



The selective orexin-2 antagonist JNJ-42847922(MIN-202) improves sleep in patients with primary insomnia

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INTRODUCTION

Insomnia disorder is a potentially disabling condition defined as sleeping difficulties not related to a specific sleeping disorder or not sufficiently explained by a medical, psychiatric or environmental condition. Clinically it is characterized by either difficulty falling asleep, maintaining sleep during the night or nonrestorative sleep [1]. Current treatments are moderately effective or demonstrate significant untoward effects on for example cognition [2]. The orexin-2 antagonists are a novel, target-specific group of drugs that are being developed for the treatment of insomnia disorder.

AIM

To investigate the effect of the selective orexin-2 receptor (OX2R) antagonist JNJ-42847922(MIN-202) (JNJ) on sleep in patients with primary insomnia.

METHODS

A multi-center, double-blind, 2-way crossover, multiple dose study consisting of two separate treatment periods of 5 consecutive nights with either oral 40 mg of JNJ or placebo and interrupted by a washout period of 5 to 9 days. 28 subjects with insomnia disorder based on subjective report using the Insomnia Severity Index (score ≥ 15) and two-night sleep assessment with mean Latency to Persistent Sleep (LPS) of ≥ 30 min with no night < 20 min, Total Sleep Time (TST) ≤ 6 hours and Wake After Sleep Onset (WASO) > 30 min objectified with polysomnography (PSG) were included. Subjects with evidence of restless leg syndrome, apnea, parasomnias or other sleep disorders were excluded.

The primary outcome was Sleep efficiency (SE) defined as the PSG ratio TST : time in bed (TIB). Secondary outcomes were LPS, TST, Time Spent in Deep Sleep (TSDS), WASO and Wake during Total Sleep Period (WTSP). All were assessed on the night of day 1 (day 1-2) and 5 (day 5-6). Subjective sleep was assessed with the Leeds Sleep Evaluation Questionnaire (LSEQ). Finally, adverse events were recorded.

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1. American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). Washington, DC.

2. Kay-Stacey, M. and H. Attarian, Advances in the management of chronic insomnia. BMJ, 2016. 354.

RESULTS

- Baseline characteristics: 28 subjects randomized, 67.9% female, median age [range] 49.5 years [22-62]. Mean SE, LPS, TST, WASO at screening were 60.9% and 83.7, 292.7, 116.5 min, respectively.
- Compared to placebo, after treatment with JNJ:
 - SE was significantly higher. LSM difference was 5.77% (3.79-7.74*, $p < 0.001$) after a single dose and 8.12% (5.39-10.86*, $p < 0.001$) after multiple dosing.
 - LPS was significantly reduced by 59% ($p < 0.001$) and 69% ($p < 0.001$) on day 1-2 and day 5-6 respectively.
 - TST was significantly increased. LSM difference after a single dose was 27.75 min (18.28-37.22*, $p < 0.001$) and 39.0 min (25.87-52.14*, $p < 0.001$) after multiple dosing.
 - WASO and WTSP were significantly reduced: 28% and 26% after a single dose and 20% and 30% after multiple dosing respectively.
 - LSEQ showed improvements in all domains.

■ * 80% confidence interval

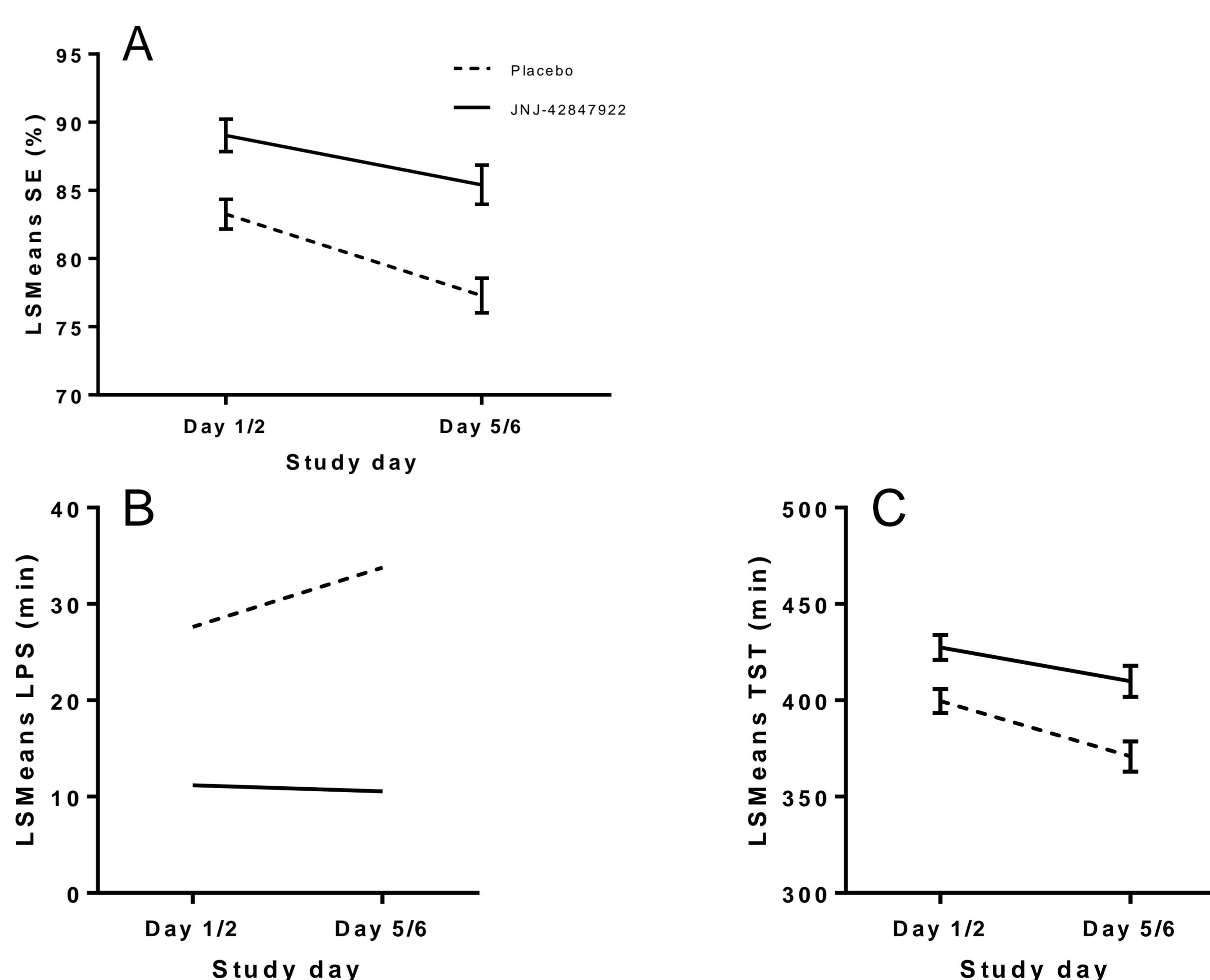


Figure 1: A. LSMMeans of Sleep Efficiency (min) \pm SE. B. LSMMeans of Latency to Persistent Sleep (min) \pm SE. C. LSMMeans Total Sleep Time (min) \pm SE. Dotted lines represent placebo, solid lines represent JNJ-42847922.

CONCLUSIONS

In comparison to placebo the selective OX2R antagonist JNJ-42847922 resulted in:

- Significantly improved objective sleep architecture
- Improved subjective sleep