KINECT 3 & KINECT 4 Pooled Long-Term Data – Underlying Disease Diagnosis & Concomitant Medication Subgroup Analyses

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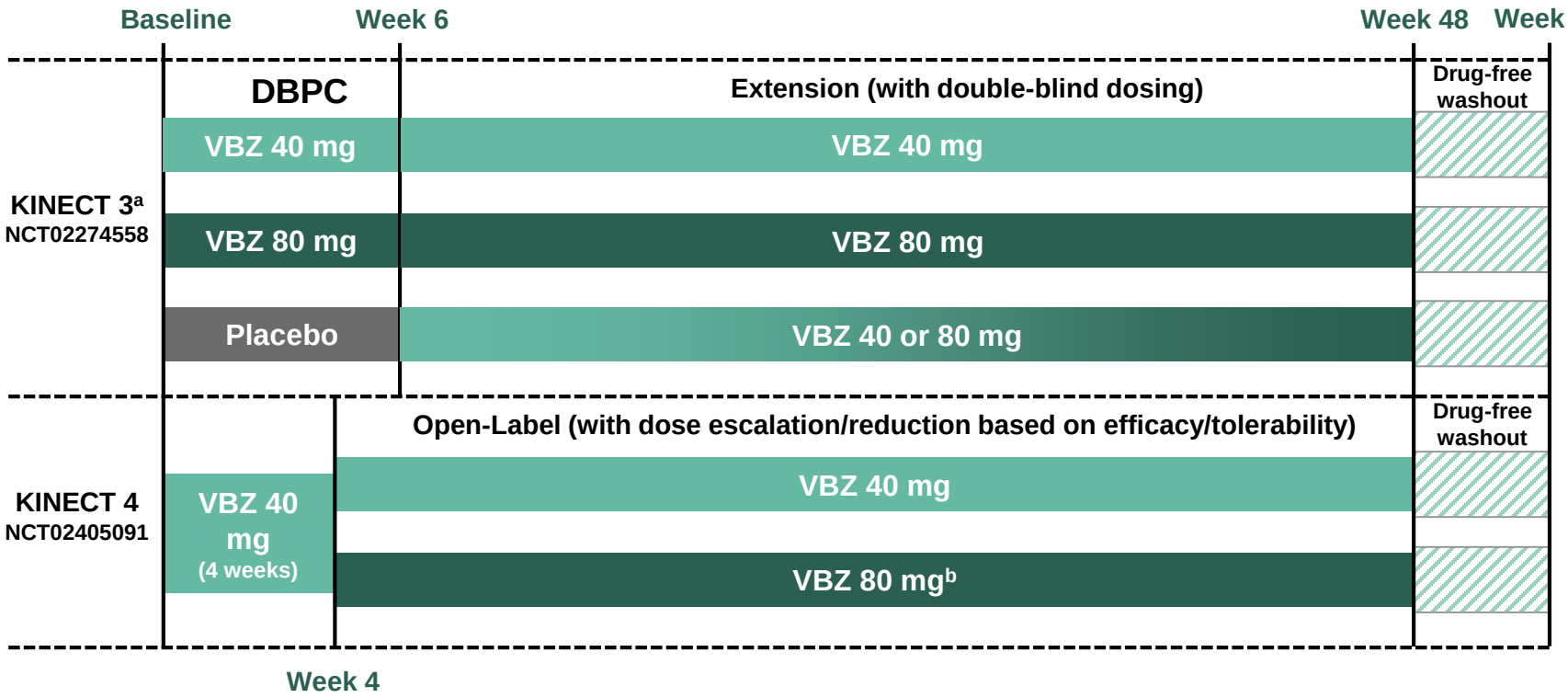
KINECT 3 & KINECT 4: Study Design



[a]KINECT 3 80 mg group received 40mg for the first week. [b]Includes participants who had a dose reduction to 40 mg due to tolerability issues. DBPC, double-blind placebo-controlled; VBZ, valbenazine.

- Stable doses of concomitant medications to treat psychiatric disorders were allowed throughout the studies
- Valbenazine dose groups were pooled as follows:
  - 40 mg: included the 40-mg group from KINECT 3 and KINECT 4 participants who remained on 40 mg
  - 80 mg: included the 80-mg group from KINECT 3 and KINECT 4 participants who were escalated to 80 mg at Week 4
  - Participants who received placebo in KINECT 3 were not included in this analysis

Giraldo E, et al. PHNS 2019; Vancouver, Canada.

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KINECT 3 & 4 – Underlying Disease Diagnosis Subgroup Analysis: Baseline Characteristics

	Schizophrenia/Schizoaffective Disorder		Mood Disorder	
	40 mg (n=75)	80 mg (n=134)	40 mg (n=32)	80 mg (n=63)
Age, mean (SD), years	56.8 (9.2)	56.9 (9.4)	54.9 (9.7)	57.3 (9.6)
Age at psychiatric diagnosis	32.1 (12.4)	28.3 (11.9)	34.3 (15.3)	35.5 (13.3)
Age at TD diagnosis	48.5 (11.0)	46.8 (12.1)	49.8 (10.4)	51.0 (11.9)
Male, n (%)	46 (61.3)	83 (61.9)	12 (37.5)	21 (33.3)
White, n (%)	37 (49.3)	80 (59.7)	24 (75.0)	48 (76.2)
BMI, mean (SD), kg/m^2	28.6 (5.8)	28.1 (5.5)	28.3 (5.6)	29.0 (5.5)
C-SSRS lifetime history, n (%)				
Suicidal ideation	24 (32.0)	38 (28.4)	12 (37.5)	30 (47.6)
Suicidal behavior	19 (25.3)	38 (28.4)	11 (34.4)	22 (34.9)
BPRS total score at screening, mean (SD)	31.4 (7.4)	28.6 (6.9)	26.5 (5.8)	27.0 (6.0)
AIMS total score at baseline, mean (SD)[a]	11.0 (5.5)	12.8 (4.8)	11.8 (4.4)	13.4 (4.4)
PANSS scores, mean (SD)				
Total score	54.3 (11.5)	49.2 (12.0)	NA	NA
Positive symptoms	12.6 (3.7)	11.3 (3.9)	NA	NA
Negative symptoms	14.7 (4.7)	13.3 (5.0)	NA	NA
General psychopathology	27.0 (6.2)	24.6 (5.6)	NA	NA
CDSS, mean (SD)	2.0 (2.3)	1.9 (2.2)	NA	NA
MADRS, mean (SD)	NA	NA	6.8 (3.6)	5.4 (3.9)
YMRS, mean (SD)	NA	NA	2.9 (2.7)	2.6 (2.7)

[a]Scored by blinded central video raters (KINECT 3) or site raters (KINECT 4); AIMS, Abnormal Involuntary Movement Scale; BMI, body mass index; BPRS, Brief Psychiatric Rating Scale; CDSS, Calgary Depression Scale for Schizophrenia; C-SSRS, Columbia-Suicide Severity Rating Scale; MADRS, Montgomery-Åsberg Depression Rating Scale; NA, not assessed; PANSS, Positive and Negative Syndrome Scale; SD, standard deviation; TD, tardive dyskinesia; YMRS, Young Mania Rating Scale.

Giraldo E, et al. PHNS 2019; Vancouver, Canada.

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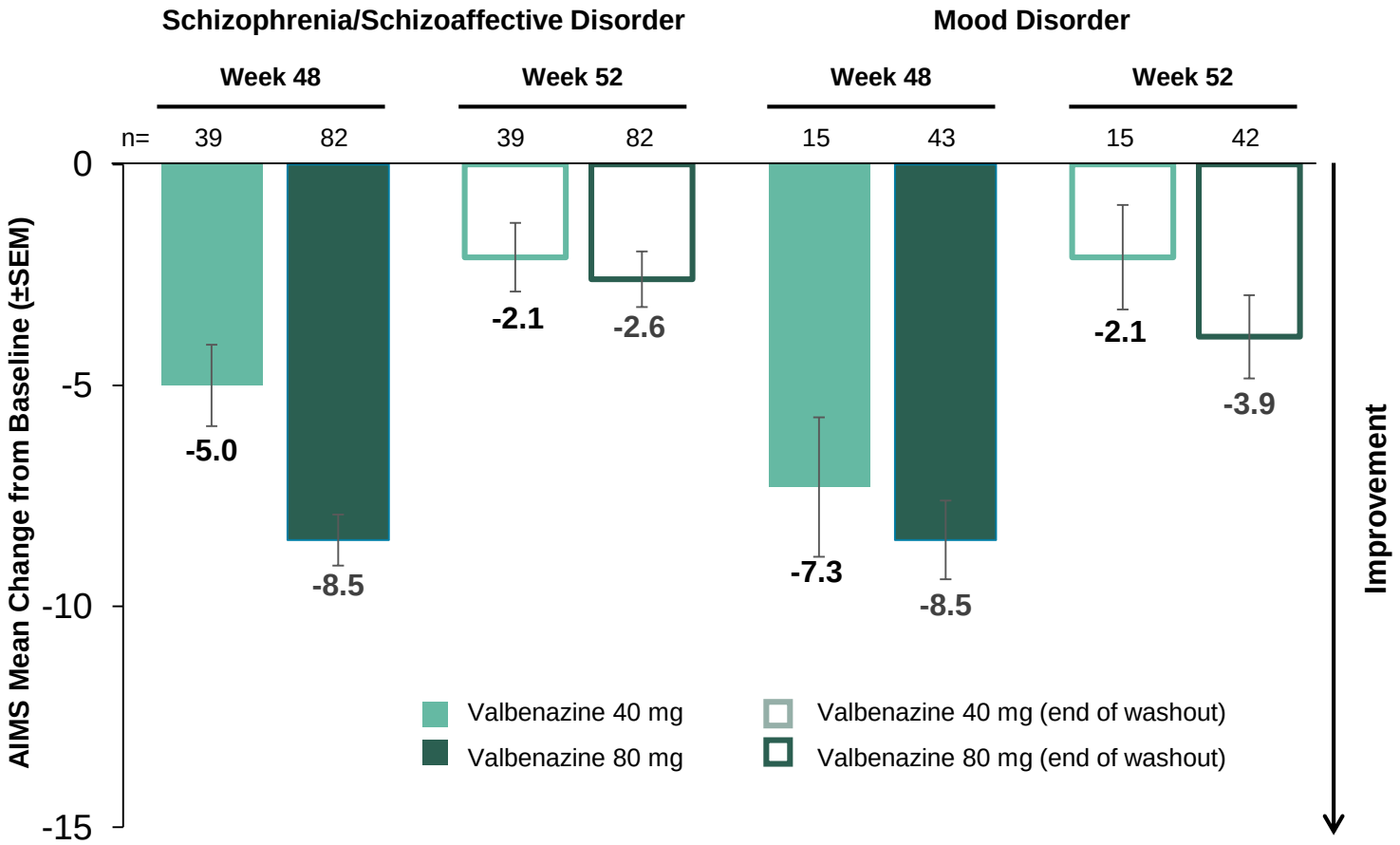
KINECT 3 & 4 – Underlying Disease Diagnosis Subgroup Analysis: AIMS Total Score Mean Change from Baseline



- Mean improvements in AIMS total score from baseline to Week 48 were observed with valbenazine (40 and 80 mg) in both diagnosis subgroups
  - Some loss of effect was observed at Week 52 (end of 4-week washout)

AIMS, Abnormal Involuntary Movement Scale; SEM, standard error of the mean

Giraldo E, et al. PHNS 2019; Vancouver, Canada.

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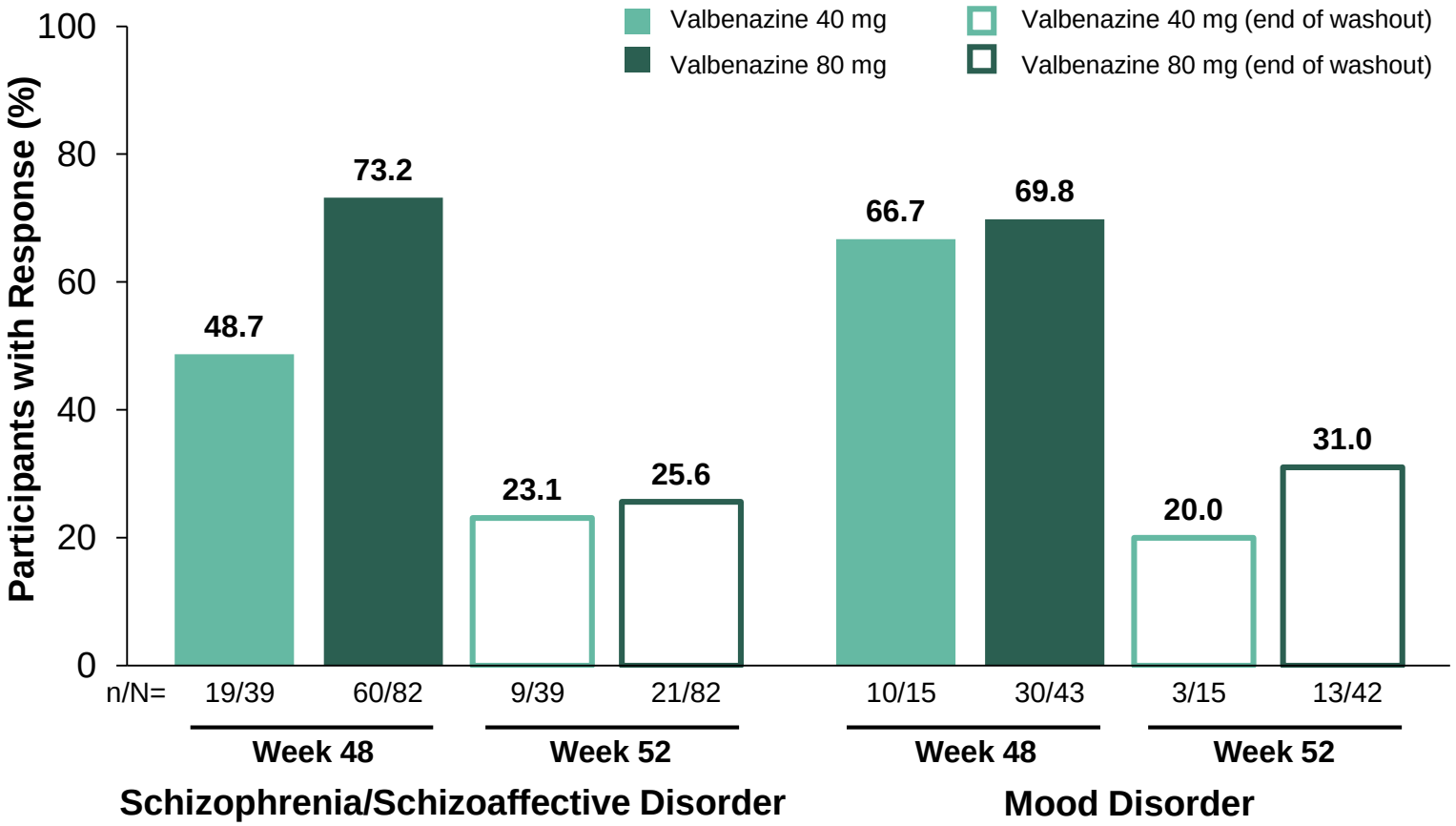
KINECT 3 & 4 – Underlying Disease Diagnosis Subgroup Analysis: AIMS Response
(≥50% Total Score Improvement from Baseline)



AIMS, Abnormal Involuntary Movement Scale.

Giraldo E, et al. PHNS 2019; Vancouver, Canada.

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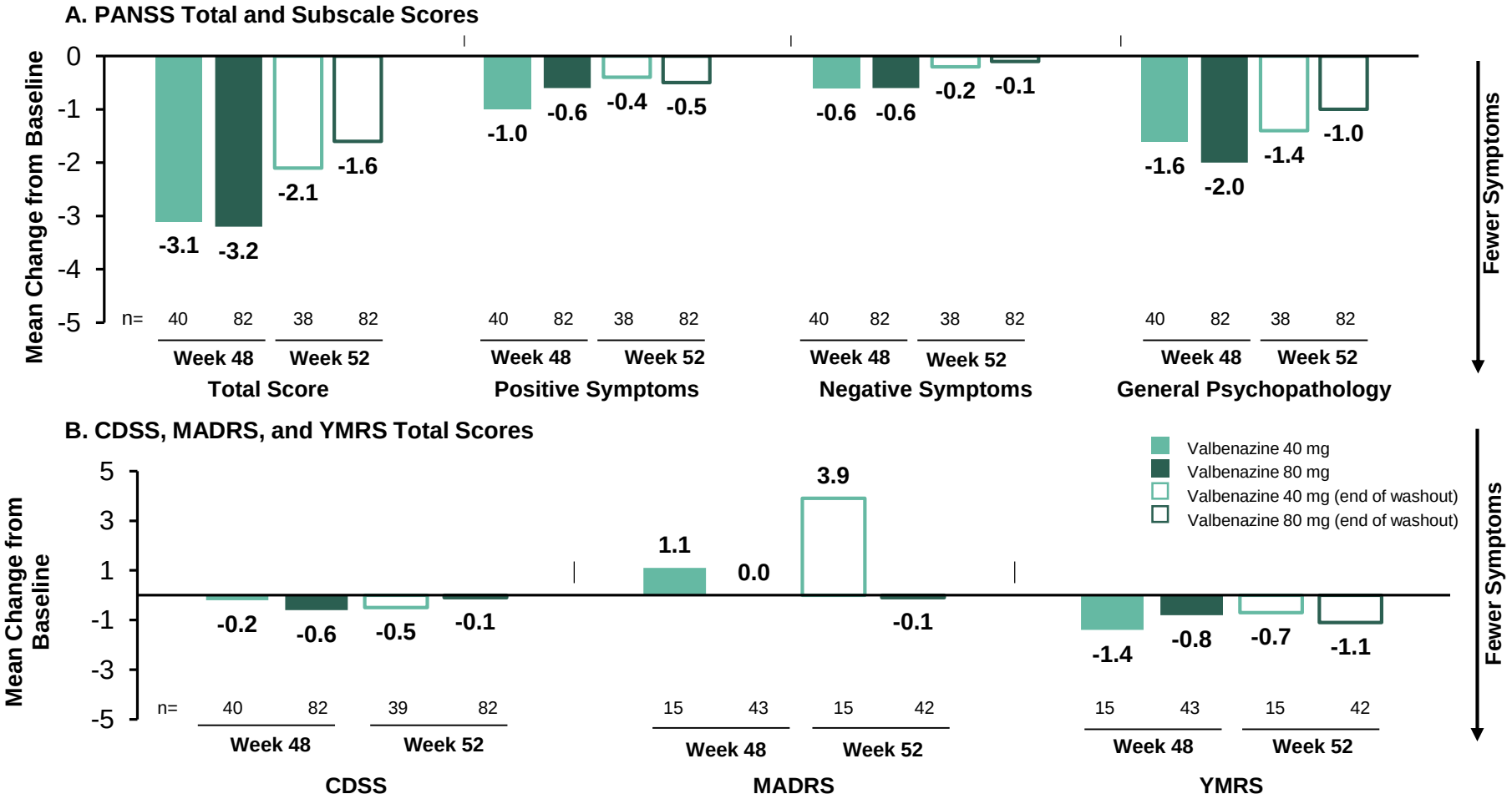
KINECT 3 & 4 – Underlying Disease Diagnosis Subgroup Analysis: Mean Changes from Baseline in Psychiatric Scale Scores



PANSS and CDSS were administered to participants with schizophrenia/schizoaffective disorder. MADRS and YMRS were administered to participants with 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.

Giraldo E, et al. PHNS 2019; Vancouver, Canada.

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KINECT 3 & 4 – Underlying Disease Diagnosis Subgroup Analysis: Columbia-Suicide Severity Rating Scale Shifts from Baseline

	Baseline Score	Maximum Suicidal Ideation Score at Any Time During the Study[a]					
		0	1	2	3	4	5
Schizophrenia/Schizoaffective Disorder (n=208)	0	189	6	3	0	2	3
	1	2	2	0	0	0	0
	2	0	0	0	0	0	0
	3	1	0	0	0	0	0
Mood Disorder (n=95)	0	87	2	3	1	0	0
	1	1	1	0	0	0	0
	2	0	0	0	0	0	0
	3	0	0	0	0	0	0

[a]0=no suicidal ideation, 1=wish to be dead, 2=non-specific active suicidal thoughts, 3=active suicidal ideation with any methods (not plan) without intent to act, 4=active suicidal ideation with some intent to act, without specific plan, 5=active suicidal ideation with specific plan and intent.

- 93.1% (189/203) of participants with schizophrenia/schizoaffective disorder and 93.5% (87/93) of participants with mood disorder who had no suicidal ideation at baseline (C-SSRS score=0) continued to have no suicidal ideation at any time during long-term treatment
- Among the few participants who had some suicidal ideation at baseline (C-SSRS score=1 to 3), none had a worsening in C-SSRS score at any time during treatment
- No participant had active suicidal ideation with intent (C-SSRS score=4 or 5) at baseline

Giraldo E, et al. PHNS 2019; Vancouver, Canada.

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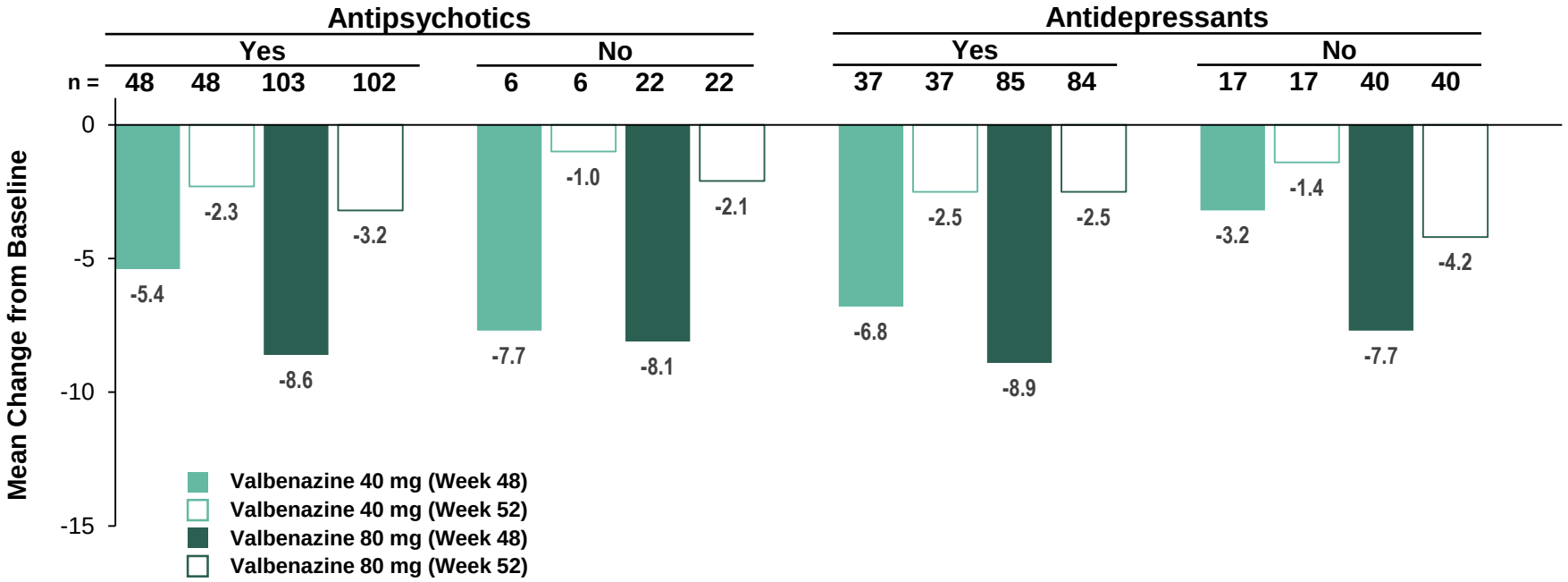
KINECT 3 & 4 – Concomitant Medication Subgroup Analysis: AIMS Mean Changes from Baseline to Week 48 & Week 52



All Week 48 mean changes were significant vs. baseline ($P<0.05$), except in the following subgroups: no antipsychotics (40 mg).
AIMS, Abnormal Involuntary Movement Scale; AC, anticholinergic; AD, antidepressant; ANX, anxiolytic; AP, antipsychotic; Benzo, benzodiazepine; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor

Comella C, et al. AAN 2019; Philadelphia, PA.

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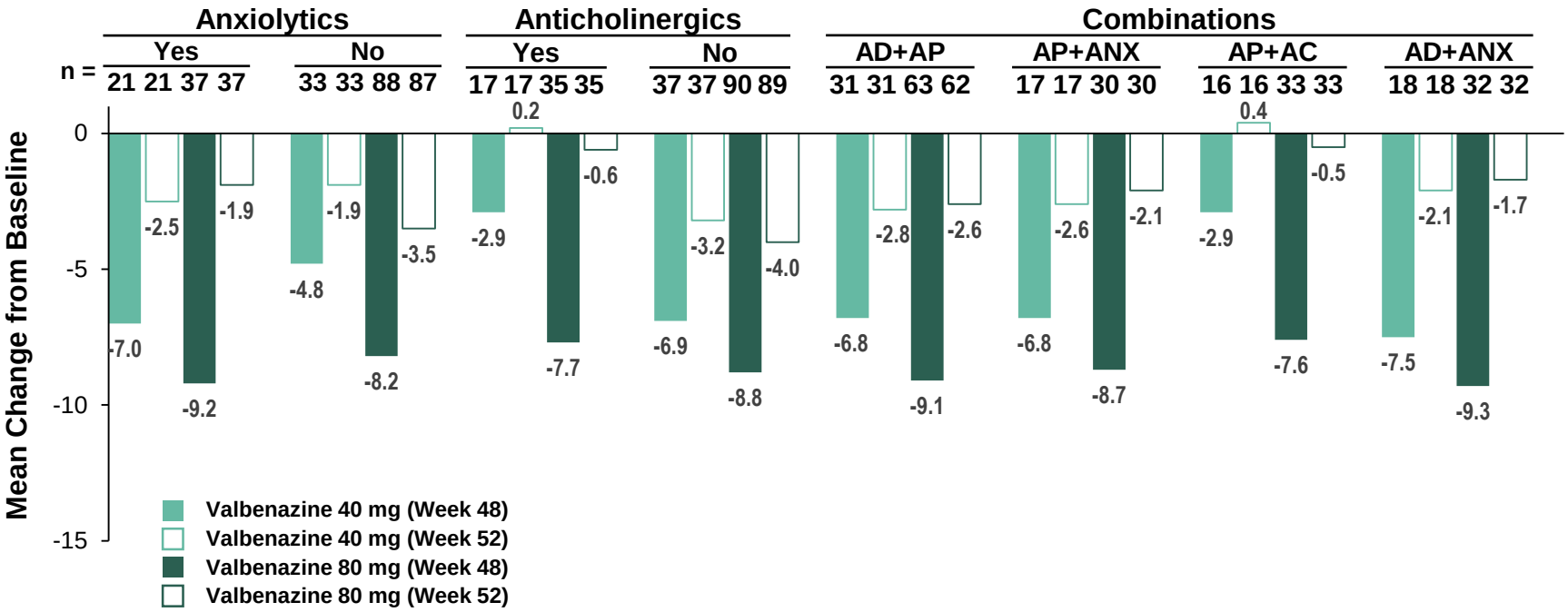
KINECT 3 & 4 – Concomitant Medication Subgroup Analysis: AIMS Mean Changes from Baseline to Week 48 & Week 52



All Week 48 mean changes were significant vs. baseline ($P<0.05$), except in the following subgroups: no antipsychotics (40 mg). AD+AP includes participants who received an atypical antipsychotic or both (atypical + typical)

AIMS, Abnormal Involuntary Movement Scale; AC, anticholinergic; AD, antidepressant; ANX, anxiolytic; AP, antipsychotic; Benzo, benzodiazepine; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor

Comella C, et al. AAN 2019; Philadelphia, PA.

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KINECT 3 & 4 – Underlying Disease Diagnosis & Concomitant Medication Subgroup Analyses: Summary

- Mean improvements in AIMS total score from baseline to Week 48 were observed with valbenazine (40 and 80 mg) in both diagnosis subgroups[1]
  - Schizophrenia/Schizoaffective disorder: -5.0 (VBZ 40mg), -8.5 (VBZ 80mg)
  - Mood Disorder: -7.3 (VBZ 40mg), -8.5 (VBZ 80mg)
- Mean psychiatric scale scores generally remained stable for both subgroups[1]
- Once daily valbenazine also provided TD improvements through Week 48 in patients taking concomitant antipsychotics, antidepressants, anxiolytics, and/or anticholinergics. Mean AIMS total score change from baseline to Week 48 were as follows:[2]
  - Antipsychotics: -5.4 (VBZ 40 mg) and -8.6 (VBZ 80 mg)
  - Antidepressants: -6.8 (VBZ 40 mg) and -8.9 (VBZ 80 mg)
  - Anxiolytics: -7.0 (VBZ 40 mg) and -9.2 (VBZ 80 mg)
  - Anticholinergics: -2.9 (VBZ 40 mg) and -7.7 (VBZ 80 mg)
- The most commonly reported TEAEs (≥ 8%) in all participants taking VBZ (n= 304) were headache (8.9%) and urinary tract infection (8.9%) [3]

VBZ, valbenazine; AIMS, Abnormal Involuntary Movement Scale; C-SSRS, Columbia-Suicide Severity Rating Scale.

1. Giraldo E, et al. PHNS 2019; Vancouver, Canada. 2. Comella C, et al. AAN 2019; Philadelphia, PA.
3. Marder SR, et al. US Psych Congress 2018; Orlando, FL.

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Back up

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KINECT 3 & KINECT 4: Key Inclusion/Exclusion Criteria

- Key inclusion criteria:
  - *Diagnostic and Statistical Manual of Mental Disorders* (e.g., DSM-IV) diagnosis of schizophrenia, schizoaffective disorder, or mood disorder; required to be psychiatrically stable prior to study entry (e.g., Brief Psychiatric Rating Scale score <50 at screening)
  - DSM-IV diagnosis of DRBA-induced TD for ≥3 months prior to screening
  - Moderate or severe TD as qualitatively assessed by blinded external reviewers at screening
- Key exclusion criteria:
  - Active, clinically significant, and unstable medical condition within 1 month prior to screening
  - Comorbid movement disorder that was more prominent than TD
  - Significant risk for active suicidal ideation, suicidal behavior, or violent behavior

Comella C, et al. AAN 2019; Philadelphia, PA.

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KINECT 3 & KINECT 4 – Underlying Disease Diagnosis Analysis

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KINECT 3 & 4 – Underlying Disease Diagnosis Analysis: Assessments

- Data from KINECT 3 & 4 were analyzed post hoc to explore the long-term effects of valbenazine (VBZ) in adults with schizophrenia/schizoaffective disorder or mood disorder (bipolar disorder and major depressive disorder)
  - All analyses were conducted in participants who received ≥1 dose of VBZ and had any available post-baseline data
- All outcomes were analyzed descriptively with no statistical testing between diagnosis subgroups (schizophrenia/schizoaffective disorder, mood disorder)
- Outcomes at end of treatment (Week 48) and end of washout (Week 52) included:
  - Mean change from baseline in the Abnormal Involuntary Movement Scale (AIMS) total score (sum of items 1-7); scored by blinded central video raters (KINECT 3) or site raters (KINECT 4)
  - AIMS response (≥50% total score improvement from baseline)
  - Clinical Global Impression of Change-Tardive Dyskinesia (CGI-TD) mean scores as assessed by site raters; score range from 1 (“very much improved”) to 7 (“very much worse”)
  - CGI-TD response (score of 1 [“very much improved”] or 2 [“much improved”])
- Changes in psychiatric symptoms were assessed at Weeks 48 and 52 using the following scales:
  - Positive and Negative Syndrome Scale (PANSS) and Calgary Depression Scale for Schizophrenia (CDSS) for participants with schizophrenia/schizoaffective disorder
  - Montgomery-Åsberg Depression Rating Scale (MADRS) and Young Mania Rating Scale (YMRS) for participants with mood disorder
  - Columbia-Suicide Severity Rating Scale (C-SSRS) for all participants

Giraldo E, et al. PHNS 2019; Vancouver, Canada.

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KINECT 3 & KINECT 4 – Concomitant Medication Subgroup Analysis

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KINECT 3 & KINECT 4: Assessments

- All participants who received ≥1 dose of study drug and had ≥1 post-baseline Abnormal Involuntary Movement Scale (AIMS) assessment were included in the pooled intent-to-treat population
  - The AIMS was scored by blinded central video raters (KINECT 3) or site raters (KINECT 4)
- Analyses at Week 48 (end of long-term treatment) and Week 52 (end of 4-week washout) included:
  - Mean change from baseline in AIMS total score (sum of items 1-7)
  - Response, defined as ≥50% total score improvement from baseline
- Concomitant medication subgroups were defined by use at baseline as follows:
  - Antipsychotic use (yes, no)
  - Antidepressant use (yes, no)
  - Anticholinergic use (yes, no)
  - Anxiolytic use (yes, no)
  - Combinations: antidepressant + atypical antipsychotics; antipsychotic + anxiolytic; antipsychotic + anticholinergic; antidepressant + anxiolytic
  - Subgroup categories were not mutually exclusive

Comella C, et al. AAN 2019; Philadelphia, PA.

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KINECT 3 & KINECT 4 – Concomitant Medication Subgroup Analysis: Concomitant Medications at Baseline or at Any Time During the Study

	Valbenazine 40 mg n=107	Valbenazine 80 mg n=197	All N=304
Any antipsychotic, n (%)[a]	98 (91.6)	169 (85.8)	267 (87.8)
Quetiapine	29 (27.1)	50 (25.4)	79 (26.0)
Risperidone	19 (17.8)	32 (16.2)	51 (16.8)
Aripiprazole	14 (13.1)	28 (14.2)	42 (13.8)
Olanzapine	17 (15.9)	24 (12.2)	41 (13.5)
Haloperidol	14 (13.1)	20 (10.2)	34 (11.2)
Ziprasidone	6 (5.6)	13 (6.6)	19 (6.3)
Any antidepressant, n (%)[a]	71 (66.4)	129 (65.5)	200 (65.8)
Trazodone	26 (24.3)	45 (22.8)	71 (23.4)
Mirtazapine	13 (12.1)	20 (10.2)	33 (10.9)
Sertraline	13 (12.1)	20 (10.2)	33 (10.9)
Citalopram	13 (12.1)	19 (9.6)	32 (10.5)
Bupropion	4 (3.7)	21 (10.7)	25 (8.2)
Escitalopram	7 (6.5)	14 (7.1)	21 (6.9)
Fluoxetine	8 (7.5)	13 (6.6)	21 (6.9)
Duloxetine	9 (8.4)	10 (5.1)	19 (6.3)
Venlafaxine	5 (4.7)	11 (5.6)	16 (5.3)
Any anxiolytic, n (%)[a]	42 (39.3)	59 (29.9)	101 (33.2)
Lorazepam	13 (12.1)	23 (11.7)	36 (11.8)
Hydroxyzine	11 (10.3)	18 (9.1)	29 (9.5)
Alprazolam	10 (9.3)	16 (8.1)	26 (8.6)
Buspirone	11 (10.3)	14 (7.1)	25 (8.2)
Any anticholinergic, n (%)[a]	41 (38.3)	68 (34.5)	109 (35.9)
Benztropine	40 (37.4)	61 (31.0)	101 (33.2)

- In all participants who received ≥1 dose of study drug (N=304), 87.8% were taking an antipsychotic medication at baseline

[a]Common medications, as reported in ≥5% of all participants, are listed

Comella C, et al. AAN 2019; Philadelphia, PA.

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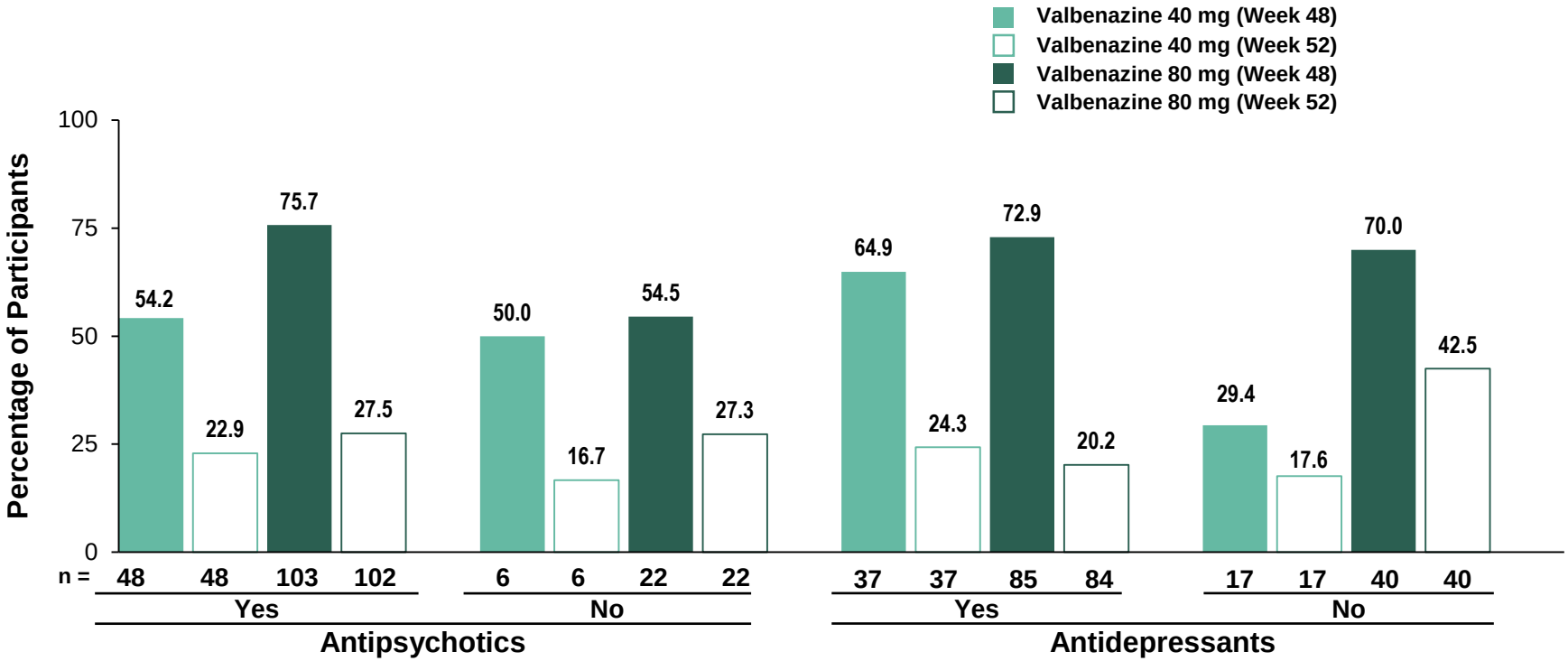
KINECT 3 & KINECT 4 – Concomitant Medication Subgroup Analysis: ≥50% AIMS Improvement from Baseline at Week 48 & Week 52



AIMS, Abnormal Involuntary Movement Scale

Comella C, et al. AAN 2019; Philadelphia, PA.

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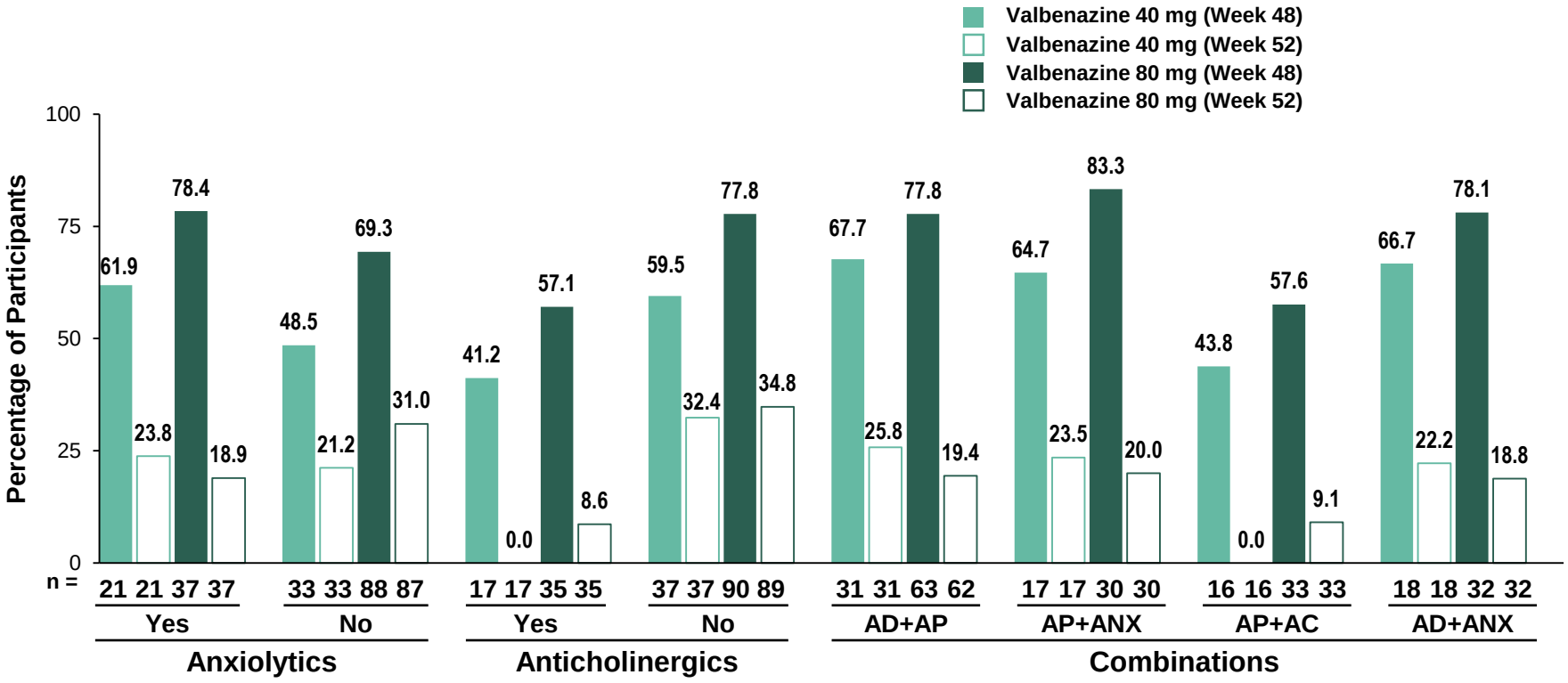
KINECT 3 & KINECT 4 – Concomitant Medication Subgroup Analysis: ≥50% AIMS Improvement from Baseline at Week 48 & Week 52



AIMS, Abnormal Involuntary Movement Scale; AC, anticholinergic; AD, antidepressant; ANX, anxiolytic; AP, antipsychotic.

Comella C, et al. AAN 2019; Philadelphia, PA.

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1506: Rollover Phase 3b Study – Underlying Disease Diagnosis Analysis

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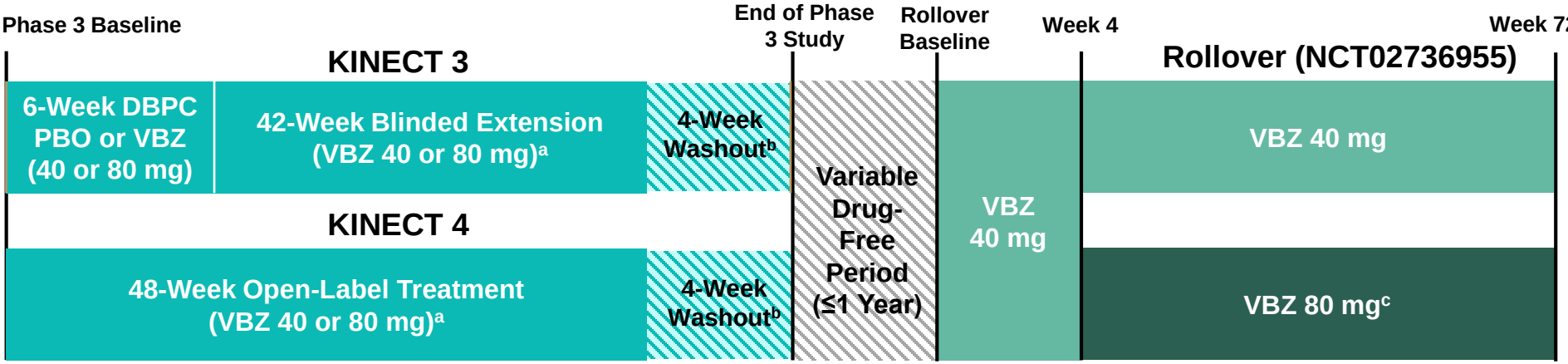
1506: Study Design



- The open-label, rollover study included participants who completed KINECT 3 or KINECT 4 (48 weeks of treatment and 4 weeks of washout)
  - All rollover study participants received once-daily valbenazine (VBZ) 40 mg for 4 weeks
  - Dosage was escalated to 80 mg at the end of Week 4 based on clinician judgment of safety/tolerability and TD improvement
  - One dose reduction to 40 mg was allowed after Week 4 if 80 mg was not tolerated
  - Participants unable to tolerate 40 mg were discontinued from the study
- Participants received treatment for up to 72 weeks or until valbenazine became commercially available
- Stable doses of concomitant medications to treat psychiatric disorders and comorbid medical conditions were allowed

[a]All KINECT 3 participants randomized to valbenazine in the DBPC period or re-randomized from placebo to valbenazine in the extension period were initiated at 40 mg for 1 week; all KINECT 4 participants were initiated at 40 mg for 4 weeks. [b]Participants who enrolled in the rollover study may have had an additional drug-free period (mean duration of additional off-drug prior to rollover study start: 66.4 days; range, 0 to 324 days). [c]Includes participants who had a dose reduction to 40 mg due to tolerability issues; DBPC, double-blind placebo-controlled; PBO, placebo VBZ, valbenazine.

Lindenmayer JP, et al. ASCP 2018; Miami, Florida.

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1506 – Underlying Disease Diagnosis Analysis: Assessments

- All outcomes were analyzed descriptively in participants who received ≥1 dose of valbenazine and had ≥1 available post-baseline assessment
- Subgroups were defined by psychiatric diagnosis: schizophrenia/schizoaffective disorder or mood disorder
- Assessments included the Clinical Global Impression of Severity-TD (CGIS-TD: range, 1 “normal, not at all ill” to 7 “extremely ill”) and the Patient Satisfaction Questionnaire (PSQ: range, 1 “very satisfied” to 5 “very dissatisfied”)
  - Mean CGIS-TD scores were analyzed at every 12-week visit in each diagnosis subgroup
  - Percentages of participants with a CGIS-TD score ≤2 (“normal, not at all ill” or “borderline ill”) or PSQ score ≤2 (“very satisfied” or “somewhat satisfied”) were also assessed
- Safety assessments included treatment-emergent adverse events (TEAEs), laboratory tests, vital sign measurements, electrocardiograms (ECGs), and the C-SSRS

Grigoriadis D, et al. ACNP 2018; Hollywood, FL.

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1506 – Underlying Disease Diagnosis Analysis: Baseline Characteristics

	Schizophrenia/Schizoaffective Disorder			Mood Disorder		
	VBZ 40 mg (n=23)	VBZ 80 mg (n=75)	All[a] (n=104)	VBZ 40 mg (n=12)	VBZ 80 mg (n=42)	All[a] (n=56)
Age, mean (SD), years	55.9 (9.4)	57.9 (9.0)	57.5 (8.9)	59.9 (7.6)	58.0 (8.7)	58.4 (8.6)
Male, n (%)	10 (43.5)	52 (69.3)	66 (63.5)	3 (25.0)	11 (26.2)	15 (26.8)
Race, n (%)						
Caucasian	11 (47.8)	49 (65.3)	62 (59.6)	10 (83.3)	37 (88.1)	49 (87.5)
African-American	12 (52.2)	26 (34.7)	41 (39.4)	2 (16.7)	4 (9.5)	6 (10.7)
BMI, mean (SD), kg/m^2	29.6 (6.0)	28.6 (5.8)	28.9 (5.8)	28.2 (4.6)	28.5 (5.0)	28.6 (4.9)
Age at diagnosis, mean (SD), years						
Psychiatric diagnosis	27.1 (8.3)	28.7 (11.4)	28.2 (10.6)	36.0 (12.0)	33.9 (13.3)	34.7 (13.2)
Tardive dyskinesia	46.3 (11.5)	46.3 (9.1)	45.8 (9.7)	51.8 (10.3)	52.1 (9.4)	52.2 (9.7)
BPRS total score at screening, mean (SD)	29.0 (6.1)	26.7 (5.7)	27.4 (6.1)	24.0 (5.5)	25.0 (5.2)	25.0 (5.6)
C-SSRS lifetime at screening, n (%)						
Suicidal ideation	6 (26.1)	21 (28.0)	29 (27.9)	4 (33.3)	15 (35.7)	20 (35.7)
Suicidal behavior	5 (21.7)	21 (28.0)	27 (26.0)	5 (41.7)	11 (26.2)	17 (30.4)

- Baseline characteristics were generally similar between valbenazine dose groups
  - Compared to the schizophrenia/schizoaffective disorder subgroup, the mood subgroup had fewer men, fewer African-American participants, and were older at time of psychiatric diagnosis and TD diagnosis

Grigoriadis D, et al. ACNP 2018; Hollywood, FL.

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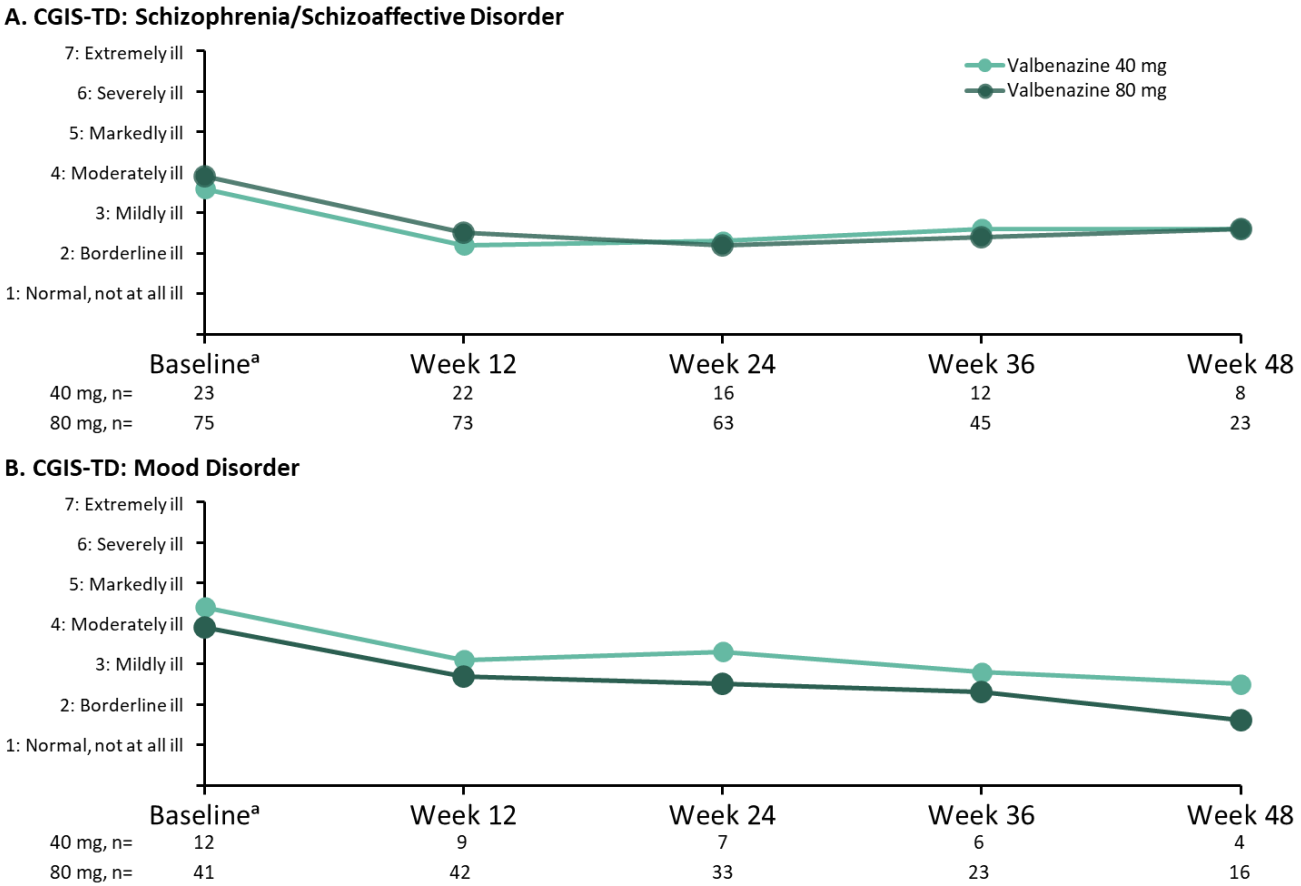
1506 – Underlying Disease Diagnosis Analysis: Global TD Improvement (Clinician-Rated)



- In both diagnosis subgroups, the percentage of participants with a CGIS-TD score ≤2 increased from baseline (prior to restarting valbenazine) to Week 48

[a]Baseline of rollover study (after variable valbenazine-free period of 0-324 days)
Data not shown for participants who had a dose reduction from 80 mg to 40 mg (schizophrenia/schizoaffective disorder, n=6; mood disorder, n=2)
CGIS-TD, Clinical Global Impression of Severity-Tardive Dyskinesia

Grigoriadis D, et al. ACNP 2018; Hollywood, FL.

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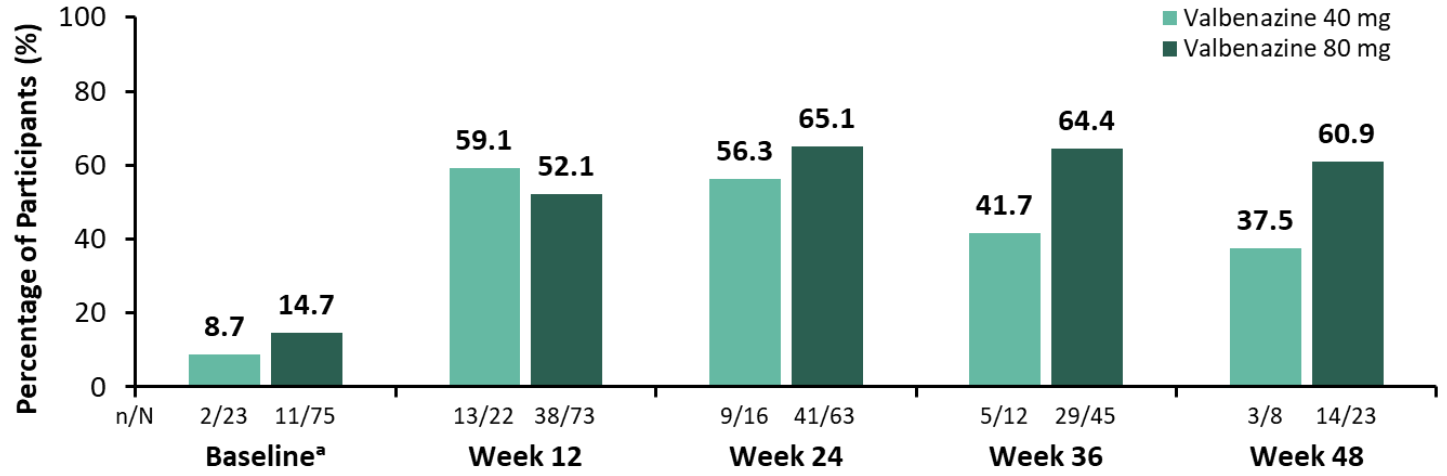
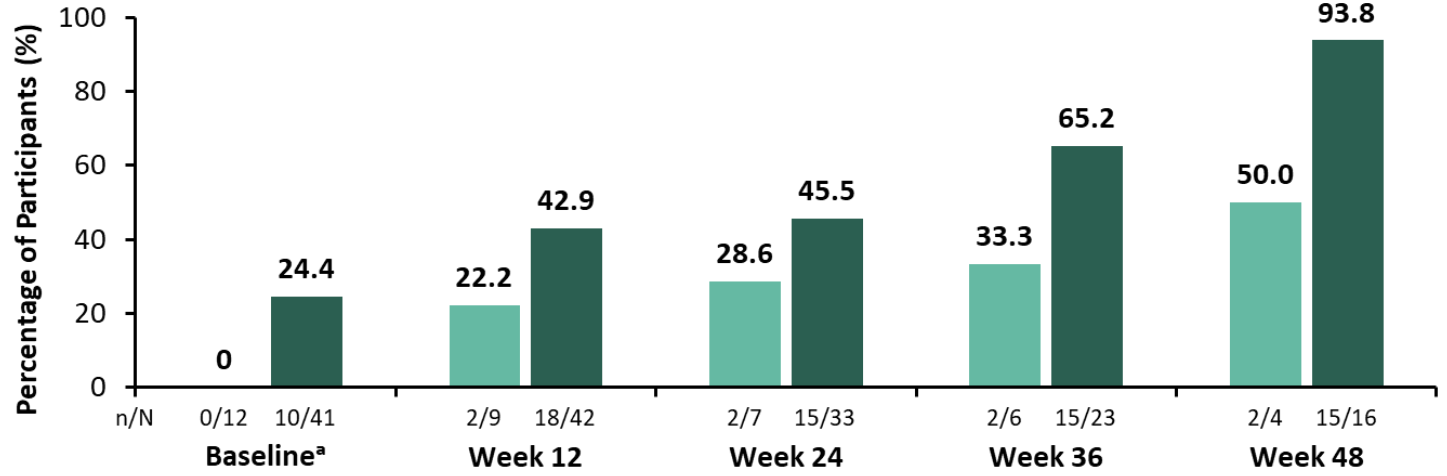
1506 – Underlying Disease Diagnosis Analysis: Meaningful TD Response (CGIS-TD Score ≤2)



B. Mood Disorder



[a]Baseline of rollover study (after variable valbenazine-free period of 0-324 days)
Data not shown for participants who had a dose reduction from 80 mg to 40 mg (schizophrenia/schizoaffective disorder, n=6; mood disorder, n=2)
CGIS-TD, Clinical Global Impression of Severity-Tardive Dyskinesia; CGIS-TD Score ≤2 : "normal, not at all ill" or "borderline ill"

Grigoriadis D, et al. ACNP 2018; Hollywood, FL.

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1506 – Underlying Disease Diagnosis Analysis: PSQ Response (Score ≤ 2)

- At baseline, 99.0% (103/104) of all schizophrenia/schizoaffective disorder participants and 98.2% (55/56) of all mood disorder participants were “very satisfied” or “somewhat satisfied” with their prior valbenazine experience (PSQ score ≤2)
- At Week 48, high levels of satisfaction with valbenazine were reported in the schizophrenia/schizoaffective disorder subgroup (97.1% [33/34]) and the mood disorder subgroup (100% [22/22])

PSQ, Patient Satisfaction Questionnaire.

Grigoriadis D, et al. ACNP 2018; Hollywood, FL.

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1506 – Underlying Disease Diagnosis Analysis: C-SSRS Shifts from Baseline

	Baseline Score	Maximum Suicidal Ideation Score At Any Time During the Study[a]					
		0	1	2	3	4	5
Schizophrenia/ Schizoaffective Disorder (n=104)	0	102	0	1	0	0	0
	1	0	1	0	0	0	0
	2	0	0	0	0	0	0
	3	0	0	0	0	0	0
Mood Disorder (n=56)	0	51	1	1	0	0	0
	1	1	0	0	0	0	0
	2	0	0	1	0	0	0
	3	0	0	0	1	0	0

[a]0=no suicidal ideation, 1=wish to be dead, 2=non-specific active suicidal thoughts, 3=active suicidal ideation with any methods (not plan) without intent to act, 4=active suicidal ideation with some intent to act, without specific plan, 5=active suicidal ideation with specific plan and intent
C-SSRS, Columbia-Suicide Severity Rating Scale

- Based on available C-SSRS data, almost all schizophrenia/schizoaffective disorder participants (99.0% [103/104]) and mood disorder participants (94.6% [53/56]) had no suicidal ideation at baseline (score=0)
  - Most of these participants continued to have no emergence of suicidal ideation at any time during the rollover study
    - schizophrenia/schizoaffective disorder: 99.0% [102/103]
    - mood disorder: 96.2% [51/53])
  - Among participants who had some suicidal ideation at baseline (score=1 to 3), none had any worsening in C-SSRS score at any time during treatment

Grigoriadis D, et al. ACNP 2018; Hollywood, FL.

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1506 – Underlying Disease Diagnosis Analysis: Treatment-Emergent Adverse Events (Week 4 to the End of Study)

	Schizophrenia/Schizoaffective Disorder			Mood Disorder		
	VBZ 40 mg (n=22)	VBZ 80 mg (n=75)	All[a] (n=103)	VBZ 40 mg (n=10)	VBZ 80 mg (n=42)	All[a] (n=54)
Summary, n (%)						
Any TEAE	9 (40.9)	36 (48.0)	50 (48.5)	5 (50.0)	20 (47.6)	27 (50.0)
Any serious TEAE	2 (9.1)	9 (12.0)	13 (12.6)	0	1 (2.4)	1 (1.9)
Any TEAE leading to discontinuation	0	6 (8.0)	7 (6.8)	0	0	0
Deaths[b]	0	3 (4.0)	4 (3.9)	0	0	0
TEAEs by preferred term, n (%)[c]						
Urinary tract infection	1 (4.5)	1 (1.3)	2 (1.9)	0	5 (11.9)	5 (9.3)
Back pain	1 (4.5)	3 (4.0)	4 (3.9)	1 (10.0)	2 (4.8)	3 (5.6)
Tremor	0	1 (1.3)	2 (1.9)	0	2 (4.8)	3 (5.6)
Cough	0	2 (2.7)	2 (1.9)	1 (10.0)	1 (2.4)	3 (5.6)
Suicidal ideation	0	1 (1.3)	1 (1.0)	1 (10.0)	2 (4.8)	3 (5.6)

- The incidence of any TEAE in all valbenazine-treated patients was similar between diagnosis subgroups
  - Less than 7% of all participants in either subgroup discontinued due to TEAEs
- There were no clinically important changes in laboratory parameters, vital signs, or ECG parameters

[a]Includes participants who had a dose reduction from 80 mg to 40 mg after Week 4
[b]Deaths occurred due to chronic obstructive pulmonary disease, sepsis syndrome, alcohol-induced coma, and hypertensive heart disease; none were judged as related to treatment.
[c]Reported in >5% of all participants in either diagnosis subgroup
40 mg: never had a dose increase to 80 mg; 80 mg: received 40 mg and increased to 80 mg, without a subsequent dose reduction
TEAE, treatment-emergent adverse event; VBZ, valbenazine

Grigoriadis D, et al. ACNP 2018; Hollywood, FL.

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1506: Rollover Phase 3b Study – Concomitant Medication Subgroup Analysis

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1506 – Concomitant Medication Subgroup Analysis: Assessments

- Data from the rollover study (1506) were analyzed post hoc to provide clinical insights into the effect of valbenazine in conjunction with common psychoactive medications
- Clinical Global Impression of Severity-Tardive Dyskinesia (CGIS-TD) data were analyzed descriptively in participants who received ≥1 dose of valbenazine and had available data
- Analyses included:
  - Mean change from baseline in CGIS-TD
    - Range, 1 “normal, not at all ill” to 7 “extremely ill”
  - Percentages of participants with a CGIS-TD score ≤2 (“normal, not at all ill” or “borderline ill”)

Farahmand K, et al. ACNP 2019; Orlando, FL.

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1506 – Concomitant Medication Subgroup Analysis: Assessments

- Concomitant medication subgroups were defined by use at baseline as follows:
  - Antipsychotic use (yes, no)
  - Antidepressant use (yes, no)
  - Anxiolytic use (yes, no)
  - Anticholinergic use (yes, no)
  - Combinations:
    - Antidepressant + Atypical Antipsychotics
    - Antipsychotic + Anxiolytic
    - Antipsychotic + Anticholinergic
    - Antidepressant + Anxiolytic
  - Subgroup categories were not mutually exclusive and only reflected concomitant medication use in the rollover study
  - Concomitant medication use in the prior studies were not considered, nor was the mean daily antipsychotic dose of the subgroups

Farahmand K, et al. ACNP 2019; Orlando, FL.

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1506 – Concomitant Medication Subgroup Analysis: Assessments

- Of the 224 participants who completed KINECT 3 or KINECT 4, 161 (71.9%) enrolled in the rollover study
  - 71 from KINECT 3; 90 from KINECT 4
  - 1 participant without post-baseline data was excluded
    - 138 (85.7%) were ongoing in the study when it was terminated
    - Few reached Week 60 (n=4) and none reached Week 72 because valbenazine became commercially available before reaching those visits
    - Reasons for discontinuation prior to study termination were withdrawal of consent (n=8), adverse events (n=5), death (n=4, not related to treatment),non-compliance (n=3), investigator decision (n=2), and lost to follow-up (n=1)
- In all 160 participants who received ≥1 dose of study drug, 82.5% were taking an antipsychotic medication at baseline or during the study
- Concomitant use of antidepressants, anxiolytics, and anticholinergics were reported in 69.4%, 36.3%, and 27.5% of participants, respectively

Farahmand K, et al. ACNP 2019; Orlando, FL.

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1506 – Concomitant Medication Subgroup Analysis: Concomitant Medication Use[a]

	Valbenazine 40 mg (n=35)	Valbenazine 80 mg (n=117)	Valbenazine 80/40 mg (n=8)
Any antipsychotic, n (%)[b]	28 (80.0)	97 (82.9)	7 (87.5)
Quetiapine	6 (17.1)	30 (25.6)	0
Haloperidol	2 (5.7)	7 (6.0)	2 (25.0)
Olanzapine	5 (14.3)	14 (12.0)	2 (25.0)
Aripiprazole	3 (8.6)	23 (19.7)	1 (12.5)
Risperidone	7 (20.0)	13 (11.1)	1 (12.5)
Ziprasidone	3 (8.6)	7 (6.0)	1 (12.5)
Lithium	1 (2.9)	7 (6.0)	1 (12.5)
Any antidepressants, n (%)[b]	22 (62.9)	85 (72.6)	4 (50.0)
Trazodone	7 (20.0)	24 (20.5)	2 (25.0)
Fluoxetine	2 (5.7)	9 (7.7)	2 (25.0)
Bupropion	3 (8.6)	13 (11.1)	0
Sertraline	7 (20.0)	13 (11.1)	0
Mirtazapine	2 (5.7)	17 (14.5)	0
Citalopram	3 (8.6)	8 (6.8)	1 (12.5)
Duloxetine	1 (2.9)	10 (8.5)	0
Escitalopram	1 (2.9)	8 (6.8)	0
Venlafaxine	2 (5.7)	7 (6.0)	0
Any anxiolytic, n (%)[b]	11 (31.4)	45 (38.5)	2 (25.0)
Alprazolam	3 (8.6)	15 (12.8)	0
Hydroxyzine	1 (2.9)	15 (12.8)	1 (12.5)
Lorazepam	4 (11.4)	10 (8.5)	1 (12.5)
Buspirone	3 (8.6)	11 (9.4)	1 (12.5)
Any anticholinergic, n (%)[b]	13 (37.1)	29 (24.8)	2 (25.0)
Benztropine	11 (31.4)	26 (22.2)	2 (25.0)

[a]At baseline or at any time during the study; [b]Reported in ≥5% of participants.

Farahmand K, et al. ACNP 2019; Orlando, FL.

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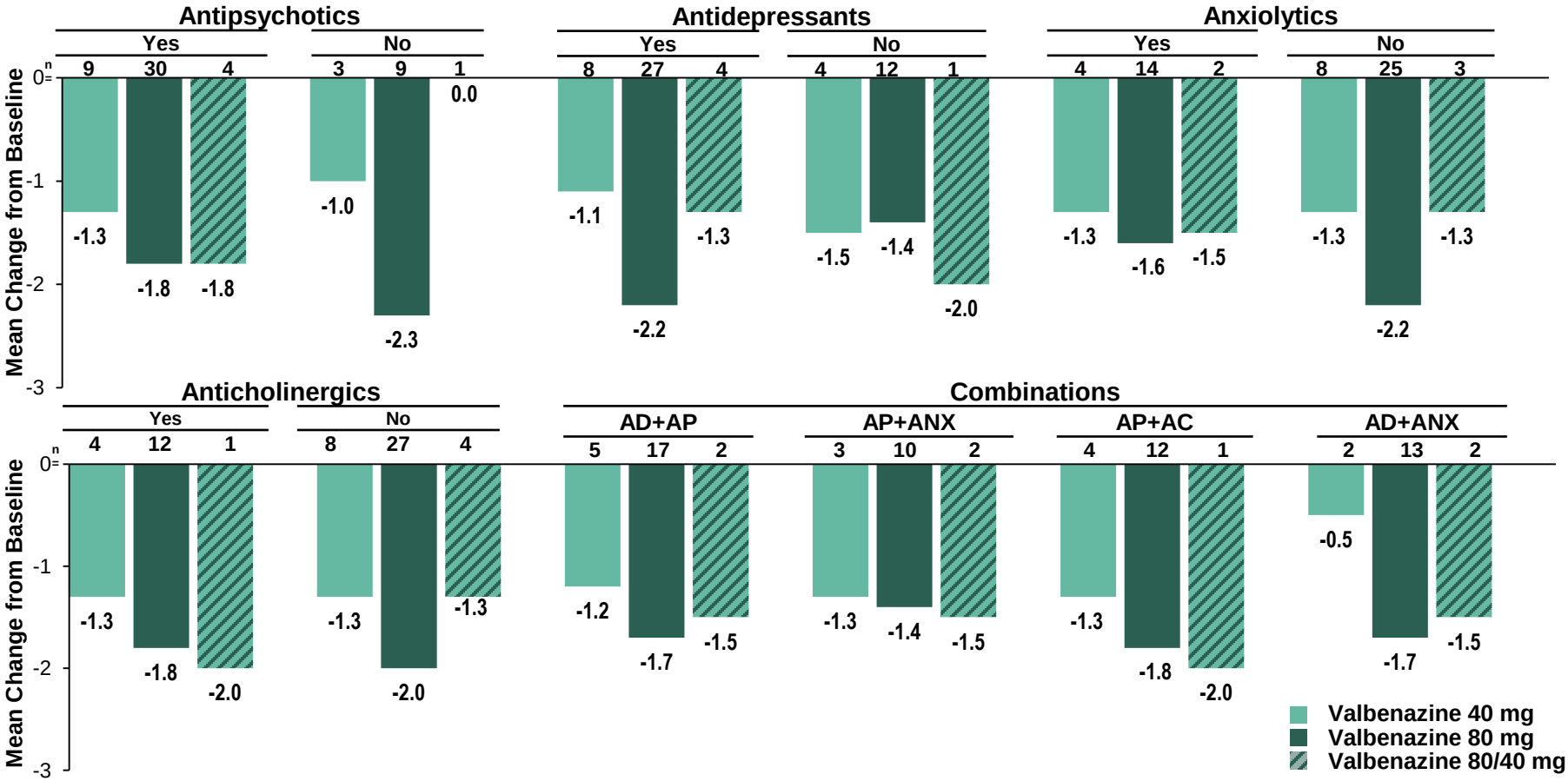
1506 – Concomitant Medication Subgroup Analysis: CGIS-TD Mean Change from Baseline at Week 48



- At Week 48 in the overall population (n=56), the mean change from baseline in CGIS-TD score was -1.8 for all doses combined; comparable mean improvements were found in all concomitant medication subgroups

AD+AP includes participants who received an atypical antipsychotic or both (atypical + typical).
AC, anticholinergic; AD, antidepressant; ANX, anxiolytic; AP, antipsychotic; CGIS-TD, Clinical Global Impression of Severity-Tardive Dyskinesia.

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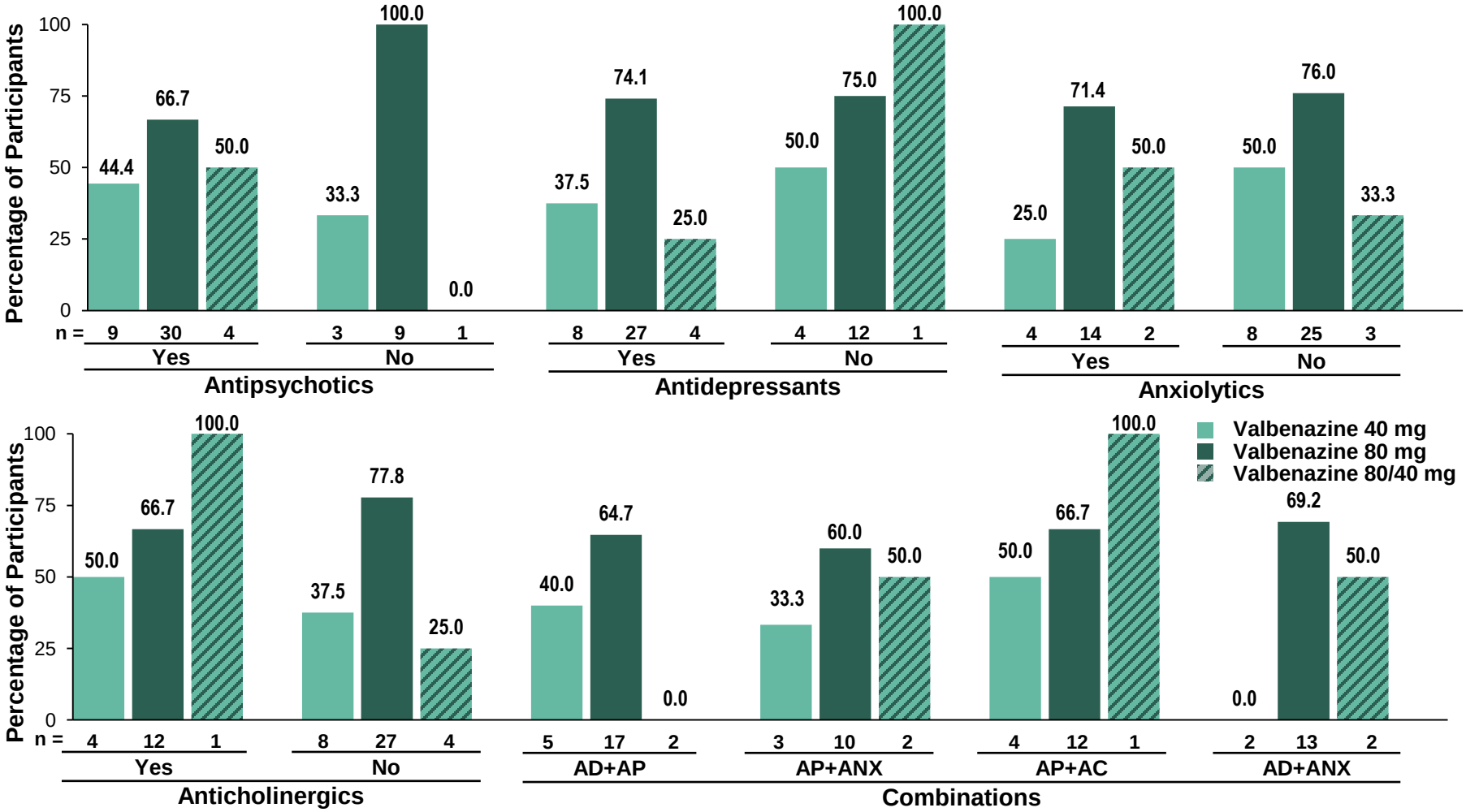
1506 – Concomitant Medication Subgroup Analysis: Percentage of Participants with CGI-TD Score ≤2* at Week 48



*CGIS-TD score ≤2 (“normal, not at all ill” or “borderline ill”); AD+AP includes participants who received an atypical antipsychotic or both (atypical + typical); AC, anticholinergic; AD, antidepressant; ANX, anxiolytic; AP, antipsychotic; CGIS-TD, Clinical Global Impression of Severity-Tardive Dyskinesia.

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