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SCIENTIFIC INVESTIGATIONS

Efficacy and safety of lemborexant in adults with insomnia: comparing Japanese and non-Japanese subgroups from the global, phase 3, randomized, double-blind, placebo-controlled SUNRISE 2 study

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Study Objective: Whether there are racial differences in the efficacy/safety of hypnotics has not been sufficiently investigated. We aimed to evaluate the efficacy/safety of lemborexant 5 mg and lemborexant 10 mg vs placebo once daily in a subset of Japanese patients with insomnia and to compare the results with those of non-Japanese patients.

Methods: This subanalysis reports the results of the first 6 months (period 1, placebo-controlled) of SUNRISE 2, a 12-month, global, randomized, double-blind, phase 3 study. Changes in patient-reported sleep onset latency, patient-reported sleep efficiency, and patient-reported wake after sleep onset with lemborexant 5 mg or lemborexant 10 mg vs placebo were evaluated. Treatment-emergent adverse events were evaluated for safety.

Results: In total, 949 patients were randomized (Japanese, n = 161; non-Japanese, n = 788). Groups were balanced at baseline except for the male/female ratio ($P = .0002$) and body mass index ($P < .0001$) in the Japanese vs non-Japanese subgroups. Overall, the efficacy and safety of lemborexant were similar between subgroups. In the Japanese subgroup, the subjective sleep onset latency change from baseline was significant after 7 nights and 6 months with lemborexant 10 mg vs placebo, the subjective sleep efficiency change from baseline was significant after 7 nights with lemborexant 10 mg vs placebo, and the subjective wake after sleep onset change from baseline was significant at 6 months with lemborexant 5 mg vs placebo. The incidence and severity of treatment-emergent adverse events were consistent between both subgroups.

Conclusions: Lemborexant 5 mg and 10 mg improved sleep onset and sleep maintenance over 6 months and was well-tolerated in both the Japanese and non-Japanese patients. The safety profiles of lemborexant 5 mg and 10 mg were consistent between the subgroups.

Clinical Trial Registration: Registry: ClinicalTrials.gov; Name: Long-term Study of Lemborexant in Insomnia Disorder (SUNRISE 2); URL: https://clinicaltrials.gov/ct2/show/NCT02952820; Identifier: NCT02952820; and Registry: ClinicalTrialsRegister.eu; Identifier: 2015-001463-39.

Keywords: chronic insomnia disorder, clinical trial, Japan, lemborexant, sleep disorder, subgroup analysis

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Lemborexant is a dual orexin receptor antagonist recently approved for the treatment of insomnia in both the United States and Japan. However, whether there are racial differences in the efficacy/safety of hypnotics, especially dual orexin receptor antagonists, had not been sufficiently investigated until now.

Study Impact: Our results showed that lemborexant improved sleep onset and sleep maintenance insomnia over 6 months and was well tolerated in Japanese patients, and that the safety profile of lemborexant was consistent between the Japanese and non-Japanese subgroups. Therefore, our findings confirm that the benefits of lemborexant reported in the overall population are also applicable to the Japanese population.

INTRODUCTION

To date, benzodiazepines or z-drugs have been the mainstream pharmaceutical treatment for insomnia. However, the effects of these drugs have some limitations, such as an apparent association with the risk of falls, fractures, dementia, cancer, and stroke in older adults[1] and the risk of dependence formation under long-term continuous use.[2] Therefore, new treatment options are warranted for patients with chronic insomnia that can lead to clinically meaningful improvement for both difficulty falling asleep and difficulty maintaining sleep that result in better daytime function and that are safe and well tolerated.

The orexin/hypocretin system is a well-established target for insomnia treatment.[3] Lemborexant (LEM) is a dual orexin receptor antagonist that was recently approved for the treatment of insomnia in the United States, Japan, and Canada. LEM shows competitive antagonism for both orexin receptor type 1 and orexin receptor type 2, with a stronger affinity for orexin receptor type 2 than orexin receptor type 1. Orexin receptor type 2

may play a more prominent role in arousal/sleep regulation and the transition from awakening to nonrapid eye movement sleep.[4–7] Therefore, stronger antagonistic action on orexin receptor type 2 is expected to yield greater clinical benefits such as faster sleep onset.

Clinical studies on healthy individuals and patients with insomnia have not reported clinically meaningful racial differences in the pharmacokinetics of the previously established dual orexin receptor antagonist suvorexant or LEM.[8–10] However, racial differences in terms of the efficacy and safety of insomnia drugs have not been sufficiently examined and should be investigated. In particular, no studies have directly examined differences in the efficacy and safety of hypnotics, particularly dual orexin receptor antagonists, between Japanese and non-Japanese patients.

The aim of the present subanalysis of SUNRISE 2[11] was to evaluate the efficacy and safety of LEM 5 mg (LEM5) or LEM 10 mg (LEM10) vs placebo in a subset of Japanese patients with insomnia and to compare these results with those of the non-Japanese population to clarify any racial differences in the efficacy and safety of this drug.

METHODS

Study design

A detailed description of the SUNRISE 2 study design and methods has been previously reported.[11] Briefly, SUNRISE 2 was a 12-month, global, multicenter, randomized, double-blind, parallel-group phase 3 study that was placebo-controlled for the first 6 months (period 1), followed by administration of the active drug only for the next 6 months (period 2). The present study focuses on the results of a subpopulation (Japanese vs non-Japanese subgroups) from period 1 (**Figure 1**).

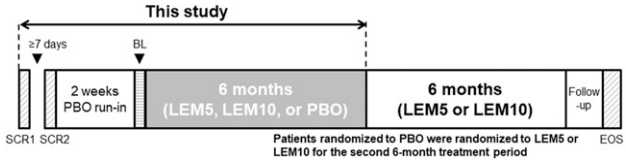
The study was conducted at 119 sites in Japan (24), North America (45), Europe (34), Asia (11), and Oceania (5) between November 15, 2016, and January 8, 2019. The 6-month placebo-controlled portion of the study (period 1) ended on May 31, 2018.

The study protocol was approved by relevant institutional review boards and independent ethics committees. All protocol amendments were approved. The study adhered to Good Clinical Practice guidelines, the Declaration of Helsinki, and local regulations. All study patients provided written informed consent.

Patients

Japanese men and women aged ≥ 18 years residing in Japan with insomnia disorder and meeting the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, criteria were eligible for the study.[12] Patients had a history of subjective sleep onset latency (sSOL) of ≥ 30 minutes and/or subjective wake after sleep onset (sWASO) of ≥ 60 minutes at least 3 times a week in the previous 4 weeks before enrollment. Patients were also required to score ≥ 15 on the Insomnia Severity Index.[13] Among the main exclusion criteria were the presence of comorbid sleep disorders, periodic limb movement disorder, restless legs syndrome, circadian rhythm sleep disorder or narcolepsy, and a history of complex sleep-related behavior.[11]

Figure 1—Study design overview.



BL = baseline, EOS = end of study, LEM5 = lemborexant 5 mg, LEM10 = lemborexant 10 mg, PBO = placebo, SCR = screening.

Procedures

Patients meeting eligibility criteria and sleep diary adherence during the run-in (at least 7 consecutive morning entries) were subsequently randomized approximately 1:1:1 to placebo, LEM5, or LEM10 once daily during period 1. LEM5 and LEM10 once daily were found to be effective for both difficulty falling asleep and difficulty maintaining sleep and had similar tolerability to the placebo group in a previous clinical trial.[14] Therefore, LEM5 and LEM10 once daily were used in the SUNRISE 2 study. Randomization was stratified by country and age group (ages 18 to < 65 years and ages ≥ 65 years). Throughout the study, patients were provided with the study drug and were instructed to take 1 tablet orally each night 5 minutes before the time they intended to try to sleep.

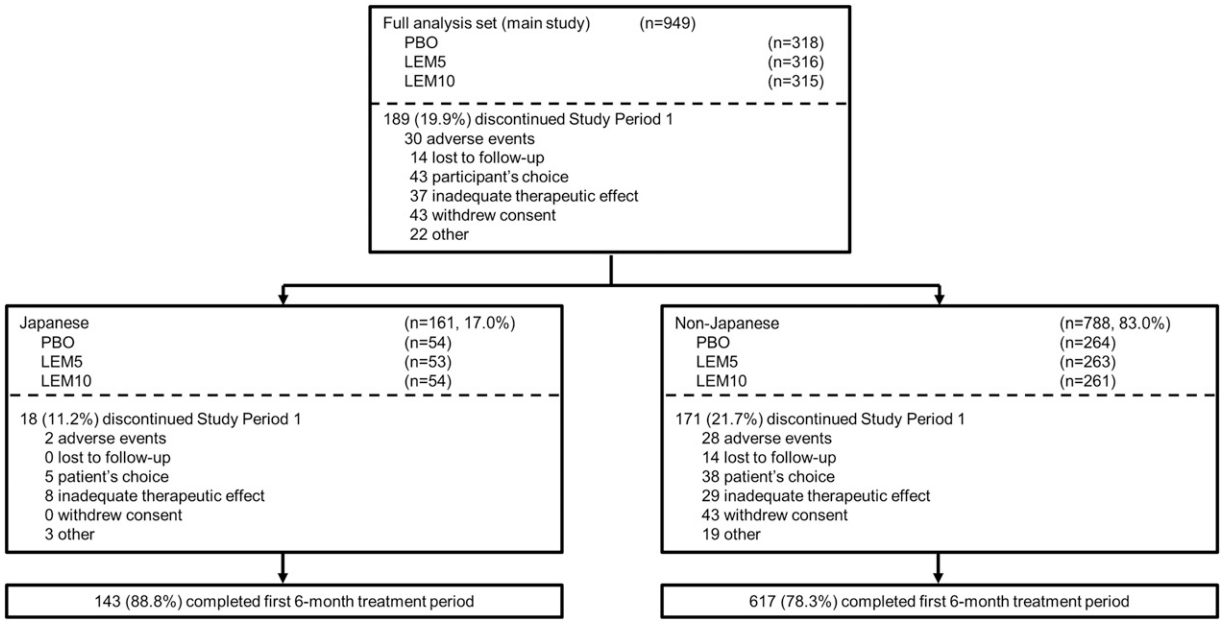
Efficacy

The sSOL, sWASO, and subjective sleep efficacy (sSE) endpoints were analyzed using data from electronic sleep diaries completed daily by each patient. The sSOL was the estimated time in minutes from the attempt to sleep until sleep onset. The sWASO was the estimated sum of wake time in minutes during the night after initial sleep onset until the patient got out of bed for the day. The subjective total sleep time was derived from the time in minutes spent asleep during the time in bed and was used to calculate sSE. We expressed sSE as the proportion of subjective total sleep time per time in bed. For all sleep diary endpoints, the above outcomes were reported as means of the final 7 nights before a given study visit (at baseline, after the first 7 nights of treatment, and at the end of months 1, 3, and 6).

Safety

Safety was assessed at each clinic visit, at follow-up phone call visits (at months 4 and 5), and at the end of the study visit and included monitoring and recording of all treatment-emergent adverse events (TEAEs). An attending physician at each study site proactively asked about falls since the last visit. Potential seizure- or cataplexy-related TEAEs were adjudicated by an external, independent committee blinded to treatment assignment. Investigators were encouraged to categorize each TEAE according to its severity and its relationship to the study treatment. TEAEs were graded on a 3-point scale as mild, moderate, or severe based on the following definitions. Mild was defined as discomfort noticed, but without disruption of

Figure 2—Patient disposition (Japanese and non-Japanese patients).



LEM5 = lemborexant 5 mg, LEM10 = lemborexant 10 mg, PBO = placebo.

normal daily activity. Moderate was defined as discomfort sufficient to reduce or affect normal daily activity. Severe was defined as incapacitating, with the inability to work or to perform normal daily activity. Notably, the criteria for assessing severity differed from those used for seriousness.

Statistical analysis

Details of the sample size calculations and statistical analysis have been previously reported.[11] Efficacy endpoints were assessed using the full analysis set (all randomized patients who received at least 1 dose of the study drug and had at least 1 postdose primary efficacy measurement). Adverse events were assessed in the safety analysis set (all randomized patients who received at least 1 dose of study drug and had at least 1 postdose safety assessment). Descriptive statistics were used for baseline demographic and clinical characteristics, with n (%) for categorical variables and mean ± standard deviation for continuous variables. Mean changes from baseline in sSOL, sSE, sWASO, and subjective total sleep time in the Japanese and non-Japanese subgroups were analyzed using a mixed-effect model repeated-measurement analysis. Age, clinic visit, and treatment-by-visit interaction were fixed effects, and the baseline value for each variable of interest was a covariate. Because sSOL data were not normally distributed, sSOL values were log-transformed, and statistical comparisons were conducted using the least-squares geometric means. Missing values for sSOL, sSE, sWASO, and subjective total sleep time were not imputed and were assumed to be missing at random.

Demographic characteristics for the Japanese and non-Japanese subgroups were analyzed by Wilcoxon test for continuous variables and chi-square test for categorical variables. The comparison between the Japanese and non-Japanese subgroups for efficacy endpoints was conducted based on an analysis of covariance with age group as a fixed effect and the baseline value for each variable of interest as a covariate. Safety parameters were analyzed in the Japanese and non-Japanese subgroups using tabulation or descriptive statistics only. The proportion of patients who experienced adverse events was compared between the Japanese and non-Japanese subgroups based on the Fisher exact test. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC).

RESULTS

Patient characteristics

Of 949 patients randomized to treatment, 161 (17.0%) were enrolled at sites in Japan, and 788 (83.0%) were from sites outside Japan (**Figure 2**). The number of patients who discontinued period 1 was 18 (11.2%) in the Japanese subgroup and 171 (21.7%) in the non-Japanese subgroup. Thus, 143 (88.8%) Japanese and 617 (78.3%) non-Japanese patients completed the first 6-month treatment period.

Table 1 summarizes the baseline demographic and clinical characteristics of the Japanese and non-Japanese subgroups. There were no clinically relevant differences in the baseline characteristics between the Japanese and non-Japanese subgroups except for the ratio of men to women and the body mass index (BMI). The mean age was 51.8 years in the Japanese subgroup and 55.1 years in the non-Japanese subgroup, and the proportion of older adult (ages ≥ 65 years) and adult (< 65 years old) patients was not significantly different between the Japanese and non-Japanese subgroups ($P = .2124$). The proportion of female patients was lower in the Japanese

Table 1—Baseline demographic and clinical characteristics of Japanese and non-Japanese subgroups.

	Japanese				Non-Japanese			
	Placebo (n = 54)	LEM5 (n = 53)	LEM10 (n = 54)	Total (n = 161)	Placebo (n = 264)	LEM5 (n = 263)	LEM10 (n = 261)	Total (n = 788)
Age, y, mean (SD)	53.4 (14.2)	51.2 (13.5)	50.7 (15.9)	51.8 (14.5)	54.7 (14.0)	54.8 (13.7)	55.7 (13.0)	55.1 (13.6)
Age group, n (%)								
< 65 y	41 (75.9)	41 (77.4)	41 (75.9)	123 (76.4)	188 (71.2)	188 (71.5)	188 (72.0)	564 (71.6)
≥ 65 y	13 (24.1)	12 (22.6)	13 (24.1)	38 (23.6)	76 (28.8)	75 (28.5)	73 (28.0)	224 (28.4)
Female sex, n (%)[a]	32 (59.3)	26 (49.1)	32 (59.3)	90 (55.9)	184 (69.7)	183 (69.6)	190 (72.8)	557 (70.7)
Race, n (%)								
Japanese	54 (100.0)	53 (100.0)	54 (100.0)	161 (100.0)	0	0	0	0
Non-Japanese	0	0	0	0	264 (100.0)	263 (100.0)	261 (100.0)	788 (100.0)
White	0	0	0	0	232 (87.9)	222 (84.4)	225 (86.2)	679 (86.2)
Black or African American	0	0	0	0	23 (8.7)	27 (10.3)	26 (10.0)	76 (9.6)
Other[b]	0	0	0	0	9 (3.4)	14 (5.3)	10 (3.8)	33 (4.2)
BMI, kg/m^2, mean (SD)[c]	22.9 (3.5)	22.3 (3.1)	22.9 (3.5)	22.7 (3.4)	28.1 (5.5)	28.3 (6.3)	28.1 (5.6)	28.2 (5.8)

[a]The proportion of female patients was significantly lower in the Japanese subgroup compared with the non-Japanese subgroup (P = .0002; chi-square test). [b]Chinese, Korean, American Indian, Alaska Native, Native Hawaiian, or other Pacific Islander. [c]The mean BMI was significantly lower in the Japanese subgroup than in the non-Japanese subgroup (P < .0001; Wilcoxon rank sum test). BMI = body mass index, LEM5 = lemborexant 5 mg, LEM10 = lemborexant 10 mg, SD = standard deviation.

subgroup vs the non-Japanese subgroup (55.9% vs 70.7%, respectively; P = .0002). The mean BMI of the Japanese subgroup was also significantly lower than that of the non-Japanese subgroup (22.7 kg/m^2 vs 28.2 kg/m^2, respectively; P < .0001). There were no clinically relevant differences in the baseline characteristics between the placebo, LEM5, and LEM10 subgroups.

The mean sSOL, sSE, and sWASO values at baseline were 63.53 minutes, 64.34%, and 111.35 minutes in the Japanese subgroup, and 63.77 minutes, 61.71%, and 138.65 minutes, respectively, in the non-Japanese subgroup. The baseline values of the efficacy measures (sSOL and sSE) were mostly comparable between the Japanese and non-Japanese subgroups (P = .3310 and P = .1015, respectively; Wilcoxon rank sum test) except for sWASO, which was significantly longer in the non-Japanese subgroup vs the Japanese subgroup (P < .0001; Wilcoxon rank sum test).

Efficacy

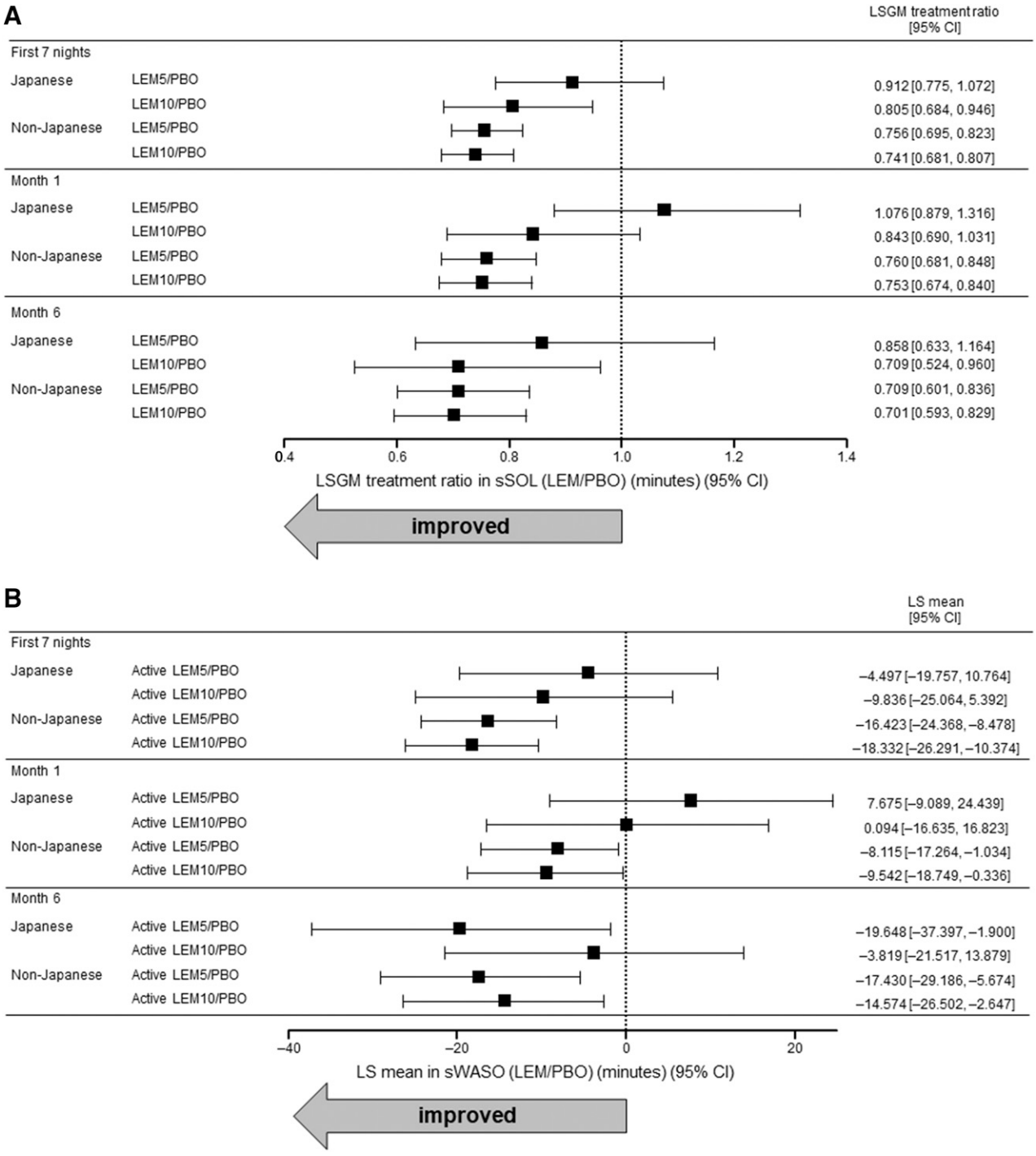
With few exceptions, the LEM group showed improvement over the placebo group at all time points and in all dose groups and subgroups, with consistent results in the Japanese and non-Japanese subgroups. **Table S1, Table S2,** and **Table S3** in the supplemental material show the values of sleep diary variables at baseline and the changes from baseline to 6 months in the Japanese and non-Japanese subgroups. **Figure 3** shows the differences between placebo vs LEM5 and LEM10 for the change from baseline to the first 7 nights, month 1, and month 6 in sSOL and sWASO in the Japanese and non-Japanese subgroups. For sSOL, the point estimates of the least-squares geometric mean ratio were all < 1; for sWASO, the point estimates of the least-squares mean difference (least squares mean–placebo) were all < 0 at month 6 in both the Japanese and non-Japanese subgroups. For sSE, the 95% confidence interval at month 6 also overlapped between the Japanese and non-Japanese subgroups (**Table S2**). Although there were some variations in these efficacy indices within the Japanese subgroup, there were no significant differences between the Japanese and non-Japanese subgroups. There were no significant differences in the change from baseline to the first 7 nights, month 1, and month 6 for sSOL and sWASO between the Japanese and non-Japanese subgroups, except for sSOL at month 1 with LEM5 (**Table 2**).

Safety

The incidence of TEAEs was significantly lower in the Japanese vs non-Japanese subgroup (**Table 3**) for placebo (P = .0202) and LEM5 (P < .0001) but not for LEM10 (P = .0683; Fisher exact test). In the non-Japanese subgroup, serious (2.7%) or severe TEAEs (3.9%) were reported, whereas no such TEAEs were reported in the Japanese subgroup.

In the Japanese subgroup, the most common TEAE, with a higher incidence in the LEM group vs the placebo group, was somnolence, with an incidence of 0% in the placebo group, 7.5% in the LEM5 group, and 11.1% in the LEM10 group. Most TEAEs of somnolence were mild or moderate in severity in the Japanese and non-Japanese subgroups. Although no statistical analysis was performed, the value obtained by subtracting the expression rate of the placebo group from the expression rate of the LEM group was similar between the Japanese and non-Japanese subgroups, suggesting no difference in the incidence of TEAEs between the subgroups.

Figure 3—Difference between PBO vs LEM5/LEM10 in **(A)** sSOL and **(B)** sWASO changes from baseline in Japanese and non-Japanese subgroups.



CI = confidence interval, LEM = lemborexant, LEM5 = lemborexant 5 mg, LEM10 = lemborexant 10 mg, LSGM = least-squares geometric mean, LS mean = least-squares mean, PBO = placebo; sSOL = subjective sleep onset latency, sWASO = subjective wake after sleep onset.

DISCUSSION

In this substudy, LEM showed clear responses in terms of sSOL, sSE, and sWASO, and this trend was observed in both the Japanese and non-Japanese subgroups. The results of the efficacy assessments in the Japanese subgroup were also consistent with those of the overall population; thus, the benefits of LEM as reported in the overall population are also applicable to the Japanese population.[11]

The American Academy of Sleep Medicine guidelines indicate that achieving a sleep efficiency of > 80%–85% is an important goal of insomnia treatment.[15] This threshold was

Table 2—Comparison of change from baseline in sSOL and sWASO between the Japanese and non-Japanese subgroups.

	Placebo	LEM5	LEM10
	Japanese (n = 54) vs Non-Japanese (n = 264)	Japanese (n = 53) vs Non-Japanese (n = 263)	Japanese (n = 54) vs Non-Japanese (n = 261)
P value for sSOL			
First 7 nights	.1437	.2963	.9637
Month 1	.1232	.0441	.8481
Month 6	.4983	.3961	.8549
P value for sWASO			
First 7 nights	.6399	.1492	.3066
Month 1	.2681	.3375	.9931
Month 6	.7136	.7843	.2870

LEM5 = lemborexant 5 mg, LEM10 = lemborexant 10 mg, sSOL = subjective sleep onset latency, sWASO = subjective wake after sleep onset.

Table 3—TEAEs with an incidence ≥ 5% in any treatment group and in Japanese and non-Japanese subgroups.

	Japanese			Non-Japanese		
	Placebo (n = 54)	LEM5 (n = 53)	LEM10 (n = 54)	Placebo (n = 265)	LEM5 (n = 261)	LEM10 (n = 260)
Category, n (%)						
Any TEAEs[a]	26 (48.1)	13 (24.5)	26 (48.1)	174 (65.7)	179 (68.6)	161 (61.9)
Treatment-related TEAEs	1 (1.9)	5 (9.4)	8 (14.8)	43 (16.2)	73 (28.0)	83 (31.9)
Severe TEAEs	0	0	0	10 (3.8)	13 (5.0)	8 (3.1)
Serious TEAEs	0	0	0	5 (1.9)	7 (2.7)	9 (3.5)
TEAEs leading to study drug withdrawal	0	0	2 (3.7)	12 (4.5)	13 (5.0)	24 (9.2)
Somnolence	0	4 (7.5)	6 (11.1)	5 (1.9)	23 (8.8)	35 (13.5)
Nasopharyngitis	11 (20.4)	7 (13.2)	11 (20.4)	29 (10.9)	23 (8.8)	18 (6.9)
Headache	1 (1.9)	1 (1.9)	1 (1.9)	20 (7.5)	27 (10.3)	20 (7.7)
Influenza	3 (5.6)	1 (1.9)	0	12 (4.5)	14 (5.4)	16 (6.2)
Upper respiratory tract infection	0	0	0	10 (3.8)	13 (5.0)	11 (4.2)
Arthralgia	0	0	0	9 (3.4)	14 (5.4)	3 (1.2)

[a]The incidence of TEAEs was significantly lower in the Japanese subgroup than in the non-Japanese subgroup for placebo ($P = .0202$) and LEM5 ($P < .0001$) but not for LEM10 ($P = .0683$; Fisher exact test). LEM5 = lemborexant 5 mg, LEM10 = lemborexant 10 mg, TEAE = treatment-emergent adverse event.

achieved or approached in both the Japanese subgroup (median sSE at month 6 = 84.56% and 79.54% with LEM5 and LEM10, respectively) and non-Japanese subgroup (median sSE at month 6 = 81.89% and 80.81%, respectively; **Table S2**).[11] Although the median sSE with LEM10 in the Japanese subgroup was < 80%, the values were > 80% with LEM5 in the Japanese subgroup and LEM5/LEM10 in the non-Japanese subgroup. Despite the smaller number of patients in the Japanese subgroup, the point estimates of LEM5 and LEM10 exceeded that of placebo, and the 95% confidence intervals overlapped at all evaluation points for sSOL and sWASO, although sWASO at baseline was different between the Japanese and the non-Japanese subgroup. Because there were fewer Japanese patients than non-Japanese patients, we considered the wider confidence intervals to be indicative of this difference in patient numbers. There was a significant difference in the improvement effect for sSOL at month 1 with LEM5 vs placebo between the Japanese and non-Japanese subgroups, possibly because of the sample size of the Japanese subgroup. There were no significant differences at all other time points except for month 1 with LEM5. These findings suggest that the effectiveness of the respective doses of lemborexant was consistent between the Japanese subgroup and the overall population, and between the Japanese and non-Japanese subgroups.

Regarding safety, both LEM5 and LEM10 were well tolerated in the Japanese and non-Japanese subgroups, with no significant differences in the dose-response trends and safety profile of LEM between the two subgroups. However, the lower incidence of TEAEs in the Japanese vs non-Japanese subgroup was possibly because of the smaller number of patients evaluated. Therefore, in clinical practice in Japan, attention should be paid to adverse events that occur after LEM administration both in the Japanese and non-Japanese population.

In this study, no difference in the efficacy and safety of LEM was shown between the Japanese and non-Japanese subgroups, even though BMI was significantly higher in the non-Japanese

subgroup than in the Japanese subgroup. Although the previous study has examined the influence of BMI on suvorexant without consideration of racial differences, BMI has been reported to affect the pharmacokinetics of suvorexant,[16] showing a higher area under the curve and maximum serum concentration in patients with higher BMI (31% and 17% increases in area under the curve and maximum serum concentration, respectively, in patients with BMI > 30 kg/m^2).[16] With suvorexant, the area under the curve increased by 46% and C_{max} increased by 25% in women who were obese compared with women who were not obese.[8] Thus, the higher exposure to suvorexant in women who are obese should be considered before increasing the dose.[8] The major metabolic enzyme of LEM and suvorexant, CYP3A4, has been reported to have no genetic differences.[17] However, many of the drugs that act as substrates for CYP3A4 have a lower clearance in patients who are obese (high BMI).[18] In comparison to suvorexant, LEM has shown a slight, not clinically relevant lower clearance and a higher area under the curve value in a subgroup with higher BMI.[10] In the same study, LEM clearance was not significantly affected by sex; in addition, exposure-response analyses of LEM indicated that small changes in exposure have negligible effects on the pharmacodynamic responses of LEM.[10] Thus, unlike with suvorexant, the impact of BMI and sex on the pharmacokinetics of LEM is not clinically relevant.[10] This characteristic may have led to similar efficacy and safety results between the Japanese and non-Japanese subgroups in this study despite differences in BMI/proportion of women.

The present study has some limitations. The main study was not originally designed to compare the efficacy and safety between Japanese and non-Japanese subgroups; thus, a forest plot was used to evaluate the consistency of treatment effect across the subgroups. The *P* values to assess treatment differences between the Japanese and non-Japanese subgroups were considered as nominal. In addition, there was a notable difference in the number of patients between the Japanese and non-Japanese subgroups. The number of Japanese patients needed to provide at least 90% statistical power for comparisons between LEM5/LEM10 and placebo for sSOL at month 6, based on the results of the SUNRISE 2 study, would have been 400 patients for the LEM5 group and 166 patients for the LEM10 group. Finally, note that the non-Japanese subgroup included small numbers of Asian patients (Chinese patients, n = 4 [0.4%], and Korean patient, n = 3 [0.3%]).

CONCLUSIONS

In conclusion, LEM5 and LEM10 taken once daily were effective in improving both sleep onset and sleep maintenance insomnia over a 6-month period and were well tolerated in the Japanese subgroup of SUNRISE 2. The safety profiles of LEM5 and LEM10 taken once daily in the Japanese subgroup were consistent with those of the overall study population.

ABBREVIATIONS

BMI, body mass index
LEM, lemborexant
LEM5, lemborexant 5 mg
LEM10, lemborexant 10 mg
sSE, subjective sleep efficiency
sSOL, subjective sleep onset latency
sWASO, subjective wake after sleep onset
TEAE, treatment-emergent adverse event

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