Once-Nightly Sodium Oxybate Improves Symptoms in People With Narcolepsy: Final Results From the Real-World REFRESH Study

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Poster 328

INTRODUCTION

- Narcolepsy is a rare, chronic disorder characterized by excessive daytime sleepiness (EDS) and can occur with or without cataplexy[1]
  - Additional narcolepsy symptoms include disturbed nocturnal sleep, sleep-related hallucinations, and sleep paralysis[1]
- These symptoms can have a negative effect on patient quality of life (QoL)[2]
- Oxybate (OXB) treatment is highly effective for the management of symptoms and improves QoL in patients with narcolepsy[3-8]
  - However, the middle-of-the-night dosing required by immediate-release, twice-nightly OXBs (TN-OXBs) can be burdensome[3,9-11]
  - 91% of patients switching from TN-OXB were better able to follow a once-nightly dosing regimen in the open-label study RESTORE[11]
- Once-nightly sodium oxybate (ON-SXB; LUMRYZ®) demonstrated efficacy and safety in the phase 3, randomized, placebo-controlled REST-ON trial and is approved for the treatment of cataplexy or EDS in patients 7 years of age and older with narcolepsy[4,12]
- The REFRESH℠ study (NCT06792708) assessed the clinical effectiveness, tolerability, and patient satisfaction of ON-SXB for the treatment of narcolepsy in a real-world setting

OBJECTIVE

- To evaluate effectiveness and tolerability of ON-SXB and effects on functional disability and disease severity in a real-world setting of patients with narcolepsy

METHODS

STUDY DESIGN AND ASSESSMENTS

- REFRESH was a prospective, multicenter, observational study (**Figure 1**)

FIGURE 1: REFRESH Study Design and Assessments

Screening and Baseline (4-6 weeks); Observation and Data Collection at Clinic Visits (4 months)

Assessments	Month 0 (Baseline)	Month 1	Month 2	Month 3	Month 4 (End of study)
ESS[a]	√	√	√	√	√
NSS	√	√	√	√	√
SDS	√	√	√	√	√
PGI-C					√
CGI-C					√

CGI-C, Clinician Global Impression of Change; ESS, Epworth Sleepiness Scale; NSS, Narcolepsy Severity Scale; PGI-C, Patient Global Impression of Change; SDS, Sheehan Disability Scale.
[a]Participants completed the ESS at weeks 1, 2, 3, 4, 5, 6, 8, 10, 12, 14, and 16 of the observation and data collection period.

DOSING

- ON-SXB dosing followed product labeling (eg, titrated at investigator discretion within a range of 4.5-9 g)

KEY INCLUSION CRITERIA

- Aged ≥18 years
- Diagnosis of narcolepsy type 1 (NT1) or type 2 (NT2)
- Participants were included in 2 cohorts:
  - OXB naive/restart: participants not taking an OXB at study onset, including those who were OXB naive or had prior TN-OXB use before study onset
  - Switch: participants currently receiving treatment with TN-OXB and switched to ON-SXB at study onset
- Prior use of ON-SXB was exclusionary

DATA ANALYSIS

- Analysis was performed using data from all enrolled study participants who received ≥1 dose of ON-SXB
- Descriptive analyses were used to describe participant characteristics and study outcomes
- Tolerability data were reported via a symptom-directed adverse reaction interview asking whether participants experienced adverse reactions from a predefined list of common adverse reactions described in the ON-SXB prescribing information (ie, nausea, dizziness, headache, vomiting, decreased appetite, decreased weight, and enuresis)
  - Each adverse reaction was categorized as mild, moderate, or severe by the investigator

RESULTS

BASELINE DEMOGRAPHICS AND CHARACTERISTICS

- From July 2024 to March 2025, 86 participants were screened, and 71 were enrolled and received ON-SXB treatment; 51 participants completed the study
- The mean (SD) age of participants was 37.8 (13.7) years (**Table 1**)
- Nearly two-thirds (62%; n=44) of participants were diagnosed with NT2
- Approximately half had prior experience with TN-OXBs (prior TN-OXB use, 14%; direct switches, 35%)
- At baseline, mean (SD) Epworth Sleepiness Scale (ESS) and Narcolepsy Severity Scale (NSS) total scores in the overall population were 13.3 (5.3) and 21.5 (10.0), respectively (**Table 2**)

TABLE 1: Baseline Demographics and Clinical Characteristics (Overall Population)

Characteristic	All participants (N=71)
Age, mean (SD), y	37.8 (13.7)
Sex, female, n (%)	54 (76)
Race, n (%)	
Asian	1 (1)
Black/African American	6 (8)
White	59 (83)
Other	2 (3)
Unknown/Not reported	3 (4)
Ethnicity, n (%)	
Hispanic or Latino	14 (20)
Not Hispanic or Latino	56 (79)
Unknown	1 (1)
Narcolepsy subtype, n (%)	
NT1	27 (38)
NT2	44 (62)
OXB experience prior to study entry, n (%)	
OXB naive	36 (51)
Prior TN-OXB use	10 (14)
Current TN-OXB use	25 (35)
Taking narcolepsy medications other than OXBs, n (%)	51 (72)

NT1, narcolepsy type 1; NT2, narcolepsy type 2; OXB, oxybate; TN-OXB, twice-nightly oxybate.

TABLE 2: Baseline Effectiveness Assessment Scores (Overall Population)

Baseline value, mean (SD)	All participants (N=71)
ESS total score	13.3 (5.3)
NT1	14.9 (5.2)
NT2	12.4 (5.2)
NSS total score	21.5 (10.0)
SDS domain scores	
Work/School	5.5 (2.9)
Social life	5.9 (2.7)
Family life/Home responsibilities	6.1 (2.8)

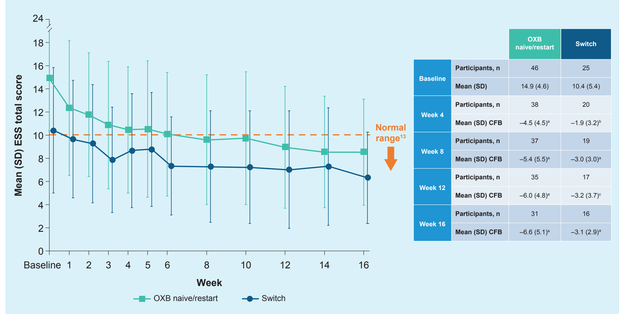
ESS, Epworth Sleepiness Scale; NSS, Narcolepsy Severity Scale; NT1, narcolepsy type 1; NT2, narcolepsy type 2; SDS, Sheehan Disability Scale.

EFFICACY

Epworth Sleepiness Scale

- Mean ESS total scores decreased with ON-SXB treatment for both OXB naive/restart and switch participants (**Figure 2**)
  - OXB naive/restart participants achieved mean ESS total scores near the threshold of normal (ie, ESS total score ≤10)[13] by week 6 and below the threshold of normal by month 2, with continued benefit observed thereafter
  - Switch participants achieved mean ESS total scores below the threshold of normal by week 1, with improvements maintained throughout the study period
- Mean (SD) change from baseline in ESS total score at week 16 was −6.6 (5.1) and −3.1 (2.9) for OXB naive/restart and switch participants, respectively

FIGURE 2: Observed ESS Total Scores Over Time



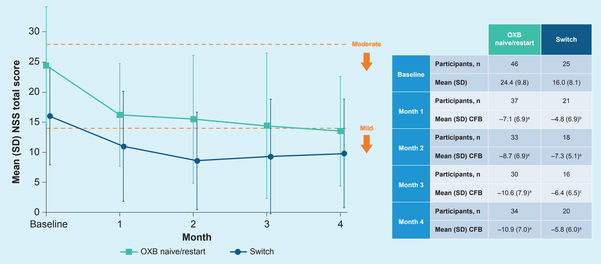
		OXB naive/restart	Switch
Baseline	Participants, n	46	25
	Mean (SD)	14.9 (4.6)	10.4 (5.4)
Week 4	Participants, n	38	20
	Mean (SD) CFB	−4.5 (4.5)[a]	−1.9 (3.2)[a]
Week 8	Participants, n	37	19
	Mean (SD) CFB	−5.4 (5.5)[a]	−3.0 (3.0)[a]
Week 12	Participants, n	35	17
	Mean (SD) CFB	−6.0 (4.8)[a]	−3.2 (3.7)[c]
Week 16	Participants, n	31	16
	Mean (SD) CFB	−6.6 (5.1)[a]	−3.1 (2.9)[a]

P values indicate differences from baseline, as determined by 2-tailed t-test. [a]*P*<0.001; [b]*P*=0.015; [c]*P*=0.002.
CFB, change from baseline; ESS, Epworth Sleepiness Scale; OXB, oxybate.

Narcolepsy Severity Scale

- Mean NSS total scores decreased with ON-SXB treatment for both OXB naive/restart and switch participants (**Figure 3**)
  - OXB naive/restart participants achieved mean NSS total scores below the threshold of mild (ie, NSS total score of 0-14) at month 4
  - Switch participants achieved mean NSS total scores below the threshold of mild by month 1, with improvements maintained throughout the study period
- Mean (SD) change from baseline in NSS total score at month 4 was −10.9 (7.0) and −5.8 (6.0) for OXB naive/restart and switch participants, respectively

FIGURE 3: Observed NSS Total Scores Over Time



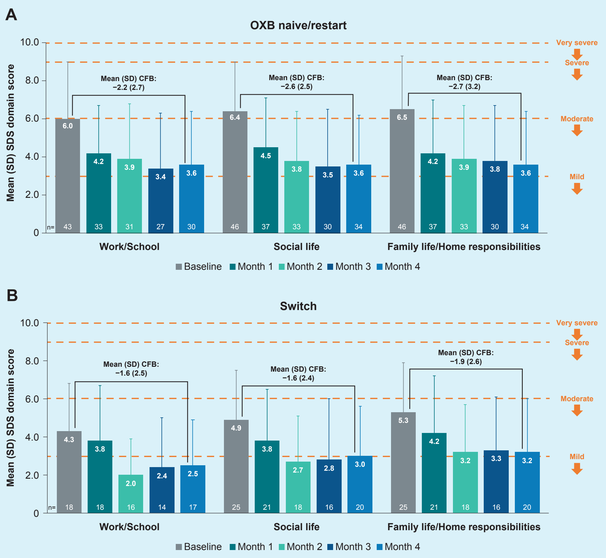
		OXB naive/restart	Switch
Baseline	Participants, n	46	25
	Mean (SD)	24.4 (9.8)	16.0 (8.1)
Month 1	Participants, n	37	21
	Mean (SD) CFB	−7.1 (6.9)[a]	−4.8 (6.9)[a]
Month 2	Participants, n	33	18
	Mean (SD) CFB	−8.7 (6.9)[a]	−7.3 (5.1)[a]
Month 3	Participants, n	30	16
	Mean (SD) CFB	−10.6 (7.9)[a]	−6.4 (6.5)[c]
Month 4	Participants, n	34	20
	Mean (SD) CFB	−10.9 (7.0)[a]	−5.8 (6.0)[a]

The NSS is a 15-item scale that assesses EDS, cataplexy, disturbed nocturnal sleep, sleep paralysis, and hallucination symptoms of narcolepsy; the NSS total score is the sum of these item scores.[14] NSS total scores of 0-14 are mild, 15-28 are moderate, 29-42 are severe, and 43-57 are very severe. Note that 62% (n=44) of the REFRESH study population were participants with NT2 for whom the 3 questions about cataplexy would not apply; maximum score for participants with NT2, 44.
P values indicate differences from baseline. [a]*P*<0.001; [b]*P*=0.005; [c]*P*=0.001.
CFB, change from baseline; EDS, excessive daytime sleepiness; NSS, Narcolepsy Severity Scale; NT2, narcolepsy type 2; OXB, oxybate.

Sheehan Disability Scale

- Mean Sheehan Disability Scale (SDS) domain scores decreased from baseline by approximately 40% at month 4 with ON-SXB treatment across all domains for both OXB naive/restart and switch participants (**Figure 4**)
  - The greatest change from baseline in mean SDS scores was observed in the family life/home responsibilities domain, with a reduction from severe to moderate interference for OXB naive/restart participants
  - OXB naive/restart participants also experienced a reduction in mean SDS scores from severe to moderate interference in the social life domain
  - Switch participants experienced a reduction in mean SDS scores from moderate to mild interference in the work/school and social life domains

FIGURE 4: Overall Observed SDS Domain Scores Over Time

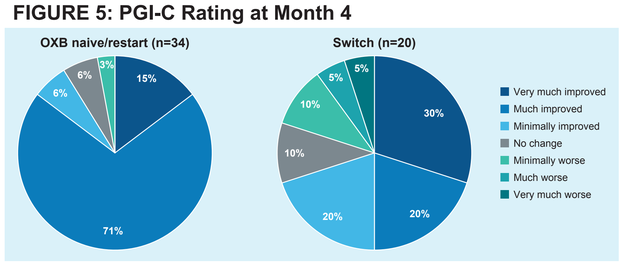


SDS domain scores of 0 indicate no interference, while scores of 1-3 indicate mild interference, 4-6 indicate moderate interference, 7-9 indicate severe interference, and 10 indicate very severe interference.[15]
CFB, change from baseline; OXB, oxybate; SDS, Sheehan Disability Scale.

Patient Global Impression of Change and Clinician Global Impression of Change

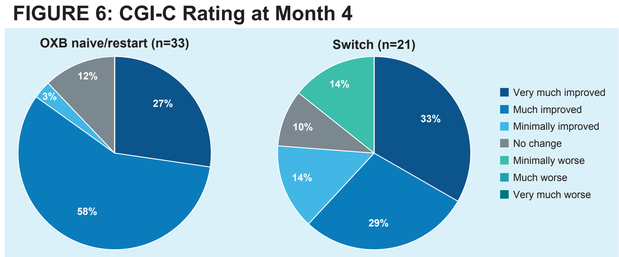
- At month 4, 91% (31/34) of OXB naive/restart and 70% (14/20) of switch participants were improved on the Patient Global Impression of Change (PGI-C; **Figure 5**)
- Similarly, 88% (29/33) of OXB naive/restart and 76% (16/21) of switch participants were improved on the Clinician Global Impression of Change (CGI-C) at month 4 (**Figure 6**)

FIGURE 5: PGI-C Rating at Month 4



Percentages may not equal 100% due to rounding.
OXB, oxybate; PGI-C, Patient Global Impression of Change.

FIGURE 6: CGI-C Rating at Month 4



CGI-C, Clinician Global Impression of Change; OXB, oxybate.

Safety

- During the symptom-directed adverse reaction interview, 45% (32/71) of participants reported an adverse reaction (**Table 3**)
  - The majority (88%; 93/106) of adverse reactions were mild or moderate in severity
  - The most common adverse reactions were nausea, dizziness, headache, and vomiting
- During the 4-month study, 48% (n=34) of participants reported missing a dose of study medication, with a median of 8.5 missed doses observed
  - Reasons for missed doses included choosing to consume alcohol, needing to wake up early, being sick, eating too late, going to sleep too late, running out of medication, and experiencing side effects

TABLE 3: Adverse Reactions (Overall Population)

Adverse reaction, n (%)	All participants (N=71)
Any adverse reaction	32 (45)
Mild	27 (38)
Moderate	18 (25)
Severe[a]	7 (10)
Adverse reaction[b]	
Nausea	25 (35)
Dizziness	13 (18)
Headache	12 (17)
Vomiting	11 (15)
Decreased appetite	8 (11)
Decreased weight	6 (8)
Enuresis	6 (8)
Early termination owing to tolerance concern	3 (4)

[a]In total, 13 severe adverse reactions were documented: dizziness (5 events), nausea (4 events), vomiting (3 events), and enuresis (1 event).
[b]From the symptom-directed adverse reaction interview.

STUDY LIMITATIONS

- Although the real-world nature of this study is a strength, the lack of blinding and absence of a placebo control introduces the potential for some results to be attributed to the open-label study design; data were tabulated as observed
- The relatively small number of participants in this study may limit the application of results to the broader population
  - There was no specific sample size requirement for analysis of the study outcomes
- NSS scores were not analyzed by narcolepsy subtype
  - Nearly two-thirds of participants in REFRESH had NT2, for whom 3 questions regarding cataplexy were not applicable; 44 was the maximum possible score for patients with NT2 vs 57 for patients with NT1
- The symptom-directed interview was limited to adverse reactions described in the ON-SXB prescribing information, which did not allow for the identification of novel adverse reactions
- All statistical analyses are descriptive in nature and no conclusions on efficacy or safety should be made

CONCLUSIONS

- Treatment with ON-SXB resulted in clinically meaningful improvements in narcolepsy symptoms, disease severity, and QoL as measured by the ESS, NSS, SDS, PGI-C, and CGI-C
  - Further, reductions observed on the NSS suggest improvements across all symptoms of the narcolepsy pentad
- ON-SXB was well tolerated, with only 4% of participants discontinuing owing to a tolerance concern
- In a real-world setting, ON-SXB treatment improved sleepiness, reduced severity of narcolepsy symptoms, and lessened the functional impairment and burden of narcolepsy on QoL for patients naive to or not currently taking OXB therapy and those switching from TN-OXB

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Disclosure information and copies of this poster can be obtained through this QR (Quick Response) code

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Poster 328

DISCLOSURES

SDM has received funding for conducting research studies from Avadel Pharmaceuticals, Axsome Therapeutics, Jazz Pharmaceuticals, and Alkermes, Inc. and has served on an advisory board for Avadel Pharmaceuticals.

GM has received funding for conducting research studies from Alkermes, Inc., Avadel Pharmaceuticals, Axsome Therapeutics, Harmony Biosciences, Jazz Pharmaceuticals, and Novo Nordisk; has served on advisory boards for Alkermes, Inc., Avadel Pharmaceuticals, Axsome Therapeutics, Harmony Biosciences, Jazz Pharmaceuticals and Lilly; and has served on speakers bureaus for Avadel Pharmaceuticals, Axsome Therapeutics, Harmony Biosciences, Idorsia, Jazz Pharmaceuticals, and Lilly.

AR has received grant/research support from Jazz Pharmaceuticals, Suven, Inspire, Nyxoah, LivaNova, and Avadel Pharmaceuticals; is a speaker for Avadel Pharmaceuticals and Lilly; is a consultant for Jazz Pharmaceuticals, Suven, Inspire, and Avadel Pharmaceuticals; and has served on speakers bureaus for Jazz Pharmaceuticals and Eisai.

AS has received research grants from Avadel Pharmaceuticals and Harmony Biosciences and has served on speakers bureaus for Avadel Pharmaceuticals, Jazz Pharmaceuticals, and Axsome Therapeutics.

RP has no disclosures to report.

OM has received research grants from and has served on speakers bureaus for Avadel Pharmaceuticals.

SI is affiliated with a hospital receiving funding for research from Avadel Pharmaceuticals and has received research grant funding from the National Institutes of Health, Harmony Biosciences, Centessa Pharmaceuticals, and Jazz Pharmaceuticals.

OB has served as a speaker for Harmony Biosciences, Idorsia, and Lilly; is a principal investigator with Centessa Pharmaceuticals and Neteera; and is Chief Executive Officer of the Sleep Doctor PLLC.

RKB is a shareholder in WaterMark Medical and Healthy Humming, LLC; serves on the board of directors for WaterMark Medical; is a consultant for Jazz Pharmaceuticals, Takeda Pharmaceutical Co., and Oventus; has received industry funding for research from Avadel Pharmaceuticals, BresoTec, Bayer, Idorsia, Suven Life Sciences Ltd., Jazz Pharmaceuticals, Balance Therapeutics, Vanda Pharmaceuticals, Merck & Co., Eisai, Philips, FRESCA Medical, Takeda Pharmaceutical Co., LivaNova, Roche, and Sommetrics; and has served on speakers bureaus for Jazz Pharmaceuticals, Eisai, and Harmony Biosciences.

LBH participates in clinical research for Alkermes, Inc., Axsome Therapeutics, Avadel Pharmaceuticals, Breas, Centessa Pharmaceuticals, Eisai, Lilly, Fisher & Paykel Healthcare, Harmony Biosciences, Idorsia, Jazz Pharmaceuticals, LivaNova/OSPREY, Merck & Co., Noctrix, Samsung, Sanofi, Suven, 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.

MD participates in clinical research for Avadel Pharmaceuticals, Axsome Therapeutics, Harmony Biosciences, and Alkermes, Inc.; has served as a speaker for Avadel Pharmaceuticals, Jazz Pharmaceuticals, Axsome Therapeutics, Harmony Biosciences, and Lilly; and has served as a consultant for Axsome Therapeutics, Jazz Pharmaceuticals, and Harmony Biosciences.

JDM has served as a consultant for Jazz Pharmaceuticals, Harmony Biosciences, Idorsia, Novo Nordisk, Lilly, Inspire, and Avadel Pharmaceuticals; has served on speakers bureaus for Harmony Biosciences, Idorsia, Novo Nordisk, Lilly, and Inspire; and has received research funding from Avadel Pharmaceuticals and Inspire.

GSR and **BA** are employees of Alkermes, Inc.

JG was an employee of Avadel Pharmaceuticals and is a consultant to Alkermes, Inc.