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Christopher L. Drake

J. Yardley

K. Pinner

M. Moline

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Poster Number: NR-32

LONG-TERM PERCEPTION OF MEDICATION EFFECTIVENESS IN ELDERLY SUBJECTS WITH INSOMNIA RECEIVING LEMBOREXANT FOR UP TO 12 MONTHS

Christopher Drake, PhD³; Jane Yardley, PhD²; Kate Pinner, MSc²; Carlos Perdomo, PhD¹; Margaret Moline, PhD¹

¹ Eisai Inc.

² Eisai Ltd.

³ Sleep Disorders and Research Center, Henry Ford Health System

Introduction: Among elderly persons (age ≥ 65 years), insomnia is a prevalent sleep disorder. Lemborexant (LEM) is a dual orexin receptor antagonist approved in multiple countries, including the United States, Japan, Canada, Hong Kong, Australia, and India, for the treatment of insomnia in adults (age ≥ 18 years). Clinical trials for insomnia therapies include data from daily sleep diaries to assess the magnitude of change quantitatively in subjective sleep outcomes, including sleep onset and maintenance. Additionally, there are instruments that assess patient estimates of time to sleep onset and duration of nighttime awakenings. Assessment of symptom improvement provides critical information on treatment effectiveness. The demonstration of improvement in sleep from the patient's perspective is important in the assessment of the effectiveness of an insomnia therapy, as insomnia is a symptom-based disorder. The Patient Global Impression–Insomnia version (PGI-I) is a self-report instrument used to evaluate a patient's perception (qualitative) of the effects of their insomnia medication on their sleep relative to their sleep before starting their treatment. The PGI-I includes 3 items related to medication effects (helped/worsened sleep; decreased/increased time to fall asleep; and increased/decreased total sleep; choices for patient responses include: 1=positive, 2=neutral, 3=negative). The PGI-I also includes 1 item related to perceived appropriateness of study medication strength with a different set of possible responses (choices for patient responses include: 1=too strong, 2=just right, 3=too weak). In Study E2006-G000-303 (Study 303; SUNRISE-2; NCT02952820), significantly greater percentages of subjects in the age ≥ 65 years subgroup reported a positive impact of LEM versus placebo (PBO) at 1, 3 and 6 months for each of the PGI-I items related to medication effects. The majority of subjects also reported medication strength as “just right” at 1, 3 and 6 months. PGI-I results at 9 and 12 months for subjects age ≥ 65 years are presented here for subjects that received continuous treatment with LEM for up to 12 months in Study 303.

Methods: Study 303 was a Phase 3, 12-month, double-blind, global study in adults age ≥ 18 years with insomnia disorder that included a 6-month PBO-controlled period (Treatment Period 1) followed by a 6-month active-only (Treatment Period 2) period. Subjects received PBO, LEM 5mg (LEM5) or LEM 10mg (LEM10) for the first 6 months. For Treatment Period 2, PBO-treated subjects were rerandomized to LEM (not reported here), while LEM-treated subjects continued their original dose. Titration to higher or lower doses was not permitted. The PGI-I was administered at Months 1, 3, 6, 9, and 12. Results for the PGI-I were analyzed by age (age ≥ 65 years).

Results: The Full Analysis Set comprised 949 subjects, of which 262 (27.6%; [PBO, n=89; LEM5, n=87; LEM10, n=86]) were age ≥ 65 y. At 9 and 12 months, the majority of elderly LEM5-treated (total treated up to 9 months, n=68; total treated up to 12 months, n=61) and LEM10-treated (total treated up to 9 months, n=61; total treated up to 12 months, n=56) subjects reported that their study medication “helped” sleep at night (9 months: LEM5=51 [75.0%], LEM10=45 [73.8%]; 12 months: LEM5=47 [77.0%], LEM10=42 [75.0%]), reduced time to fall asleep (9 months: LEM5=59 [86.8%], LEM10=47 [77.0%]; 12 months: LEM5=53 [86.9%], LEM10=44 [78.6%]), and increased total sleep time (9 months: LEM5=43 [63.2%], LEM10=45 [73.8%]; 12 months: LEM5=38 [62.3%], LEM10=33 [58.9%]). Also, at both 9 and 12 months, the majority of subjects in the LEM5 and LEM10 groups responded that their medication strength was “just right” (9 months: LEM5=46 [67.6%], LEM10=37 [60.7%]; 12 months: LEM5=43 [70.5%], LEM10=37 [66.1%]). LEM was well tolerated. Most adverse events were mild or moderate.

Conclusions: The majority of elderly subjects receiving LEM5 or LEM10 for up to 12 months reported a positive medication effect and perceived their medication strength as “just right” at both 9 and 12 months. These results demonstrate that the similar positive perceptions of the effects of LEM achieved during Treatment Period 1 in the elderly subgroup were sustained through Treatment Period 2.

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SUBJECTIVE RATINGS OF MEDICATION STRENGTH OVER 6 MONTHS IN ELDERLY SUBJECTS WITH MODERATE OR SEVERE INSOMNIA TREATED WITH LEMBOREXANT

Christopher Drake, PhD³; Jane Yardley, PhD²; Kate Pinner, MSc²; Margaret Moline, PhD¹

¹ Eisai Inc.

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³ Sleep Disorders and Research Center, Henry Ford Health System

Introduction: Lemborexant (LEM) is a dual orexin receptor antagonist approved in multiple countries including the United States, Japan, Canada, Hong Kong, Australia, and India, for the treatment of adults with insomnia. Patient-reported perceptions of medication effectiveness and strength, and perceptions of insomnia severity can be assessed by the Patient Global Impression – Insomnia (PGI-I) and Insomnia Severity Index (ISI) questionnaires, respectively. PGI-I items 1-3 assess perceived effects (positive, neutral, or negative) of the study medication on sleep (helped/worsened sleep; decreased/increased time to fall asleep; and increased/decreased total sleep). PGI-I item 4 assesses the perceived appropriateness of study medication strength (“too strong,” “just right,” or “too weak”).

In Study E2006-G000-303 (Study 303; SUNRISE-2; NCT02952820), significantly greater percentages of subjects with insomnia disorder age ≥ 65 y (elderly) treated with LEM indicated a positive effect of their medication compared with placebo (PBO), as assessed by items 1-3 of the PGI-I at 1, 3, and 6 months. A significantly greater percentage of these elderly subjects also indicated on PGI-I item 4 that their medication strength was “just right” at these time points. Additionally, significantly greater decreases from baseline in ISI total score were also observed with LEM vs PBO in elderly subjects, as assessed at 1, 3, and 6 months.

In this post hoc analysis, potential tolerance to LEM was evaluated in the elderly subgroup by analyzing ratings of medication strength on PGI-I item 4 in the subsets of elderly subjects who had moderate (ISI total score 15-21) or severe (ISI total score 22-28) insomnia at baseline.

Methods: Study 303 was a 12-month, double-blind, PBO-controlled (first 6 months [Treatment Period 1]), phase 3 study in subjects ≥ 18 y with insomnia disorder and baseline ISI total score ≥ 15 . Subjects were randomized to PBO, LEM 5mg (LEM5), or LEM 10mg (LEM10). During the second 6 months (Treatment Period 2, not reported here), PBO-treated subjects were rerandomized to LEM, while LEM-treated subjects continued their originally assigned dose. During Treatment Period 1, the PGI-I and ISI were administered at 1, 3, and 6 months; the ISI was also administered at baseline. Titration to higher or lower doses was not permitted during the study.

Results: Of 949 subjects in the Full Analysis Set, 262 (27.6%; [PBO, n=89; LEM5, n=87; LEM10, n=86]) were age ≥ 65 y. Among these subjects, 193 (73.7% [PBO, n=66; LEM5, n=63; LEM10, n=64]) had moderate insomnia, and 61 (23.3%; [PBO, n=20; LEM5, n=21; LEM10, n=20]) had severe insomnia at baseline, respectively. In both insomnia severity groups, greater percentages of LEM-treated than PBO-treated subjects rated their medication strength as “just right” at 1 month (moderate: LEM5=47.4%; LEM10=46.4%; PBO=21.3%; severe: LEM5=47.6%; LEM10=44.4%; PBO=5.3%), at 3 months (moderate: LEM5=60.4%; LEM10=53.8%; PBO=34.4%; severe: LEM5=47.4%; LEM10=64.7%; PBO=22.2%) and at 6 months (moderate: LEM5=59.6%; LEM10=51.0%; PBO=34.4%; severe: LEM5=76.5%; LEM10=68.8%; PBO=25.0%). The majority of LEM-treated subjects who rated their medication strength as “just right” had an ISI total score ≤ 14 (ie, subthreshold insomnia) at each of the time points.

Ratings of “too weak” were greater with PBO than with LEM and did not increase over time (Months 1, 3, and 6) in subjects with moderate (LEM10: 42.9%; 34.6%; 38.8%; LEM5: 50.9%; 39.6%, 40.4%; PBO: 75.4%, 65.6%, 65.6%) or severe (LEM10: 55.6%, 35.3%, 31.3%; LEM5: 52.4%, 52.6%, 23.5%; PBO: 89.5%, 77.8%, 75.0%) insomnia at baseline. In subjects with moderate insomnia, ratings of “too strong” at 1, 3, and 6 months were higher with LEM10 (10.7%, 11.5%, 10.2%) than with LEM5 (1.8%, 0%, 0%) or PBO (3.3%, 0%, 0%). However, no LEM5- or LEM10-treated subjects with severe insomnia at baseline rated their medication as “too strong” at any time point. LEM was well tolerated with adverse events being mild or moderate in severity.

Conclusions: These analyses suggest that tolerance to LEM5 and LEM10 does not develop over time, as ratings of “too weak” did not increase across the study period. In both insomnia severity groups, ratings of “just right” were more common in subjects treated with LEM5 or LEM10 than PBO. These data support LEM as a long-term treatment option in adults ≥ 65 y with insomnia.

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PSYCHOSOMATIC OR PSYCHOTROPIC POLYPHARMACY? A CASE HIGHLIGHTING THE IMPORTANCE OF PHARMACOKINETICS

Alexandra Moore, DO

Dell Medical School - UT Austin

Introduction: Psychotropic drugs are among the most common medications prescribed to elderly patients. The number of psychotropic drugs has increased significantly over the past few decades with a proportional increase in adverse medication outcomes including drug-drug interactions. Advancing age is accompanied by changes in pharmacokinetics and pharmacodynamics that put older patients at greater risk for adverse medication outcomes. The majority of psychotropic agents