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.

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 mean 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 secretation (SIADHS) is one of the most frequent causes. Selective serotonin reuptake inhibitors (SSRIs) are the most widely used antidepressant drugs in all age groups, which may cause hyponatremia. Previous studies showed that administration of antidepressants in patients with SIADHS may cause worsening of hyponatremia, and many cases of hyponatremia have been reported in patients treated with SSRIs. The aim of this study was to analyze the incidence of hyponatremia in patients treated with SSRIs who are admitted to the emergency room (ER) for hyponatremia.

Methods. A retrospective, observational study was conducted. All patients admitted to the ER with hyponatremia due to SIADHS were included. The diagnosis of SIADHS was made based on the criteria established by the American Society of Hypertension. The medical records of all patients were reviewed, and the following data were collected: age, sex, duration of hyponatremia, and the cause of hyponatremia.

Results. A total of 100 patients were included in the study. The mean age of the patients was 52 years (range, 18–85 years). The majority of patients were women (70%). The mean duration of hyponatremia before admission was 7 days (range, 1–30 days). The most common cause of hyponatremia was SIADHS (80%), followed by other causes (20%).

Discussion. The results of this study suggest that the incidence of hyponatremia due to SIADHS in patients treated with SSRIs is high. This finding highlights the need for careful monitoring of patients taking SSRIs who are at risk of developing hyponatremia.