Time to therapeutic effect with daridorexant: Weekly analysis of patient-reported outcomes from a Phase 3 randomized, placebo-controlled study in patients with insomnia disorder

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Background

- Reducing night-time disturbances and improving daytime functioning are key goals for patients with insomnia disorder
- Daridorexant, a dual orexin receptor antagonist, is approved for the treatment of insomnia disorder in adults in the US, EU, UK, Switzerland, Canada, Hong-Kong and Japan
- Daridorexant 50 mg has been shown to significantly improve objective sleep parameter of wake time after sleep onset and latency to persistent sleep, and subjective total sleep time (sTST) and daytime functioning (Insomnia Symptoms and Impacts Questionnaire [IDSIQ] total and domain scores)[1]

Study objective

- Evaluate the patient-perceived effect of daridorexant on both sleep (sTST) and daytime functioning (IDSIQ domain scores) over time (week by week), compared with placebo in patients with insomnia disorder

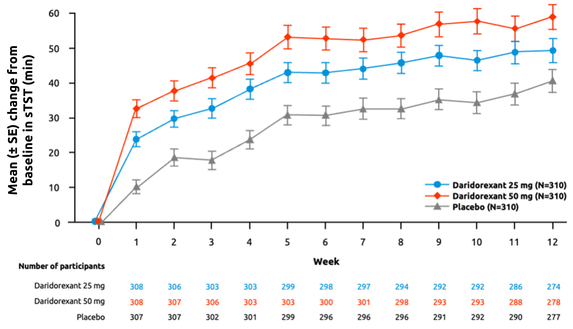
Methods

- Post hoc analysis of the randomized, double-blind, placebo-controlled, parallel-group phase 3 study (NCT03545191) in adult patients (≥18 years) with insomnia disorder, investigating the efficacy and safety of daridorexant versus placebo
- Participants were randomized (1:1:1) to receive daridorexant 25mg (n=310), 50mg (n=310) or placebo (n=310) every evening for 12 weeks
- Participants completed daily eDiary entries throughout the study. Weekly mean changes from baseline in sTST and IDSIQ domain scores (sleepiness, alert/cognition, and mood) were calculated and used to assess how patients perceived the changes in duration of sleep and daytime functioning, respectively, over the 12-weeks treatment period.
- Observed values and changes from baseline are summarized

Results

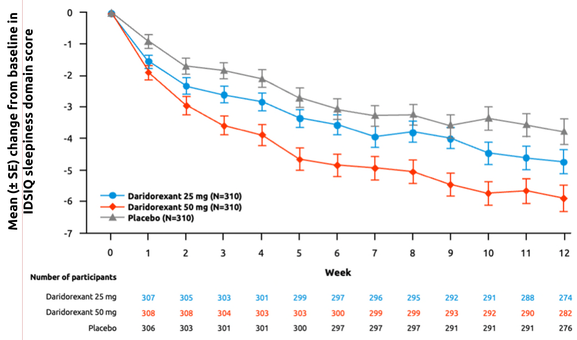
- Weekly mean changes from baseline in sTST (Figure 1) and each of the IDSIQ domain scores (Figures 2–4) from Week 1 to Week 12 of treatment showed improved outcomes over time in all treatment groups
- At each week, the observed improvements from baseline were numerically larger for daridorexant 25 and 50 mg than placebo, with daridorexant 50 mg showing the greatest treatment effect
- For sTST, treatment differences versus placebo were seen from Week 1 (mean increases from baseline for placebo, daridorexant 25 mg and 50 mg of +10.07 min, +23.83 min, and +32.63 min, respectively), and were maintained up to the end of the 12-week treatment period (Figure 1)
- For the IDSIQ domain scores, treatment differences versus placebo were seen from Week 1 and continued to increase until Week 4 with daridorexant 50 mg
- Mean decrease in IDSIQ domain scores from baseline to Week 1 for placebo, daridorexant 25 mg and 50 mg, respectively:
  - IDSIQ sleepiness domain (Figure 2): –0.92, – 1.56, and –1.90 points
  - IDSIQ alert/cognition domain (Figure 3): –1.36, –2.30, and –2.75 points
  - IDSIQ mood domain (Figure 4): –0.43, –1.51, and –2.04 points

Figure 1: Mean ± SE change from baseline in subjective total sleep time (sTST [min]) by week



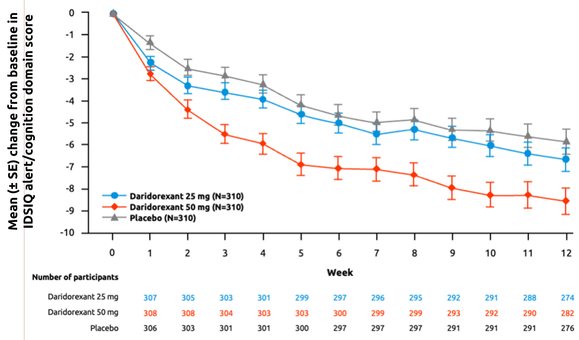
Number of participants	0	1	2	3	4	5	6	7	8	9	10	11	12
Daridorexant 25 mg	308	306	303	303	299	298	297	294	292	292	286	274	
Daridorexant 50 mg	308	307	306	303	303	300	301	298	293	293	288	278	
Placebo	307	307	302	301	299	296	296	296	291	292	290	277	

Figure 2: Mean ± SE change from baseline in IDSIQ sleepiness domain score by week



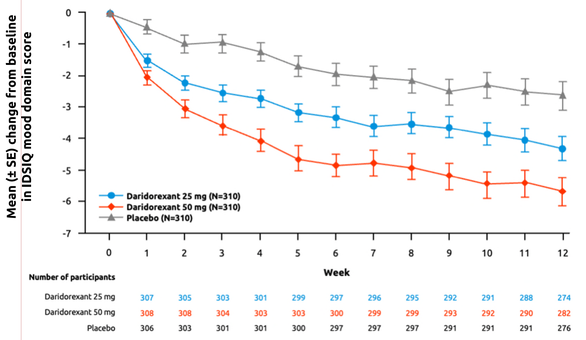
Number of participants	0	1	2	3	4	5	6	7	8	9	10	11	12
Daridorexant 25 mg	307	305	303	301	299	297	296	295	292	291	288	274	
Daridorexant 50 mg	308	308	304	303	303	300	299	299	293	292	290	282	
Placebo	306	303	301	301	300	297	297	297	291	291	291	276	

Figure 3: Mean ± SE change from baseline in IDSIQ alert/cognition domain score by week



Number of participants	0	1	2	3	4	5	6	7	8	9	10	11	12
Daridorexant 25 mg	307	305	303	301	299	297	296	295	292	291	288	274	
Daridorexant 50 mg	308	308	304	303	303	300	299	299	293	292	290	282	
Placebo	306	303	301	301	300	297	297	297	291	291	291	276	

Figure 4: Mean ± SE change from baseline in IDSIQ mood domain score by week



Number of participants	0	1	2	3	4	5	6	7	8	9	10	11	12
Daridorexant 25 mg	307	305	303	301	299	297	296	295	292	291	288	274	
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Conclusions

- The patient-perceived benefits of daridorexant treatment on sTST and the three IDSIQ domain scores were apparent from Week 1
- Compared with placebo, the treatment effect was generally more pronounced for daridorexant 50 mg than for the 25 mg dose
- With consistent nightly use, the patient-perceived efficacy on sleep and daytime functioning continued to build over the course of the 12-week treatment period, with the greatest effect being observed with daridorexant 50 mg

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Reference

1. Mignot et al. Lancet Neurol 2022; 21:125-139.