90.0)	78 (94.0)
Lower Extremities	20 (100)	82 (98.8)	19 (95.0)	74 (89.2)
Trunk	19 (95.0)	81 (97.6)	18 (90.0)	77 (92.8)

[a]Includes 9 participants with available data who had a dose reduction from 80 mg to 40 mg; AIMS, Abnormal Involuntary Movement Scale.

- More than 95% of all 103 participants had a score ≤2 at Week 48 for all 7 AIMS items
  - Highest rates found in lips (100%), upper extremities (100%), jaw (99.0%), and lower extremities (99.0%)
- More than 75% of all participants had a score ≤1 in all 7 AIMS items at Week 48
  - Highest rates found in upper extremities (93.2%), face (92.2%), trunk (92.2%), and lower extremities (90.3%)

Marder SR, et al. NEI 2019; CO Springs, CO.

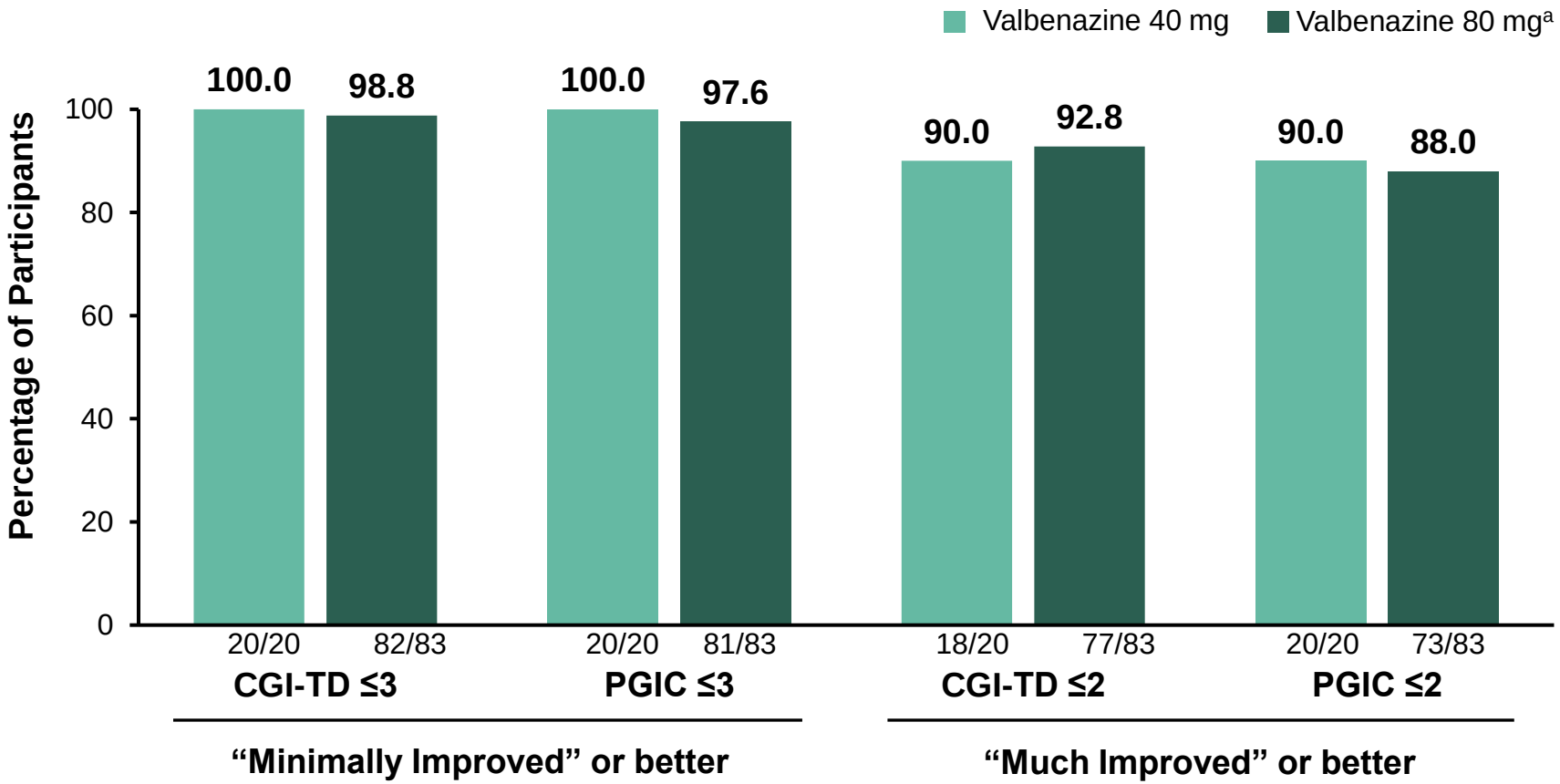
KINECT 4 – Response and Shift Analyses: AIMS Item Shifts



[a]N represents the number of participants who had a score ≥3 ("moderate" or "severe") at baseline; n represents the number of those participants who shifted to a score ≤2 ("none" to "mild") at Week 48;
[b]Includes participants who had a dose reduction from 80 to 40 mg.
AIMS, Abnormal Involuntary Movement Scale.

Marder SR, et al. NEI 2019; CO Springs, CO.

KINECT 4 – Response and Shift Analyses: Response Thresholds for CGI-TD and PGIC



[a]Includes 9 participants who had a dose reduction from 80 mg to 40 mg.
CGI-TD, Clinical Global Impression of Change-Tardive Dyskinesia; PGIC, Patient Global Impression of Change.

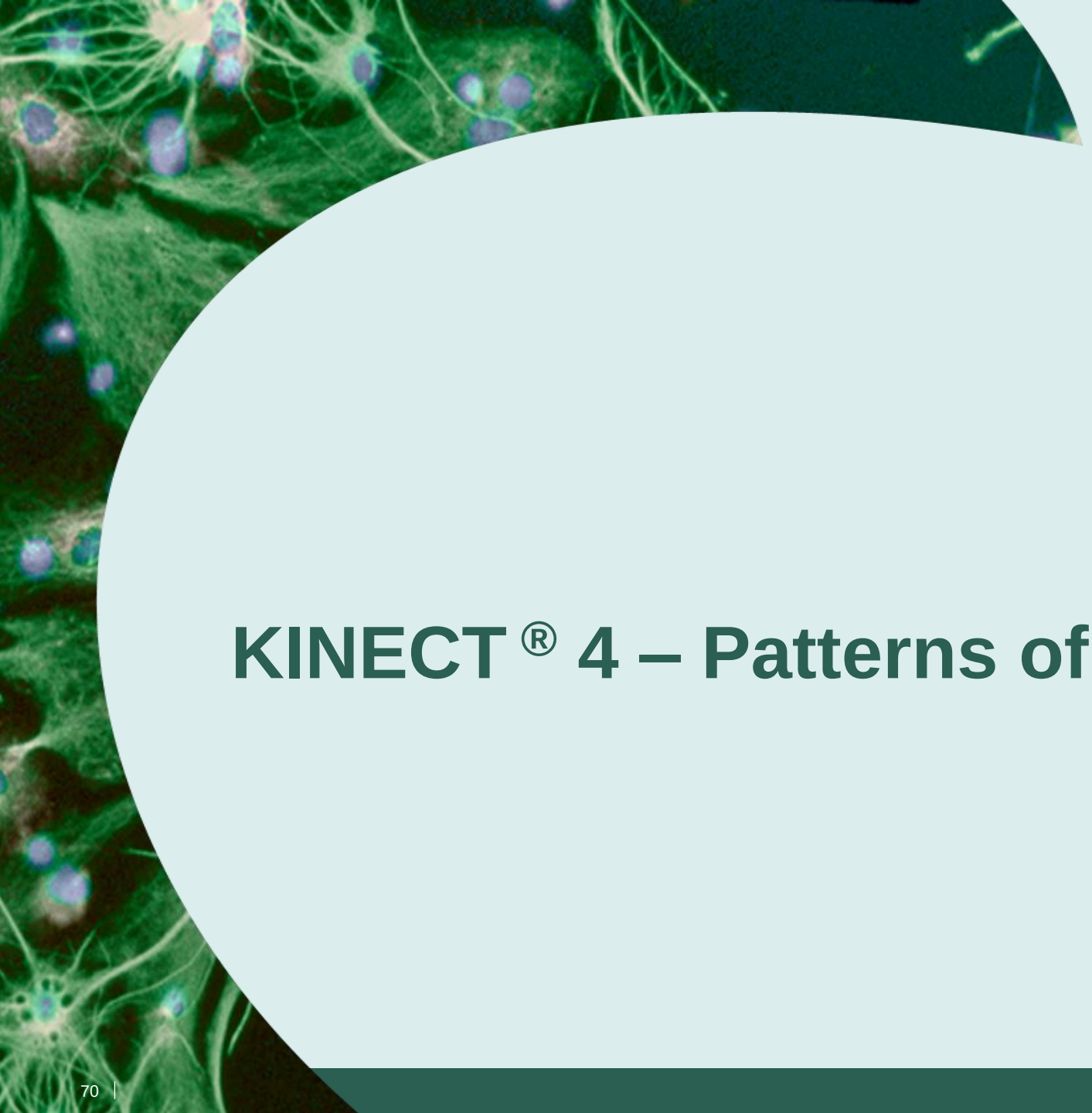
Singer C, et al. MDS-PAS 2020; Miami, FL.

KINECT 4 – Response and Shift Analyses: Summary

- After 48 weeks of once-daily valbenazine (40 or 80 mg), AIMS response thresholds ranged from 9.7% (100% improvement) to 97.1% (≥10% improvement) in all participants with available data[1]
- Percentage of participants meeting AIMS shift criteria* at Week 481:
  - Face: 100% (40mg), 96.9% (80mg)
  - Lips, Upper Extremities, Lower Extremities: 100% (both doses)
  - Jaw: 100% (40mg), 97.6% (80mg)
  - Tongue: 100% (40mg), 97.9% (80mg)
  - Trunk: 87.5% (40mg), 88.9% (80mg)
- After 48 weeks of once-daily valbenazine (40 or 80 mg), almost all participants had a global score of “minimally improved” or better and most had a global score of “much improved” or better[2]
  - CGI-TD ≤3 : 99.0%; PGIC ≤3 : 98.1%
  - CGI-TD ≤2: 92.2%; PGIC ≤2: 88.3%
- 64.7% of all participants had ≥1 treatment-emergent adverse event after Week 4 through Week 483

*AIMS Shift criteria: AIMS item score ≥3 (“moderate or “severe”) at baseline to a score ≤2 (“none” to “mild”) at Week 48.

1. Marder SR, et al. NEI 2019; CO Springs, CO. 2. Singer C, et al. MDS-PAS 2020; Miami, FL. 3. Marder SR, et al. ACNP 2017; Palm Springs, CA.



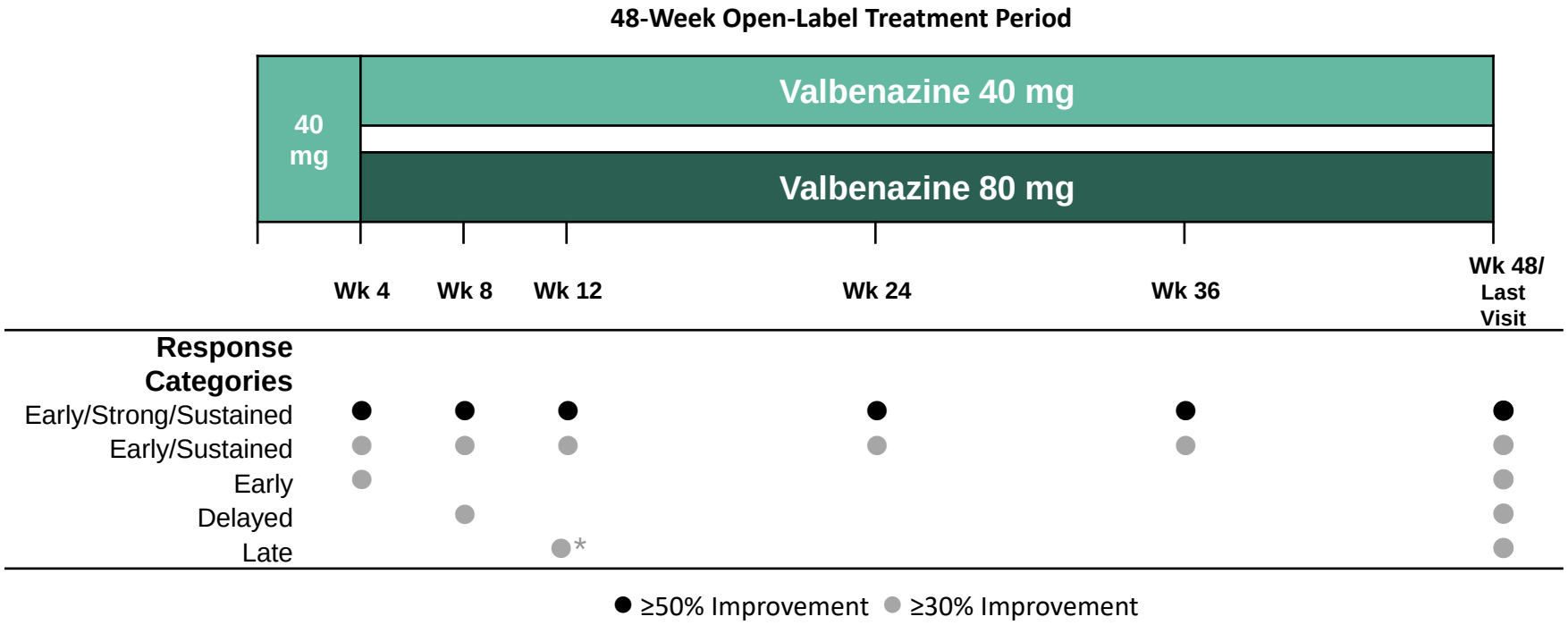
KINECT ® 4 – Patterns of TD Improvement

KINECT 4 – Patterns of Improvement: Assessments

- KINECT 4 post-hoc analysis to characterize different patterns of TD improvement[1]
- Data from study participants who received study drug and had ≥1 post-baseline AIMS assessment were analyzed descriptively[1]
- Based on the minimal clinically important difference (MCID) for AIMS total score[2], the proportion of participants with a ≥2-point decrease (improvement) or increase (worsening) were analyzed by study visit (Weeks 4, 8, 12, 24, 36, 48)[1]
- Based on the MCID for clinically meaningful response2 and protocol-defined response (≥30% and ≥50% AIMS total score improvement from baseline, respectively), participants were categorized as follows[1]:
  - Early/sustained/strong response; early/sustained response; early response; delayed response; late response; poor/no response
- Based on Schooler-Kane criteria for TD,[3] remission was defined as absence of TD (i.e., score of 2 [“mild”] in ≤1 AIMS item and all other item scores ≤1)[1]
  - At last available study visit = Remission
  - At last 2 visits = Sustained remission

1. Correll CU, et al. APA 2021. 2. Stacy M, et al. *Mov Disord.* 2019;34:1203-9. 3. Schooler NR, et al. *Arch Gen Psychiatry.* 1982;39:486-7.

KINECT 4 – Patterns of Improvement: Response Categories



*Week 12 or later; Wk, week.

Correll CU, et al. APA 2021.

KINECT 4 – Patterns of Improvement: Response Categories Defined*

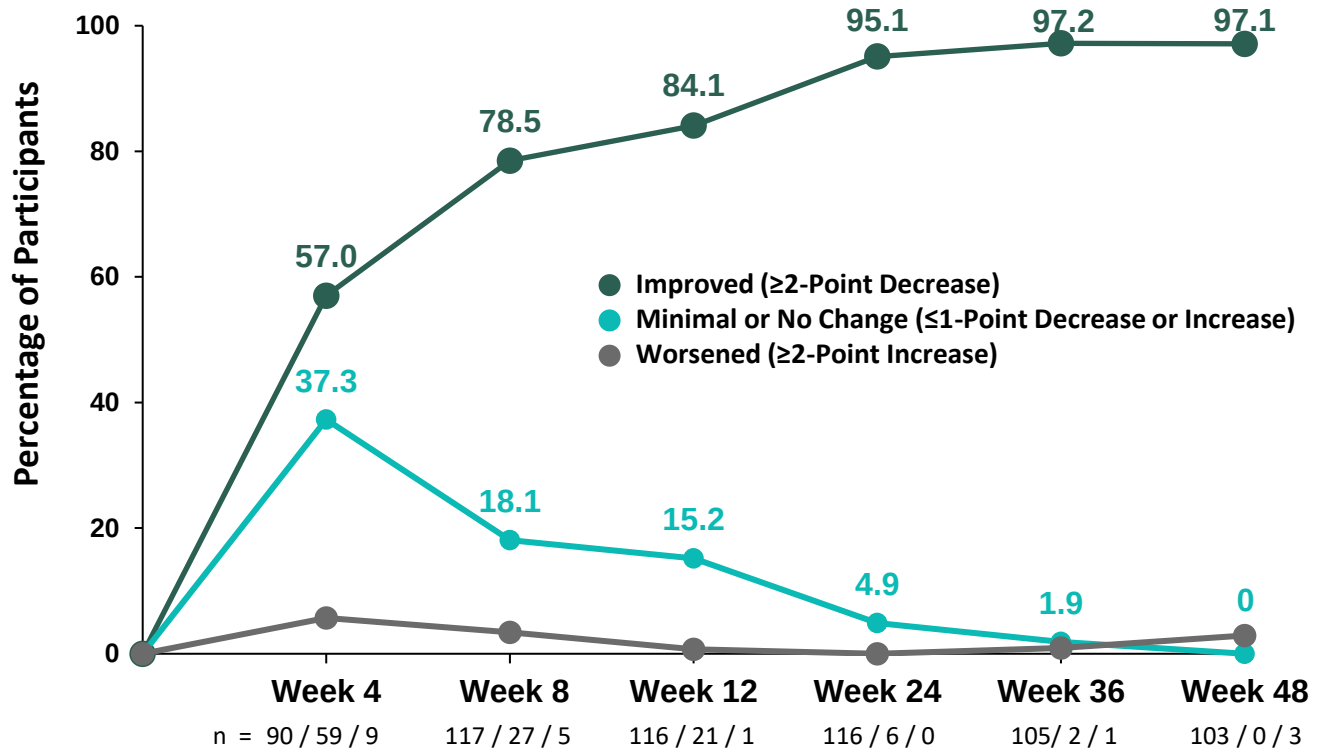
- **Early/sustained/strong response:** ≥50% improvement by Week 4 through all visits until Week 48 (or last visit for participants with no Week 48 data)
- **Early/sustained response:** ≥30% improvement by Week 4 through all visits until Week 48
- **Early response**: ≥30% improvement at Week 4 and Week 48
- **Delayed response:** ≥30% improvement at Week 8 and Week 48
- **Late response:** ≥30% improvement at Week 12 or later and Week 48
- **Poor/no response:** none of the 5 response groups above

*Participants were categorized into these response categories based on the minimal clinically important difference (MCID) for clinically meaningful response and protocol-defined response (≥30% and ≥50% AIMS total score improvement from baseline, respectively).

Correll CU, et al. APA 2021.

KINECT 4 – Patterns of Improvement: AIMS Total Score Changes with Long-Term Once-Daily Valbenazine Treatment

- 158 participants received study drug and had ≥1 post-baseline AIMS assessment
- The percentage of participants with a clinically meaningful (MCID) ≥2-point improvement in AIMS total score increased over time, with ≥95% having a clinically meaningful improvement at Weeks 24, 36, and 48

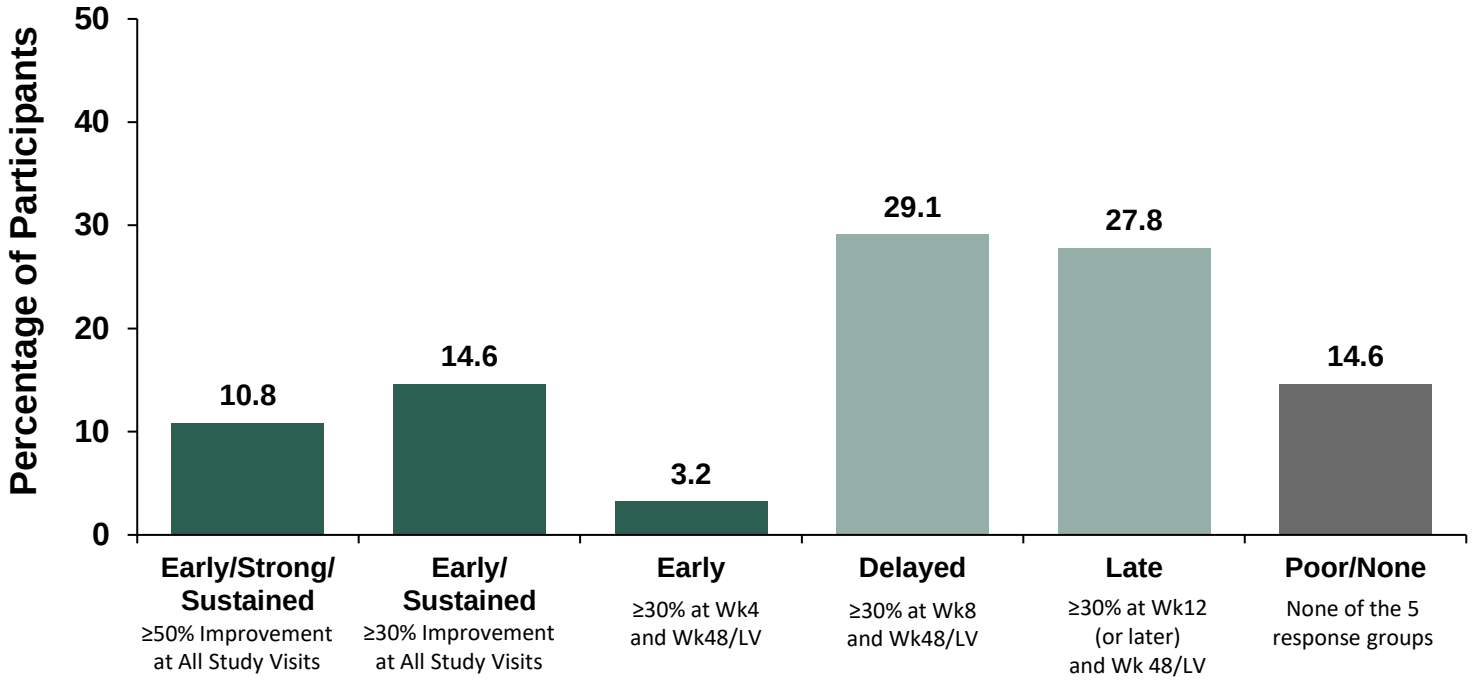


AIMS, Abnormal Involuntary Movement Scale; n, number of available assessments for improved/minimal or no change/worsened.

Correll CU, et al. APA 2021.

KINECT 4 – Patterns of Improvement: AIMS Response Patterns with Long-Term Once-Daily Valbenazine Treatment*

- At Week 48 or last visit, 85.4% (135/158) of participants met the criteria for a response
  - 28.5% (45/158) had ≥30% or ≥50% improvement by Week 4 (“early” response)
  - 57.0% (90/158) had ≥30% improvement at Week 8 or later, but their Week 48 outcomes were comparable to early responders (“delayed” or “late” response)

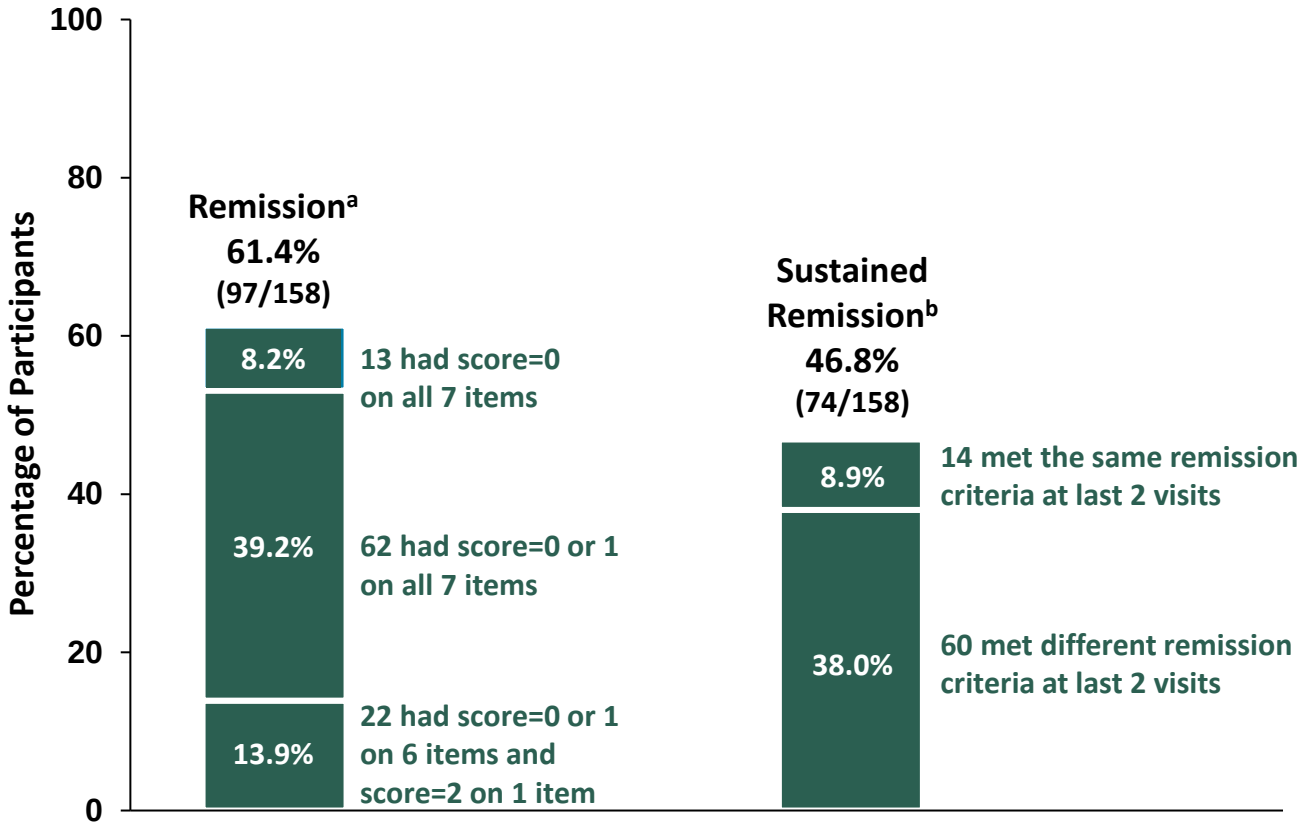


*Based on all 158 participants; AIMS, Abnormal Involuntary Movement Scale; LV, last visit; Wk, week.

Correll CU, et al. APA 2021.

KINECT 4 – Patterns of Improvement: Remission and Sustained Remission

- 61.4% and 46.8% of participants met the criteria for remission and sustained remission, respectively



[a]Remission defined as score of 2 ["mild"] in ≤1 AIMS item and all other item scores ≤1. The numbers are presented for participants with each possible score combination; [b]Sustained remission defined as meeting a remission definition at last 2 visits. The numbers are presented for participants who met the same remission criteria for the last 2 visits or different criteria at the last 2 visits (e.g., score=1 on several items and then score=0 on all 7 items). Results include participants who had only 1 post-baseline AIMS assessment (categorized as having no sustained remission); AIMS, Abnormal Involuntary Movement Scale.

Correll CU, et al. APA 2021.

KINECT 4 – Patterns of Improvement: Baseline Characteristics by Response Categories

- Mean AIMS total scores were higher (worse) among early and delayed responders (P<0.05 across response categories)
- Late and poor responders had relatively fewer participants with ≥1 maximum AIMS item score of 4 (severe) at baseline (P<0.05), which may have left less “room” for improvement

	Early/ Strong/ Sustained (n=17)	Early/ Sustained (n=23)	Early (n=5)	Delayed (n=46)	Late (n=44)	Poor/ None (n=23)	*P*-Value
Age, mean (SD)	57.6 (8.80)	57.9 (8.82)	59.0 (3.08)	58.7 (7.91)	57.4 (10.54)	57.0 (10.89)	0.7638
Sex, n (%)							
Male	6 (35.3)	13 (56.5)	2 (40.0)	27 (58.7)	22 (50.0)	15 (65.2)	0.4602
Female	11 (64.7)	10 (43.5)	3 (60.0)	19 (41.3)	22 (50.0)	8 (34.8)	
Race, n (%)							
White/Caucasian	11 (64.7)	12 (52.2)	4 (80.0)	35 (76.1)	29 (65.9)	16 (69.6)	0.4767
Black/African-American	5 (29.4)	10 (43.5)	1 (20.0)	11 (23.9)	13 (29.5)	7 (30.4)	
Other[a]	1 (5.9)	1 (4.3)	0 (0)	0 (0)	2 (4.5)	0 (0)	
BMI, mean (SD), kg/m^2	28.4 (5.65)	28.7 (5.09)	32.4 (4.55)	27.3 (4.94)	29.4 (5.97)	28.8 (5.61)	0.7614
Psychiatric diagnosis, n (%)							
Schizophrenia/ schizoaffective disorder	12 (70.6)	15 (65.2)	5 (100.0)	35 (76.1)	31 (70.5)	16 (69.6)	0.7583
Mood disorder	5 (29.4)	8 (34.8)	0 (0)	11 (23.9)	13 (29.5)	7 (30.4)	
AIMS total score, mean (SD)	15.8 (4.59)	15.5 (4.88)	14.2 (5.40)	15.8 (4.16)	13.5 (4.78)	13.6 (5.47)	0.0371
Highest AIMS item score, n (%)[b]							
1 = Minimal	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0.0412
2 = Mild	1 (5.9)	2 (8.7)	0 (0)	0 (0)	0 (0)	0 (0)	
3 = Moderate	7 (41.2)	10 (43.5)	3 (60.0)	24 (52.2)	32 (72.7)	15 (65.2)	
4 = Severe	9 (52.9)	11 (47.8)	2 (40.0)	22 (47.8)	12 (27.3)	6 (26.1)	

[a]Includes Asian, Native Hawaiian/Pacific Islander, and other; [b]In any (1 or more) of the 7 body regions; AIMS, Abnormal Involuntary Movement Scale; BMI, body mass index; SD, standard deviation.

Correll CU, et al. APA 2021.

KINECT 4 – Patterns of Improvement: Baseline Characteristics by Remission Status

- No significant differences were found between remitters and non-remitters

	Remission (n=97)	No Remission (n=61)	P-Value
Age, mean (SD)	58.6 (9.32)	56.7 (8.94)	0.2100
Sex, n (%)			
Male	46 (47.4)	39 (63.9)	0.0500
Female	51 (52.6)	22 (36.1)	
Race, n (%)			
White/Caucasian	66 (68.0)	41 (67.2)	0.2998
Black/African-American	29 (29.9)	18 (29.5)	
Other	2 (2.1)	2 (3.3)	
BMI, mean (SD), kg/m^2	28.6 (5.58)	28.7 (5.28)	0.8922
Psychiatric diagnosis, n (%)			
Schizophrenia/schizoaffective disorder	67 (69.1)	47 (77.0)	0.3622
Mood disorder	30 (30.9)	14 (23.0)	
AIMS total score, mean (SD)	14.2 (4.52)	15.6 (5.09)	0.0822
Highest AIMS item score, n (%)[a]			
1 = Minimal	0 (0)	0 (0)	0.2418
2 = Mild	3 (3.1)	2 (3.3)	
3 = Moderate	61 (62.9)	30 (49.2)	
4 = Severe	33 (34.0)	29 (47.5)	

[a]Includes Asian, Native Hawaiian/Pacific Islander, and other; [b]In any (1 or more) of the 7 body regions; AIMS, Abnormal Involuntary Movement Scale; BMI, body mass index; SD, standard deviation.

Correll CU, et al. APA 2021.

KINECT 4 – Patterns of Improvement: Summary

- Patterns of improvement may vary, but sustained clinically meaningful or robust responses (≥30% or ≥50% AIMS total score decrease) were observed with once-daily valbenazine in this KINECT 4 post-hoc analysis[1]
  - 85.4% (135/158) of participants met criteria for a response at Week 48
- 61.4% and 46.8% of participants met the criteria for remission[a] and sustained remission[b], respectively[1]
- In the KINECT 4 study, the most common TEAEs were urinary tract infection (8.5%) and headache (5.2%) in all participants taking valbenazine (40 mg and 80 mg)[2]

[a]Remission defined as score of 2 [“mild”] in ≤1 AIMS item and all other item scores ≤1 at last available study visit. [b]Sustained remission defined as meeting a remission definition at last 2 visits. AIMS, Abnormal Involuntary Movement Scale.

1. Correll CU, et al. APA 2021. 2. Marder SR, et al. *J Clin Psychopharmacology*. 2019;39(6):620-627.

KINECT® 4 – AIMS Items 8,9,&10 Analysis

KINECT 4 – AIMS Items 8,9,&10 Analysis: Assessments

- AIMS total score was defined as the sum of items 1 to 7
  - Rates the severity of abnormal movements in different body regions (i.e., face, lips, jaw, tongue, upper extremities, lower extremities, and trunk)
- AIMS items 8,9, & 10 defined:
  - AIMS Item 8: Overall severity of abnormal movements
  - AIMS Item 9: Incapacitation due to abnormal movements
  - AIMS Item 10: Patient's awareness of abnormal movements and if aware, the level of distress
- AIMS Items were scored by site investigator raters
- Mean changes from baseline to Weeks 48 and 52 were analyzed descriptively for AIMS total score (sum of items 1 to 7) and individual items 8, 9, and 10
- Baseline characteristics were analyzed in all participants who received ≥1 dose of VBZ (safety population)
- All other analyses were conducted in participants who received ≥1 dose of VBZ and had a relevant postbaseline AIMS assessment
  - No significance testing was conducted

VBZ, valbenazine; AIMS, Abnormal Involuntary Movement Scale

Marder SR, et al. APA 2019; San Francisco, CA.

KINECT 4 – AIMS Items 8,9,&10 Analysis: Assessments

- Response and shift analyses were conducted for AIMS items 8 and 9, which have the same scale for scoring (0=none to 4=severe)
  - These analyses were not conducted for item 10 because the scoring represents 2 different patient types: unaware (score=0) and aware with increasing levels of distress (score=1 to 4)
- Two thresholds were used to assess response:
  - Score ≤2 (none to mild) at Week 48 or 52, regardless of baseline score
  - Score ≤1 (none or minimal) at Week 48 or 52, regardless of baseline score
- Two sets of criteria were used to assess shifts:
  - Score ≥3 (moderate or severe) at baseline and score ≤2 at Week 48 or 52
  - Score ≥2 (mild to severe) at baseline and score ≤1 at Week 48 or 52

AIMS, Abnormal Involuntary Movement Scale

Marder SR, et al. APA 2019; San Francisco, CA.

KINECT 4 – AIMS Items 8,9,&10 Analysis: Baseline Characteristics

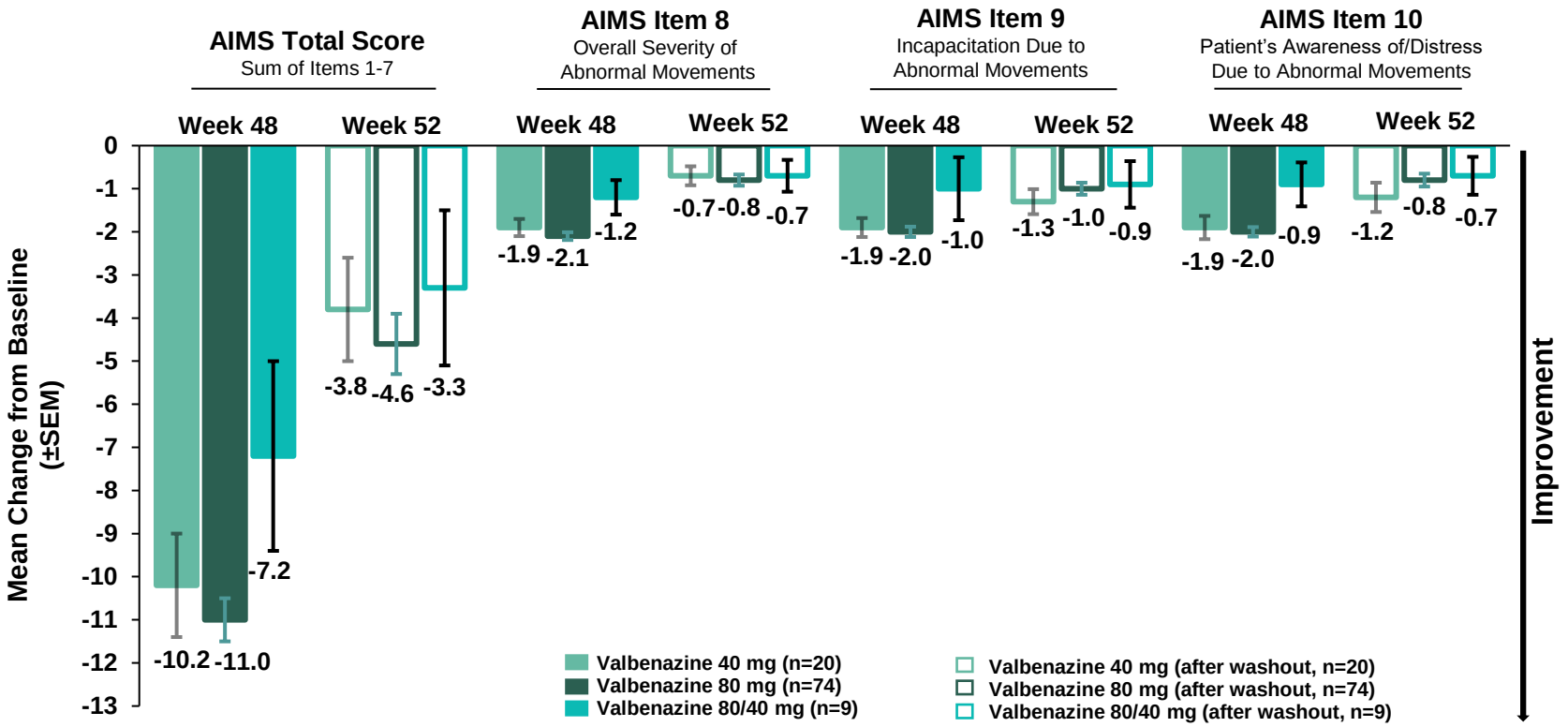
	VBZ 40 mg (n=45)	VBZ 80 mg (n=107)	VBZ 80/40 mg (n=11)	All VBZ (n=163)
Age, mean (SD), years	56.8 (11.2)	57.8 (9.0)	56.3 (8.6)	57.4 (9.6)
Male, n (%)	21 (46.7)	59 (55.1)	6 (54.5)	86 (52.8)
White, n (%)	26 (57.8)	74 (69.2)	10 (90.9)	110 (67.5)
BMI, mean (SD), kg/m^2	27.8 (6.0)	29.0 (5.4)	27.5 (3.3)	28.5 (5.5)
BPRS score at screening, mean (SD)	29.2 (6.8)	27.3 (6.6)	28.4 (7.4)	27.9 (6.7)
C-SSRS lifetime suicidal ideation or behavior, n (%)	17 (37.8)	48 (44.9)	4 (36.4)	69 (42.3)
AIMS scores, mean (SD)[a]				
Total score: sum of items 1-7 (site raters)	14.2 (5.5)	15.0 (4.5)	12.8 (4.6)	14.6 (4.8)
Item 8: overall severity of abnormal movements	3.1 (0.5)	3.2 (0.5)	2.7 (0.6)	3.2 (0.5)
Item 9: incapacitation due to abnormal movements	2.4 (0.9)	2.6 (0.8)	2.0 (1.3)	2.5 (0.9)
Item 10: patient's awareness of abnormal movements and distress level	2.8 (0.9)	2.7 (0.7)	2.5 (1.0)	2.7 (0.8)

[a]Score ranges: total (0-28 [none to severe in all 7 body regions]); items 8 and 9 (0-4 [none to severe]); item 10 (0 [no awareness], 1-4 [aware with no distress to severe distress]).
AIMS, Abnormal Involuntary Movement Scale; BMI, body mass index; BPRS, Brief Psychiatric Rating Scale; C-SSRS, Columbia-Suicide Severity Rating Scale; SD, standard deviation; VBZ, valbenazine

- Baseline characteristics and demographics were generally similar across dosage groups

Marder SR, et al. APA 2019; San Francisco, CA.

KINECT 4 – AIMS Items 8,9,&10 Analysis: Results: Mean Score Changes from Baseline

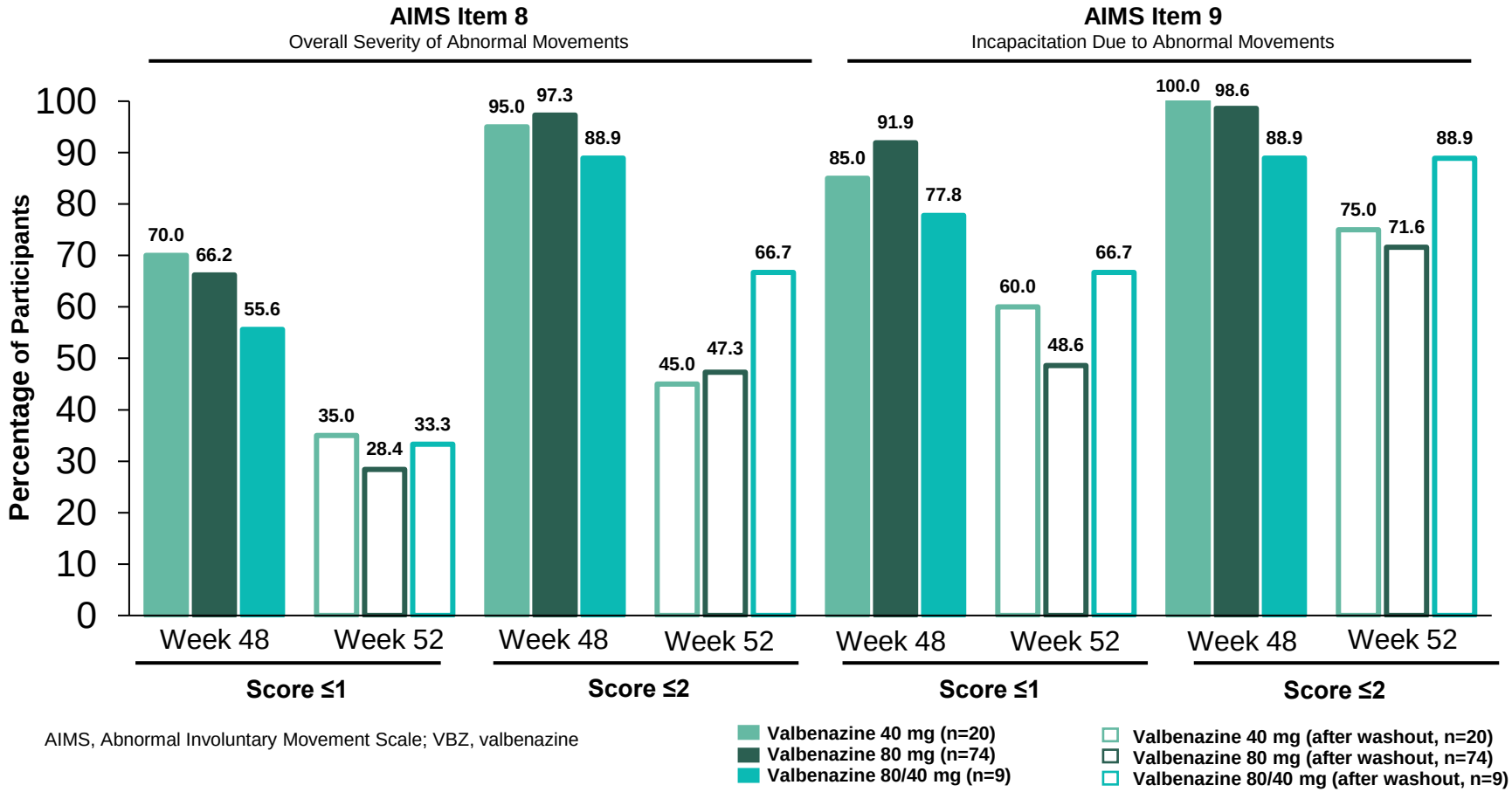


AIMS items 8 and 9 scoring: 0=none, 1=minimal, 2=mild, 3=moderate, and 4=severe; AIMS item 10 scoring: 0=unaware, 1=aware, no distress, 2=aware, mild distress, 3=aware, moderate distress, 4=aware, severe distress.
AIMS, Abnormal Involuntary Movement Scale; SEM, standard error of the mean.

- AIMS Items were scored by site investigator raters

Marder SR, et al. APA 2019; San Francisco, CA.

KINECT 4 – AIMS Items 8,9,&10 Analysis: Participants Meeting Response Thresholds



AIMS, Abnormal Involuntary Movement Scale; VBZ, valbenazine

- In all VBZ-treated participants, response rates at Week 48 were >85% for AIMS item 8 (score ≤2) and item 9 (score ≤2), indicating none to mild overall severity and incapacitation due to abnormal movements, respectively
- Response rates decreased for AIMS items 8 & 9 at Week 52

Marder SR, et al. APA 2019; San Francisco, CA.

KINECT 4 – AIMS Items 8,9,&10 Analysis: Participants Meeting Shift Criteria

		VBZ 40 mg	VBZ 80 mg	VBZ 80/40 mg	All VBZ
Shift from score ≥3 at baseline to score ≤2, n/N (%)					
AIMS item 8	Week 48 Week 52	17/18 (94) 8/18 (44)	71/73 (97) 34/73 (47)	6/7 (86) 4/7 (57)	94/98 (96) 46/98 (47)
AIMS item 9	Week 48 Week 52	10/10 (100) 6/10 (60)	45/46 (98) 27/46 (59)	3/3 (100) 2/3 (67)	58/59 (98) 35/59 (59)
Shift from score ≥2 at baseline to score ≤1, n/N (%)					
AIMS item 8	Week 48 Week 52	14/20 (70) 7/20 (35)	49/74 (66) 21/74 (28)	5/8 (63) 3/8 (38)	68/102 (67) 31/102 (30)
AIMS item 9	Week 48 Week 52	16/18 (89) 11/18 (61)	62/68 (91) 32/68 (47)	6/6 (100) 4/6 (67)	84/92 (91) 47/92 (51)

AIMS, Abnormal Involuntary Movement Scale; N, number of participants with score ≥3 or ≥2 at baseline; n, number of participants who shifted to score ≤2 or ≤1 at Week 48 or 52; VBZ, valbenazine.

Marder SR, et al. APA 2019; San Francisco, CA.

KINECT 4 – AIMS Items 8,9,&10 Analysis: Summary

- Mean changes from baseline (CFB) in AIMS scores indicated that long-term treatment with once-daily VBZ (40 or 80 mg) was effective in improving the following (based on AIMS Items analysis)
  - AIMS total score (items 1-7; across 7 body regions)
  - Overall severity of abnormal movements (item 8)
  - Incapacitation due to abnormal movements (item 9)
  - awareness/distress in patients with TD (item 10)

VBZ, valbenazine.

Marder SR, et al. APA 2019; San Francisco, CA.

KINECT® 4 – AIMS Item 8 as an Independent Clinical Measure

KINECT 4 – AIMS Item 8 Analysis: Assessments

- Data from KINECT 4 were analyzed post hoc to evaluate the potential of AIMS item 8 (clinician's global impression of severity) as a simple clinical measure that could be used in lieu of the AIMS total score
- Analyses were based on AIMS item 8 using two sets of AIMS item 8 scores:
  - Protocol-based method: based on investigators' ratings of item 8 using protocol-defined descriptors
  - Post hoc method: based on investigators' highest single score from items 1–7
- Mean AIMS item 8 scores with standard deviation (SD) were analyzed at baseline and by study visit
- Three shift analyses were conducted based on the following criteria:
  - Score 4 at baseline (severe) and score ≤3 at Week 48 (none to moderate)
  - Score ≥3 at baseline (moderate or severe) and score ≤2 at Week 48 (none to mild)
  - Score ≥2 at baseline (mild to severe) and score ≤1 at Week 48 (none or minimal)

AIMS, Abnormal Involuntary Movement Scale

Citrome L, et al. Psych Congress 2020.

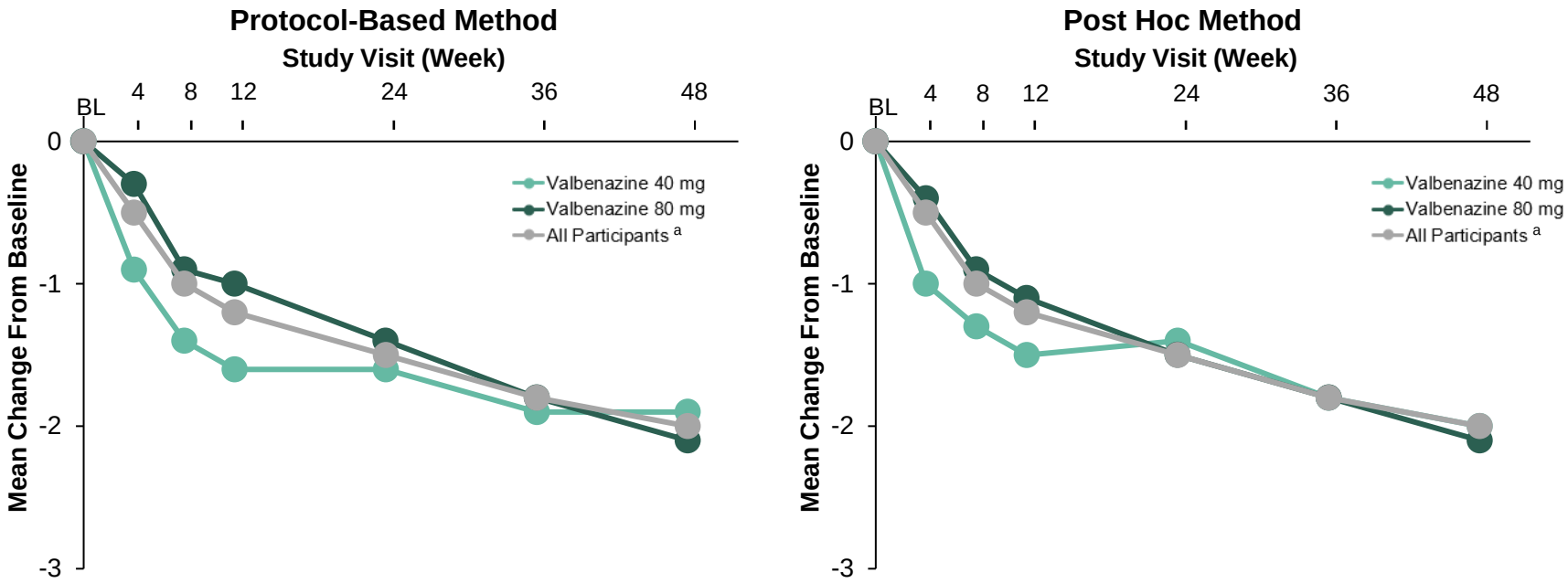
KINECT 4 – AIMS Item 8 Analysis: AIMS Scoring and Descriptors in KINECT 4a

Score	Protocol-Defined Descriptors[1]
0	**No dyskinesia**
1	**Minimal or slight dyskinesia:** Low amplitude, present during some but not most of exam
2	**Mild dyskinesia:** Low amplitude and present during most of exam (or moderate amplitude and present during some of exam)
3	**Moderate dyskinesia:** Moderate amplitude and present during most of exam
4	**Severe dyskinesia:** Maximal amplitude and present during most of exam

[a]For AIMS items 1-7.
No other specific or additional direction was provided for AIMS item 8; scores were based on each investigator's individual judgement. When used clinically, a common practice is to score AIMS item 8 using the highest single score from items 1-7.[2]

1. Citrome L, et al. Psych Congress 2020. 2. Marder SR, et al. J Clin Psychopharmacology. 2019;39(6):620-627.

KINECT 4 – AIMS Item 8 Analysis: AIMS Mean Change From Baseline By Visit

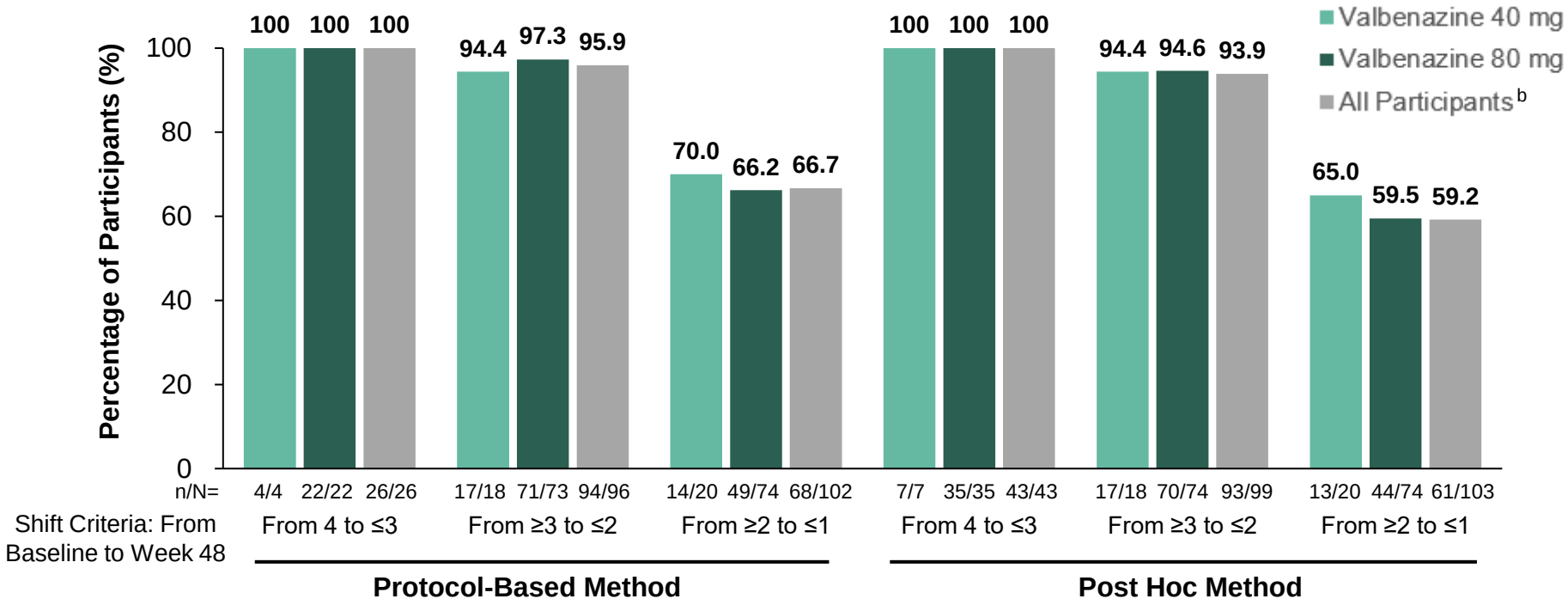


[a]Includes 11 participants who had a dose reduction from 80 to 40 mg after Week 4.
AIMS, Abnormal Involuntary Movement Scale

- In all participants (N=163), mean scores for AIMS item 8 and changes from baseline (±SD) were as follows:
  - At baseline: protocol, 3.2 ± 0.6; post hoc, 3.3 ± 0.6 (moderate-to-severe)
  - At Week 48: protocol, 1.2 ± 0.7; post hoc, 1.4 ± 0.7 (minimal-to-mild)
  - Mean change from baseline to Week 48: protocol, -2.0 ± 0.8; post hoc, -2.0 ± 0.9

Citrome L, et al. Psych Congress 2020.

KINECT 4 – AIMS Item 8 Analysis: Participants Meeting Shift Criteriaa



[a]Based on participants who had available AIMS assessments at baseline and Week 48.
[b]Includes 9 participants who had a dose reduction from 80 to 40 mg after Week 4.

- Results from AIMS item 8 shift analyses were similar between the scoring methods
  - Participants with a score of 4 at baseline (severe), 100% shifted to a score ≤3 at Week 48 (none to moderate)
  - Participants with a score ≥3 at baseline (moderate or severe), >90% shifted to a score ≤2 at Week 48 (none to mild)
  - Participants with a score ≥2 at baseline (mild to severe), >50% shifted to a score ≤1 at Week 48 (none or minimal)

Citrome L, et al. Psych Congress 2020.

KINECT 4 – AIMS Item 8 Analysis: Summary

- Once-daily valbenazine treatment resulted in improved AIMS item 8 scores (clinician's global impression of severity) in patients with TD (N=163)[1]
- Similar results were found whether AIMS item 8 scores were based on report by site raters (protocol-based method) or the highest items 1–7 scores (post hoc method)[1]
  - At baseline: protocol, 3.2 ± 0.6; post hoc, 3.3 ± 0.6 (moderate-to-severe)
  - At Week 48: protocol, 1.2 ± 0.7; post hoc, 1.4 ± 0.7 (minimal-to-mild)
  - Mean change from baseline to Week 48: protocol, -2.0 ± 0.8; post hoc, -2.0 ± 0.9
- Shift analyses indicated that most participants had a clinically meaningful improvement at Week 48 (end of treatment)[1]
- These results demonstrate that AIMS item 8 scores may be an appropriate clinical measure for assessing changes in TD severity[1]
- The convention of scoring AIMS item 8 based on the highest single score from AIMS items 1-7 is simple to communicate and can yield clinically useful and actionable data[1]
  - This approach avoids the need to interpret the AIMS total score (sum of AIMS items 1-7), which can be ambiguous when viewed in isolation
- In the KINECT 4 study, the most common TEAEs were urinary tract infection (8.5%) and headache (5.2%) in all participants taking valbenazine (40 mg and 80 mg)[2]

1. Citrome L, et al. Psych Congress 2020. 2. Marder SR, et al. J Clin Psychopharmacology. 2019;39(6):620-627.

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