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Baseline Features of Participants With Narcolepsy: Insights From the DUET Study

DUET STUDY 407

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Introduction

- Low-sodium oxybate (LXB, Xywav®) is approved by the US Food and Drug Administration for the treatment of excessive daytime sleepiness (EDS) or cataplexy in patients ≥7 years of age with narcolepsy and for the treatment of idiopathic hypersomnia in adults[1-4]
- Jazz DUET (Develop hypersomnia Understanding by Evaluating low-sodium oxybate Treatment) is a phase 4, prospective, multicenter, single-arm, open-label interventional study (NCT05875974)
- This patient-centric study assesses the association of LXB treatment with changes in sleep architecture (polysomnography [PSG]), nighttime/daytime symptoms, and functional outcomes in adults diagnosed with narcolepsy (type 1 [NT1] or type 2 [NT2]) or idiopathic hypersomnia
- The DUET study is actively recruiting participants in the United States and Canada; reported here are baseline features of the participants with narcolepsy enrolled thus far
  - For further insights into the DUET study, including patient-centric and novel design elements and other cohort findings, please refer to Abstract 655/Poster 283, Abstract 1106/Poster 304, and Abstract 1337/Poster 432, respectively

Objective

- The primary objective of DUET is to evaluate the change in EDS in participants with narcolepsy (NT1 or NT2) or idiopathic hypersomnia treated with LXB

Methods

Figure 1. Study Design

EoT, end-of-treatment period; LXB, low-sodium oxybate; PK, pharmacokinetics; PSG, polysomnography; SDP, stable-dose period; V, visit.

- DUET consists of a screening period (including a washout for participants currently taking an oxybate), a baseline period, a titration period (participants begin LXB treatment with individualized dosing adjustments to achieve their optimal dose), a stable-dose period (at optimal LXB dose), an end-of-treatment period, and a safety follow-up

Table 1. Key Inclusion and Exclusion Criteria

Key Inclusion Criteria

1. 18–75 years of age (inclusive) at time of signing informed consent form
2. Primary diagnosis of idiopathic hypersomnia (*International Classification of Sleep Disorders – Third Edition* [ICSD-3] criteria) or narcolepsy type 1 or type 2 (ICSD-3 or *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* criteria)
3. If not currently taking an oxybate medication, has clinically significant symptoms of excessive daytime sleepiness, with Epworth Sleepiness Scale (ESS) score >10 at screening visit 1; if currently taking an oxybate medication, has ESS score >10 at baseline visit 2 (after washout period)
4. If currently taking an anticataplectic or an alerting agent, has been taking same dosage for ≥1 month before screening visit 1 and is not planning to adjust dosage during study period

Key Exclusion Criteria

1. Evidence of a previous untreated or inadequately treated sleep disorder considered by investigator to negatively impact study conduct. Disorders include sleep-disordered breathing, parasomnias, circadian rhythm sleep disorders, and restless legs syndrome and are determined by a previous sleep-laboratory diagnosis or interview using Diagnostic Interview for Sleep Patterns and Disorders modules
2. Evidence of untreated or inadequately treated sleep-disordered breathing, defined by apnea-hypopnea index >10,[a] during baseline visit 2
3. History or presence of an unstable or clinically significant medical condition (eg, chronic pain condition that may impact sleep), behavioral or psychiatric disorder (including active suicidal ideation or current or past [within 1 year] major depressive episode), or history or presence of another neurologic disorder or surgical history that might affect participant's safety or interfere with study conduct, based on investigator's judgment
4. Took within 1 month before screening, is taking, or plans to take any of the following:
   a. Substance or medication contraindicated with low-sodium oxybate (LXB) use (specifically, alcohol or a sedative hypnotic)
   b. Medication with known drug–drug interaction with LXB
   c. Medication that may have electroencephalography effects similar to those of LXB
   d. Medication known to have clinically significant central nervous system sedative effects
   e. Another medication, natural health product, or substance from which participant experiences clinically significant sedation, based on investigator's clinical judgment

[a]According to the rules of the US Centers for Medicare & Medicaid Services.

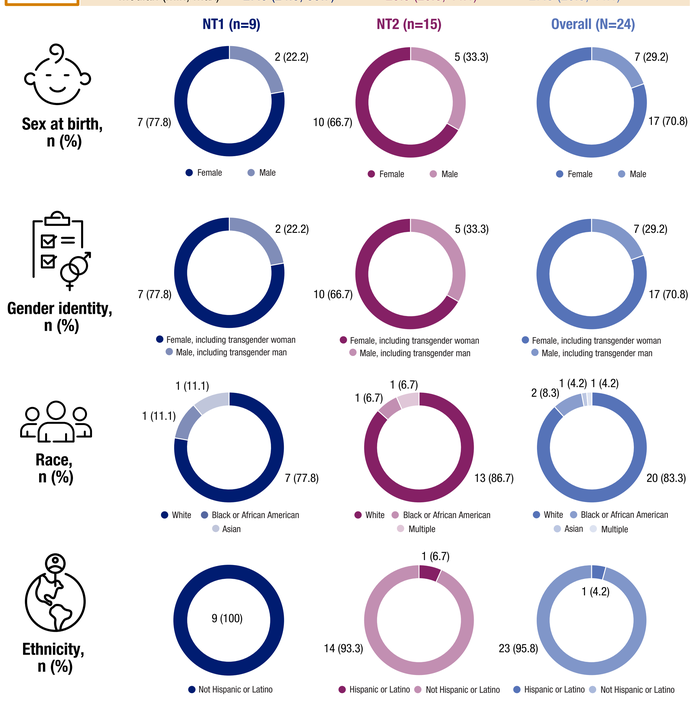
- The primary endpoint of the DUET study is change in Epworth Sleepiness Scale[5] (ESS) total score from baseline to end of treatment
- Secondary efficacy endpoints for the narcolepsy cohort include PSG measurements, pharmacokinetic parameters (optional sub-study), Patient Global Impression of Severity, and Patient Global Impression of Change from baseline to end of treatment
- Baseline data for the first 24 participants with narcolepsy who provided informed consent, passed screening, and have taken ≥1 dose of LXB as of February 5, 2024, are reported here (anticipated n=54 dosed participants)

Results

Figure 2. Baseline Demographics for First 24 Dosed Participants With Narcolepsy

Age, years	NT1 (n=9)	NT2 (n=15)	Overall (N=24)
Mean (SD)	30.7 (10.9)	30.2 (11.7)	30.4 (11.2)
Median (min, max)	24 (20, 47)	25 (20, 62)	25 (20, 62)

Body mass index, kg/m²	NT1 (n=9)	NT2 (n=15)	Overall (N=24)
Mean (SD)	30.5 (5.8)	29.7 (7.8)	30.0 (7.0)
Median (min, max)	27.5 (24.3, 39.7)	25.5 (20.5, 44.1)	27.3 (20.5, 44.1)



Participant of childbearing potential, n (%)[a]	NT1 (n=9)	NT2 (n=15)	Overall (N=24)
Yes	5 (55.6)	10 (66.7)	15 (62.5)

[a]Out of N=24 participants.
max, maximum; min, minimum; NT1, narcolepsy type 1; NT2, narcolepsy type 2; SD, standard deviation.

- Baseline demographics for the first 24 dosed DUET participants with narcolepsy are similar to those reported in a larger real-world study of people with narcolepsy[6]
  - Most participants are female (70.8%, n=17) and White (83.3%, n=20)

Table 3. Key Concomitant Alerting Medications at Study Entry for First 24 Dosed Participants With Narcolepsy

ATC Level 4 Term and Preferred Terms, n (%)	NT1 (n=9)	NT2 (n=15)	Overall (N=24)
Centrally acting sympathomimetics	4 (44.4)	5 (33.3)	9 (37.5)
Amphetamine aspartate, amphetamine sulfate, dexamphetamine saccharate, dexamphetamine sulfate	3 (33.3)	1 (6.7)	4 (16.7)
Lisdexamfetamine dimesylate	0	2 (13.3)	2 (8.3)
Methylphenidate	1 (11.1)	1 (6.7)	2 (8.3)
Solriamfetol hydrochloride	1 (11.1)	1 (6.7)	2 (8.3)
Armodafinil	0	1 (6.7)	1 (4.2)
Dexmethylphenidate hydrochloride	1 (11.1)	0	1 (4.2)
Modafinil	0	1 (6.7)	1 (4.2)
Other antidepressants	0	2 (13.3)	2 (8.3)
Bupropion hydrochloride	0	1 (6.7)	1 (4.2)
Other nervous system drugs	1 (11.1)	2 (13.3)	3 (12.5)
Pitolisant hydrochloride	1 (11.1)	2 (13.3)	3 (12.5)

ATC, Anatomical Therapeutic Chemical; NT1, narcolepsy type 1; NT2, narcolepsy type 2.

- At study entry, some participants were taking alerting agents, most commonly amphetamines (16.7%)

Table 2. Oxybate Use Before Study Entry for First 24 Dosed Participants With Narcolepsy

Oxybate Type at Screening, n (%)	NT1 (n=9)	NT2 (n=15)	Overall (N=24)
Not currently taking oxybate	8 (88.9)	12 (80.0)	20 (83.3)
Currently taking oxybate	1 (11.1)	3 (20.0)	4 (16.7)
Low-sodium oxybate	0	1 (6.7)	1 (4.2)
Sodium oxybate	1 (11.1)	2 (13.3)	3 (12.5)

NT1, narcolepsy type 1; NT2, narcolepsy type 2.

- Of the 24 dosed DUET participants with narcolepsy, 4 participants were taking oxybate at screening, while 20 were not currently taking oxybate

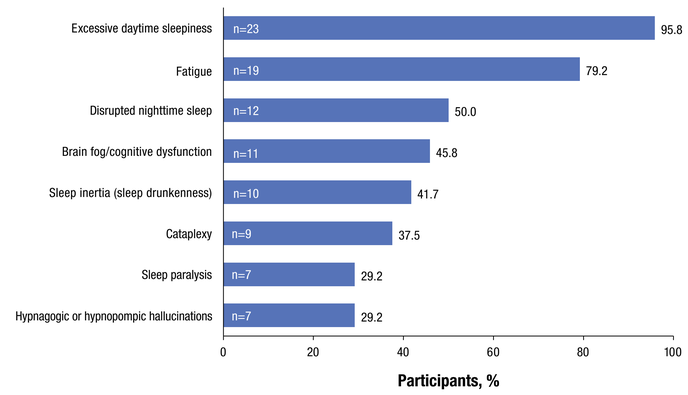
Figure 3. Symptom Analysis for First 24 Dosed Participants With Narcolepsy

Average Time From Symptom Onset to Diagnosis

N=24

- Participants reported a long delay between symptom onset and when they received a diagnosis of narcolepsy (overall, mean [SD] 8.0 [10.8] years; median [min, max], 4.0 [0.0, 39.0] years)
  - Participants with NT1 reported a mean (SD) delay of 11.2 (12.0) years (median [min, max], 8.0 [1.0, 36.0] years)
  - Those with NT2 reported a mean (SD) delay of 6.1 (9.9) years (median [min, max], 3.0 [0.0, 39.0] years)

Current Symptoms at Study Entry



- The most common symptoms reported at study entry were EDS (95.8%), fatigue (79.2%), and disrupted nighttime sleep (50.0%)

Conclusions

- Demographic features of participants with narcolepsy enrolled in DUET thus far generally align with those reported in other studies of narcolepsy[6,7]
  - These initial results include only the first 24 dosed participants with narcolepsy as of February 5, 2024
- Once completed, the DUET study is anticipated to enhance the understanding of narcolepsy and the treatment effects of LXB

References: 1. Xywav® (calcium, magnesium, potassium, and sodium oxybates) oral solution, CIII [prescribing information]. Palo Alto, CA: Jazz Pharmaceuticals, Inc. **2.** Szarfman A, et al. *N Engl J Med.* 1995;333(19):1291. **3.** US Food and Drug Administration. Clinical review for Binosto, NDA 202344. 2012. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/202344Orig1s000MedR.pdf. Accessed February 28, 2023. **4.** US Food and Drug Administration. Quantitative labeling of sodium, potassium, and phosphorus for human over-the-counter and prescription drug products. Guidance for industry. 2022. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/quantitative-labeling-sodium-potassium-and-phosphorus-human-over-counter-and-prescription-drug. Accessed October 11, 2022. **5.** Johns MW. *Sleep.* 1991;14(6):540-545. **6.** Ohayon MM, et al. *Sleep Med.* 2021;84:405-414. **7.** Bogan RK, et al. *Sleep.* 2021;44(3):zsaa206.

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