

# Improvement in Sleepiness With Once-Nightly Sodium Oxybate in People With Narcolepsy Type 1 and Narcolepsy Type 2: A Specialty Pharmacy Data Analysis

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Poster 327

## INTRODUCTION

- Narcolepsy is a rare, chronic sleep disorder that is classified as narcolepsy type 1 (NT1; ie, with cataplexy and/or low hypocretin 1) or narcolepsy type 2 (NT2; ie, without cataplexy)<sup>1</sup>
- NT1 and NT2 are characterized by excessive daytime sleepiness (EDS),<sup>2</sup> and patients with both narcolepsy subtypes have reported that EDS has a significant impact on their life<sup>3</sup>
- Once-nightly sodium oxybate (ON-SXB; LUMRYZ<sup>®</sup> [sodium oxybate] for extended-release oral suspension, Avadel Pharmaceuticals) was approved to treat cataplexy or EDS in adults with narcolepsy in May 2023 and subsequently approved for patients 7 years of age and older with narcolepsy in October 2024<sup>4,6</sup>
- ON-SXB demonstrated significant improvements in both objective (ie, Maintenance of Wakefulness Test) and subjective (ie, Epworth Sleepiness Scale [ESS] total score) measurements of EDS in the REST-ON trial (NCT02720744) and via the ESS in the real-world REFRESH<sup>SM</sup> study (NCT06792708)<sup>7,8</sup>
  - In REFRESH, patients achieved mean ESS total scores near or within the clinically meaningful improvement threshold (ie,  $\geq 2$ -point ESS total score reduction<sup>9</sup>) by week 6, regardless of prior oxybate (OXB) therapy use status<sup>8</sup>
  - For more information about ESS improvements with ON-SXB in REFRESH, please see poster 328<sup>8</sup>
- Evaluating the effect of ON-SXB on EDS in a larger, more diverse narcolepsy patient population will further inform the effectiveness of ON-SXB in clinical practice

## OBJECTIVE

- To assess real-world ESS scores over time, based on narcolepsy subtype, in patients who received ON-SXB from a single specialty pharmacy

## METHODS

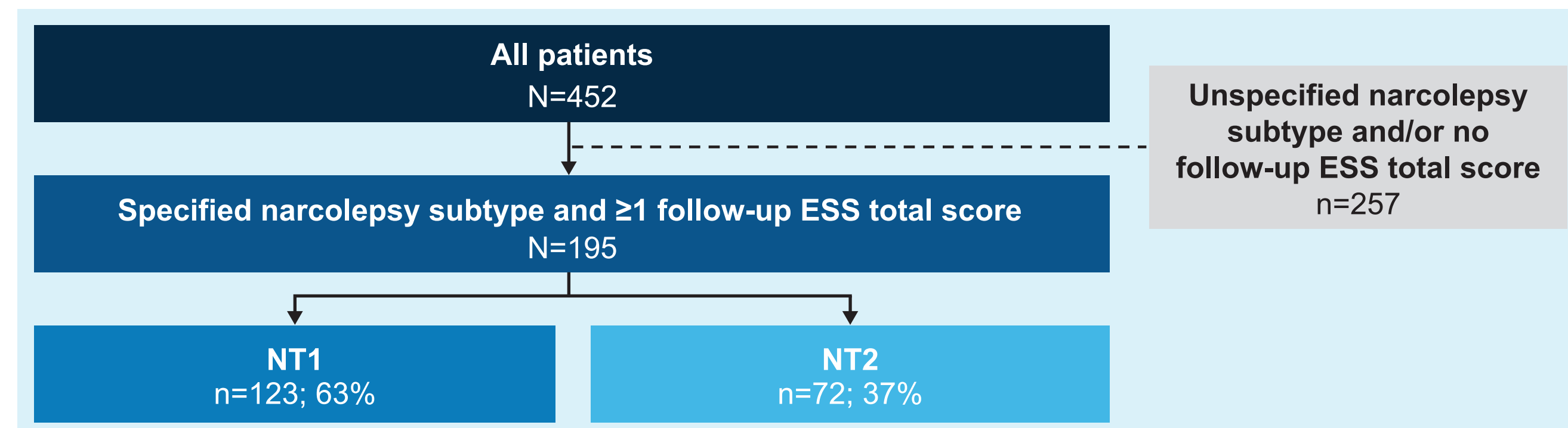
- Demographics, clinical characteristics, and ESS total score data were collected from Optum Frontier Therapies specialty pharmacy from June 1, 2023 to September 30, 2024 for patients who had:
  - $\geq 1$  filled ON-SXB prescription
  - $\geq 1$  ON-SXB-related clinical assessment
  - A documented baseline ESS total score at index and  $\geq 1$  follow-up ESS total score post-index (participation in the ESS assessment was voluntary)
- Index date: first ON-SXB prescription fill during the study period
- Data were stratified by narcolepsy subtype (ie, NT1 and NT2)
- Demographic, clinical, and ESS total score data at baseline and ESS total score data at the first follow-up were summarized descriptively, without statistical testing
- A log-rank test was used to assess statistical significance ( $P < 0.05$ ) of the difference in time (in days) to meaningful clinical improvement (ie, ESS total score reduction of  $\geq 2$  points<sup>9</sup>) between patients with NT1 and NT2 based on Kaplan-Meier analysis

## RESULTS

### BASELINE DEMOGRAPHICS AND CLINICAL CHARACTERISTICS

- Of 452 identified patients, 195 had  $\geq 1$  follow-up ESS total score and a documented narcolepsy subtype (NT1, 63% [n=123]; NT2, 37% [n=72]; Figure 1)

### FIGURE 1: Patient Population by Narcolepsy Subtype



Percentages were calculated based on the total number of patients with a specified narcolepsy subtype and  $\geq 1$  follow-up ESS total score. ESS, Epworth Sleepiness Scale; NT1, narcolepsy type 1; NT2, narcolepsy type 2.

- Mean (SD) age was 38.6 (14.1) years and 40.7 (12.5) years for patients with NT1 and NT2, respectively (Table 1)
- The majority of patients were female (NT1, 69%; NT2, 74%), had prior OXB therapy use (NT1, 72%; NT2, 58%), and had commercial insurance (NT1, 80%; NT2, 86%)

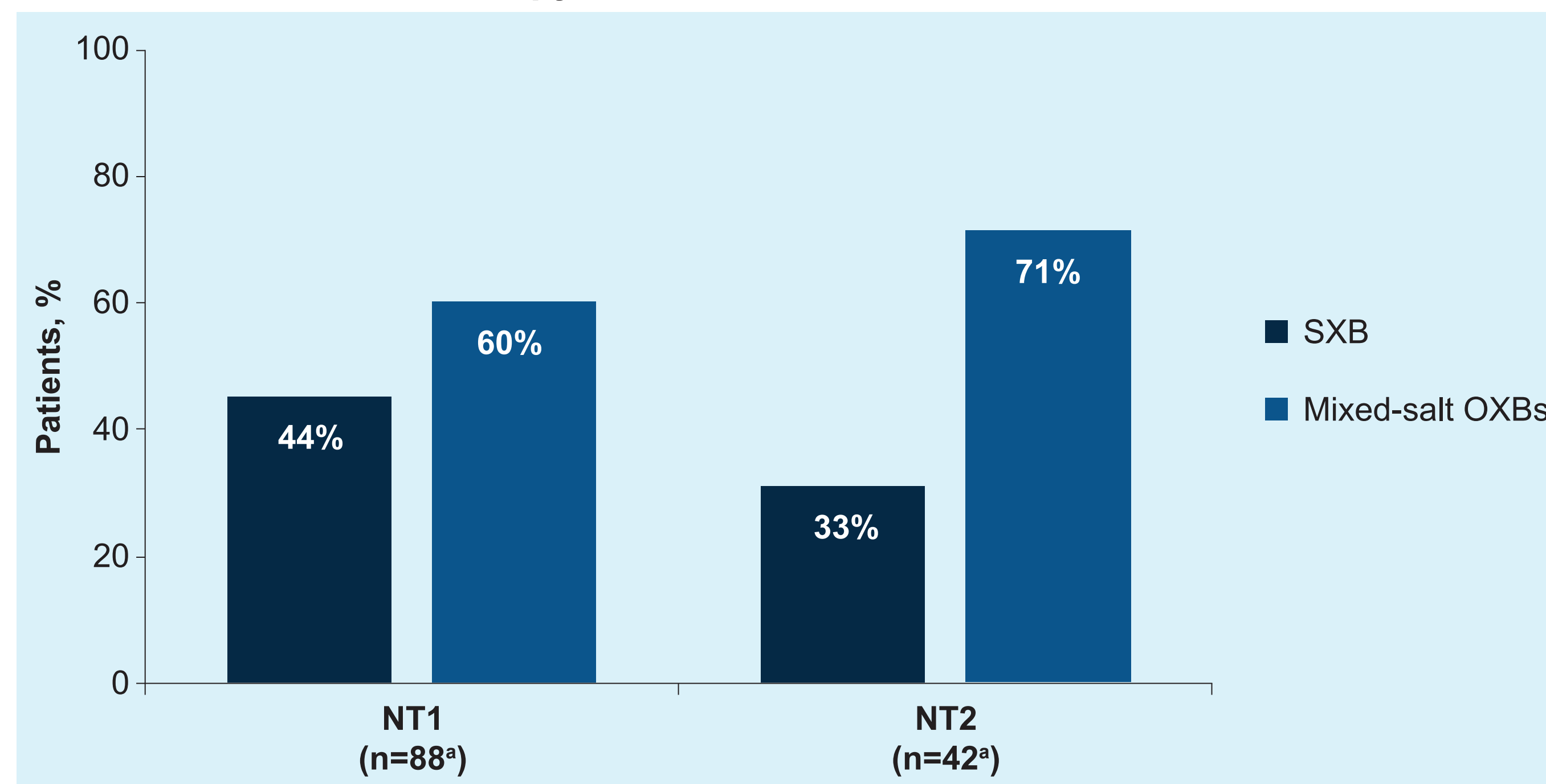
TABLE 1: Baseline Demographics and Clinical Characteristics by Narcolepsy Subtype

Characteristic	NT1 (n=123)	NT2 (n=72)
Age, mean (SD), y	38.6 (14.1)	40.7 (12.5)
Sex, n (%)		
Female	85 (69)	53 (74)
Male	38 (31)	19 (26)
Prior OXB therapy use status, n (%)		
Prior OXB therapy use	88 (72)	42 (58)
OXB naive	35 (28)	30 (42)
Insurance type, n (%)		
Commercial	99 (80)	62 (86)
Medicare or Medicaid	24 (20)	10 (14)
ESS total score, mean (SD)	12.1 (5.7)	12.2 (5.3)

ESS, Epworth Sleepiness Scale; NT1, narcolepsy type 1; NT2, narcolepsy type 2; OXB, oxybate.

- Among the 130 patients (NT1, n=88; NT2, n=42) with prior OXB therapy use, the most common previously used OXB therapy was mixed-salt OXBs (NT1, 60%; NT2, 71%; Figure 2)

FIGURE 2: Prior OXB Therapy Medication for Patients With NT1 and NT2



NT1, narcolepsy type 1; NT2, narcolepsy type 2; OXB, oxybate; SXB, sodium oxybate. \*Patients who had previously received OXB therapy. Six patients (NT1, n=4; NT2, n=2) had previously received SXB and mixed-salt OXBs.

### MEDICATION USE AT BASELINE

- The majority of patients were prescribed alerting/wake-promoting agents and/or stimulants regardless of prior OXB therapy use status (NT1, 58%; NT2, 64%; Table 2)

TABLE 2: Medication Use at Baseline

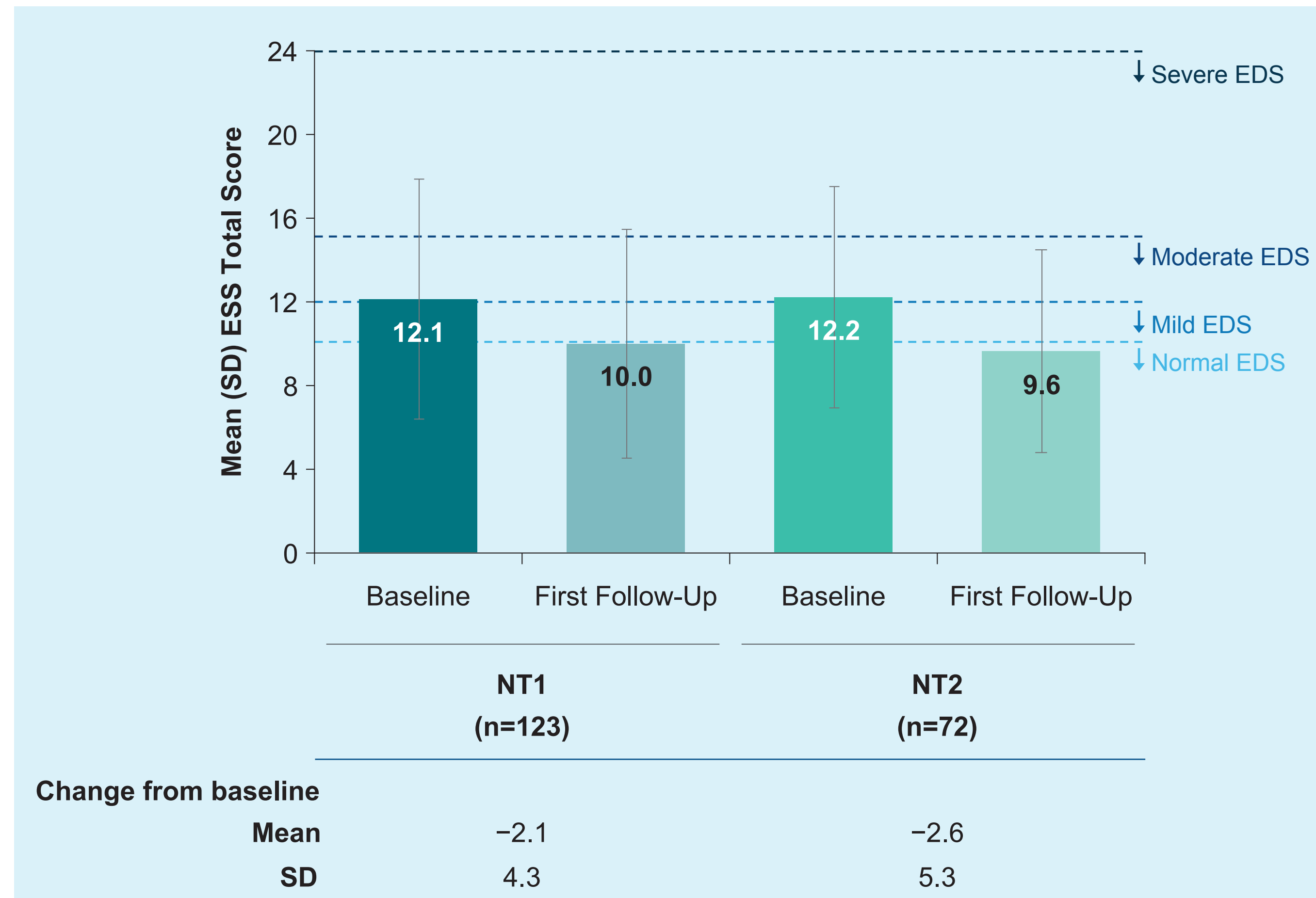
Medication, n (%)	NT1 (n=123)	NT2 (n=72)
Alerting/wake-promoting agents and/or stimulants	71 (58)	46 (64)
Alerting/wake-promoting agents <sup>a</sup>	51 (41)	33 (46)
Stimulants	37 (30)	26 (36)
Amphetamine, short-acting <sup>b</sup>	16 (13)	14 (19)
Amphetamine, long-acting <sup>c</sup>	13 (11)	11 (15)
Methylphenidate, short-acting <sup>d</sup>	10 (8)	5 (7)
Methylphenidate, long-acting <sup>e</sup>	4 (3)	4 (6)
Antidepressants <sup>f</sup>	43 (35)	29 (40)
Antihypertensives <sup>g</sup>	26 (21)	20 (28)

NT1, narcolepsy type 1; NT2, narcolepsy type 2. <sup>a</sup>Includes modafinil, armodafinil, and solvantolol; pitolisant was also captured in this category. <sup>b</sup>Includes amphetamine, amphetamine sulfate, dextroamphetamine, dextroamphetamine sulfate, mixed amphetamine salts, and methamphetamine HCl. <sup>c</sup>Includes amphetamine, dextroamphetamine sulfate, mixed amphetamine salts, and lisdexamfetamine dimesylate. <sup>d</sup>Includes methylphenidate HCl and dexmethylphenidate HCl. <sup>e</sup>Includes methylphenidate HCl, dexmethylphenidate HCl, and serdexmethylphenidate/dexmethylphenidate. <sup>f</sup>Includes antidepressants (atypical), anxiolytics, general anesthetics (nonbarbiturates), monoamine oxidase inhibitors, selective serotonin reuptake inhibitors, serotonin and norepinephrine reuptake inhibitors, and tricyclic antidepressants. <sup>g</sup>Includes angiotensin-converting enzyme inhibitors, angiotensin II receptor antagonists, beta blockers, calcium channel blockers, thiazide and thiazide-like diuretics, aldosterone receptor antagonists, alpha blockers, centrally acting alpha-2 adrenergic agonists, loop diuretics, potassium-sparing diuretics, direct renin inhibitors, and vasodilators.

### ESS TOTAL SCORES AND SEVERITY OF EDS

- Baseline mean (SD) ESS total score was 12.1 (5.7) for patients with NT1 and 12.2 (5.3) for those with NT2 (Table 1)
  - Mean ESS scores indicated moderate EDS both for patients with NT1 and NT2 at baseline (Figure 3)
- Mean (SD) ESS total score by the first follow-up (median [IQR] 52 [29-94] days) was 10.0 (5.5) for patients with NT1 and 9.6 (4.8) for those with NT2; for both groups, mean ESS total score was in the normal EDS range (Figure 3)
  - Mean (SD) change from baseline to first follow-up in ESS total score was  $-2.1$  (4.3) for patients with NT1 and  $-2.6$  (5.3) for those with NT2

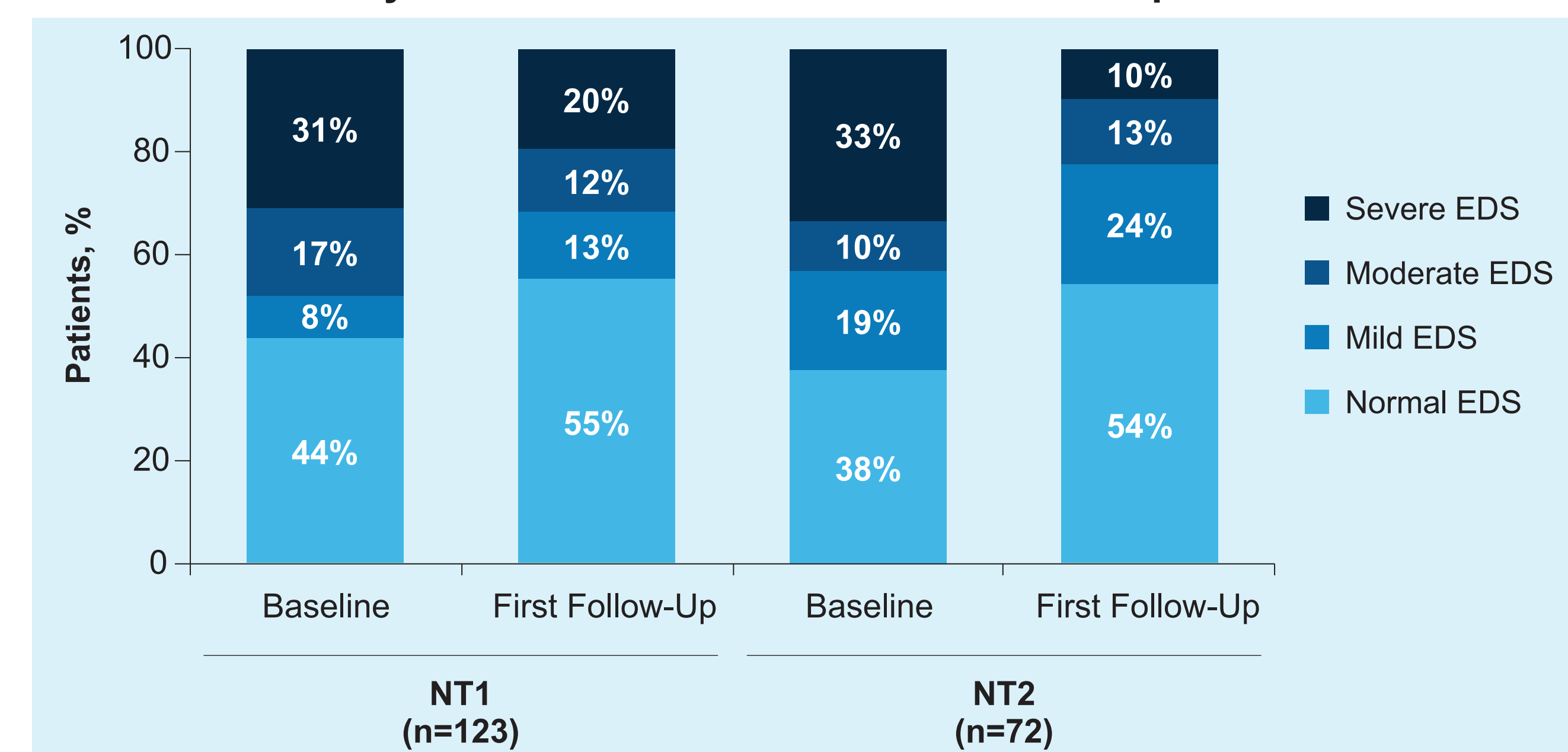
FIGURE 3: ESS Total Scores at Baseline and First Follow-Up



Normal, mild, moderate, and severe EDS defined as ESS total score of  $\leq 10$ , 11-12, 13-15, and  $\geq 16$ , respectively.<sup>10,11</sup> Clinically meaningful improvement threshold of  $\geq 2$ -point reduction in ESS total score, as defined by the American Academy of Sleep Medicine 2021 Clinical Practice Guidelines.<sup>9</sup>

- At baseline, 56% of patients with NT2 and 62% of those with NT1 experienced mild-to-severe EDS (Figure 4)
- By the first follow-up, the majority of patients with both NT1 (55%) and NT2 (54%) reported normal levels of daytime sleepiness

FIGURE 4: Severity of EDS at Baseline and First Follow-Up



Normal, mild, moderate, and severe EDS defined as ESS total score of  $\leq 10$ , 11-12, 13-15, and  $\geq 16$ , respectively.<sup>10,11</sup> EDS, excessive daytime sleepiness; ESS, Epworth Sleepiness Scale; NT1, narcolepsy type 1; NT2, narcolepsy type 2.

- Median (95% CI) time to clinically meaningful improvement of ESS total score (ie,  $\geq 2$ -point reduction) was 3.7 (2.9, 4.6) months for patients with NT1 and 3.3 (2.1, 5.0) months for those with NT2 ( $P=0.535$ )

## STUDY LIMITATIONS

- As these data originated from patients who received ON-SXB through a single specialty pharmacy of the 4 that dispense ON-SXB, their applicability to wider narcolepsy patient populations may be constrained
- Reliance on prescription fill data means that patient adherence to the intended regimen cannot be confirmed
- Given that this was a descriptive analysis, statistical significance was not assessed to formally compare difference between NT1 and NT2 subgroups
- Variation in patient follow-up may have led to an overestimation of the time required to achieve a clinically meaningful improvement in ESS total score, since patients could have met this threshold before the documented assessment point

## CONCLUSIONS

- In this real-world dataset,  $>50\%$  of patients achieved normal levels of EDS (ie, ESS total score  $\leq 10$ ) by first follow-up (median, 1.7 months) after initiating ON-SXB, regardless of narcolepsy subtype
- Patients with NT1 and those with NT2 experienced clinically meaningful improvement in EDS (ie,  $\geq 2$ -point ESS total score reduction) 3.7 months and 3.3 months after starting ON-SXB, respectively
- To support patient expectations, clinicians may wish to consider discussing the expected timeframe for clinically meaningful improvement in EDS when counseling patients

### ACKNOWLEDGMENTS

Medical writing support was provided by Kelly Kilroy, PhD, from Citrus Health Group, Inc. (Chicago, IL), and was funded by Avadel Pharmaceuticals (Chesterfield, MO).

### FUNDING

This study was funded by Avadel Pharmaceuticals (Chesterfield, MO). \*Avadel Pharmaceuticals Limited (formerly Avadel Pharmaceuticals plc) is an affiliate of Alkermes plc. LUMRYZ<sup>®</sup> is a registered trademark and REFRESH<sup>SM</sup> is a service mark of Flamel Ireland Limited, an affiliate of Alkermes plc.

### DISCLOSURES

SM has served on an advisory board for Avadel Pharmaceuticals and has received research funding from Alkermes, Inc., Avadel Pharmaceuticals, Axsome Therapeutics, and Jazz Pharmaceuticals. LBH has participated in clinical research for Alkermes, Inc., Axsome Therapeutics, Avadel Pharmaceuticals, Bress Medical, Centessa Pharmaceuticals, Eisai, Fisher & Paykel Healthcare, Harmony Biosciences, Idorsia, Jazz Pharmaceuticals, Lilly, LivaNova/OSPREY, Merck & Co., Noctrix Health, Samsung, Sanofi, Suvven Life Sciences Ltd., Takeda Pharmaceutical Co., and Vanda Pharmaceuticals and served as a speaker or consultant for Avadel Pharmaceuticals, Fisher & Paykel Healthcare, Harmony Biosciences, Idorsia, and Jazz Pharmaceuticals. MJT has served as a consultant or on advisory boards for Axsome Therapeutics, Balance Therapeutics, Avadel Pharmaceuticals, Eisai, Harmony Biosciences, Jazz Pharmaceuticals, NLS Pharmaceuticals, Suvven Life Sciences Ltd., and Takeda Pharmaceutical Co. CMR has served as an advisory board member for Alkermes, Inc., Eisai, Jazz Pharmaceuticals, and Takeda Pharmaceutical Co. and has received grant funding from Jazz Pharmaceuticals. DC is an employee of Optum Frontier Therapies and a stockholder of UnitedHealth Group. EB and MV are employees of Optum Life Sciences and stockholders of UnitedHealth Group. BA is an employee of Alkermes, Inc. JG was an employee of Avadel Pharmaceuticals and is currently a consultant to Alkermes, Inc.

### REFERENCES

- Kornum BR, et al. *Nat Rev Dis Primers*. 2017;3(1):16100.
- American Academy of Sleep Medicine. *International Classification of Sleep Disorders*. 3rd ed. American Academy of Sleep Medicine; 2014.
- Manski K, et al. *J Clin Sleep Med*. 2017;13(3):419-425.
- LUMRYZ<sup>®</sup> (sodium oxybate for extended-release oral suspension, CII). Full Prescribing Information. Avadel Pharmaceuticals; 2025.
- Avadel Pharmaceuticals. Avadel Pharmaceuticals announces final FDA approval of LUMRYZ<sup>®</sup> (sodium oxybate) for extended-release oral suspension as the first and only once-at-bedtime oxybate for cataplexy or excessive daytime sleepiness in adults with narcolepsy [press release]. 2023. Accessed March 10, 2026. <https://investors.avadel.com/news-releases/news-release-details/avadel-pharmaceuticals-announces-final-fda-approval-lumryzm>
- Avadel Pharmaceuticals. Avadel Pharmaceuticals Announces FDA Approval of LUMRYZ<sup>®</sup> (sodium oxybate) Extended-Release Oral Suspension (CII) for the Treatment of Cataplexy or Excessive Daytime Sleepiness in Patients 7 Years of Age and Older with Narcolepsy. 2024. Accessed 11 November, 2024. <https://investors.avadel.com/news-releases/news-release-details/avadel-pharmaceuticals-announces-fda-approval-lumryzm-sodium>
- Kushida CA, et al. *Sleep*. 2022;45(6):1-11.
- Meskill S, et al. Once-nightly sodium oxybate improves symptoms in people with narcolepsy: final results from the real-world REFRESH study [abstract #752]. Presented at: SLEEP 2026; June 14-17, 2026; Baltimore, MD, USA.
- Manski K, et al. *J Clin Sleep Med*. 2021;17(9):1895-1945.
- Johns MW. About the ESS. Accessed March 5, 2026. <https://epworthsleepinessscale.com/about-the-ess/>
- Johns MW. *Sleep*. 1991;14(6):540-545.



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