SLEEP 2026

BALTIMORE, MD | JUNE 14-17

A JOINT MEETING

AASM American Academy of SLEEP MEDICINE™

Sleep Research Society® Advancing Sleep & Circadian Science

Clinical Responders to Low-Sodium Oxybate in Narcolepsy and Idiopathic Hypersomnia

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Introduction

- Narcolepsy and idiopathic hypersomnia are central disorders of hypersomnolence characterized by a constellation of symptoms that impact nighttime sleep and daytime functioning, including excessive daytime sleepiness (EDS)[1]

- The Epworth Sleepiness Scale (ESS) is a validated subjective assessment of EDS[2]; the Idiopathic Hypersomnia Severity Scale (IHSS) is a validated subjective measure of the severity, frequency, and functional impact of idiopathic hypersomnia symptoms[3,4]

- Low-sodium oxybate (LXB; Xywav®) is approved by the US Food and Drug Administration for the treatment of cataplexy or EDS in people with narcolepsy ≥7 years of age and for the treatment of idiopathic hypersomnia in adults[5]

- LXB has demonstrated clinically meaningful improvements in EDS in both narcolepsy and idiopathic hypersomnia, and clinically meaningful improvements in idiopathic hypersomnia symptom severity based on the IHSS[6,7]

1. American Academy of Sleep Medicine. International classification of sleep disorders – third edition, text revision. Darien, IL: American Academy of Sleep Medicine; 2023. 2. Johns MW. *Sleep*. 1991;14(6):540-546. 3. Dauvilliers Y, et al. *Neurology*. 2019;92:e1-e9. 4. Rassu AL, et al. *J Clin Sleep Med*. 2022:18(2):617-629. 5. Xywav® (calcium, magnesium, potassium, and sodium oxybates) oral solution, CIII [prescribing information]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; 2025. 6. Schneider LD, et al. *Neurol Ther*. 2026. doi:10.1007/s40120-026-00921-3. 7. Plante DT, et al. *CNS Drugs*. 2026. doi:10.1007/s40263-025-01262-9.

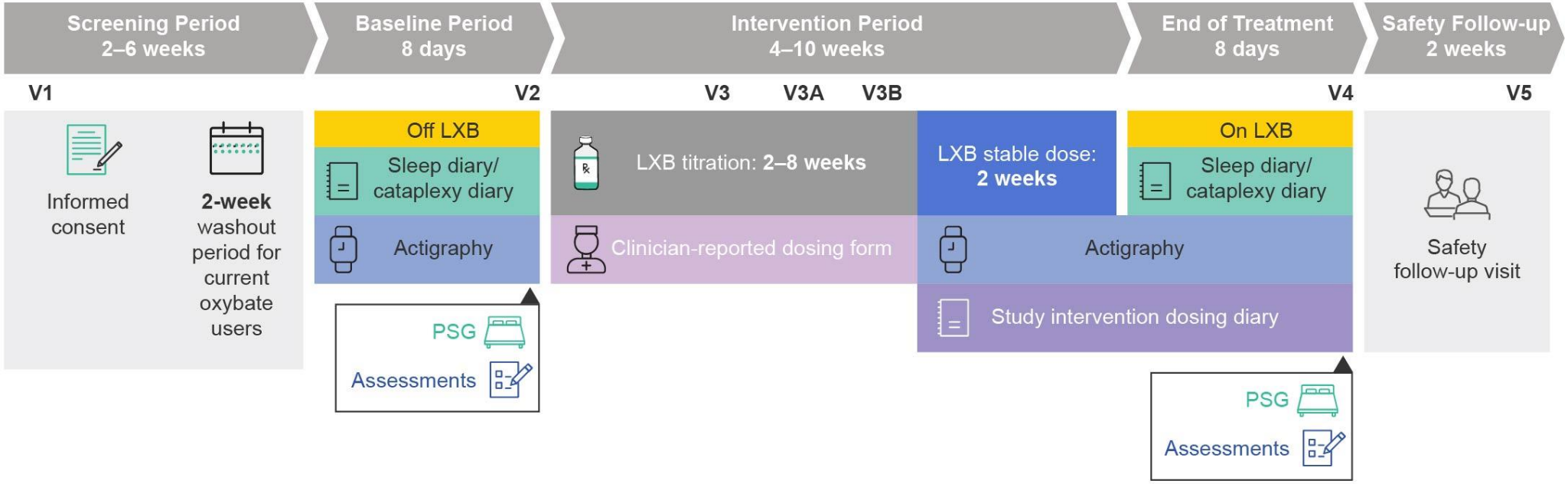
Objective

- Jazz DUET (**D**evelop hypersomnia **U**nderstanding by **E**valuating low-sodium oxybate **T**reatment) was a phase 4, prospective, single-arm, open-label study (NCT05875974) evaluating the effectiveness of LXB in treating sleep and daytime symptoms[1,2]

This analysis aimed to describe the proportions of DUET participants with narcolepsy or idiopathic hypersomnia who achieved a clinically important response to LXB treatment based on established thresholds and normal score ranges on the ESS (both cohorts) and IHSS (idiopathic hypersomnia cohort only)

1. Schneider LD, et al. *Neurol Ther*. 2026. doi:10.1007/s40120-026-00921-3. 2. Plante DT, et al. *CNS Drugs*. 2026. doi:10.1007/s40263-025-01262-9.
ESS, Epworth Sleepiness Scale; IHSS, Idiopathic Hypersomnia Severity Scale; LXB, low-sodium oxybate.

DUET Study Design



- **Key Inclusion Criteria**: Age 18–75 with a primary diagnosis of NT1 or NT2 (ICSD-3 or DSM-5) or idiopathic hypersomnia (ICSD-3); ESS score >10; concomitant stable use of anticataleptic or alerting agents allowed
- **Key Exclusion Criteria**: Untreated/inadequately treated sleep-disordered breathing (AHI >10); history/presence of other untreated, inadequately treated, or unstable disorder or condition (eg, sleep, medical, behavioral/psychiatric, neurological)

Figure adapted from Nichols DA, et al. *Neurol Ther*. 2025;14:1705-1727. http://creativecommons.org/licenses/by-nc/4.0/.

AASM, American Academy of Sleep Medicine; AHI, apnea-hypopnea index; DSM-5, *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*; ESS, Epworth Sleepiness Scale; ICSD-3, *International Classification of Sleep Disorders – Third Edition*; LXB, low-sodium oxybate; NT1, narcolepsy type 1; NT2, narcolepsy type 2; PSG, polysomnography; V, visit.

Outcomes: Responder Definitions

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- Proportions of participants who responded to treatment based on these MCIDs and normal range cutoffs were descriptively analyzed
- **ESS:** Assesses daytime sleepiness (8 items on a 4-point scale, total score range 0–24)[1]
  - MCID for ESS: ≥2-point decrease[2]
  - Normal score: ESS ≤10 points[1]
- **IHSS:** Assesses the severity, frequency, and functional impacts of idiopathic hypersomnia symptoms, including prolonged nighttime sleep, sleep inertia, and daytime sleepiness (14 items, total score range 0–50)[3]
  - MCID for IHSS: ≥4-point decrease[4]
  - Normal score: IHSS <22 points[3]

1. Johns MW. *Sleep*. 1991;14(6):540-546. 2. Maski K, et al. *J Clin Sleep Med*. 2021;17(9):1895–1945. 3. Dauvilliers Y, et al. *Neurology*. 2019;92:e1-e9. 4. Rassu AL, et al. *J Clin Sleep Med*. 2022:18(2):617-629.
AASM, American Academy of Sleep Medicine; BL, baseline; EOT, end of treatment; ESS, Epworth Sleepiness Scale; IHSS, Idiopathic Hypersomnia Severity Scale; MCID, minimally clinically important difference.

Results

Demographics/Baseline Characteristics for Narcolepsy[1] and Idiopathic Hypersomnia Cohorts[2,a]

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Characteristic	Total Narcolepsy Cohort n=34	Total Idiopathic Hypersomnia Cohort n=40
Age (years)		
Mean (SD)	35.7 (14.2)	38.7 (12.3)
Female at birth, n (%)	25 (73.5)	31 (77.5)
Race, n (%)		
White	27 (79.4)	34 (85.0)
Black or African American	4 (11.8)	2 (5.0)
Asian	2 (5.9)	2 (5.0)
Native Hawaiian or Other Pacific Islander	–	1 (2.5)
Unknown	1 (2.9)	–
Multiple[b]	–	1 (2.5)
Body mass index (kg/m²)		
Mean (SD)	29.1 (6.2)	29.2 (6.5)
Concomitant alerting agents,[c] n (%)	20 (58.8)	15 (37.5)

[a]Completer analysis set. [b]Participants reported more than 1 race. [c]Alerting agents were defined as stimulants or wake-promoting agents; participants must have taken the same dosage for ≥1 month before screening visit 1 with no plans to adjust dosage during the study.

SD, standard deviation.

1. From Schneider LD, et al. *Neurol Ther*. 2026. doi:10.1007/s40120-026-00921-3. http://creativecommons.org/licenses/by-nc/4.0/.
2. From Plante DT, et al. *CNS Drugs*. 2026. doi:10.1007/s40263-025-01262-9. . http://creativecommons.org/licenses/by-nc/4.0/.

DUET Primary Endpoint: Mean ESS Scores Improved With Optimized LXB Treatment in Participants With Narcolepsy or Idiopathic Hypersomnia[a]

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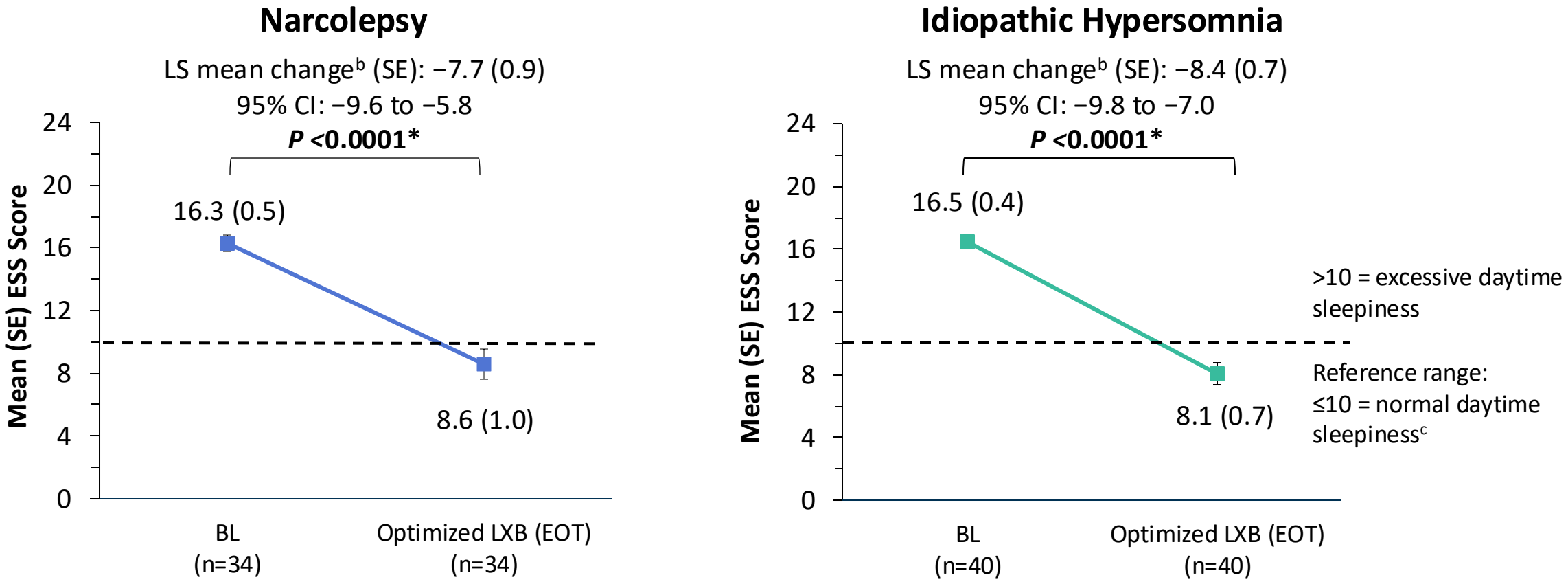
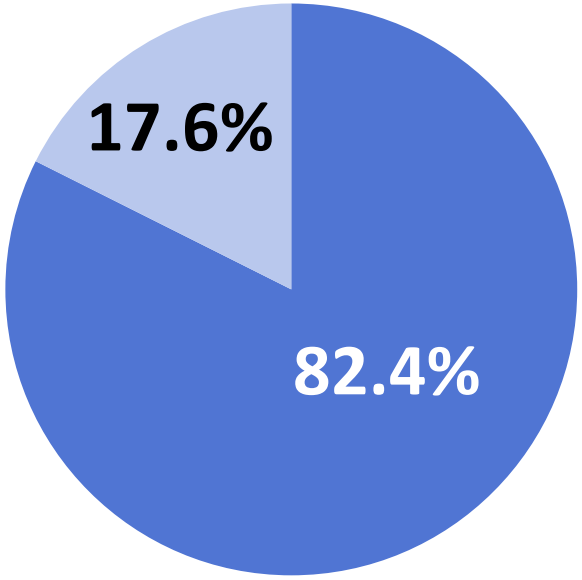


[a]Completer analysis set. [b]Difference between EOT and BL. LS mean and 95% CI are provided at EOT visit using ANCOVA model adjusted for the BL value. [c]Established categories consider scores up to 10 normal.
*Controlled for multiplicity in prespecified sequential testing. *P*<0.05 are statistically significant.
ANCOVA, analysis of covariance; BL, baseline; CI, confidence interval; EOT, end of treatment; ESS, Epworth Sleepiness Scale; LS, least squares; LXB, low-sodium oxybate; SE, standard error.

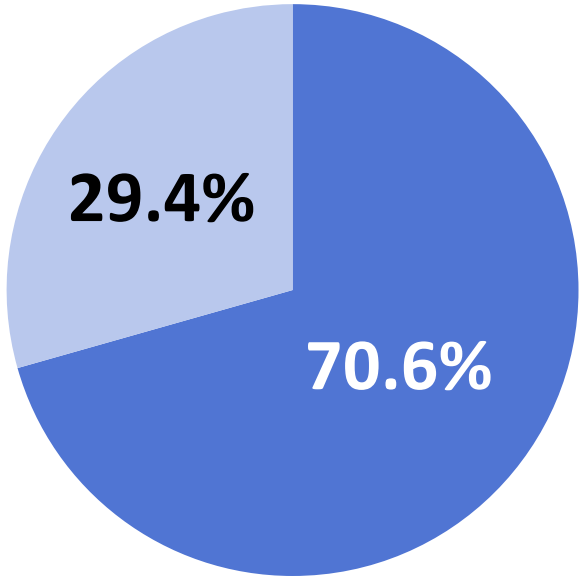
Most Participants With Narcolepsy Achieved Clinically Meaningful Improvement and ESS Scores Within Normal Range (≤10) With Optimized LXB Treatment[a]

ESS MCID Responder (≥2-point decrease) from BL to EOT



(n=34)

ESS Score Normal Range (≤10) at EOT



(n=34)

Yes No

- The majority of participants with narcolepsy (82.4%; n=28/34) met MCID criteria for ESS; 70.6% (n=24/34) achieved normal range ESS scores with optimized LXB at EOT

[a]Completer analysis set.

BL, baseline; EOT, end of treatment; ESS, Epworth Sleepiness Scale; LXB, low-sodium oxybate; MCID, minimally clinically important difference.

Most Participants With Narcolepsy Achieved Clinically Meaningful Improvement and ESS Scores Within Normal Range (≤10) With Optimized LXB Treatment, *Regardless of Concomitant Alerting Agent Use*[a,b,c]

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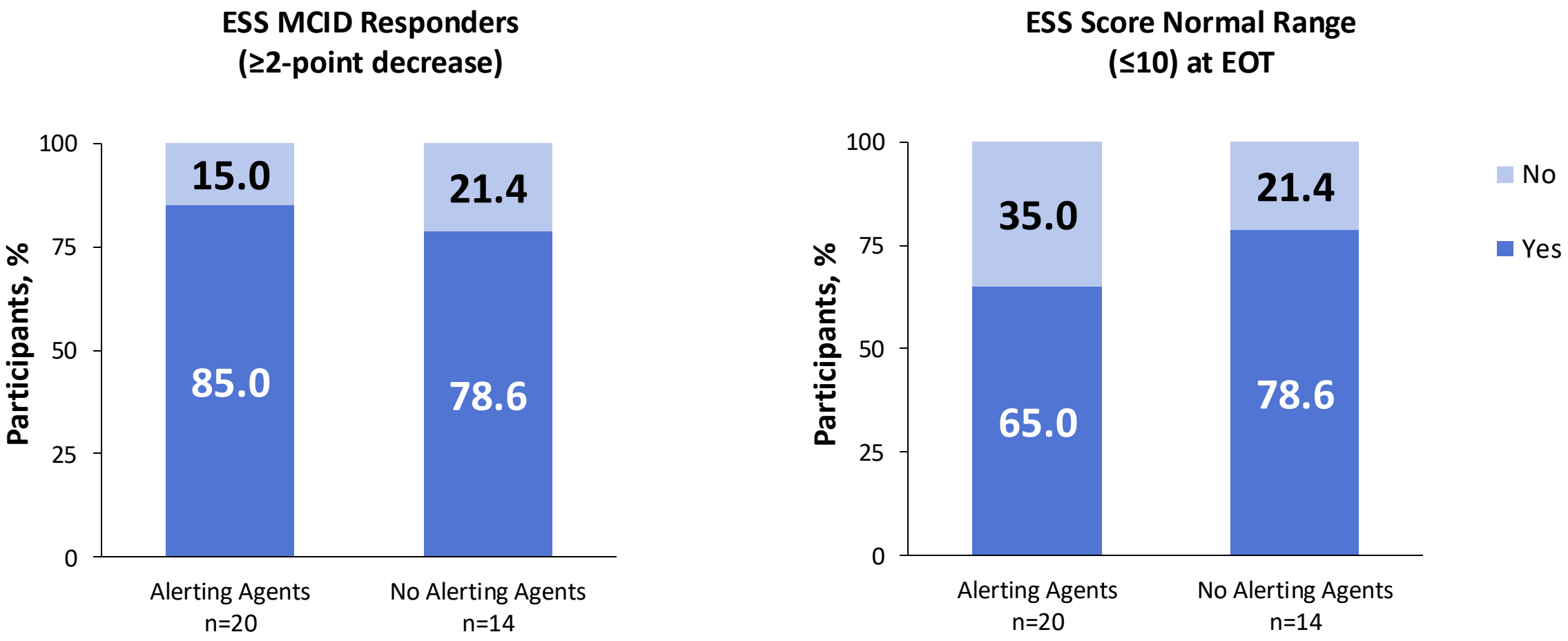
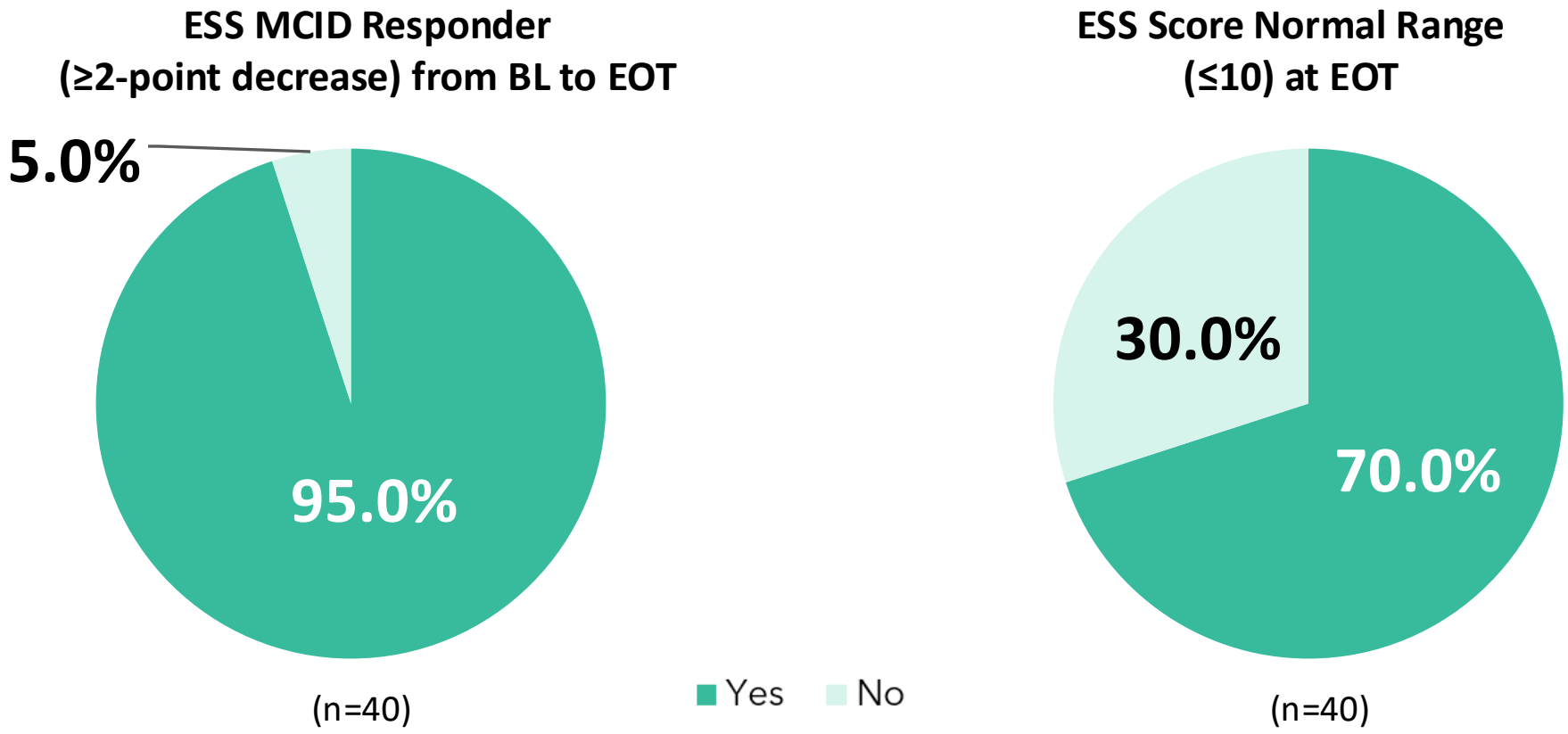


[a]Completer analysis set. [b]Alerting agents were defined as stimulants or wake-promoting agents; participants must have taken the same dosage ≥1 month before screening visit 1 with no plans to adjust dosage during the study.
[c]Inclusion criteria included ESS score >10; therefore, participants with controlled EDS (taking alerting agents and not on alerting agents) were not eligible for the study.
EOT, end of treatment; EDS, excessive daytime sleepiness; ESS, Epworth Sleepiness Scale; LXB, low-sodium oxybate; MCID, minimally clinically important difference.

Most Participants With Idiopathic Hypersomnia Achieved Clinically Meaningful Improvement and ESS Scores Within Normal Range (≤10) With Optimized LXB Treatment[a]



- Most participants with idiopathic hypersomnia (95.0%; n=38/40) met MCID criteria for ESS; 70.0% (n=28/40) achieved normal range ESS scores with optimized LXB at EOT

[a]Completer analysis set.
BL, baseline; EOT, end of treatment; ESS, Epworth Sleepiness Scale; LXB, low-sodium oxybate; MCID, minimally clinically important difference.

Most Participants With Idiopathic Hypersomnia Achieved Clinically Meaningful Improvement and ESS Scores Within Normal Range (≤10) With Optimized LXB Treatment, *Regardless of Concomitant Alerting Agent Use*[a,b,c]

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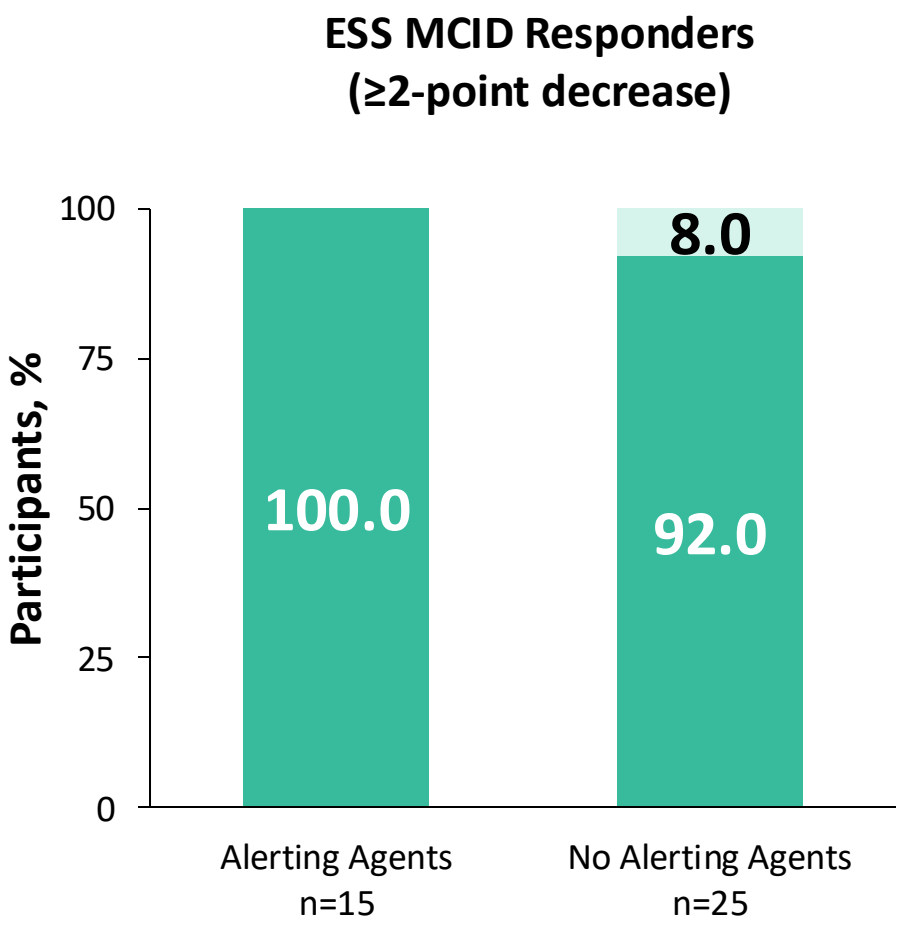

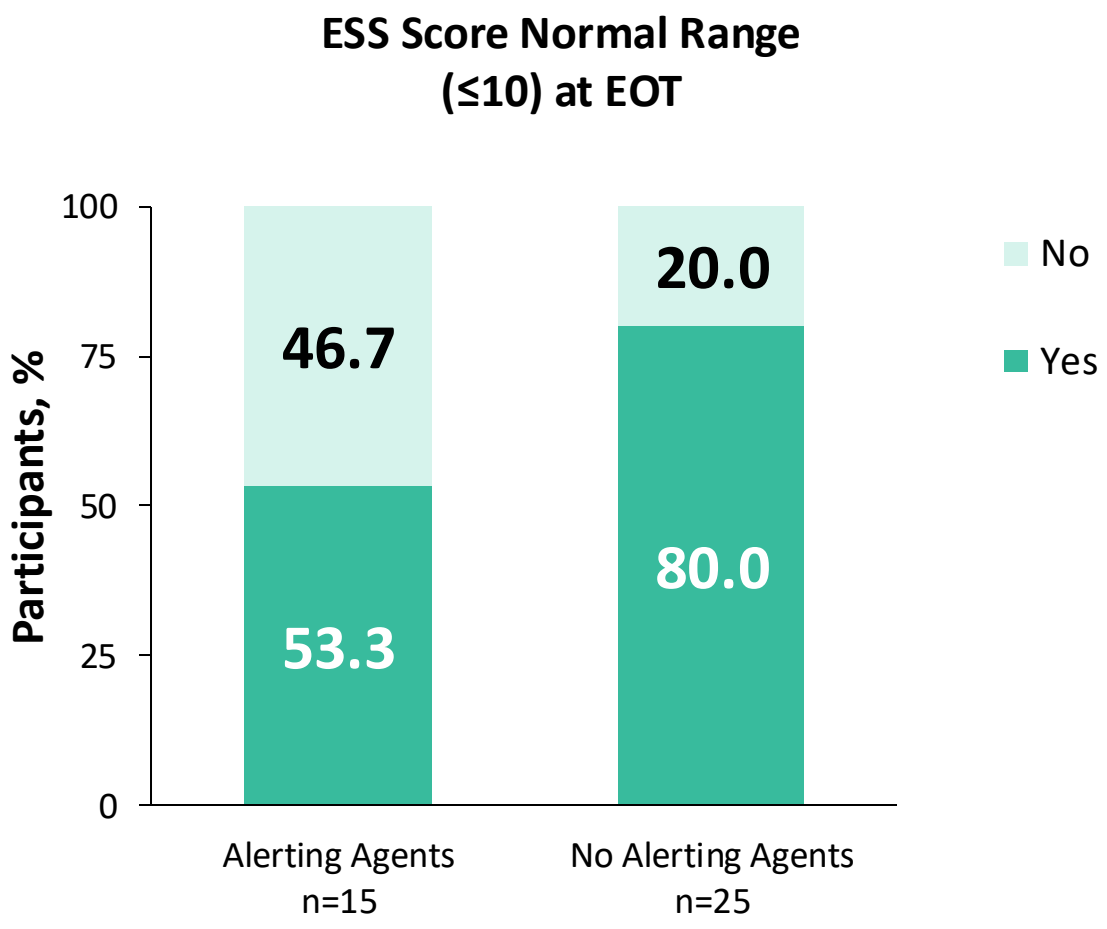

[a]Completer analysis set. [b]Alerting agents were defined as stimulants or wake-promoting agents; participants must have taken the same dosage ≥1 month before screening visit 1 with no plans to adjust dosage during the study.
[c]Inclusion criteria included ESS score >10; therefore, participants with controlled EDS (taking alerting agents and not on alerting agents) were not eligible for the study.
EOT, end of treatment; EDS, excessive daytime sleepiness; ESS, Epworth Sleepiness Scale; LXB, low-sodium oxybate; MCID, minimally clinically important difference.

DUET Key Secondary Endpoint: Mean Idiopathic Hypersomnia Severity Scale Scores Improved With Optimized LXB Treatment in Participants With Idiopathic Hypersomnia[a]

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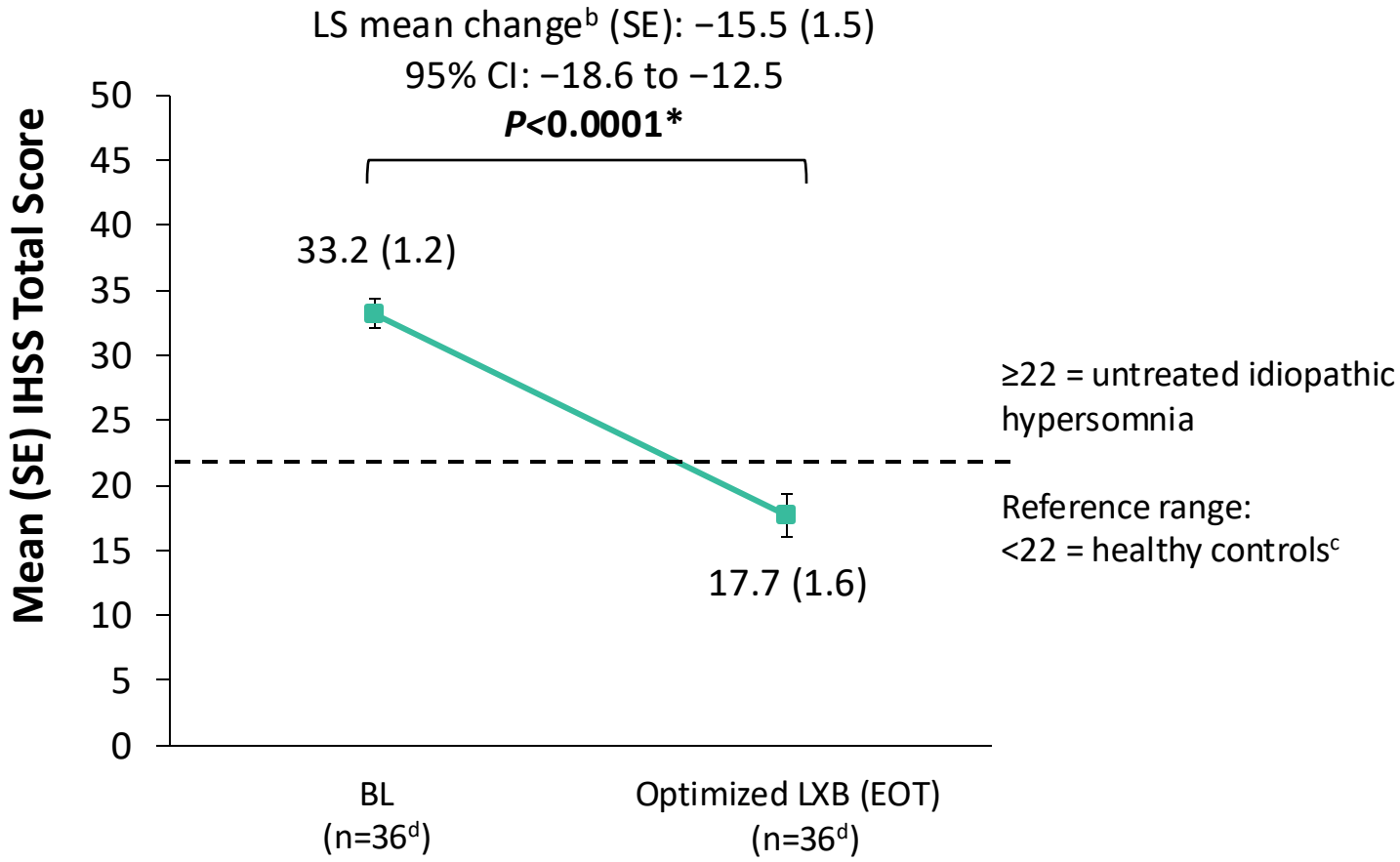

Figure (with color modification) from Plante DT, et al. *CNS Drugs*. 2026. doi:10.1007/s40263-025-01262-9.[1] http://creativecommons.org/licenses/by-nc/4.0/.

[a]Completer analysis set includes all participants who enrolled in the study, took their prescribed LXB regimen for ≥1 night after the BL period, completed the SDP, and completed the PSG EOT visit. [b]Difference between BL and EOT. [c]An IHSS score of 22 is the optimal cutoff for distinguishing between untreated patients with idiopathic hypersomnia and community-dwelling controls.[2] [d]Not all participants completed all assessments. *Controlled for multiplicity.

1. Plante DT, et al. *CNS Drugs*. 2026. doi:10.1007/s40263-025-01262-9. 2. Dauvilliers Y, et al. *Neurology*. 2019;92:e1-e9.

BL, baseline; CI, confidence interval; EOT, end of treatment; IHSS, Idiopathic Hypersomnia Severity Scale; LS, least squares; LXB, low-sodium oxybate; PSG, polysomnography; SDP, stable-dose period; SE, standard error.

Most Participants With Idiopathic Hypersomnia Achieved Clinically Meaningful Improvement and IHSS Scores Within Normal Range (<22) With Optimized LXB Treatment[a]

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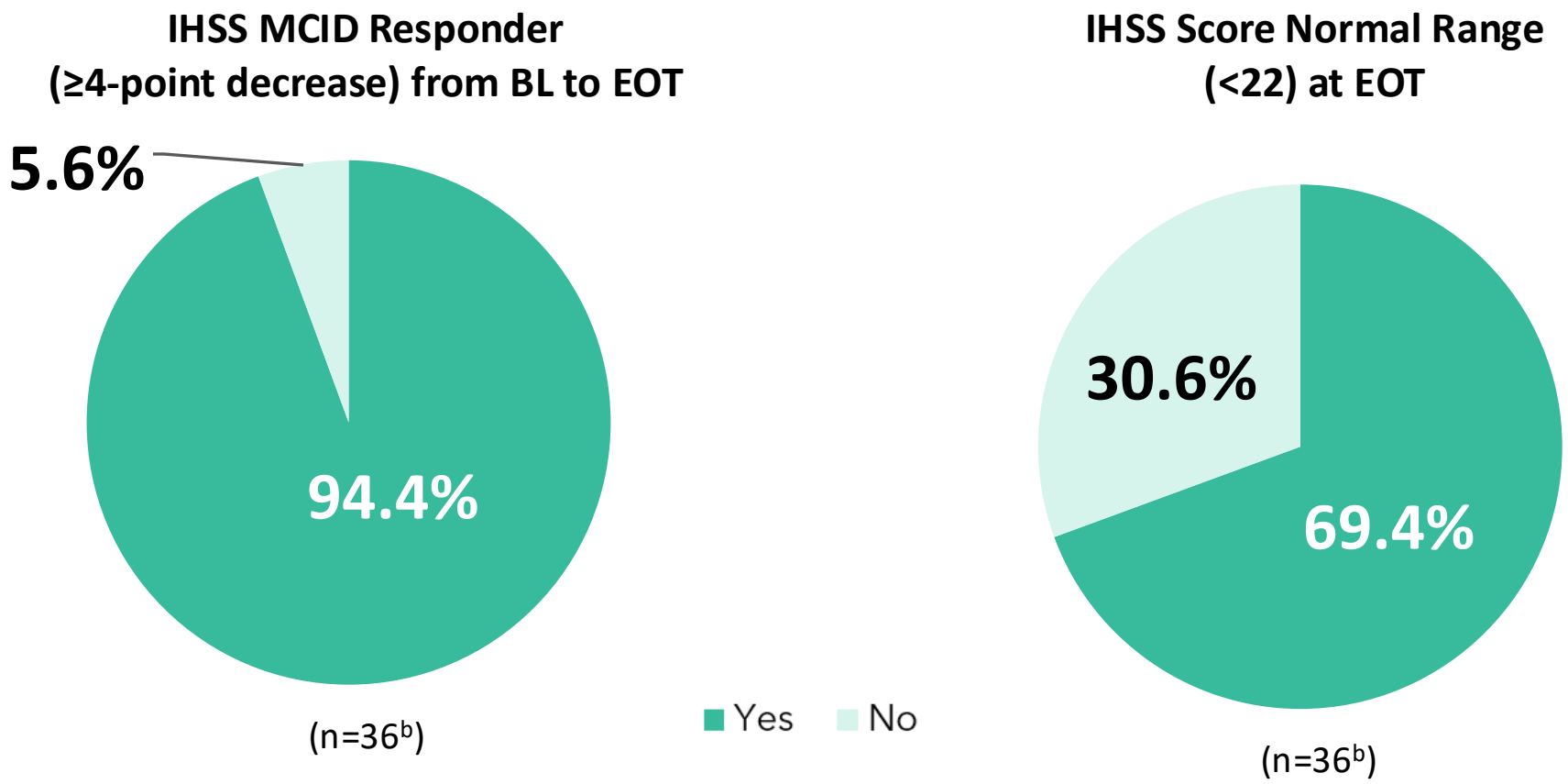

Most participants with idiopathic hypersomnia (94.4%; n=34/36) achieved MCID for IHSS; 69.4% (n=25/36) achieved a normal IHSS score with optimized LXB at EOT.

[a]Completer analysis set. [b]Not all participants completed all assessments.
BL, baseline; EOT, end of treatment; IHSS, Idiopathic Hypersomnia Severity Scale; LXB, low-sodium oxybate; MCID, minimal clinically important difference.

Most Participants With Idiopathic Hypersomnia Achieved Clinically Meaningful Improvement and IHSS Scores Within Normal Range (<22) With Optimized LXB Treatment, *Regardless of Concomitant Alerting Agent Use*[a,b,c]

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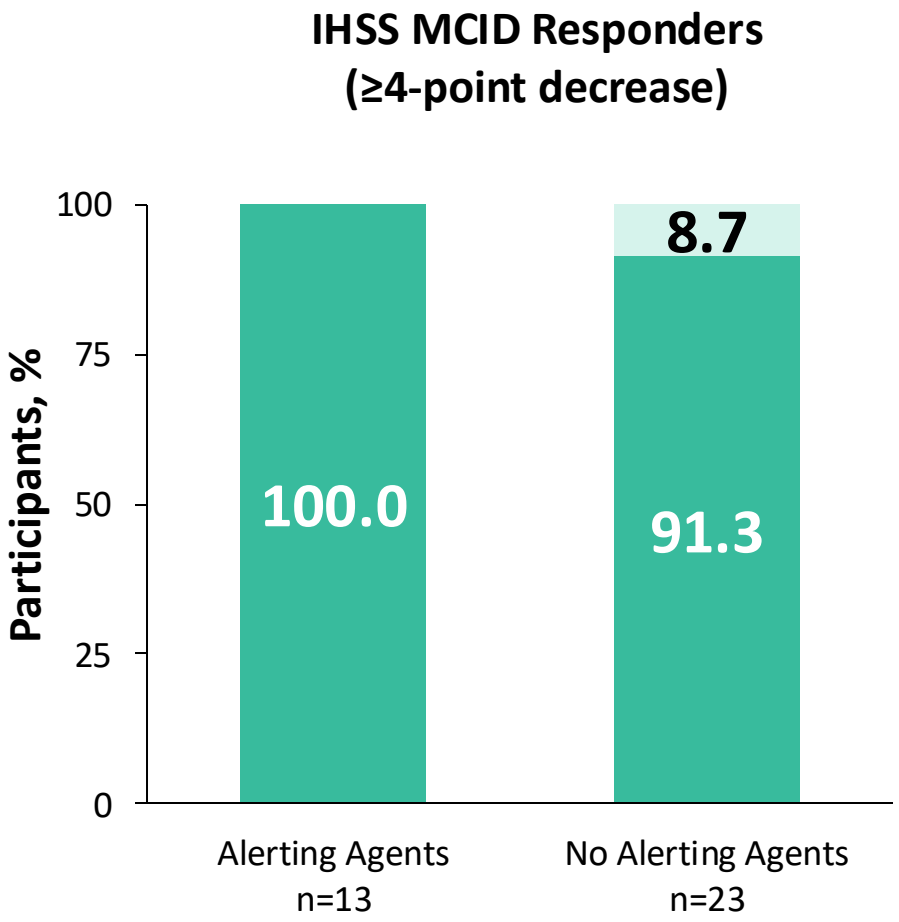
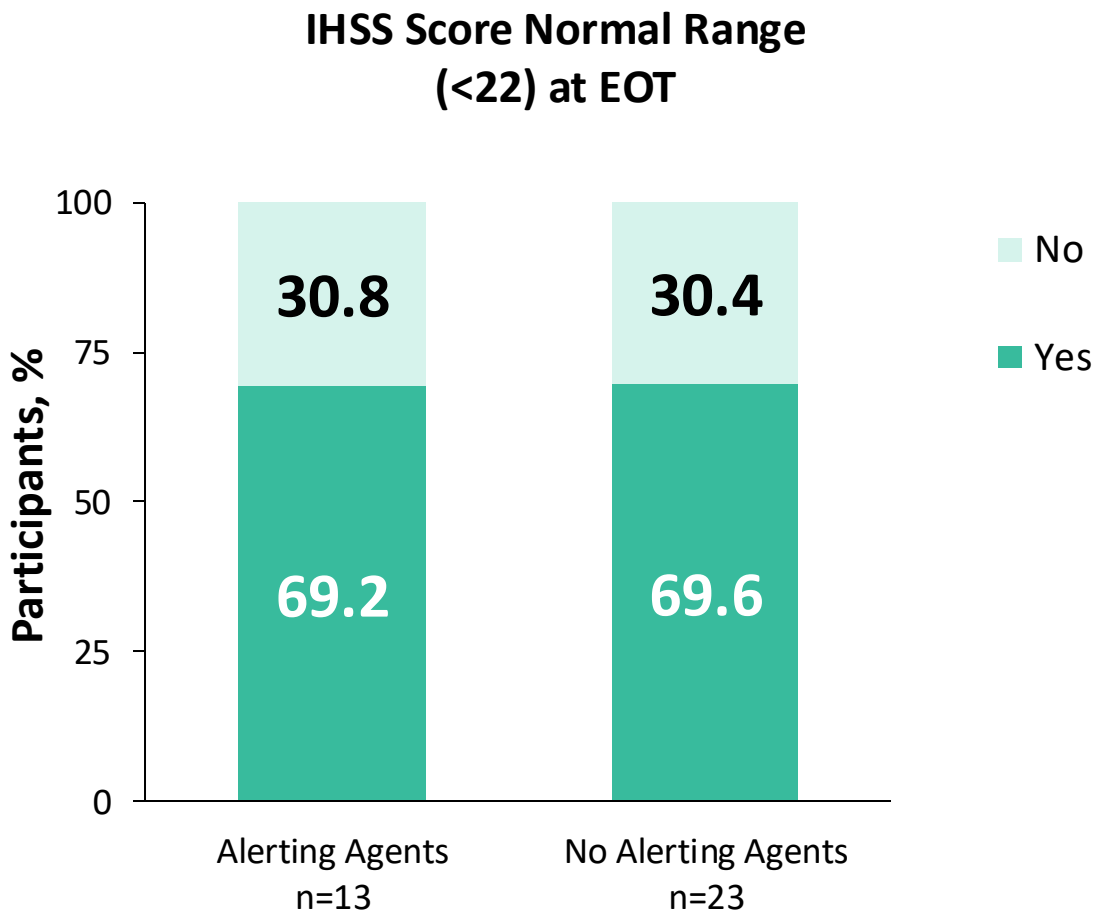




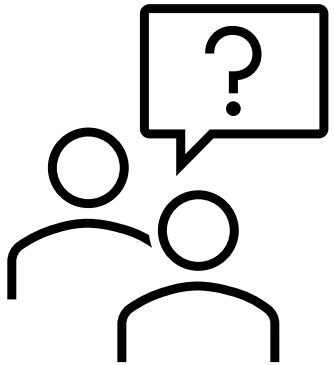
[a]Completer analysis set. [b]Alerting agents were defined as stimulants or wake-promoting agents; participants must have taken the same dosage ≥1 month before screening visit 1 with no plans to adjust dosage during the study.
[c]Inclusion criteria included ESS score >10; therefore, participants with controlled EDS (taking alerting agents and not on alerting agents) were not eligible for the study.
EOT, end of treatment; EDS, excessive daytime sleepiness; IHSS, Idiopathic Hypersomnia Severity Scale; LXB, low-sodium oxybate; MCID, minimal clinically important difference.

Conclusions

- The majority of DUET participants met the AASM ≥2-point **ESS** clinical improvement criterion (narcolepsy, 82.4%; idiopathic hypersomnia, 95.0%) and achieved an **ESS** score within normal range (≤10; narcolepsy, 70.6%; idiopathic hypersomnia, 70.0%) after optimization of LXB treatment
- The majority of participants with idiopathic hypersomnia achieved clinically meaningful **IHSS** improvement (reduction ≥4 points; 94.4%), as well as an **IHSS** score within normal range (<22; 69.4%) after optimization of LXB treatment
- Clinically meaningful improvements were observed in the majority of participants with narcolepsy or idiopathic hypersomnia, including in those **with and without concomitant alerting agents use**
  - Limitations include the open-label and single arm design; causality cannot be established
- These findings suggest a consistent, robust, and clinically meaningful response to LXB treatment in people with narcolepsy or idiopathic hypersomnia

AASM, American Academy of Sleep Medicine; BL, baseline; EOT, end of treatment; ESS, Epworth Sleepiness Scale; IHSS, Idiopathic Hypersomnia Severity Scale; LXB, low-sodium oxybate.

Questions?



Back-Up Slides

Most Participants With NT1 and NT2 Achieved Clinically Meaningful Improvement and ESS Scores Within Normal Range (≤10) With Optimized LXB at EOT[a]

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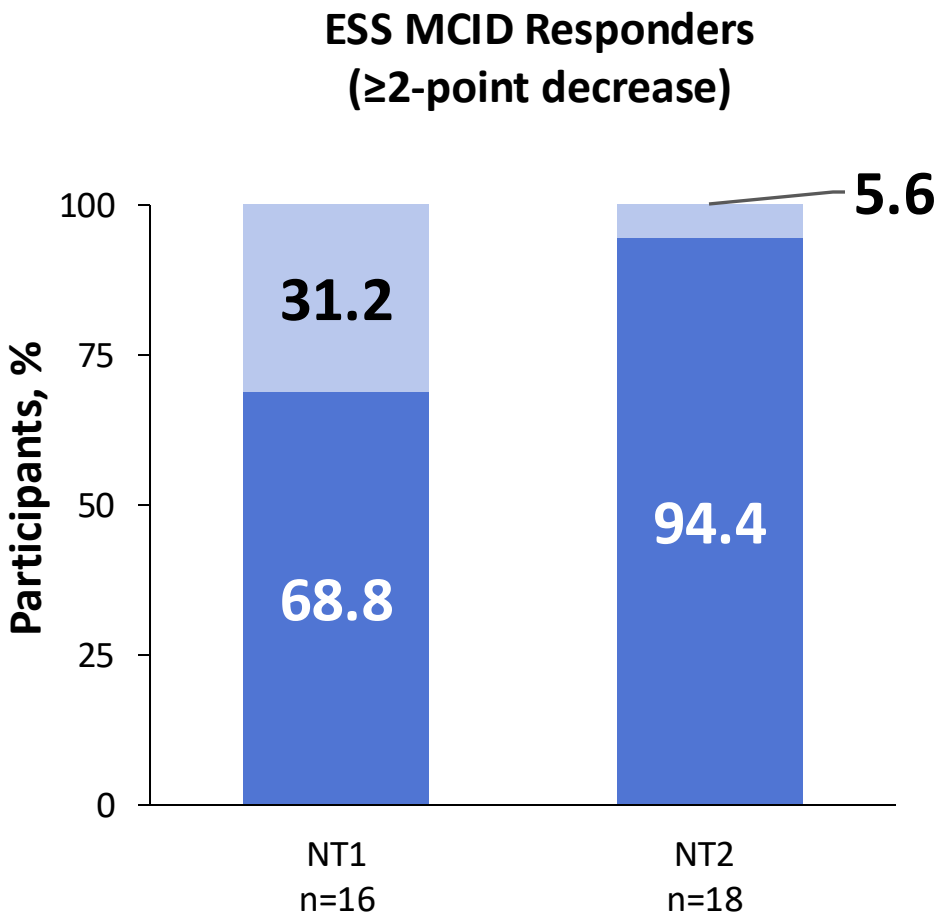

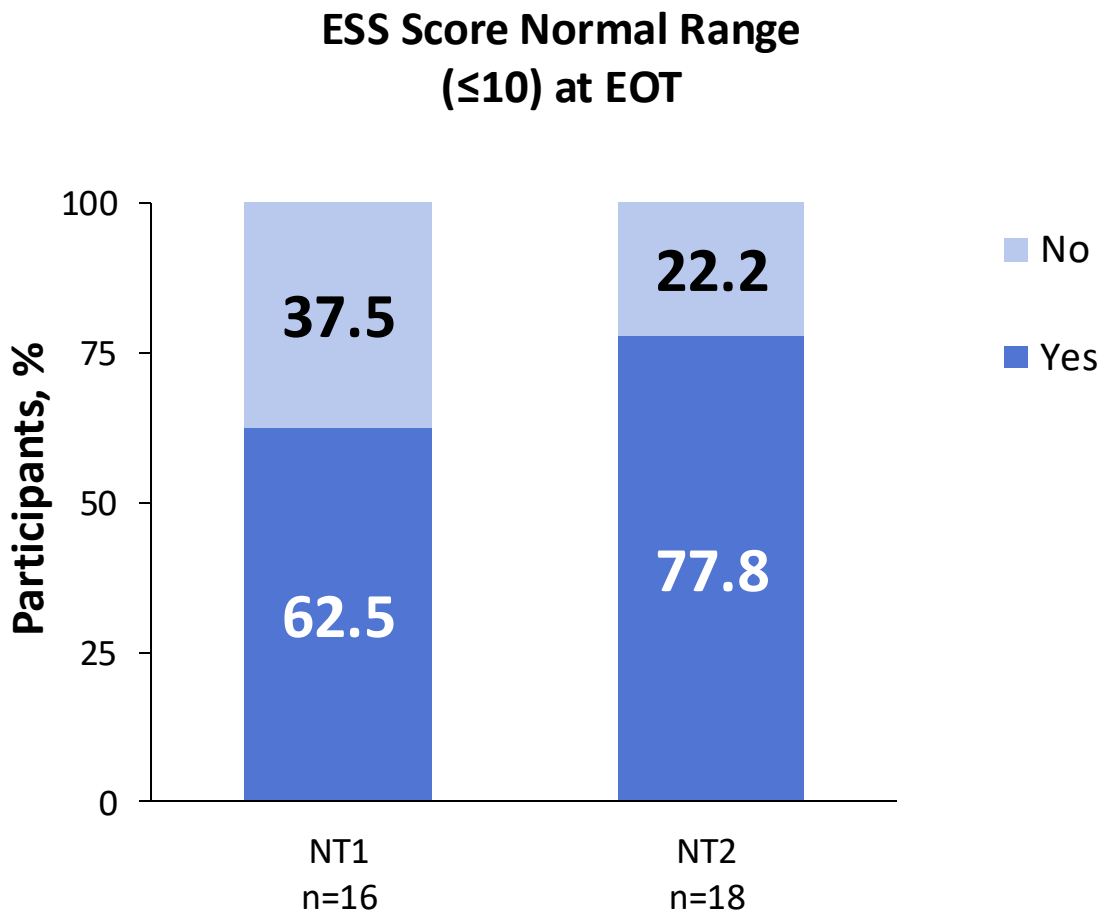

[a]Completer analysis set.

EOT, end of treatment; ESS, Epworth Sleepiness Scale; LXB, low-sodium oxybate; MCID, minimally clinically important difference; NT1, narcolepsy type 1; NT2, narcolepsy type 2.

Demographics/Baseline Characteristics for Narcolepsy Cohort Based on ESS Response[a]

Characteristic	MCID-Responders: ≥2-point Decrease n=28	Non–MCID-Responders: <2-point Decrease n=6	Normal Range: ≤10 at EOT n=24	Not Within Normal Range: >10 at EOT n=10	Total Narcolepsy Cohort n=34
Age (years)					
Mean (SD)	34.3 (14.5)	42.7 (11.7)	35.3 (15.4)	36.8 (11.6)	35.7 (14.2)
Female at birth, n (%)	20 (71.4)	5 (83.3)	18 (75.0)	7 (70.0)	25 (73.5)
Race, n (%)					
White	23 (82.1)	4 (66.7)	19 (79.2)	8 (80.0)	27 (79.4)
Black or African American	4 (14.3)	0	3 (12.5)	1 (10.0)	4 (11.8)
Asian	1 (3.6)	1 (16.7)	1 (4.2)	0	2 (5.9)
Unknown	0	1 (16.7)	1 (4.2)	0	1 (2.9)
Body mass index (kg/m^2)					
Mean (SD)	28.6 (5.7)	31.4 (8.3)	27.0 (5.1)	34.1 (5.7)	29.1 (6.2)
Comorbid OSA, n (%)	4 (14.3)	1 (16.7)	3 (12.5)	2 (20.0)	5 (14.7)
Without comorbid OSA, n (%)	24 (85.7)	5 (83.3)	21 (87.5)	8 (80.0)	29 (85.3)

[a]Completer analysis set.

EOT, end of treatment; ESS, Epworth Sleepiness Scale; MCID, minimally clinically important difference; OSA, obstructive sleep apnea; SD, standard deviation.

Demographics/Baseline Characteristics for Idiopathic Hypersomnia Cohort Based on ESS Response[a]

Characteristic	MCID Responders: ≥2-point Decrease n=38	Non–MCID-Responders: <2-point Decrease n=2	Normal Range: ≤10 at EOT n=28	Not Within Normal Range: >10 at EOT n=12	Total Idiopathic Hypersomnia Cohort n=40
Age (years)					
Mean (SD)	38.7 (12.5)	38.5 (10.6)	37.5 (12.0)	41.3 (13.0)	38.7 (12.3)
Female at birth, n (%)	30 (78.9)	1 (50.0)	22 (78.6)	9 (75.0)	31 (77.5)
Race, n (%)					
White	32 (84.2)	2 (100)	24 (85.7)	10 (83.3)	34 (85.0)
Black or African American	2 (5.3)	0	1 (3.6)	1 (8.3)	2 (5.0)
Asian	2 (5.3)	0	2 (7.1)	0	2 (5.0)
Native Hawaiian or other Pacific Islander	1 (2.6)	0	0	1 (8.3)	1 (2.5)
Multiple[b]	1 (2.6)	0	1 (3.6)	0	1 (2.5)
Body mass index (kg/m^2)					
Mean (SD)	29.1 (6.5)	31.3 (7.9)	28.9 (6.6)	29.8 (6.4)	29.2 (6.5)
LXB regimen, n (%)					
Once-nightly LXB	15 (39.5)	0	12 (42.9)	3 (25.0)	15 (37.5)
Twice-nightly LXB	23 (60.6)	2 (100)	16 (57.1)	9 (75.0)	25 (62.5)
Comorbid OSA, n (%)	10 (26.3)	0	6 (21.4)	4 (33.3)	10 (25.0)
Without comorbid OSA, n (%)	28 (73.7)	2 (100)	22 (78.6)	8 (66.7)	30 (75.0)
Long sleep need[c]					
> 9 hours	19 (50.0)	1 (50.0)	16 (57.1)	4 (33.3)	20 (50.0)
≤9 hours	18 (47.4)	1 (50.0)	12 (42.9)	7 (58.3)	19 (47.5)

[a]Completer analysis set. [b]Participants reported >1 race. [c]Based on participants' response to Item 1 on the Idiopathic Hypersomnia Severity Scale at baseline. Not all participants completed the IHSS assessment at BL.
EOT, end of treatment; ESS, Epworth Sleepiness Scale; LXB, low-sodium oxybate; MCID, minimally clinically important difference; SD, standard deviation.

Demographics/Baseline Characteristics for Idiopathic Hypersomnia Cohort Based on IHSS Response[a]

Characteristic	MCID Responders: ≥4-point Decrease n=34	Non–MCID-Responders: <4-point Decrease n=2	Normal Range: <22 at EOT n=25	Not Within Normal Range: ≥22 at EOT n=11	Total Idiopathic Hypersomnia Cohort n=36
Age (years)					
Mean (SD)	38.0 (12.3)	34.5 (16.3)	39.6 (13.1)	33.9 (9.6)	37.8 (12.3)
Female at birth, n (%)	28 (82.4)	1 (50.0)	21 (84.0)	8 (72.7)	29 (80.6)
Race, n (%)					
White	29 (85.3)	1 (50.0)	22 (88.0)	8 (72.7)	30 (83.3)
Black or African American	1 (2.9)	1 (50.0)	1 (4.0)	1 (9.1)	2 (5.6)
Asian	2 (5.9)	0	1 (4.0)	1 (9.1)	2 (5.6)
Native Hawaiian or other Pacific Islander	1 (2.9)	0	0	1 (9.1)	1 (2.8)
Multiple[b]	1 (2.9)	0	1 (4.0)	0	1 (2.8)
Body mass index (kg/m^2)					
Mean (SD)	29.5 (6.6)	31.3 (8.0)	29.4 (5.4)	29.9 (9.0)	29.6 (6.6)
LXB regimen, n (%)					
Once-nightly LXB	13 (38.2)	0	9 (36.0)	4 (36.4)	13 (36.1)
Twice-nightly LXB	21 (61.8)	2 (100)	16 (64.0)	7 (63.6)	23 (63.9)
Long sleep need[c]					
>9 hours	19 (55.9)	0	13 (52.0)	6 (54.5)	19 (52.8)
≤9 hours	15 (44.1)	2 (100)	12 (48.0)	5 (45.5)	17 (47.2)

[a]Completer analysis set. [b]Participants reported >1 race. [c]Based on participants' response to Item 1 on the Idiopathic Hypersomnia Severity Scale at baseline. Not all participants completed the IHSS assessment at BL.
EOT, end of treatment; IHSS, Idiopathic Hypersomnia Severity Scale; MCID, minimally clinically important difference; SD, standard deviation.

Treatment-Emergent Adverse Events[a]

Participants, n (%)	Total Narcolepsy (N=55)	Total Idiopathic Hypersomnia (N=46)
TEAEs in ≥10% of participants		
Nausea	13 (23.6)	9 (19.6)
Dizziness	8 (14.5)	8 (17.4)
Headache	7 (12.7)	8 (17.4)
Vomiting	6 (10.9)	5 (10.9)
Somnolence	6 (10.9)	—[b]

[a]Safety analysis set.
TEAE, treatment-emergent adverse event.