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Efficacy and Safety in People Transitioning to Lower-Sodium Oxybate: Data From the Transition Experience of Patients With Narcolepsy Taking Oxybate in the Real-World (TENOR) Study

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Introduction

- Lower-sodium oxybate (LXB) is an oxybate medication, containing 92% less sodium than sodium oxybate (SXB), that is approved by the US Food and Drug Administration (FDA) for treating cataplexy or excessive daytime sleepiness in patients with narcolepsy ≥7 years of age and idiopathic hypersomnia in adults[1,2]
  - LXB has been recognized by the FDA in the narcolepsy population for its significant reduction in chronic sodium burden compared with SXB, which "will be clinically meaningful in reducing cardiovascular morbidity in a substantial proportion of patients for whom the drug is indicated"[3]
- When transitioning from SXB to LXB, the recommendation is to initiate LXB treatment at the same dose and regimen as SXB (gram-for-gram) and titrate based on efficacy and tolerability, if necessary[1]
- Controlled clinical trial data have demonstrated successful transitions from SXB to LXB[1,2]; however, real-world data are needed to inform expectations of the patient population and medical community regarding transitioning from SXB to LXB
- *The Transition Experience of persons with Narcolepsy taking Oxybate in the Real-world* (TENOR) study collected data from patients transitioning from SXB to LXB in a real-world setting

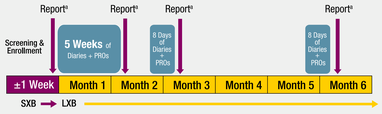
Objective

- This analysis evaluated measures of efficacy and safety in participants with narcolepsy who transitioned from SXB to LXB in TENOR

Methods

- TENOR was a patient-centric, prospective, observational, noninterventional, virtual-format study (NCT04803786)
- Eligible participants included US adults with confirmed narcolepsy (type 1 or 2) transitioning from SXB to LXB within the previous or upcoming 7 days
- Longitudinal data were collected for 21 weeks post-transition (including data collected at initiation of LXB treatment) via daily and weekly diaries and questionnaires completed by participants
  - Efficacy measures (Epworth Sleepiness Scale [ESS]; Functional Outcomes of Sleep Questionnaire, Short Version [FOSQ-10]; and British Columbia Cognitive Complaint Inventory [BC-CCI]) were collected at baseline (taking SXB) and weekly beginning at week 1 (taking LXB)
  - Participants were prospectively queried about changes in tolerability during the transition
- These analyses comprise an interim data cut (as of October 13, 2021) and include baseline data (taking SXB) from all enrolled participants and 1-week follow-up data (taking LXB) for those who had completed this timepoint
- Continuous variables were summarized with descriptive statistics (n, mean, standard deviation [SD], median, quartiles, minimum, and maximum); frequency counts and percentage of participants within each category were provided for categorical data
- Due to no adjustments for multiplicity, the *P* values presented are nominal

Figure 1. Study Design



LXB, lower-sodium oxybate; PRO, patient-reported outcome; SXB, sodium oxybate.
[a]Each participant engagement report includes a different combination of personal, aggregate, and study-related data.

Results

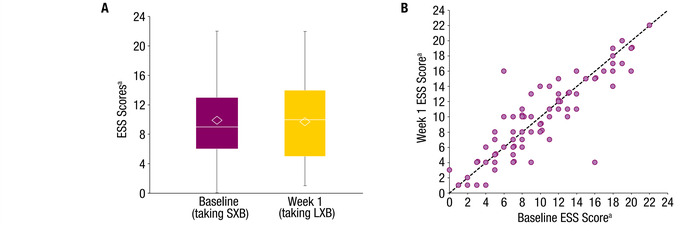
Table 1. Participant Demographics and Baseline Characteristics

Characteristic	Total N=85
Age, years, mean (SD)	40.3 (13.0)
Female, n (%)	62 (72.9)
BMI, kg/m^2, mean (SD)	28.0 (9.6)
Ethnicity, n (%)	
Hispanic, Latino, or Spanish origin	5 (5.9)
Not Hispanic, Latino, or Spanish origin	80 (94.1)
Race, n (%)[a]	
American Indian or Alaska Native	3 (3.5)
Asian	4 (4.7)
Black or African American	6 (7.1)
White	74 (87.1)
Other	5 (5.9)
Current employment status, n (%)[a]	
Employed full time	46 (54.1)
Employed part time	10 (11.8)
Unemployed	7 (8.2)
Student	13 (15.3)
Homemaker	8 (9.4)
Retired	8 (9.4)
Geographic region, n (%)	
Midwest	19 (22.4)
Northeast	15 (17.6)
South	39 (45.9)
West	12 (14.1)
Comorbidities at study enrollment, n (%)[a]	
Depression	46 (54.1)
Anxiety	39 (45.9)
Obstructive sleep apnea	23 (27.1)
Hypertension	20 (23.5)
Other mental health conditions	11 (12.9)
Cancer	5 (5.9)
Diabetes	4 (4.7)
Other cardiovascular disease	4 (4.7)
Other	12 (14.1)

BMI, body mass index; SD, standard deviation.
[a]Selection of multiple categories was allowed; percentages may sum to greater than 100%.

- This analysis included 85 participants (narcolepsy type 1, n=45; narcolepsy type 2, n=40) at baseline and 79 participants (narcolepsy type 1, n=42; narcolepsy type 2, n=37) at week 1
- At baseline, most participants took ≥1 concomitant medication for narcolepsy (79%) in addition to SXB
- Because participants could enroll up to 7 days after the transition from SXB to LXB, there was potential for recall bias when reporting baseline values (ie, when SXB was still being taken)
  - Enrollment was generally balanced in terms of the number of participants who enrolled prior to (34.1%) or following (29.4%) the transition, with a plurality of participants (36.5%) enrolling on the day of transition

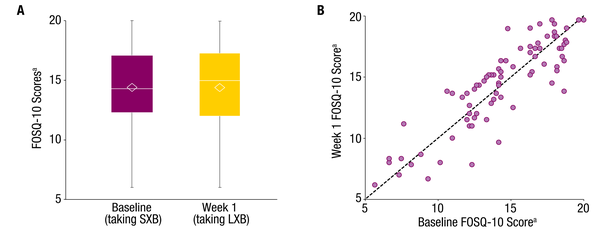
Figure 2. Average (A) and Individual (B) ESS Scores in Participants 1 Week After Transitioning to LXB Were Similar to Baseline



ESS, Epworth Sleepiness Scale; LXB, lower-sodium oxybate; Q1, first quartile; Q3, third quartile; SXB, sodium oxybate.
In panel A, the bottom and top edges of the box indicate Q1 and Q3, the line inside the box is the median, and the marker inside the box is the mean. The whiskers extending from the box indicate the minimum and maximum values. In panel B, the dashed line indicates no change. Overlapping values are shifted slightly for visibility.
[a]Range of possible ESS scores is 0–24; higher scores indicate greater sleepiness.

- At baseline (taking SXB) and week 1 (taking LXB), mean (SD) ESS scores were 9.9 (5.2) and 9.7 (5.2), respectively (mean [SD] change: −0.3 [2.7]). The median (interquartile range) ESS scores were 9.0 (6.0–13.0) at baseline and 10.0 (5.0–14.0) at week 1

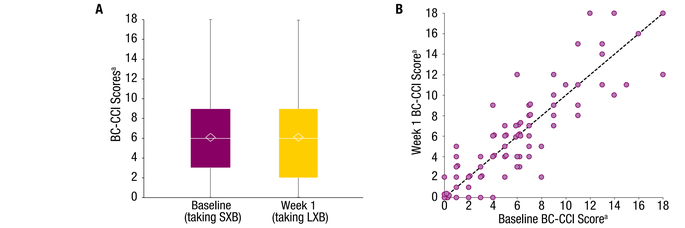
Figure 3. Average (A) and Individual (B) FOSQ-10 Scores in Participants 1 Week After Transitioning to LXB Were Similar to Baseline



FOSQ-10, Functional Outcomes of Sleep Questionnaire, short version; LXB, lower-sodium oxybate; Q1, first quartile; Q3, third quartile; SXB, sodium oxybate.
In panel A, the bottom and top edges of the box indicate Q1 and Q3, the line inside the box is the median, and the marker inside the box is the mean. The whiskers extending from the box indicate the minimum and maximum values. In panel B, the dashed line indicates no change. Overlapping values are shifted slightly for visibility.
[a]Range of possible FOSQ-10 scores is 5–20; lower scores indicate worse impairment.

- At baseline (taking SXB) and week 1 (taking LXB), mean (SD) FOSQ-10 scores were 14.4 (3.4) and 14.4 (3.6), respectively (mean [SD] change: 0.1 [1.8])

Figure 4. Average (A) and Individual (B) BC-CCI Scores in Participants 1 Week After Transitioning to LXB Were Similar to Baseline



BC-CCI, British Columbia Cognitive Complaints Inventory; LXB, lower-sodium oxybate; SXB, sodium oxybate.
In panel A, the bottom and top edges of the box indicate Q1 and Q3, the line inside the box is the median, and the marker inside the box is the mean. The whiskers extending from the box indicate the minimum and maximum values. In panel B, the dashed line indicates no change. Overlapping values are shifted slightly for visibility.
[a]Range of possible BC-CCI scores is 0–18; higher scores indicate worse impairment.

- At baseline (taking SXB) and week 1 (taking LXB), mean (SD) BC-CCI scores were 6.1 (4.4) and 6.1 (4.7), respectively (mean [SD] change: 0.0 [2.3])

Table 2. Symptoms Related to Tolerability in Participants at Baseline and 1 Week After Transitioning to LXB

Symptom, n (%)	Baseline (Taking SXB) n=84	Week 1 (Taking LXB) n=79	P Value[a]
Grogginess in the morning	38 (45.2)	36 (45.6)	0.85
Excessive sweating	34 (40.5)	21 (26.6)	0.008
Dizziness	23 (27.4)	11 (13.9)	0.01
Anxiety	20 (23.8)	20 (25.3)	0.83
Peripheral edema	16 (19.0)	10 (12.7)	0.20
Headache	16 (19.0)	18 (22.8)	0.67
GERD	14 (16.7)	10 (12.7)	0.10
Short-term nausea	12 (14.3)	15 (19.0)	0.25
Decreased appetite	11 (13.1)	10 (12.7)	1.0
Tremor	11 (13.1)	7 (8.9)	0.16
Bedwetting	9 (10.7)	4 (5.1)	0.16
Diarrhea	7 (8.3)	9 (11.4)	0.56
Long-term nausea	6 (7.1)	11 (13.9)	0.10
Vomiting	3 (3.6)	3 (3.8)	1.0

GERD, gastroesophageal reflux disease; LXB, lower-sodium oxybate; SXB, sodium oxybate.
[a]*P* values are nominal and were generated using McNemar's Chi-Square test for paired proportions (n=79).

- Tolerability symptoms reported with LXB treatment were consistent with the known safety profile of SXB[4]
- Fewer participants reported experiencing dizziness or excessive sweating 1 week after transitioning to LXB

Conclusions

- In the TENOR study, efficacy measures of excessive daytime sleepiness, quality of life, and cognition were similar from baseline (taking SXB) to 1 week after transitioning (taking LXB) in people with narcolepsy
- Tolerability symptoms were consistent with the known safety profile of SXB
- Longer-term assessments of efficacy and safety will be reported following study completion

References: 1. XYWAV® (calcium, magnesium, potassium, and sodium oxybates) oral solution, CIII [prescribing information]. Palo Alto, CA: Jazz Pharmaceuticals. **2.** Bogan RK, et al. *Sleep*. 2021;44:zsaa206. **3.** US Food and Drug Administration. Clinical superiority findings. 2021. Available at: https://www.fda.gov/industry/designating-orphan-product-drugs-and-biological-products/clinical-superiority-findings. **4.** XYREM® (sodium oxybate) oral solution, CIII [prescribing information]. Palo Alto, CA: Jazz Pharmaceuticals.

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