Sleepiness Improvement With Once-Nightly Sodium Oxybate in Patients With and Without Prior Twice-Nightly Oxybate Use: Specialty Pharmacy Data Analysis

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INTRODUCTION

- Narcolepsy is a rare, chronic sleep disorder that is characterized by excessive daytime sleepiness (EDS)[1,2]
- In a cross-sectional survey of >1200 patients with narcolepsy, >75% reported that EDS has a significant impact on their life[3]
- Once-nightly sodium oxybate (ON-SXB; LUMRYZ® [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 aged ≥7 years with narcolepsy in October 2024[4-6]
- ON-SXB demonstrated significant improvements in both objective (ie, mean sleep latency on the 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℠ study (NCT06792708)[7,8]
  - In REFRESH, mean (SD) ESS total scores near or within the clinically meaningful improvement threshold (ie, ≥2-point ESS total score reduction[9]) were achieved by week 6 in patients who transitioned from twice-nightly OXB (TN-OXB) to ON-SXB (–4.5 [4.5]) and those who were not on oxybate (OXB) therapy at study entry (–1.9 [3.2])[8]
  - For more information about ESS improvements with ON-SXB in REFRESH, please see poster 328[8]
- Assessing real-world ESS data from patients who received ON-SXB further informs the generalizability of ON-SXB effectiveness

OBJECTIVE

- To assess ESS scores over time in patients with narcolepsy who received ON-SXB from a single specialty pharmacy, stratified by prior OXB therapy use

METHODS

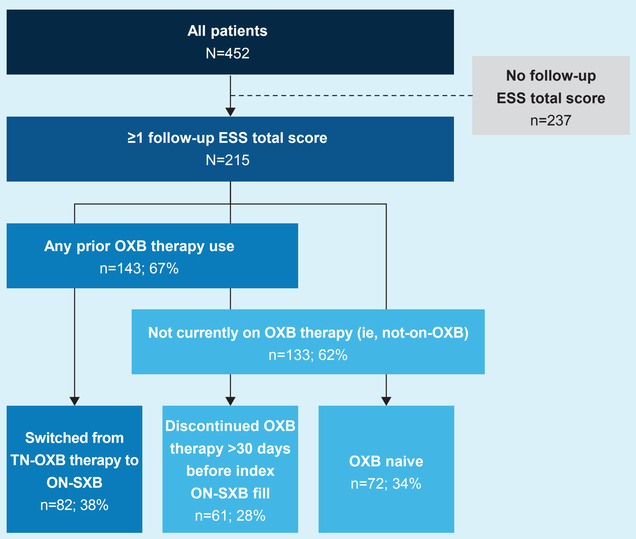
- Demographics, clinical characteristics, and ESS total score data were collected using electronic health records from Optum Frontier Therapies specialty pharmacy from June 1, 2023 to September 30, 2024 for patients who had:
  - ≥1 filled ON-SXB prescription
  - ≥1 ON-SXB-related clinical assessment
  - A documented baseline ESS total score at index and ≥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 status of prior OXB therapy use for:
  - Patients who transitioned from TN-OXB treatment to ON-SXB ≤30 days of index (ie, switch patients)
  - Patients who were OXB naive or who discontinued OXB >30 days before index ON-SXB fill (ie, not-on-OXB patients)
- 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 ≥2 points[9]) between switch and not-on-OXB patients based on Kaplan-Meier analysis

RESULTS

BASELINE DEMOGRAPHICS AND CLINICAL CHARACTERISTICS

- Of 452 identified patients, 215 (switch, 38% [n=82]; not-on-OXB, 62% [n=133]) had ≥1 follow-up ESS score (**Figure 1**)

FIGURE 1: Patient Population by Prior OXB Therapy Use Status



Percentages were calculated based on the total number of patients with ≥1 follow-up ESS total score.
ESS, Epworth Sleepiness Scale; ON-SXB, once-nightly sodium oxybate; OXB, oxybate; TN-OXB, twice-nightly oxybate.

- Mean (SD) age was 38.4 (12.6) years and 40.0 (14.2) years for switch patients and not-on-OXB patients, respectively (**Table 1**)
- The majority of patients were female (71% in both switch and not-on-OXB patients) and had commercial insurance (switch, 88%; not-on-OXB, 80%)

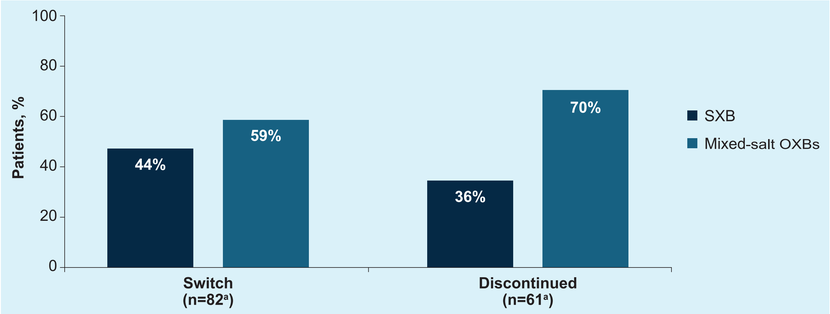
TABLE 1: Baseline Demographics and Clinical Characteristics by Prior OXB Therapy Use Status

Characteristic	Switch (n=82)	Not-on-OXB[a] (n=133)
Age, mean (SD), y	38.4 (12.6)	40.0 (14.2)
Sex, n (%)		
Female	58 (71)	94 (71)
Male	24 (29)	39 (29)
Insurance type, n (%)		
Commercial	72 (88)	106 (80)
Medicare or Medicaid	10 (12)	27 (20)
ESS total score, mean (SD)	11.3 (5.5)	12.5 (5.6)

ESS, Epworth Sleepiness Scale; ON-SXB, once-nightly sodium oxybate; OXB, oxybate.
[a]Not-on-OXB patients included those who were OXB naive and those who discontinued an OXB therapy >30 days before index ON-SXB fill.

- Among the 133 not-on-OXB patients, 61 (46%) had previously used but discontinued an OXB therapy >30 days before index ON-SXB fill
- Among 143 patients (switch, n=82; discontinued, n=61) with any prior OXB therapy use, the most common OXB therapy medication was mixed-salt OXBs (switch, 59%; discontinued, 70%; **Figure 2**)

FIGURE 2: Prior OXB Medication for Switch Patients and Discontinued Patients



OXB, oxybate; SXB, sodium oxybate.
[a]Patients who had previously received OXB therapy. Six patients (switch, n=2; discontinued, n=4) 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 (switch, 51%; not-on-OXB, 65%; **Table 2**)

TABLE 2: Medication Use at Baseline

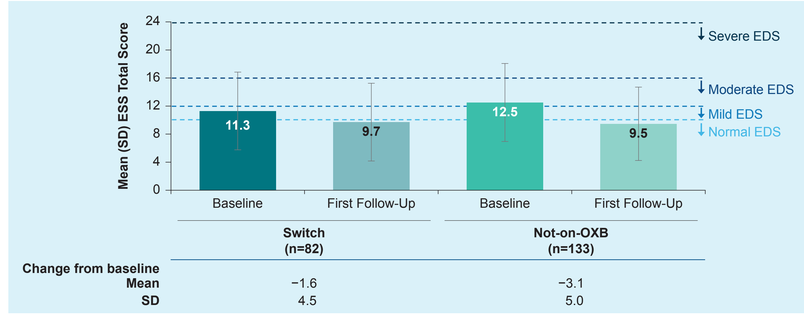
Medication, n (%)	Switch (n=82)	Not-on-OXB (n=133)
Alerting/wake-promoting agents and/or stimulants	42 (51)	86 (65)
Alerting/wake-promoting agents[a]	30 (37)	61 (46)
Stimulants	23 (28)	45 (34)
Amphetamine, short-acting[b]	13 (16)	19 (14)
Amphetamine, long-acting[c]	8 (10)	18 (14)
Methylphenidate, short-acting[d]	5 (6)	11 (8)
Methylphenidate, long-acting[e]	5 (6)	4 (3)
Antidepressants[f]	27 (33)	49 (37)
Antihypertensives[g]	15 (18)	34 (26)

OXB, oxybate.
[a]Includes modafinil, armodafinil, and solriamfetol; pitolisant was also captured in this category. [b]Includes amphetamine, amphetamine sulfate, dextroamphetamine, dextroamphetamine sulfate, mixed amphetamine salts, and methamphetamine HCl. [c]Includes amphetamine, dextroamphetamine sulfate, mixed amphetamine salts, and lisdexamfetamine dimesylate. [d]Includes methylphenidate HCl and dexmethylphenidate HCl. [e]Includes methylphenidate HCl, dexmethylphenidate HCl, and serdexmethylphenidate/dexmethylphenidate. [f]Includes antidepressants (atypical), anxiolytics, general anesthetics (nonbarbiturates), monoamine oxidase inhibitors, selective serotonin reuptake inhibitors, serotonin and norepinephrine reuptake inhibitors, and tricyclic antidepressants. [g]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 scores were 11.3 (5.5) for switch and 12.5 (5.6) for not-on-OXB patients (**Table 1**)
  - Mean ESS scores indicated mild EDS for switch patients and moderate EDS for not-on-OXB patients at baseline (**Figure 3**)
- At median first follow-up of 49 (IQR 28-94) days, mean (SD) ESS total score after treatment with ON-SXB was 9.7 (5.5) for switch and 9.5 (5.2) for not-on-OXB patients; for both groups, mean ESS total score was in the normal EDS range (**Figure 3**)
  - Mean (SD) change from baseline in ESS total score was –1.6 (4.5) for switch and –3.1 (5.0) for not-on-OXB patients

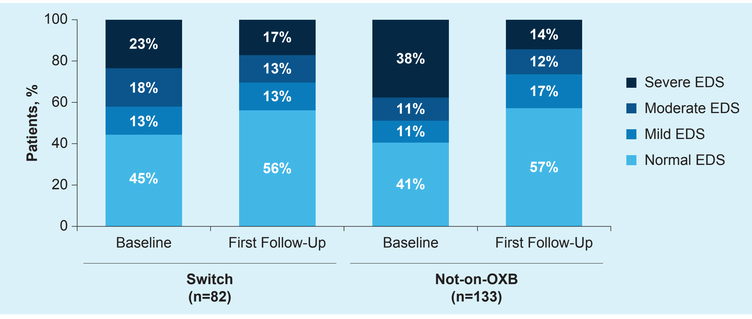
FIGURE 3: ESS Total Scores at Baseline and First Follow-Up and Change From Baseline



Normal, mild, moderate, and severe EDS defined as ESS total score of ≤10, 11-12, 13-15, and ≥16, respectively.[10,11]
Clinically meaningful improvement threshold defined as ≥2-point reduction in ESS total score per American Academy of Sleep Medicine 2021 Clinical Practice Guidelines.[9]
EDS, excessive daytime sleepiness; ESS, Epworth Sleepiness Scale; OXB, oxybate.

- At baseline, 55% of switch patients and 59% of not-on-OXB patients experienced mild-to-severe EDS (**Figure 4**)
- By the first follow-up, more than half of both switch (56%) and not-on-OXB (57%) patients 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 ≤10, 11-12, 13-15, and ≥16, respectively.[10,11]
EDS, excessive daytime sleepiness; ESS, Epworth Sleepiness Scale; OXB, oxybate.

- Median (95% CI) time to clinically meaningful improvement of ESS total score (ie, ≥2-point reduction) was 4.2 (3.3, 5.6) months for switch patients and 2.6 (2.0, 3.2) months for not-on-oxybate patients (P=0.016)

STUDY LIMITATIONS

- Data were obtained for patients who received ON-SXB from a single specialty pharmacy, of the 4 that dispense ON-SXB, which may limit the generalizability to broader populations of patients with narcolepsy
- The dataset was derived from prescription records; therefore, actual adherence to the prescribed regimen could not be verified
- Given that this was a descriptive analysis, statistical significance was not assessed to formally compare differences between switch vs not-on-OXB groups
- Follow-up intervals varied across patients and, thus, the time to clinically meaningful improvement in ESS total score may be overestimated, as patients could have reached this threshold before the recorded timepoint
- The proportion of switch patients on a maintenance dose of SXB or mixed-salts OXBs at baseline was not determined

CONCLUSIONS

- In this real-world dataset, patients switching from TN-OXB and those not on OXB at index had mild-to-moderate EDS at baseline; after initiating ON-SXB, >50% of patients achieved normal levels of daytime sleepiness (ie, ESS total score ≤10) by first follow-up (median, 1.6 months) regardless of prior TN-OXB use
- Patients switching from TN-OXB and those not on OXB at index experienced clinically meaningful improvement in EDS (ie, ≥2-point ESS total score reduction) at 4.2 months and 2.6 months after starting ON-SXB, respectively

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DISCLOSURES

LBH has participated in clinical research for Alkermes, Inc., Axsome Therapeutics, Avadel Pharmaceuticals, Breas Medical, Centessa Pharmaceuticals, Eisai, Fisher & Paykel Healthcare, Harmony Biosciences, Idorsia, Jazz Pharmaceuticals, Lilly, LivaNova/OSPREY, Merck & Co., Noctrix Health, Samsung, Sanofi, Suven 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, Suven Life Sciences Ltd., and Takeda Pharmaceutical Co. **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. **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.

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