double-blind AMPH ER TAB 5 mg starting dose or matching placebo, once daily in the morning beginning the day after the Baseline Visit. Subjects were titrated up (5 mg increments) each week. Safety and efficacy assessments were done weekly. After Visit 3, subjects received 20 mg for 14 (3) days before Visit 5 (V5). Subjects who could not tolerate study drugs discontinued. A Permanent Product Measure of Performance (PERMP) placement test was done at Screening or Baseline. At V5, efficacy assessments included the administration of serial PERMPs predose, 0.5, 1, 2, 4, 8, 10, 12, 13, and 14 hours postdose. The primary efficacy endpoint was the mean PERMP-T score across postdose time points during the Visit 5 serial PERMPs. Safety was monitored by AEs assessed at each visit, C-SSRS, vital signs, weight, and assessment of sleep, appetite, mood, and psychotic AEs.

Results. The mean postdose PERMP-T score over all postdose time points at V5 was statistically significantly higher in the AMPH ER TAB group vs placebo (302.8 vs 279.6; $P = .0043$). Common adverse events were decreased appetite, insomnia, and dry mouth. The majority of TEAEs were mild to moderate in severity, and no SAEs were reported.

Conclusion. The AMPH ER TAB demonstrated efficacy in the treatment of symptoms of ADHD in adults, with an anticipated safety profile.

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Post Hoc Analysis of the Impact of Lemborexant on Patient-Reported Sleep and Insomnia Severity in Adults with Insomnia and Depression Histories

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Abstract

Introduction. The dual orexin receptor antagonist lemborexant (LEM) is approved in multiple countries including the United States, Japan, Canada, and Australia for insomnia treatment in adults. In phase 3 study E2006-G000-303 (Study 303; SUNRISE-2; NCT02952820), LEM provided significant benefit vs placebo (PBO) on subjective sleep outcomes over 6 months and was well tolerated. This post hoc analysis evaluated the effect of LEM on sleep outcome measures and insomnia severity as assessed by the Insomnia Severity Index (ISI) over 6 months in subjects with a lifetime history of depression (DepHx subgroup). We performed this analysis as insomnia in DepHx subjects could be a residual symptom of unresolved depression, and therefore, these subjects may respond differently to insomnia treatment.

Methods. Study 303 was a randomized, double-blind, 12 months global study in adults (≥18 years) with DSM-5 insomnia disorder. For 6 months (Treatment Period 1), subjects were randomized to PBO or LEM (5 mg [LEM5]; 10 mg [LEM10]). For the next 6 months (Treatment Period 2; not reported), PBO subjects were rerandomized to LEM and LEM subjects continued their original dose. The inclusion criteria allowed for participation of subjects with a lifetime DepHx, concomitant antidepressant medication use and/or mild depression (maximum Beck Depression Inventory II score of 19). Subjects had a baseline ISI total score (ISI-ts) ≥15.

Results. The Full Analysis Set comprised 949 subjects, including 112 subjects in the DepHx subgroup (PBO, n = 34; LEM5, n = 39; LEM10, n = 39). Baseline median subjective sleep onset latency (sSOL; minutes) was 52.9, 57.1, and 70.7 for PBO, LEM5, and LEM10, respectively. At 6 months, greater median decreases from baseline in sSOL were observed with LEM5 (−21.7) and LEM10 (−40.1) vs PBO (−12.9). Baseline mean subjective sleep efficiency (sSE; %) was 62.2, 59.2, and 62.4 for PBO, LEM5, and LEM10, respectively. At 6 months, greater mean (SD) increases from baseline in sSE were observed with LEM5 (17.2 [18.3]) and LEM10 (20.9 [19.0]) vs PBO (14.9 [15.4]). Baseline mean subjective wake after sleep onset (sWASO; minutes) was 123.7, 151.0, and 132.6 for PBO, LEM5, and LEM10, respectively. At 6 months, greater mean (SD) decreases from baseline in sWASO were observed with LEM5 (−52.7 [69.2]) and LEM10 (−68.8 [81.9]) vs PBO (−46.7 [69.4]). Mean baseline ISI-ts were 18.6, 19.9, and 19.0 PBO, LEM5, and LEM10, respectively. At 6 months, greater mean (SD) decreases from baseline in ISI-ts were observed with LEM5 (−9.1 [6.8]) and LEM10 (−10.0 [5.9]) vs PBO (−7.9 [5.6]). Treatment-emergent adverse event rates in the DepHx subgroup were similar to those in the overall study population.

Discussion. At 6 months, LEM improved patient-reported sleep outcomes and reduced patient-reported insomnia severity in subjects with DepHx. These results suggest that LEM may be a therapeutic option for patients with insomnia and DepHx.

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Hyponatremia Secondary Treatment with SSRI Antidepressants in Adults and Elderly

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Abstract

Introduction. Hyponatremia is an electrolyte disorder that can be caused by multiple factors, among which the syndrome of inappropriate antidiuretic hormone secretion (SIAHS) is one of the most frequent causes. Selective serotonin reuptake inhibitors (SSRIs) are the most widely used antidepressant drugs in all age

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