003

Long-Term Effects of Lower-Sodium Oxybate on Functioning and Work Productivity in Participants With Idiopathic Hypersomnia

The 74th Annual Meeting of the American Academy of Neurology (AAN)
April 2-7, 2022 • Seattle, WA

Richard K. Bogan, MD[1]; Isabelle Arnulf, MD, PhD[2]; Michael J. Thorpy, MD[3]; Nancy Foldvary-Schaefer, DO, MS[4]; Patricia Chandler, MD[5]; Luke Hickey, MSc[6]; Jed Black, MS[5,7]; Yves Dauvilliers, MD, PhD[8,9]

[1]University of South Carolina School of Medicine, Columbia, SC, USA; [2]Sleep Disorder Unit, Pitié-Salpêtrière Hospital and Sorbonne University, Paris, France; [3]Albert Einstein College of Medicine, Bronx, NY, USA; [4]Cleveland Clinic Lerner College of Medicine, Cleveland, OH, USA; [5]Jazz Pharmaceuticals, Palo Alto, CA, USA; [6]Jazz Pharmaceuticals, Philadelphia, PA, USA; [7]Stanford Center for Sleep Sciences and Medicine, Palo Alto, CA, USA; [8]Sleep and Wake Disorders Centre, Department of Neurology, Gui de Chauliac Hospital, Montpellier, France; [9]University of Montpellier, INSERM Institute Neuroscience Montpellier (INM), Montpellier, France

Introduction

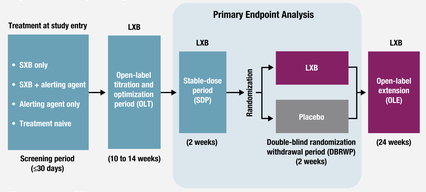
- Idiopathic hypersomnia is a debilitating neurologic sleep disorder characterized by chronic excessive daytime sleepiness (EDS; the inability to stay awake and alert during the day, resulting in the irrepressible need to sleep or unplanned lapses into sleep or drowsiness).[1-3] In addition to EDS, symptoms may include severe sleep inertia (prolonged difficulty waking with frequent reentries into sleep, confusion, and irritability), a core symptom of idiopathic hypersomnia, as well as prolonged nighttime sleep, cognitive impairment, and long and unrefreshing naps[2,3]
- Most individuals with idiopathic hypersomnia report difficulty with functioning and work due to EDS[3-5]
- Lower-sodium oxybate (LXB) was evaluated in a double-blind, placebo-controlled, randomized withdrawal clinical study that established its efficacy and safety for the treatment of idiopathic hypersomnia (NCT03533114)[6]
  - LXB is an oxybate medication with the same active moiety at the same concentration as sodium oxybate (SXB) and a unique composition of cations resulting in 92% less sodium[7]
  - The US Food and Drug Administration approved LXB in July 2020 for the treatment of cataplexy or EDS in patients 7 years of age and older with narcolepsy, and in August 2021 for the treatment of idiopathic hypersomnia in adults[8]

Objective

- This analysis evaluated functioning, quality of life, and safety during the open-label extension period (OLE) of the randomized, placebo-controlled study of LXB in adults with idiopathic hypersomnia

Methods

Figure 1. Study Design

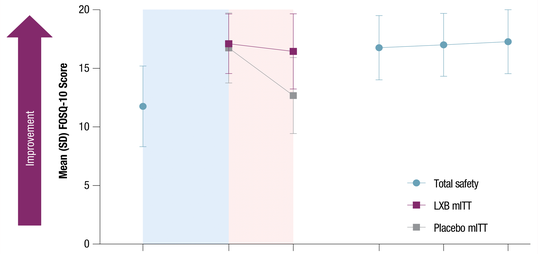


LXB, lower-sodium oxybate; SXB, sodium oxybate.

- Eligible participants were adults (18–75 years of age) with a primary diagnosis of idiopathic hypersomnia according to *International Classification of Sleep Disorders*, 2nd or 3rd Edition criteria and an average nocturnal total sleep time ≥7 hours
  - Participants were either treatment naive or were taking medications for idiopathic hypersomnia symptoms, including SXB and/or alerting agents (ie, traditional stimulants or wake-promoting agents)
- A secondary efficacy outcome was the Functional Outcomes of Sleep Questionnaire, short version (FOSQ-10; normal score, ≈18[9,10])
- An exploratory efficacy outcome was the Work Productivity and Activity Impairment Questionnaire: Specific Health Problem (WPAI:SHP), with idiopathic hypersomnia as the health problem for the following measures: work time missed (absenteeism), impairment while working (presenteeism), overall work impairment (absenteeism + presenteeism), and activity impairment
  - FOSQ-10 and WPAI:SHP were assessed at end of stable-dose period (SDP), end of double-blind randomized withdrawal period (DBRWP), OLE week 6, OLE week 14, and end of OLE (or early termination)
- Safety assessments included collection of treatment-emergent adverse events (TEAEs), vital signs, physical examination, electrocardiogram, clinical laboratory tests, and the Columbia-Suicide Severity Rating Scale
- The safety population included participants who received ≥1 dose of study drug
- The modified intent-to-treat population comprised participants who received at least 1 dose of double-blind study drug and had at least 1 post-randomization set of efficacy assessments

Results

Figure 2. FOSQ-10 Scores Improved From Baseline to End of SDP and Remained Stable Through OLE



	Baseline	End SDP	End DBRWP	OLE W6	OLE W14	End OLE
Total Safety n =	153			105	96	96
LXB mITT n =		56	54			
Placebo mITT n =		59	56			

mITT population for randomized treatment groups and safety population for combined groups. Data during OLE have not been analyzed by randomized treatment.
Note: FOSQ-10 score is the mean of the non-missing 5 subscales multiplied by 5. Scores range is 5–20 points, with higher scores indicating better functional status.
DBRWP, double-blind randomized withdrawal period; FOSQ-10, Functional Outcomes of Sleep Questionnaire, short version; LXB, lower-sodium oxybate; mITT, modified intent to treat; OLE, open-label extension period; SD, standard deviation; SDP, stable-dose period; W, week.

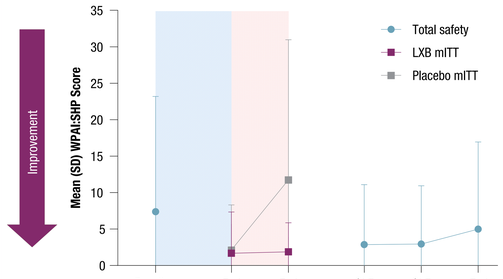
Table 1. Demographics and Baseline Disease Characteristics

		mITT Population by Randomized Treatment Group[a]	
Characteristic	**Safety Population (N=154)**	**LXB (n=56)**	**Placebo (n=59)**
Age, years, mean (SD)	40.3 (13.7)	43.4 (14.4)	38.5 (13.0)
Female, n (%)	105 (68.2)	39 (69.6)	43 (72.9)
Body mass index, kg/m^2, mean (SD)	27.4 (7.4)	28.7 (9.7)	27.2 (6.1)
Race, n (%)			
White	129 (83.8)	48 (85.7)	45 (76.3)
Black or African American	9 (5.8)	3 (5.4)	4 (6.8)
Other[b]	16 (10.4)	5 (8.9)	10 (16.9)
Region, n (%)			
North America	104 (67.5)	35 (62.5)	42 (71.2)
Europe	50 (32.5)	21 (37.5)	17 (28.8)
Baseline disease severity at study entry			
ESS score, mean (SD)	16.1 (3.6)	15.6 (3.3)	15.9 (4.2)
IHSS total score, mean (SD)	32.1 (8.0)	31.1 (8.2)	32.0 (8.6)

ESS, Epworth Sleepiness Scale; IHSS, Idiopathic Hypersomnia Severity Scale; LXB, lower-sodium oxybate; mITT, modified intent-to-treat; SD, standard deviation.
[a]Two participants did not meet the randomization criteria due to a lack of response to treatment.
[b]Includes declined to state.

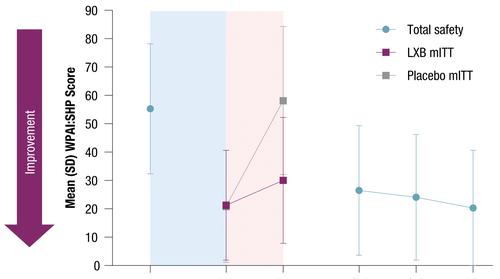
Figure 3. WPAI:SHP Scores Improved From Baseline to End of SDP and Remained Stable Through OLE[a]

A. Percent Work Time Missed Due to Idiopathic Hypersomnia (Absenteeism)



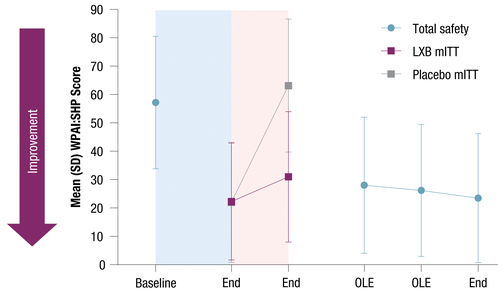
	Baseline	End SDP	End DBRWP	OLE W6	OLE W14	End OLE
Total Safety n =	120			77	65	70
LXB mITT n =		39	35			
Placebo mITT n =		46	43			

B. Percent Impairment While Working Due to Idiopathic Hypersomnia (Presenteeism)



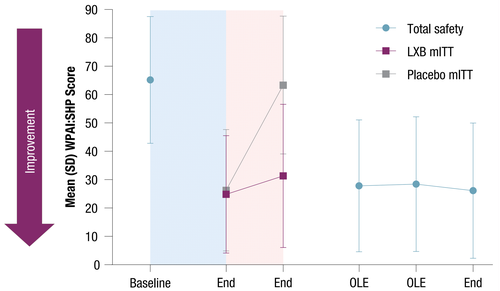
	Baseline	End SDP	End DBRWP	OLE W6	OLE W14	End OLE
Total Safety n =	121			77	66	70
LXB mITT n =		39	35			
Placebo mITT n =		46	44			

C. Percent Overall Work Impairment Due to Idiopathic Hypersomnia (Absenteeism + Presenteeism)



	Baseline	End SDP	End DBRWP	OLE W6	OLE W14	End OLE
Total Safety n =	120			77	65	70
LXB mITT n =		39	35			
Placebo mITT n =		46	43			

D. Percent Activity Impairment Due to Idiopathic Hypersomnia (Activity Impairment)



	Baseline	End SDP	End DBRWP	OLE W6	OLE W14	End OLE
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mITT population for randomized treatment groups and safety population for combined groups. Data during OLE have not been analyzed by randomized treatment.
DBRWP, double-blind randomized withdrawal period; LXB, lower-sodium oxybate; mITT, modified intent to treat; OLE, open-label extension period; SD, standard deviation; SDP, stable-dose period; W, week; WPAI:SHP, Work Productivity and Activity Impairment: Specific Health Problem.
[a]Items relating to work productivity were completed only by participants who were employed; the item relating to activity impairment was completed by all participants.

Table 2. TEAEs Across All Study Periods in ≥5% of Safety Population, by Treatment at Study Entry[a]

		Treatment at Study Entry	
TEAE, n (%)	**Safety Population (N=154)**	**Baseline Idiopathic Hypersomnia Medication[b] (n=88)**	**Treatment Naive[c] (n=66)**
Participants with ≥1 TEAE	123 (79.9)	73 (83.0)	50 (75.8)
Nausea	34 (22.1)	21 (23.9)	13 (19.7)
Headache	27 (17.5)	15 (17.0)	12 (18.2)
Dizziness	19 (12.3)	8 (9.1)	11 (16.7)
Anxiety	17 (11.0)	10 (11.4)	7 (10.6)
Vomiting	17 (11.0)	14 (15.9)	3 (4.5)
Decreased appetite	14 (9.1)	7 (8.0)	7 (10.6)
Diarrhea	12 (7.8)	9 (10.2)	3 (4.5)
Nasopharyngitis	12 (7.8)	6 (6.8)	6 (9.1)
Upper respiratory tract infection	12 (7.8)	7 (8.0)	5 (7.6)
Urinary tract infection	12 (7.8)	6 (6.8)	6 (9.1)
Fatigue	11 (7.1)	7 (8.0)	4 (6.1)
Insomnia	11 (7.1)	9 (10.2)	2 (3.0)
Dry mouth	10 (6.5)	8 (9.1)	2 (3.0)
Night sweats	9 (5.8)	7 (8.0)	2 (3.0)
Tremor	9 (5.8)	9 (10.2)	0
Muscle spasms	8 (5.2)	7 (8.0)	1 (1.5)

SXB, sodium oxybate; TEAE, treatment-emergent adverse event.
[a]Excludes placebo data.
[b]Includes participants who were taking SXB and/or an alerting agent at study entry.
[c]Includes participants not taking SXB or an alerting agent at study entry.

- Three participants discontinued during the OLE due to TEAE

Conclusions

- In addition to the previously reported efficacy on primary disease symptoms,[6] LXB demonstrated long-term maintenance of improvement in daytime functioning and work productivity over the course of the OLE (up to 24 weeks) in adults with idiopathic hypersomnia
- The safety profile of LXB in participants with idiopathic hypersomnia during this study was consistent with that of LXB in narcolepsy

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Support and Acknowledgments: This study was supported by Jazz Pharmaceuticals. Under the direction of the authors, Michael J. Theisen, PhD of Peloton Advantage, LLC, an OPEN Health company, provided medical writing and editorial support for this poster, which was funded by Jazz Pharmaceuticals.

Disclosures: RK Bogan has served on the speakers' bureau and participated in advisory boards for Jazz Pharmaceuticals. **I Arnulf** has participated in an advisory board for Idorsia. **MJ Thorpy** has received research/grant support and consultancy fees from Jazz Pharmaceuticals, Harmony Biosciences, Balance Therapeutics, Axsome Therapeutics, and Avadel Pharmaceuticals. **N Foldvary-Schaefer** has served on an advisory committee for Jazz Pharmaceuticals and participated in clinical trials supported by Jazz Pharmaceuticals, Suven, and Takeda. **P Chandler** and **L Hickey** are full-time employees of Jazz Pharmaceuticals who, in the course of this employment, have received stock options exercisable for, and other stock awards of, ordinary shares of Jazz Pharmaceuticals, plc. **J Black** is a part-time employee of Jazz Pharmaceuticals and shareholder of Jazz Pharmaceuticals plc. **Y Dauvilliers** is a consultant for and has participated in advisory boards for Jazz Pharmaceuticals, UCB Pharma, Avadel, Idorsia, Takeda, Theranexus, and Bioprojet.

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