**Title:** Efficacy of Lower-Sodium Oxybate by Baseline Sleep Inertia in a Phase 3 Clinical Study in Patients With Idiopathic Hypersomnia

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**Has or will this research be presented or published prior to SLEEP 2023?**

**Yes___**

**No _x_**

**ABSTRACT**

**Introduction:** Idiopathic hypersomnia is a debilitating neurologic sleep disorder. Sleep inertia (difficulty awakening) is a common symptom that can significantly impair functioning and quality of life. This post hoc analysis evaluated response to lower-sodium oxybate (LXB; Xywav®) by baseline sleep inertia in a phase 3 trial (NCT03533114).

**Methods:** Eligible participants began LXB treatment with an open-label treatment titration and optimization period (10–14 weeks), followed by a 2-week stable-dose period (SDP). Participants were randomized to placebo or continued LXB treatment during a 2-week, double-blind, randomized withdrawal period (DBRWP). Using the visual analog scale for sleep inertia (VAS-SI), participants rated their difficulty awakening during baseline, SDP, and DBRWP on a 100-mm line with anchors at 0 (very easy) and 100 (very difficult). VAS-SI terciles comprised score segments of <44 (group A), ≥44 to <70 (group B), and ≥70 (group C). Efficacy assessments included the Epworth Sleepiness Scale (ESS), Idiopathic Hypersomnia Severity Scale (IHSS), Clinical Global Impression of Severity (CGIs), and Patient Global Impression of Change (PGIc).

**Results:** Participants (A, n=34; B, n=33; C, n=32) were a mean (SD) 40.7 (13.5) years of age and primarily female (74%). At baseline, participants with the highest VAS-SI scores had numerically higher mean (SD) ESS (A=16.0 [3.1], B=15.6 [2.6], C=17.1 [2.4]) and IHSS (A=26.7 [7.7], B=34.5 [5.9], C=36.3 [5.5]) scores. Participants with the highest baseline sleep inertia were more frequently rated severely ill on the CGIs

(A=17.6%, B=12.1%, C=34.4%). Baseline total sleep time trended higher with increasing VAS-SI scores. From baseline to end of SDP, mean (SD) scores decreased (improved) on the ESS (A=−9.9 [5.1], B=−9.8 [3.5], C=−10.0 [5.1]) and IHSS (A=−14.1 [9.9], B=−19.0 [9.0], C=−18.1 [9.9]), regardless of baseline sleep inertia; nearly all (99%) participants reported improvement on the PGIc. Mean (SD) VAS-SI scores decreased by 9.3 (11.9), 31.5 (14.8), and 42.8 (22.9) in groups A, B, and C, respectively, at end of SDP. Spearman correlation coefficients for VAS-SI and IHSS items assessing sleep inertia were moderate (≥0.3) to strong (≥0.6).

**Conclusion:** Participants with higher baseline sleep inertia generally had greater baseline disease burden. LXB treatment was efficacious across subgroups regardless of baseline sleep inertia.

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**Disclosures**

**Y Dauvilliers** is a consultant for and has participated in advisory boards for Jazz Pharmaceuticals, UCB Pharma, Avadel, Idorsia, Harmony Biosciences, Takeda, and Bioprojet**.**

**A Chen, M Whalen,** and **W Macfadden** are full-time employees of Jazz Pharmaceuticals who, in the course of this employment, have received stock options

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