Efficacy and safety of daridorexant in patients with chronic insomnia disorder and comorbid nocturia

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Introduction

- Chronic insomnia and nocturia are frequently associated, particularly in older adults.
- Both chronic insomnia and nocturnal voids ≥2/night significantly impact sleep quality, daytime functioning and quality of life.[1,2]
- Despite the high prevalence of sleep disruptions in patients suffering from nocturia, only a limited number of studies have assessed the efficacy of hypnotics in improving sleep and/or nocturia in these patients.[3-7]
- In patients with chronic insomnia, daridorexant 50 mg reduces time to sleep onset, increases total sleep time and improves sleep maintenance and daytime functioning without next-day residual effects , as compared to placebo.[8]

Study objective

- **To evaluate the efficacy and safety of daridorexant 50 mg versus placebo in patients with chronic insomnia and comorbid nocturia.**

Methods

Study design

- A double-blind, placebo-controlled, 2-way crossover study (NCT05597020).
- Patients were randomized (1:1) to daridorexant 50 mg or placebo for 4 weeks. This was followed by a 14–21-day washout period, after which patients received the alternate treatment for 4 weeks (**Figure 1**).

Key inclusion criteria

- Age ≥55 years
- Insomnia complaints ≥3 months and insomnia severity index [ISI] score ≥13
- Self-reported nocturia: ≥3 voids/night for ≥1 month

Primary endpoint (assessed using a sleep diary)

- Self-reported total sleep time (sTST): change from baseline to Week 4
- Analysis carried out via Mixed Model for Repeated Measurements (MMRM)

Other insomnia endpoints

- ISI: change from baseline to Weeks 2 and 4
- sTST: change from baseline to Weeks 1, 2 and 3
- Visual analogue scale (VAS) for quality and depth of sleep: change from baseline to Weeks 1, 2, 3 and 4

Nocturia endpoints (evaluated using the Minze diary Pod)

- Number of nocturnal voids and time to first nocturnal void: change from baseline to Weeks 1 and 4

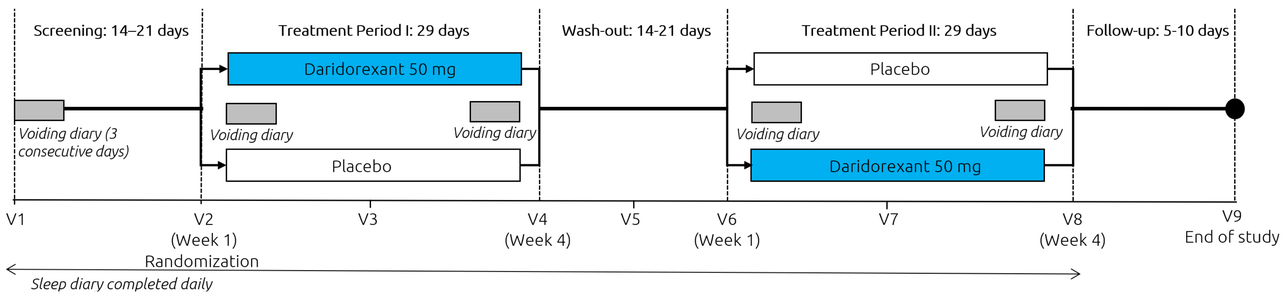
Daytime functioning endpoints

- Insomnia Daytime symptoms and Impacts Questionnaire [IDSIQ] total score: change from baseline to Weeks 1, 2, 3 and 4

Safety endpoints

- Adverse events (AEs) and AEs of special interest: falls, urinary incontinence

Figure 1. Study design



Results

Patients

- Patients had moderate/severe insomnia and clinically significant nocturia (**Table 1**).

Table 1. Demographics and baseline characteristics

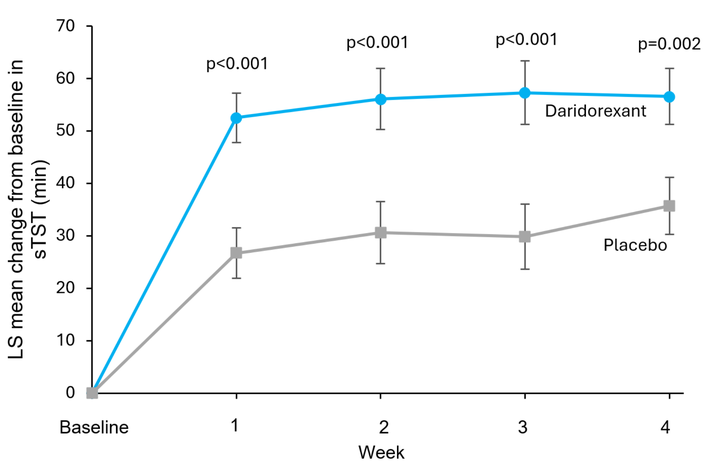
	All patients, N=60
Male / Female, %	52% / 48%
Age (years)	64.0 (6.4)
Race %	
White	70%
Black or African American	30%
Countries %	
US / Germany / Spain	70% / 22% / 8%
Baseline sleep characteristics	
sTST, min	360.3 (56.7)
ISI, range 0–28[a]	19.0 (3.7)
Quality of sleep, VAS; 0–100 mm[b]	47 (20)
Depth of sleep, VAS; 0–100 mm[b]	49 (20)
Baseline nocturia characteristics	
Number of voids per night	3.63 (0.97)
Median (range) time to first void, hours	1 h 40 (1 h 26 – 1 h 49)
Daytime functioning	
IDSIQ total score, 0–140[c]	67.0 (24.4)

Results: mean (SD) unless otherwise stated.
[a]15–21, moderate insomnia; 22–28, severe insomnia; [b]higher VAS scores indicate better quality or depth of sleep; [c]lower IDSIQ scores indicate better patient-perceived daytime functioning.

Primary endpoint: sTST

- At Week 4, daridorexant (vs. placebo) significantly increased mean sTST: LS mean difference: +20.9 min (95% CI 8.0, 33.7; p=0.002) (**Figure 2**).
- Significant improvements were also seen at Weeks 1, 2 and 3.

Figure 2. Mean change from baseline in sTST



Two-sided p values shown are versus placebo. Error bars, SEM.

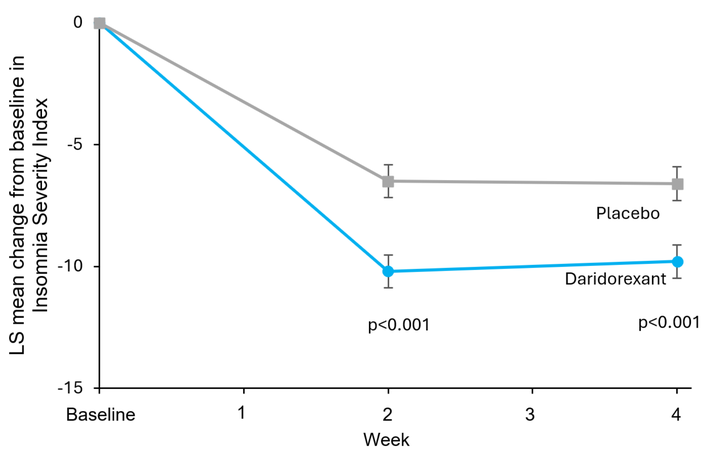
VAS quality and depth of sleep

- Improvements in quality and depth of sleep, as assessed by VAS, were significantly greater (p<0.05) with daridorexant than placebo at all weekly timepoints, except at Week 4 for VAS quality of sleep (p=0.058).

Insomnia severity index score

- ISI scores significantly decreased (i.e. improved) with daridorexant 50 mg vs. placebo at Weeks 2 and 4 (**Figure 3**).

Figure 3. Mean change from baseline in ISI score



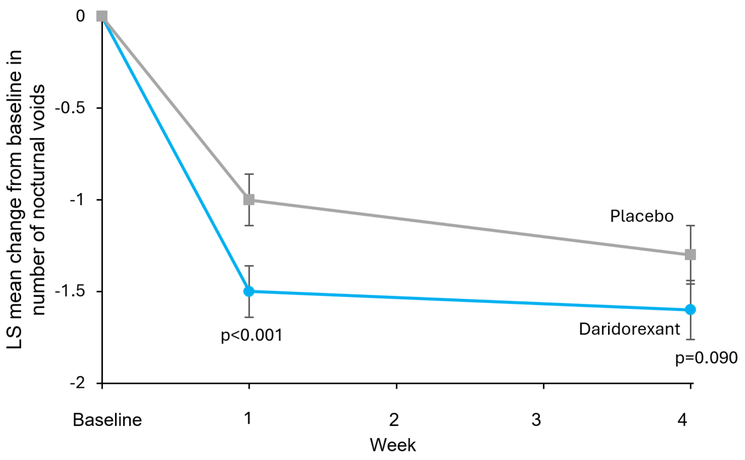
Two-sided p values shown are versus placebo. Error bars, SEM.

- A greater proportion of patients on daridorexant had an ISI score <7 (i.e. no clinically significant insomnia) vs. placebo at Week 2 (46% vs. 18%) and Week 4 (43% vs. 21%).

Number of voids per night

- Daridorexant decreased the number of voids per night vs. placebo at Weeks 1 and 4 (**Figure 4**).
- A greater proportion of patients on daridorexant reported <2 voids per night vs. placebo at Week 1 (46.6% vs. 19%) and Week 4 (52.7% vs. 31.6%).

Figure 4. Mean change in the number of voids per night



Two-sided p values shown are versus placebo. Error bars, SEM.

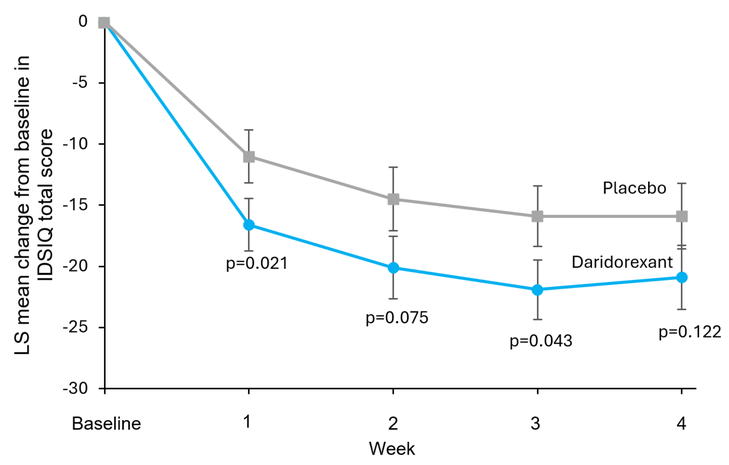
Time to first nocturnal void

- Daridorexant increased median time to first void at Weeks 1 and 4.
- Median time to first void at baseline = 1.67 h (95% CI 1.44, 1.82).
- This increased to 2.36 h (1.95, 2.95) on daridorexant and 1.85 h (1.43, 2.14) on placebo at Week 1, and to 2.46 h (1.93, 2.77) on daridorexant and 2.09 h (1.70, 2.71) on placebo at Week 4.
- The median difference between daridorexant and placebo was +31 min (p=0.0027) and +23 min (p=0.2026) at Week 1 and 4 respectively.

Daytime functioning

- IDSIQ total score decreased (i.e. improved) over time with both treatments, with greater improvements observed with daridorexant compared to placebo (**Figure 5**).

Figure 5. Mean change from baseline in IDSIQ total score



Two-sided p values shown are versus placebo. Error bars, SEM.

Safety

- No serious AEs, AEs leading to discontinuation of study treatment or deaths were reported during the study.
- No AEs of special interest were reported on daridorexant (**Table 2**).

Table 2. Summary of adverse events

	Daridorexant N=60	Placebo N=60	Total N=60
Patients with ≥1 AE, n (%)	15 (25%)	10 (17%)	22 (37%)
AEs in ≥1 patient, n (%)			
Dry mouth	3 (5%)	2 (3.4)	4 (7%)
Nausea	2 (3%)	0	2 (3%)
Fatigue	3 (5%)	0	3 (5%)
Hangover	2 (3%)	0	2 (3%)
AEs of special interest, n (%)	0	2 (3%)	2 (3%)
Fall	0	1 (2%)	1 (2%)
Incontinence	0	1 (2%)	1 (2%)

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Conclusions

- **In patients with chronic insomnia and comorbid nocturia, daridorexant 50 mg improves the duration and quality of sleep, as well as daytime functioning.**
- **Daridorexant also improves nocturia symptoms, with no increased risk of falls or urinary incontinence.**

Disclosures

The study was funded by Idorsia Pharmaceuticals Ltd. **JK** is an employee of Idorsia Pharmaceuticals UK Ltd. **J-EBM** reports research honorarium for the present study. **AO, MM and RR** are employees of Idorsia Pharmaceuticals Ltd. **KL and SS** have no conflicts to declare.

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