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Blood Pressure Changes After Treatment With Low-Sodium Oxybate in Oxybate-Naive Patients With Narcolepsy or Idiopathic Hypersomnia: A Post hoc Analysis

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Introduction

- Narcolepsy and idiopathic hypersomnia are etiologically distinct central hypersomnolence disorders associated with increased rates of cardiometabolic comorbidities[1-3]
- Excess sodium intake is associated with increased blood pressure (BP) and cardiovascular risk[4-6]
  - In addition to dietary consumption, pharmacotherapy represents a modifiable source of sodium intake[7]
- Low-sodium oxybate (LXB; Xywav®), a US Food and Drug Administration (FDA)-approved treatment for excessive daytime sleepiness or cataplexy in patients 7 years and older with narcolepsy and for idiopathic hypersomnia in adults, contains the same active moiety as high-sodium oxybates (including Xyrem® [sodium oxybate; SXB] and Lumryz™ [fixed-dose, high-sodium oxybate]) but with 92% less sodium[8-10]
  - The FDA has recognized LXB in the narcolepsy population for its significant reduction in chronic sodium burden compared with high-sodium oxybate products and formulations, which "will be clinically meaningful in reducing cardiovascular morbidity in a substantial proportion of patients for whom the drug is indicated"[11]

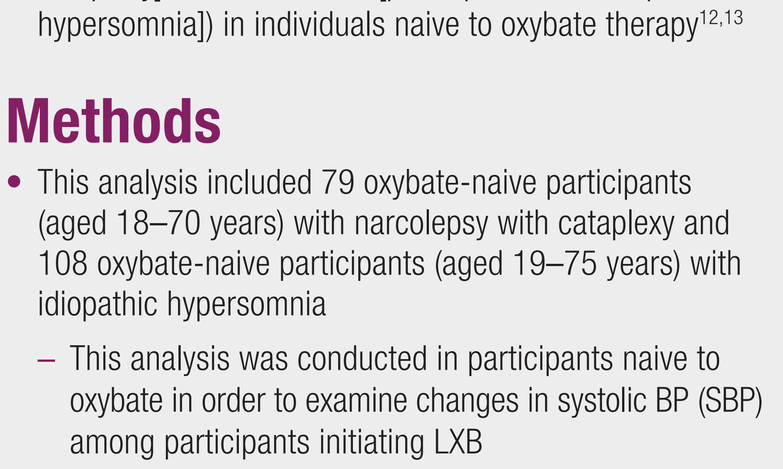
Objective

- The objective of this post hoc analysis was to determine the changes from baseline in BP during 2 phase 3 trials of LXB (NCT03030599 [participants with narcolepsy with cataplexy]; NCT03533114 [participants with idiopathic hypersomnia]) in individuals naive to oxybate therapy[12,13]

Methods

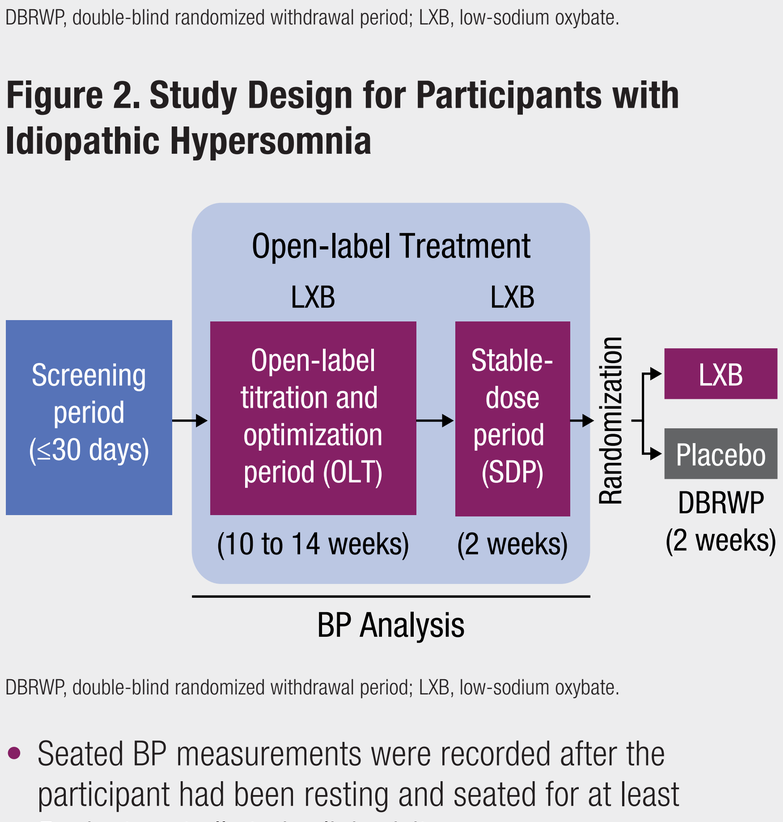
- This analysis included 79 oxybate-naive participants (aged 18–70 years) with narcolepsy with cataplexy and 108 oxybate-naive participants (aged 19–75 years) with idiopathic hypersomnia
  - This analysis was conducted in participants naive to oxybate in order to examine changes in systolic BP (SBP) among participants initiating LXB
- Participants received LXB during a 12-week (narcolepsy) or 10- to 14-week (idiopathic hypersomnia), open-label, optimized treatment and titration period, followed by a 2-week stable-dose period
  - Participants with hypertension or antihypertensive use were not excluded from either trial

Figure 1. Study Design for Participants with Narcolepsy



DBRWP, double-blind randomized withdrawal period; LXB, low-sodium oxybate.

Figure 2. Study Design for Participants with Idiopathic Hypersomnia

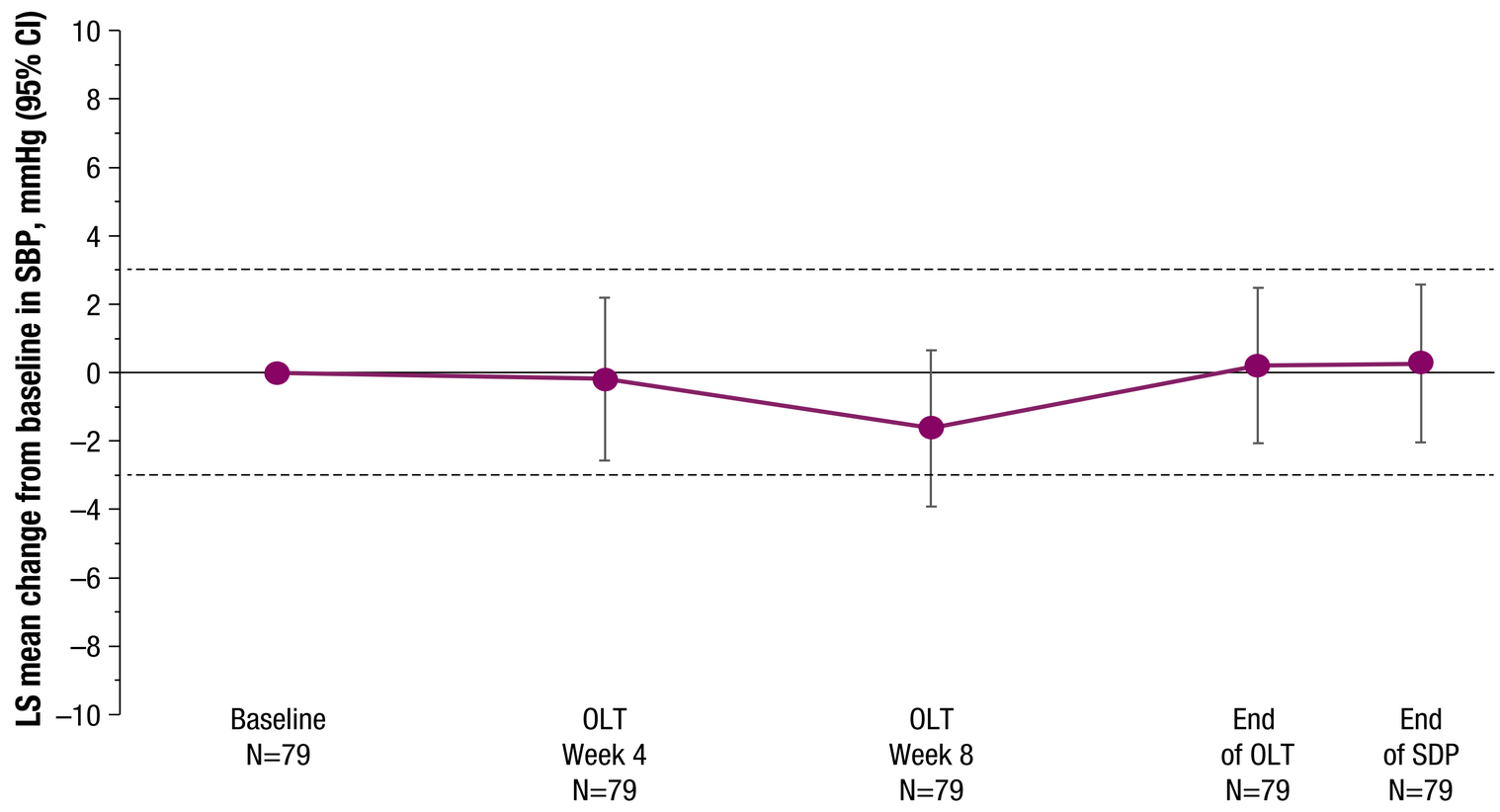


DBRWP, double-blind randomized withdrawal period; LXB, low-sodium oxybate.

- Seated BP measurements were recorded after the participant had been resting and seated for at least 5 minutes at all study clinic visits
- Change from baseline in mean SBP at each visit was analysed using 2 linear mixed models (1 for each trial) for repeated measures controlling for baseline SBP, study visit, and within-subject repeated visits

Results

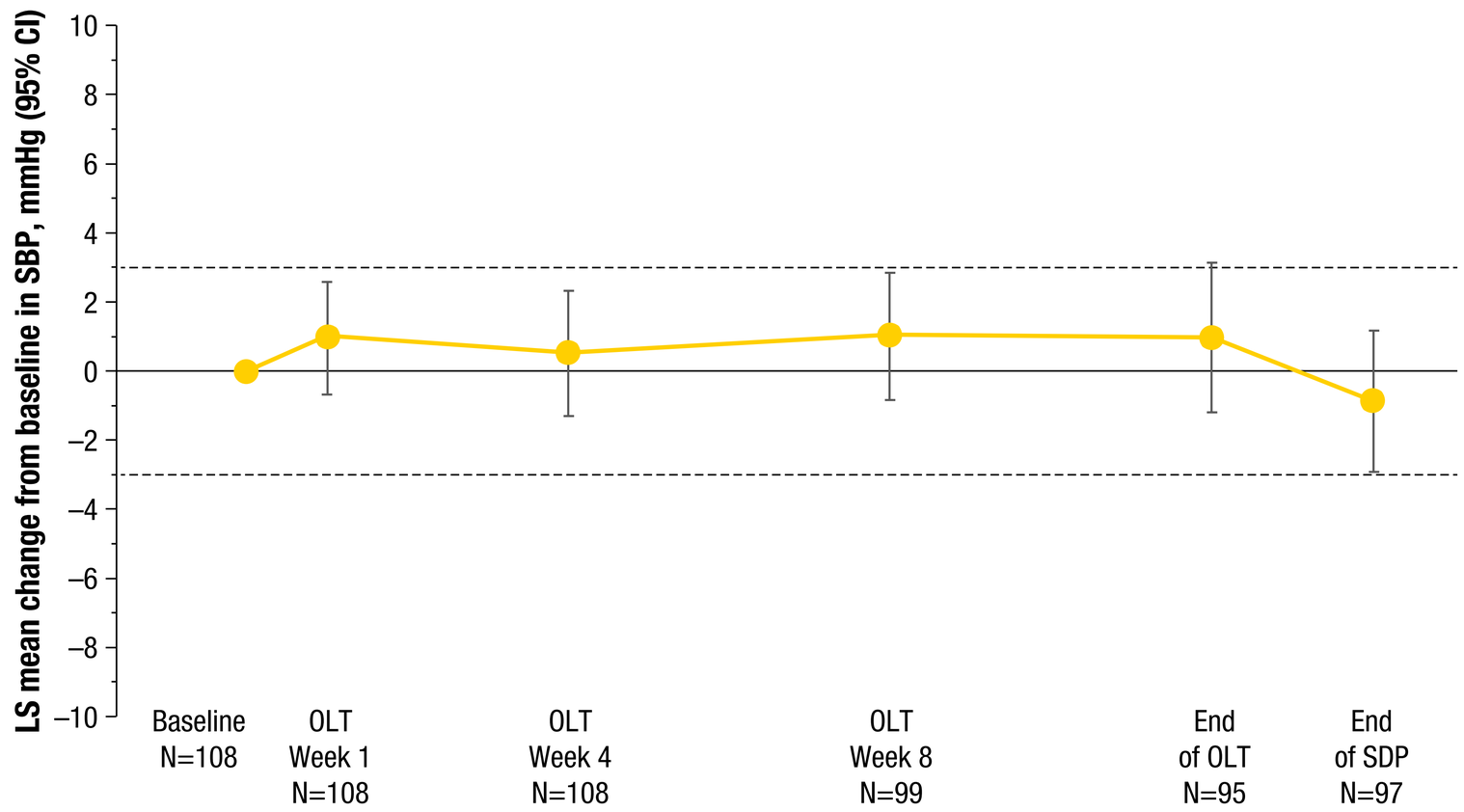
Figure 3. LS Mean Changes From Baseline in SBP for Participants With Narcolepsy (N=79)



Dotted lines denote a clinically meaningful difference of ±3 mmHg for patients with intermediate to high cardiovascular risk.[14]
CI, confidence interval; LS, least squares; OLT, open-label titration; SBP, systolic blood pressure; SDP, stable-dose period.

- In participants with narcolepsy naive to oxybate, LS mean (95% CI) changes in SBP were <3 mmHg throughout the majority of the open-label period (–0.2 [–2.6, 2.2] at OLT Week 4, –1.6 [–3.9, 0.7] at OLT Week 8, 0.2 [–2.1, 2.5] at End of OLT, and 0.3 [–2.1, 2.6] at End of SDP)

Figure 4. LS Mean Changes From Baseline in SBP for Participants With Idiopathic Hypersomnia (N=108)



Dotted lines denote a clinically meaningful difference of ±3 mmHg for patients with intermediate to high cardiovascular risk.[14]
CI, confidence interval; LS, least squares; OLT, open-label titration; SBP, systolic blood pressure; SDP, stable-dose period.

- In participants with idiopathic hypersomnia naive to oxybate, LS mean (95% CI) changes in SBP were <3 mmHg throughout the majority of the open-label period (1.0 [–0.7, 2.6] at OLT Week 1, 0.5 [–1.3, 2.4] at OLT Week 4, 1.0 [–0.8, 2.9] at OLT Week 8, 1.0 [–1.2, 3.2] at End of OLT, and –0.9 [–2.9, 1.2] at End of SDP)

Table 1. Demographics and Baseline Characteristics

Variable	Participants With Narcolepsy (N=79)	Participants With Idiopathic Hypersomnia (N=108)
Age, mean (SD), years	36.8 (12.3)	40.7 (13.7)
Sex		
Male, n (%)	24 (30.4)	30 (27.8)
Female, n (%)	55 (69.6)	78 (72.2)
SBP, mean (SD), mmHg	122.1 (12.8)	122.8 (13.8)

SBP, systolic blood pressure; SD, standard deviation.

Limitations

- This was a post hoc analysis of open-label trials that were not designed to examine changes in SBP
- Participants with hypertension or who were using antihypertensives were not exlcuded from these analyses, while those who were taking oxybate at study entry were excluded, which may limit the generalizability of these findings

Conclusions

- This post hoc analysis found no substantial changes in SBP based on a clinically meaningful difference from baseline of ±3 mmHg in 2 patient populations naive to oxybate treated with LXB during open-label study periods (12 weeks for participants with narcolepsy; 10–14 weeks for participants with idiopathic hypersomnia)
- These data suggest that treatment with LXB was not associated with SBP changes in these 2 patient populations
- In the context of the increased risk for cardiovascular and cardiometabolic comorbidities in patients with narcolepsy and idiopathic hypersomnia, these data help inform clinicians' treatment decisions

References: 1. Black J, et al. *Sleep Med.* 2017;33:13-8. **2.** Ben-Joseph RH, et al. *Sleep.* 2023:zsad161. **3.** Saad R, et al. *Sleep Epidemiol.* 2023;3:100059. **4.** Strazzullo P, et al. *BMJ.* 2009;339:b4567. **5.** Ma Y, et al. *N Engl J Med.* 2022;386(3):252-63. **6.** Gardener H, et al. *Stroke.* 2012;43(5):1200-5. **7.** Zeng C, et al. *Eur Heart J.* 2022;43(18):1743-55. **8.** Lumryz™ (sodium oxybate) for extended-release oral solution, CIII [prescribing information]. Chesterfield, MO: Avadel CNS Pharmaceuticals; 2023. **9.** Xyrem® (sodium oxybate) oral solution, CIII [prescribing information]. Palo Alto, CA: Jazz Pharmaceuticals, Inc. **10.** Xywav® (calcium, magnesium, potassium, and sodium oxybates) oral solution, CIII [prescribing information]. Palo Alto, CA: Jazz Pharmaceuticals, Inc. **11.** Clinical superiority findings. 2021. Available at: https://www.fda.gov/industry/designating-orphan-product-drugs-and-biological-products/clinical-superiority-findings. Accessed: July 9, 2021. **12.** Bogan RK, et al. *Sleep.* 2021;44(3):zsaa206. **13.** Dauvilliers Y, et al. *Lancet Neurol.* 2022;21(1):53-65. **14.** Assessment of Pressor Effects of Drugs: Guidance for Industry. 2022. Available at: https://www.fda.gov/media/113477/download. Accessed: September 27, 2023.

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Disclosures: W Macfadden, S Candler, DS Fuller, and **TJ Measey** 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. **WB White** is a cardiovascular safety consultant to Jazz Pharmaceuticals, plc.

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