The impact of insomnia disorder on the night and the day: analysis of polysomnography and subjective parameters from a large clinical trial database

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Introduction

- Insomnia is a heterogenic disorder, defined by subjective dissatisfaction with sleep quantity and/or quality accompanied by significant daytime impairments.[1,2]
- According to diagnostic criteria, these night and daytime symptoms must occur ≥ 3 nights/week for ≥ 3 months despite adequate opportunities to sleep.[1,2]
- Effective management of insomnia disorder requires addressing both the nighttime symptoms and daytime impairments, yet studies assessing both nocturnal and diurnal clinical features of insomnia disorder remain limited.
- The phase 3 clinical program for daridorexant, a dual orexin receptor antagonist, provides a large, well-characterized dataset that includes extensive baseline data on objective and subjective measures of nighttime sleep and daytime functioning in individuals with insomnia disorder.[3]
- This dataset, therefore, represents a valuable opportunity to provide a contemporary description of the multidimensional clinical characteristics of patients with insomnia disorder.

Study objective

To comprehensively evaluate the objective and subjective clinical features of sleep symptoms and daytime functioning in a large sample of subjects with insomnia disorder screened in the two Phase 3 daridorexant trials.

Methods

- Both trials (NCT03545191, NCT03575104) were global, multicenter, randomized, double-blind, placebo-controlled trials of similar design.[3]
- ~7000 subjects aged ≥18 years with insomnia disorder and an Insomnia Severity Index (ISI) score ≥ 15 were screened between 2018 and 2020 for recruitment into one of the two studies.
- Insomnia disorder was defined according to DSM-5 criteria[2], plus a self-reported history of ≥30 min to fall asleep, wake time during sleep ≥30 min, and subjective total sleep time [sTST] ≤ 6.5 h on ≥ 3 days/week and for ≥ 3 months.

Assessments during the screening period (7-18 days)

One-night polysomnography (PSG) in the sleep laboratory.

- PSG measurements included: wake after sleep onset (WASO), latency to persistent sleep (LPS), total sleep time (TST), rapid eye movement (REM) quantity, number of awakenings and number/duration of wake bouts.

eDiary, completed daily by the patient, which included:

- Visual analog scales (VAS):
  - Morning VAS to assess quality and depth of sleep, and morning sleepiness;
  - Evening VAS to assess ability to function and daytime alertness.
  - *VAS scores range: 0-100; higher scores indicate better outcomes.*
- Insomnia Daytime Symptoms and Impacts questionnaire (IDSIQ) completed every evening to assess daytime functioning.
  - *IDSIQ total scores range: 0-140; lower scores indicate better daytime functioning.*
- ISI scale to assess the severity of insomnia.
  - *ISI total score range: 0-28; higher scores indicate more severe insomnia.*
- Morning questionnaire to assess self-reported TST (sTST), self-reported WASO (sWASO) and self-reported latency to sleep onset (sLSO).

Statistics

- This was a post hoc analysis of all subjects screened with ≥1 data record on the selected parameters.
- Subjects with an apnea or hypopnea index ≥15 events/hour or an event associated with oxygen saturation <80%, or with periodic limb movement index ≥15 events/hour, restless legs syndrome, circadian rhythm disorder, REM sleep behavior disorder or narcolepsy were excluded.
- Pearson correlation coefficients were calculated to assess correlations between different variables (r <±0.3, weak or no relationship; ±0.3 < r < ± 0.7, moderate relationship; r > ± 0.7, strong relationship).
- Descriptive statistics are presented for all endpoints.

Results

Patients

- 5474 screened subjects were included in this analysis (Table 1).
- The majority were female (66%) and White (83%); 40% were aged ≥65 years.

Table 1. Demographics and baseline characteristics

	Total screened subjects N=5474
Male / Female, %	34% / 66%
Age, mean (range), years	55.4 (18, 91)
Race, %	
White	83%
Black or African American	13%
Asian	3%
Other / unknown	1%
Body mass index, mean (SD) kg/m²*	26.5 (4.4)*
Patients with ≥1 concomitant condition, %	40%
Patients with ≥1 medication, %	16%
Time since insomnia diagnosis, mean (range), years†	11.0 (0.1, 64.1)

*BMI: n=2867; †Time since diagnosis: n=1841, only includes patients randomized to study treatment, not available for screening failures.

Sleep parameters

- Objective (PSG) and subjective measures of sleep are summarized in Table 2.
- Mean ISI total score was 20.2, indicating moderate/severe intensity of insomnia symptoms.
- Mean objective TST was 320.5 minutes, with >1 hour to fall asleep and wakefulness progressively increasing as night progressed from the first to the last quarter.
- Patients reported poor quality and depth of sleep as reflected by low mean VAS values.

Table 2. Objective and subjective nighttime sleep characteristics of screened subjects

	n	Mean (SD)
Objective (PSG) sleep parameters		
TST, min	3929	320.5 (81.1)
LPS, min	3908	63.1 (61.7)
WASO, min	3908	102.6 (57.5)
WASO per quarter, min		
Quarter 1	3400	10.9 (12.6)
Quarter 2	3804	26.0 (24.3)
Quarter 3	3887	29.5 (27.2)
Quarter 4	3903	38.5 (29.9)
REM sleep duration, min	3929	59.1 (27.6)
REM sleep latency, min	3855	156.5 (83.2)
Number of awakenings	3921	12.4 (5.5)
Wake bouts		
Total number	3898	29.8 (13.2)
Mean duration, min	3898	4.5 (8.4)
Number >6 min[a]	3898	2.8 (1.9)
Total duration of wake bouts >6 min[a], min	3581	77.8 (56.1)
Subjective sleep parameters		
sTST, min	4062	325.5 (68.2)
sWASO, min	4062	81.3 (66.0)
sLSO, min	4062	62.1 (49.5)
VAS depth of sleep (0-100)[b]	4062	39.4 (17.2)
VAS quality of sleep (0-100)[b]	4062	38.7 (16.9)
Total ISI score[c]	4874	20.2 (3.6)

[a]>6-min defines a long wake bout[4]; [b]higher VAS scores indicate better quality and depth of sleep; [c]ISI total score 0–7 = absence of insomnia; 8–14 = sub-threshold insomnia; 15–21 = moderate insomnia; 22–28 = severe insomnia.

ISI, insomnia severity index; LPS, latency to persistent sleep; REM, rapid eye movement; sLSO, self-reported latency to sleep onset; sTST, self-reported total sleep time; sWASO, self-reported wake after sleep onset; TST, total sleep time; VAS, visual analog scale; WASO, wake after sleep onset.

Daytime functioning

- IDSIQ total scores indicated moderate/severe daytime impairment (Table 3). Impairment was observed in all three individual IDSIQ domain scores (alert/cognition, mood, and sleepiness).
- Mean VAS daytime ability to function, daytime alertness and morning sleepiness scores also indicated moderate/severe daytime impairment.

Table 3. Subjective daytime characteristics of screened subjects

	n	Mean (SD)
IDSIQ scores		
Total (0-140)	3995	71.6 (22.5)
Alert/cognition domain (0-60)	3995	30.9 (9.3)
Mood domain (0-40)	3995	18.7 (8.1)
Sleepiness domain (0-40)	3995	22.0 (6.5)
VAS scores (0-100)		
Ability to function	3995	43.2 (18.5)
Daytime alertness	3995	41.6 (18.8)
Morning sleepiness	4062	39.6 (17.6)

IDSIQ, Insomnia Daytime Symptoms and Impacts Questionnaire; VAS, visual analog scale. Lower IDSIQ scores indicate better patient-perceived daytime functioning; Higher VAS scores indicate better scores.

Correlations between variables

Objective sleep measures:

- WASO and LPS (measured by PSG) showed moderate / strong negative correlations with TST (Fig 1):
  - WASO vs TST: r = -0.71; LPS vs TST: r = -0.57.

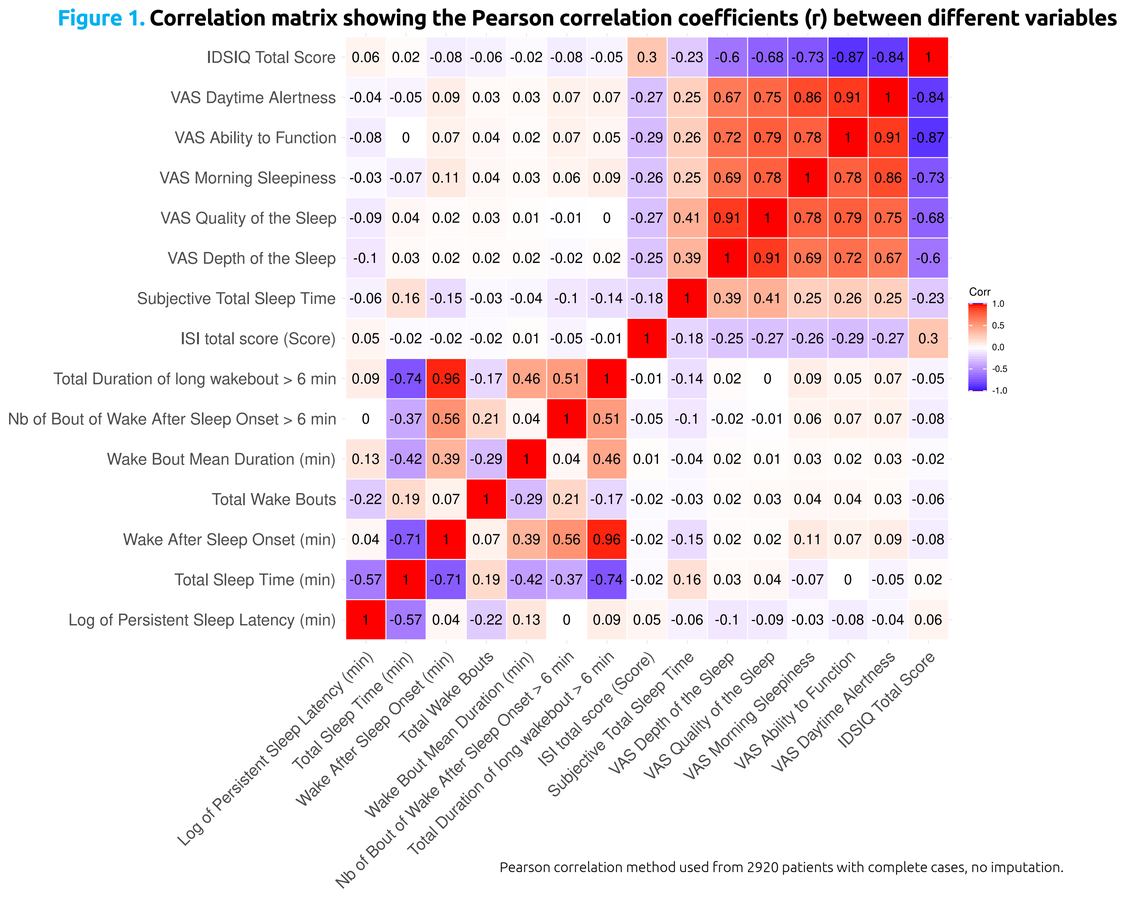
Subjective measures (VAS, IDSIQ and ISI)

- Moderate / strong correlations were observed:
  - Between VAS variables: r = 0.67 to 0.91;
  - Between IDSIQ total score and VAS variables: r = -0.87 to -0.60.
- ISI total score was weakly correlated with IDSIQ total score (r = 0.3) and VAS variables (r < -0.3).

Subjective vs objective measures

- Only weak / no correlations were found between subjective and objective sleep variables.

Figure 1. Correlation matrix showing the Pearson correlation coefficients (r) between different variables



Pearson correlation method used from 2920 patients with complete cases, no imputation.

Disclosures

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Conclusions

- **This large dataset provides much-needed comprehensive data on the high burden of insomnia disorder from a broad population of patients.**
- **These data provide valuable insights to help clinicians better understand the clinical characteristics of patients with insomnia disorder and the need to improve not only sleep but also daytime impairment.**

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