REFRESH Real-World Experience in Narcolepsy: Burden of Twice-Nightly Oxybate and Changes in Symptoms and Quality of Life With Extended-Release, Once-Nightly Sodium Oxybate

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INTRODUCTION

- Sodium oxybate is strongly recommended by American and European clinical practice guidelines for the treatment of excessive daytime sleepiness (EDS) and cataplexy in people with narcolepsy[1,2]
- Immediate-release, twice-nightly formulations of oxybates (TN-OXB) require patients to take 1 dose at bedtime and a second dose 2.5 to 4 hours later[3-5]
- Extended-release, once-nightly sodium oxybate (ER-OXB; LUMRYZ®) is approved by the US Food and Drug Administration (FDA) for the treatment of cataplexy or EDS in patients 7 years of age and older with narcolepsy[6]
- ER-OXB was granted orphan drug exclusivity by the FDA[7]
- In the open-label study RESTORE (NCT04451668) that demonstrated the tolerability of ER-OXB, 94% (92/98) of participants preferred the once-nightly dosing regimen of ER-OXB over the twice-nightly regimen of TN-OXB[8]
- REFRESH℠ (NCT06792708) was a real-world study that assessed the clinical effectiveness, tolerability, and patient satisfaction of ER-OXB for the treatment of narcolepsy

OBJECTIVE

- To evaluate the burden of TN-OXB, changes in symptoms and quality of life (QoL) following treatment with ER-OXB, and preference for ER-OXB or TN-OXB in a real-world setting of patients with narcolepsy and their partners

METHODS

STUDY DESIGN AND DOSING

- REFRESH was a prospective, multicenter, observational study
- ER-OXB dosing followed product labeling (eg, titrated at investigator discretion within a range of 4.5-9 g)

KEY INCLUSION CRITERIA

- Age ≥18 years
- Diagnosis of narcolepsy type 1 (NT1) or type 2 (NT2)
- Participants were included in 2 cohorts
  - Oxybate (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 ER-OXB at study onset
- Prior use of ER-OXB was exclusionary

ASSESSMENTS

- Switch participants completed a 9-question switch survey at baseline to characterize their experience with TN-OXB
- All participants completed a 7-question survey at baseline (month 0) and end of study (EOS; month 4) to characterize overall QoL, mood, depression, anxiety, effect of narcolepsy on QoL, fatigue, and brain fog
- All participants completed a 14-question EOS questionnaire at their final study visit to characterize their experience with ER-OXB
  - Switch participants answered 4 additional questions about their transition from TN-OXB to ER-OXB
- Partners of participants completed an optional, 7-question survey at baseline and EOS regarding the effect of the participant's narcolepsy symptoms on the partner's QoL, as well as an optional 2-question EOS survey
  - Partners of switch participants completed an optional, 3-question survey at baseline and 2 additional optional EOS questions

DATA ANALYSIS

- Analysis was performed using data from all enrolled participants who received ≥1 dose of ER-OXB
- All data were analyzed descriptively

RESULTS

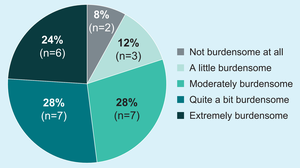
BASELINE DEMOGRAPHICS

- A total of 86 individuals were screened for REFRESH; of these, 71 participants initiated treatment with ER-OXB and are included in the overall population (OXB naive/restart, n=46; switch, n=25)
- The majority of participants were female (76%), white (83%), had a diagnosis of NT2 (62%), were OXB naive (51%; prior TN-OXB use, 14%; current TN-OXB use, 35%), and were using a medication for narcolepsy other than an OXB (72%)
  - Mean (SD [range]) age was 37.8 (13.7 [18-72]) years

SWITCH SURVEY

- All 25 switch participants completed the switch survey
- 76% (n=19) of switch participants were taking equal TN-OXB doses each night
  - The remaining switch participants (24%; n=6) were taking a higher first dose of TN-OXB
    - Reasons for asymmetrical dosing included difficulty falling and staying asleep after first dose administration, being able to wake up in the morning, and alleviation of anxiety experienced as a side effect during the day
- 92% (n=23) of switch participants found the second TN-OXB dose a little to extremely burdensome (**Figure 1**)

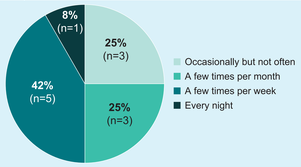
FIGURE 1: Burden of Second TN-OXB Dose (n=25)



Q. How burdensome is the second dose of medication?
TN-OXB, twice-nightly oxybate.

- 48% (n=12) of switch participants reported that they needed another person to help them wake up to take their second TN-OXB dose; of these, 50% (n=6) required help at least a few times per week (**Figure 2**)

FIGURE 2: Frequency of Needing Another Person to Wake Up for a Second TN-OXB Dose (n=12)



Q. How often?
Asked of the 12 participants who answered "yes" to "have you ever needed to have another person wake up with you to ensure you take your second dose of medicine?"
TN-OXB, twice-nightly oxybate.

- 80% (n=20) of switch participants reported missing their second TN-OXB dose in the previous 3 months
  - Most (55%; n=11) of these participants reported missing their second dose ≥1 time per week (**Figure 3**)
    - Missed second doses led to worsening of fatigue or sleepiness in ≥80% of these participants

FIGURE 3: Frequency of Missed Second TN-OXB Doses (n=20)



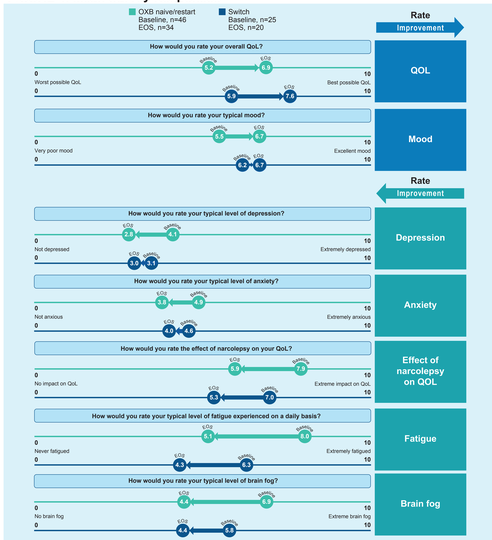
Worsening symptoms if second dose of TN-OXB is missed:
- Fatigue, 85% (n=17)
- Sleepiness, 80% (n=16)
- Anxiety/depression, 5% (n=1)
- Brain fog, 5% (n=1)
- Cataplexy (NT1 only), 5% (n=1)
- Difficulty falling asleep after second dose, 10% (n=2)

Q. How often did you miss your second dose?
Asked of the 20 participants who answered "yes" to "in the last 3 months of twice-nightly oxybate use, did you take your first dose of oxybate but not your second dose?"
NT1, narcolepsy type 1; TN-OXB, twice-nightly oxybate.

SURVEY FOR ALL PARTICIPANTS

- Participants experienced numerical improvements from baseline to EOS in overall QoL, mood, depression, anxiety, effect of narcolepsy on QoL, fatigue, and brain fog (**Figure 4**)

FIGURE 4: Mean Survey Responses

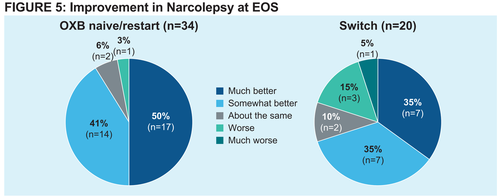


EOS, end of the study; OXB, oxybate; QoL, quality of life.

EOS QUESTIONNAIRE

- 76% (n=54) of participants completed the EOS questionnaire (OXB naive/restart, 63% [n=34]; switch, 37% [n=20])
- 83% (n=45) of participants across the overall population felt that their narcolepsy was "much" or "somewhat" better with ER-OXB (**Figure 5**; OXB naive/restart, 91% [n=31]; switch, 70% [n=14])

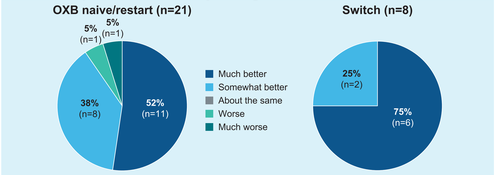
FIGURE 5: Improvement in Narcolepsy at EOS



Q. How is your narcolepsy?
EOS, end of study; OXB, oxybate.

- Mental clarity was reported as "much" better or "somewhat" better with ER-OXB by ≥50% of participants (OXB naive/restart, 65% [n=22]; switch, 50% [n=10])
- Among participants who had previously experienced drowsy driving, 90% (19/21) of OXB naive/restart participants and all (100% [8/8]) switch participants reported that their experience with drowsy driving was "much" or "somewhat better" with ER-OXB (**Figure 6**)

FIGURE 6: Experience With Drowsy Driving



Q. Have you noticed a difference in your experience with drowsy driving?
Data shown are for participants who previously experienced drowsy driving.
OXB, oxybate.

- Among participants who used as-needed stimulants to treat their narcolepsy, approximately half of OXB naive/restart and switch participants reported reductions in their use of as-needed stimulants (**Figure 7**)

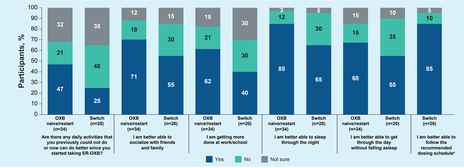
FIGURE 7: Reduction in As-Needed Stimulant Use



Q. Have you been able to reduce your use of as-needed stimulants?
Data shown are for participants who reported as-needed stimulant use.
OXB, oxybate.

- Participants reported benefits in QoL from treatment with ER-OXB (**Figure 8**)
  - Improvements in daily activities described by participants included driving, cleaning, exercising, hobbies, time with family and friends, cooking, getting up easily in the morning, completing activities during and after work, and the ability to sleep

FIGURE 8: Benefits From Treatment With ER-OXB



ER-OXB, extended-release oxybate; OXB, oxybate.
*Only answered by switch participants.

- When asked which oxybate they prefer overall, 75% (15/20) of switch participants preferred ER-OXB over TN-OXB and 10% (2/20) were not sure or had no opinion
- 90% (18/20) of switch participants reported that once-nightly dosing fits better into their routine than twice-nightly dosing

PARTNER SURVEYS

- Partners of participants (n=19) reported improvements, as reflected in decreases from baseline to EOS in mean (SD) scores (0=no effect to 10=extreme effect), for their own sleep quality (−1.2 [3.1]), intimacy (−1.2 [2.8]), QoL (−1.0 [3.4]), mood (−0.6 [3.2]), social life (−0.1 [3.1]), and interactions with family (−0.1 [2.7])
- Of the 8 partners of switch participants who completed the survey, all (100% [8/8]) reported that the twice-nightly dosing regimen of TN-OXB was burdensome for themselves, ranging from a little to extremely burdensome
- 88% (7/8) of switch participants' partners reported that once-nightly dosing fits better into their routine than twice-nightly dosing

STUDY LIMITATIONS

- This analysis relied exclusively on survey responses; limitations of REFRESH include its observational design, lack of a control group, relatively small sample size, reliance on self-reported data, lack of statistical analyses, and selection bias owing to the potential enrollment of participants dissatisfied with TN-OXB treatment
- This study was not designed to compare the safety and efficacy of ER-OXB with other medications used to treat narcolepsy
- Doses of TN-OXB for switch group patients were not collected and maintenance status on entering REFRESH was not documented

CONCLUSIONS

- After 4 months of treatment with ER-OXB, REFRESH participants described improvements in narcolepsy symptoms and QoL, even for those who switched from TN-OXB
- Participants who had been taking TN-OXB prior to study onset described the twice-nightly dosing regimen as burdensome, with missed middle-of-the-night doses leading to fatigue or sleepiness the next day
- Switch participants preferred ER-OXB over TN-OXB
- ER-OXB was the preferred treatment option among partners of switch participants, with ER-OXB leading to improvements in their own well-being and relationships

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FUNDING

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

ACKNOWLEDGMENTS

Medical writing support was provided by Taylor Johnson, PharmD, from Citrus Health Group, Inc. (Chicago, IL) and was funded by Avadel Pharmaceuticals (Chesterfield, MO).

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DISCLOSURES

SDM has received funding for conducting research studies from Alkermes, Inc., Avadel Pharmaceuticals, Axsome Therapeutics, and Jazz Pharmaceuticals 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, Takeda Pharmaceutical Co., and Lilly; has served as an advisor for Eisai; and has served on speakers bureaus for Avadel Pharmaceuticals, Axsome Therapeutics, Harmony Biosciences, Idorsia, Jazz Pharmaceuticals, Takeda Pharmaceutical Co., and Lilly.

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

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

RP has nothing to disclose.

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

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

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 has served as an advisor and/or consultant for Alkermes, Inc., Axsome Therapeutics, Daiichi Sankyo, Eisai, Jazz Pharmaceuticals, Noctrix Health, and Takeda Pharmaceutical Co.; has received industry funding for research from Apnimed, Avadel Pharmaceuticals, Bayer, BresoTec, Centessa Pharmaceuticals, Clinilabs, Eisai, FRESCA Medical, Harmony Biosciences, Idorsia, Jazz Pharmaceuticals, Lilly, LivaNova, Merck & Co., NLS Pharmaceutics, Novo Nordisk, Pfizer, Philips, Roche, Samsung, Sommetrics, Suven Life Sciences Ltd., Takeda Pharmaceutical Co., and Vanda Pharmaceuticals; and has served on speakers bureaus for Axsome Therapeutics, Eisai, Harmony Biosciences, Jazz Pharmaceuticals, and Noctrix Health.

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 has served as a speaker or consultant for Avadel Pharmaceuticals, Axsome Therapeutics, Fisher & Paykel Healthcare, Harmony Biosciences, Noctrix Health, Takeda Pharmaceutical Co., and Jazz Pharmaceuticals.

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

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

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

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

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