# EFFICACY AND SAFETY OF LEMBOREXANT IN ELDERLY PATIENTS WITH INSOMNIA DISORDER: A RANDOMIZED CONTROLLED STUDY

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## ABSTRACT

Insomnia disorder is very common in the older adults and tends to be accompanied with poor functioning during the day and likelihood of adverse outcomes. Hypnotics like benzodiazepines and Z-drugs are contraindicated because of their side effects on safety in older patients. This was a randomized, double-blind, placebo-controlled trial that compared the effectiveness and safety of a dual orexin receptor antagonist, lemborexant, in patients with insomnia disorder aged 55 years and above. One thousand one hundred subjects were randomized to get lemborexant 5 mg, lemborexant 10 mg, zolpidem extended-release 6.25 mg and placebo during 30 nights. There were subjective and polysomnographic outcomes of sleep. Both lemborexant doses showed a significant improvement in the sleep onset, sleep maintenance and sleep efficiency among the placebo and zolpidem in terms of effects lasting one month. The severity of insomnia and the functioning in the daytime were also improved significantly. There was an overall positive safety profile of lemborexant and it was generally well tolerated.

**Keywords:** Insomnia disorder, Lemborexant, Dual orexin receptor antagonist, Elderly population and Polysomnography

## INTRODUCTION

Insomnia disorder is a widespread disease that is defined by problems with falling asleep and/or sleep 3 or more, and continuing to sleep 3 or more, 3 months or more, with health risks in older adults [1]. Cognitive behavior therapy is an insomnia therapy which is a first line insomnia therapy and has been shown to enhance sleep in insomnia patients of old age [2,3]. Pharmacologic treatment, however, might be required when cognitive behavior therapy of insomnia is ineffective or not available to the patient [4]. The use of benzodiazepines and other sedative-hypnotic drugs is common to treat insomnia in elderly individuals, even though numerous treatment alternatives fail to offer proper response to both sleep onset and sleep maintenance symptoms in the elderly [5,6]. Such poor quality is especially problematic since older people are more likely to have more problems with falling asleep [7]. The side effects of these drugs can be linked to falls, hip fracture, and chances of accidental injury [8-11].

Dual orexin receptor antagonists can be used as an alternative to the current treatments. The orexins are significant in regulating the aspects of wake and sleep/wake. Dual orexin receptor antagonists inhibit orexin receptors 1, 2, suppressing orexin and controlling sleep/wake activity [12]. E2006, an orally active dual orexin receptor antagonist (code name: Lemborexant), is a competitive reversible antagonist, which binds both orexin receptor 1 and 2, with higher affinity to orexin receptor 2 [13]. Lemborexant 5 mg and 10 mg therapy administered in the objective (polysomnography [PSG]) and subjective (self-reported sleep diary) end points of a randomized double-blind placebo-controlled phase 2 study was effective with minimal next-morning residual sleepiness in adults and elderly participants with insomnia disorder [14]. The present research, Study of the Efficacy and Safety of Lemborexant in Subjects 55 Years and Older With Insomnia Disorder, recruited elderly individuals with insomnia disorder and determined the efficacy and tolerability of lemborexant therapy compared with the placebo and an active comparator, zolpidem tartrate extended release.

## MATERIALS AND METHODOLOGY

### Clinical Trials Oversight and Study Subjects

The criteria used to select women aged 55 years or older and men aged 65 years or older were Diagnostic and Statistical Manual of Mental Disorders requirements of insomnia disorder. The participants had to say that they had at least 60 minutes of subjective wake after sleep onset (sWASO) on at least 3 nights per week of the past 4 weeks, a regular time in bed of 7 9 hours, sleep maintenance insomnia, and an Insomnia Severity Index (ISI) of 13 or higher. Difficulties in getting sleep onset were also allowed but not compulsory. Sleep history, sleep diaries, and polysomnography (PSG) (mean wake-after-sleep onset (WASO) of 60 minutes or longer on two consecutive PSG nights, neither of which had the WASO of less than 45 minutes) were used to confirm that eligibility criteria were met [1517].

### Trial Procedures

After screening, the participants were sent into single-blind placebo run-in, lasting around 2 weeks (with baseline PSG) to filter out placebo responders and also to detect noncompliance with sleep diary provisions. Participants who had proved eligible were then randomized (in a 5:5:5:4 ratio) to receive lemborexant 5 mg, lemborexant 10 mg, zolpidem 6.25 mg or placebo over a 30-night period plus a 14-18 days follow up. The dosage of the zolpidem was determined according to the prescription guidelines in old age [18]. The stratification of randomization in terms of the country and age group was centralized and performed using a computer-generated scheme. During the study, the participants were asked to fill the electronic sleep diaries on a daily basis. At baseline and baseline as well as baseline and the end of treatment, PSG tests were conducted. The evaluation of PSG data conducted by centralized scorers was done using standardized 30-second epochs.

### Outcomes and Safety

Change in baseline latency to persistent sleep (LPS) at night 29 and 30 was the main end point of efficacy. Major secondary outcomes were sleep efficiency, WASO and WASO in the second half of the night. Sleep diaries were used to obtain subjective outcomes of sleep. The severity of diseases and the daily functioning were evaluated with the help of ISI scores [19]. Safety tests involved adverse event monitoring, lab tests, vital signs, electrocardiograms, Columbia-Suicide Severity Rating Scale, and physical tests. Validated measures were used to measure withdrawal symptoms and rebound insomnia [20].

### Statistical Analysis

The repeated measures mixed-effect models were used to carry out the efficacy analyses, and the nonnormal data were transformed accordingly. The relevant statistical methods were found to be Kaplan-Meier and covariance analysis, and as a result of controlling type I error, sequential gatekeeping procedures were employed. The results on safety were described in a descriptive manner [21-23].

## RESULTS

Out of 2500 screened participants, 1010 passed the eligibility criterion and were randomized to placebo, zolpidem ER 6.25 mg, lemborexant 5 mg, or lemborexant 10mg.

**Table 1.** Baseline Characteristics of Participants

| Characteristic | Total (N = 1010) | Placebo (n = 210) | Zolpidem ER 6.25 mg (n = 265) | Lemborexant 5 mg (n = 267) | Lemborexant 10 mg (n = 268) |
|---|---|---|---|---|---|
| **Age, y** | | | | | |
| Mean (SD) | 64.0 (6.9) | 63.5 (6.5) | 64.4 (7.1) | 63.8 (6.8) | 64.3 (6.9) |
| Median (range) | 63 (55–88) | 62 (55–82) | 63 (55–84) | 63 (55–88) | 64 (55–85) |
| ≥55 to <65 | 556 (55.0) | 116 (55.2) | 144 (54.3) | 149 (55.8) | 147 (54.9) |
| ≥65 | 454 (45.0) | 94 (44.8) | 121 (45.7) | 118 (44.2) | 121 (45.1) |
| **Sex** | | | | | |
| Male | 138 (13.7) | 25 (11.9) | 38 (14.3) | 37 (13.9) | 38 (14.2) |
| Female | 872 (86.3) | 185 (88.1) | 227 (85.7) | 230 (86.1) | 230 (85.8) |
| **Race** | | | | | |
| White | 731 (72.4) | 154 (73.3) | 175 (66.0) | 201 (75.3) | 201 (75.0) |
| Black | 257 (25.4) | 52 (24.8) | 81 (30.6) | 62 (23.2) | 62 (23.1) |
| Asian (total) | 16 (1.6) | 2 (1.0) | 5 (1.9) | 3 (1.1) | 6 (2.2) |
| Other | 6 (0.6) | 2 (1.0) | 4 (1.5) | 1 (0.4) | 0 |
| **Polysomnography sleep variables, mean (SD)** | | | | | |
| Latency to persistent sleep, min | 44.6 (35.7) | 44.1 (33.8) | 44.7 (38.5)a | 45.0 (36.6) | 44.8 (33.1) |
| Sleep efficiency, % | 68.2 (11.0) | 68.8 (9.7) | 68.0 (11.5)a | 68.3 (11.2) | 67.8 (10.9) |
| Wake-after-sleep onset, min | 113.9 (39.3) | 112.0 (37.4) | 114.5 (40.1)a | 113.6 (39.1) | 115.0 (40.2) |
| Wake-after-sleep onset in second half of night, min | 76.8 (32.6) | 74.6 (30.3) | 78.3 (34.0)a | 76.7 (33.0) | 77.1 (32.2) |
| **ISI total score, mean (SD)** | 19.1 (3.5) | 19.4 (3.6) | 19.2 (3.5) | 18.9 (3.5) | 19.0 (3.4) |

Table 1 represents the baseline demographic, clinical, and polysomnographic characteristics of 1010 study participants who were randomly assigned. All in all, the treatment groups were balanced, which means that randomization and intergroup comparability were achieved. The median age of the overall study population was 63 years (SD, 6.9), the mean age of 64 years with a range of 55 to 88 years. About 55 percent of persons interviewed aged 55-64 years, and 45 percent aged 65 years and above. The age distributions were similar in all treatment arms, such as placebo, zolpidem extended-release (ER) 6.25 mg, lemborexant 5mg, and lemborexant 10mg.

The population of the study was mostly women (86.3%), and only 13.7% were men. The treatment groups did not differ clinically on sex distribution. Regarding race, the majority of the participants were White (72.4%), and Black participants came in (25.4%). Only a minor percentage of respondents belonged to Asians (1.6%), or other races (0.6%). The composition of race was typically similar in all

treatment arms, though Zolpidem ER treatment was slightly disproportionate to the other treatment groups with more Black participants than the rest.

Baseline polysomnography (PSG) variables showed significant sleep disturbance in all the treatment groups. The mean latency to persistent sleep was between 44.1 and 45.0 minutes and mean sleep efficiency was about 68% across all groups, meaning that there was a decrease in sleep consolidation. The mean wake-after-sleep onset (WASO) in both groups was more than 110 minutes and wake-after-sleep onset in the later half of the night was between 74.6 and 78.3 minutes, which indicated severe sleep maintenance insomnia. It was moderate to severe with the total ISI scores of 18.9 to 19.4 across the treatment arms. In general, the similarity between the demographic characteristics, objective sleep measurements, and ISI scores between groups justifies the validity of the further comparisons of treatment efficacy and safety.

**Table 2.** Sleep Onset and Sleep Maintenance End Points by Treatment Group (N = 1010)

| End Point | Placebo (n = 209) | Zolpidem ER 6.25 mg (n = 265) | Lemborexant 5 mg (n = 268) | Lemborexant 10 mg (n = 268) |
|---|---|---|---|---|
| **Latency to Persistent Sleep, min** | | | | |
| Nights 1 & 2, mean (SD) | 37.4 (32.5) | 31.9 (23.7) | 28.3 (24.4) | 25.1 (16.7) |
| Change from baseline, mean (SD) | –6.5 (32.6) | –12.6 (32.5) | –16.6 (28.7) | –19.5 (31.8) |
| LSGM ratio vs placebo (95% CI) | NA | 0.97 (0.86–1.10) | 0.85 (0.75–0.96) | 0.80 (0.70–0.90) |
| P value | NA | .66 | .009 | <.001 |
| LSGM ratio vs zolpidem (95% CI) | NA | NA | 0.87 (0.78–0.98) | 0.82 (0.73–0.92) |
| P value | NA | NA | .02 | <.001 |
| Nights 29 & 30, mean (SD) | 36.0 (32.1) | 37.1 (28.4) | 25.8 (24.3) | 22.8 (17.5) |
| Change from baseline, mean (SD) | –7.9 (32.0) | –7.5 (35.1) | –19.5 (33.1) | –21.5 (32.4) |
| LSGM ratio vs placebo (95% CI) | NA | 1.22 (1.06–1.40) | 0.77 (0.67–0.89) | 0.72 (0.63–0.83) |
| P value | NA | .006 | <.001 | <.001 |
| **Sleep Efficiency, %** | | | | |
| Nights 1 & 2, mean (SD) | 73.1 (10.8) | 79.9 (8.5) | 82.0 (8.4) | 84.3 (7.6) |
| Change from baseline, mean (SD) | 4.2 (9.0) | 11.7 (9.7) | 13.6 (9.7) | 16.5 (9.6) |
| LSM difference vs placebo (95% CI) | NA | 7.0 (5.7–8.3) | 9.0 (7.7–10.3) | 11.6 (10.3–12.9) |
| P value | NA | <.001 | <.001 | <.001 |
| Nights 29 & 30, mean (SD) | 74.5 (9.8) | 77.2 (10.2) | 81.3 (8.8) | 82.0 (8.8) |
| Change from baseline, mean (SD) | 5.4 (9.9) | 9.1 (11.2) | 12.9 (9.7) | 14.1 (10.5) |
| **Wake-After-Sleep Onset, min** | | | | |

| | | | | |
|---|---|---|---|---|
| Nights 1 & 2, mean (SD) | 96.7 (41.3) | 69.9 (33.5) | 63.5 (31.5) | 55.2 (30.5) |
| Change from baseline, mean (SD) | –15.1 (36.9) | –44.4 (38.1) | –50.0 (39.6) | –59.6 (37.7) |
| Nights 29 & 30, mean (SD) | 92.1 (41.0) | 77.7 (39.9) | 69.1 (34.5) | 68.6 (35.2) |
| Change from baseline, mean (SD) | –18.6 (41.9) | –36.5 (43.4) | –43.9 (39.3) | –46.4 (39.6) |
| **Wake-After-Sleep Onset in Second Half of Night, min** | | | | |
| Nights 1 & 2, mean (SD) | 67.4 (32.9) | 53.3 (27.7) | 46.3 (25.6) | 39.8 (23.7) |
| Change from baseline, mean (SD) | –7.1 (31.1) | –24.6 (33.3) | –30.3 (32.1) | –37.1 (30.8) |
| Nights 29 & 30, mean (SD) | 64.4 (32.4) | 56.7 (31.1) | 49.1 (28.2) | 48.2 (27.8) |
| Change from baseline, mean (SD) | –8.9 (31.9) | –21.4 (36.3) | –27.2 (33.0) | –28.8 (33.1) |

Table 2 provides the overall comparison of the results of the sleep onset and sleep maintenance in the four treatment groups placebo, zolpidem ER 6.25 mg, lemborexant 5mg and lemborexant 10 mg through polysomnographic evaluation of the initial state of treatment (night 1 and 2) and final state of treatment (night 29 and 30). Latency to persistent sleep is the primary endpoint of sleep onset, which significantly improved dose-dependently with lemborexant. The mean sleep latency of the lemborexant 10 mg group took the shortest time during night 1 and 2, followed by lemborexant 5 mg, zolpidem, and placebo. Baseline reductions were also found to be significantly more with the two doses of lemborexant than with placebo, and ratio of treatments featured statistically significant better lemborexant relative to placebo and zolpidem especially with 10mg dose. The effects were observed to be sustained with night 29 and 30 which implies that the effects are durable.

Sleep efficiency, which is one of the major indicators of the general quality of sleep, was enhanced in all the active treatment groups in comparison with the placebo. Lemborexant 10mg, lemborexant 5mg and zolpidem recorded the greatest increases. The mean difference of least-squares of placebo and active treatments were statistically significant in all early and late evaluation and the differences between lemborexant and zolpidem were always higher which means that lemborexant has stronger effects on improving sleep in the sense of consolidation of sleep. Lemborexant also maintained a better result in terms of sleep maintenance. The Wake-after-sleep onset (WASO) was significantly lower in the night 1 and 2 of the lemborexant groups, and the highest amounts were lowered at the 10 mg dose. These decreases continued during the 29th and 30th night showing that it is effective in supporting sleep during the night. The same trends were found in the case of the wake-after-sleep onset in the second half of the night, which is a clinically relevant parameter in the early awakenings in the morning. In general, it can be seen that lemborexant, especially that dose of 10 mg, can be beneficial and strength and stable in the processes of sleep initiation and maintenance in comparison to placebo and zolpidem ER.

**Table 3.** Insomnia Severity and Daily Functioning End Points at the End of Month 1 (N = 1010)

| End Point | Placebo (n = 209) | Zolpidem ER 6.25 mg (n = 265) | Lemborexant 5 mg (n = 268) | Lemborexant 10 mg (n = 268) |
|---|---|---|---|---|
| **ISI Total Score (Items 1–7)** | | | | |
| Baseline, mean (SD) | 19.4 (3.6) | 19.2 (3.5) | 18.9 (3.5) | 19.0 (3.3) |
| Month 1, mean (SD) | 13.3 (5.4) | 11.0 (5.4) | 11.2 (5.4) | 11.1 (5.6) |
| Change from baseline, mean (SD) | –6.1 (5.5) | –8.3 (6.0) | –7.8 (5.5) | –7.9 (5.9) |
| LSM difference vs placebo (95% CI) | NA | –2.3 (–3.3 to –1.3) | –1.9 (–2.9 to –1.0) | –2.1 (–3.1 to –1.1) |
| P value | NA | <.001 | <.001 | <.001 |
| LSM difference vs zolpidem (95% CI) | NA | NA | 0.4 (–0.6 to 1.3) | 0.2 (–0.7 to 1.2) |
| P value | NA | NA | .45 | .64 |
| **ISI Daytime Functioning (Items 4–7)** | | | | |
| Baseline, mean (SD) | 11.2 (2.4) | 11.1 (2.5) | 10.9 (2.4) | 10.8 (2.3) |
| Month 1, mean (SD) | 7.3 (3.6) | 5.9 (3.4) | 6.1 (3.5) | 6.1 (3.6) |
| Change from baseline, mean (SD) | –3.9 (3.6) | –5.2 (3.8) | –4.8 (3.6) | –4.8 (3.7) |
| LSM difference vs placebo (95% CI) | NA | –1.4 (–2.1 to –0.8) | –1.1 (–1.7 to –0.5) | –1.1 (–1.7 to –0.5) |
| P value | NA | <.001 | .001 | .001 |
| LSM difference vs zolpidem (95% CI) | NA | NA | 0.3 (–0.3 to 0.9) | 0.3 (–0.3 to 0.9) |
| P value | NA | NA | .23 | .27 |

The table 3 shows the outcomes of the treatment on the severity of insomnia and functioning during the day after a month of therapy as measured with Insomnia Severity Index (ISI) in a total of 1010 participants who were randomly selected. At baseline, there was no significant difference in the mean ISI total scores among all treatment groups (18.9-19.4), and this demonstrates that there was an equal level of moderate-severe insomnia in all treatment groups prior to the intervention and successful randomization. One month of treatment showed that all the active treatment groups showed larger decreases in ISI total scores than placebo. The mean score of the placebo group was 6.1, and the greatest change was observed in the participants who were treated with zolpidem ER 6.25mg, which was 8.3. Lemborexant 5mg and 10mg too yielded significant gains of 7.8 and 7.9 points respectively. All active treatments (P <.001) showed statistically significant treatment difference between least squares mean (LSM) versus placebo, which implies clinically meaningful differences between overall insomnia severity. Conversely, the results showed no statistically significant differences when the lemborexant doses were directly compared to zolpidem so that there was no difference between active treatments of overall insomnia severity.

The same was the case with daytime functioning, measured with ISI items 4 7. There was consistency in baseline scores of daytime functioning between groups (10.8 to 11.2) who showed similar impairment before treatment. Month 1 showed more improvements in all the active treatment groups than placebo. The baseline to mean reductions were -5.2 points on zolpidem ER, -4.8 points, on lemborexant 5 mg, and on lemborexant 10mg, versus -3.9 points in the placebo group. All the active treatments were statistically significant in the LSM differences over placebo, which showed improvements in daytime alertness, performance, and quality of life. Measures of lemborexant to zolpidem in daytime functioning showed no statistically significant differences, showing the same benefits in active therapies. On the whole, these results suggest that lemborexant and zolpidem have a considerable positive effect on insomnia severity and daytime impairment in one month of treatment with similar active treatment groups demonstrating the same effect.

**Table 4.** Treatment-Emergent Adverse Events During Treatment and Follow-up Periods, Safety Analysis Set[a]

| Event | Placebo (n = 210) | Zolpidem ER 6.25 mg (n = 265) | Lemborexant 5 mg (n = 267) | Lemborexant 10 mg (n = 268) |
|---|---|---|---|---|
| **Any TEAE** | 54 (25.7) | 95 (35.8) | 75 (28.1) | 83 (31.0) |
| **Treatment-related TEAE** | 16 (7.6) | 42 (15.8) | 30 (11.2) | 39 (14.6) |
| **Severe TEAE** | 3 (1.4) | 8 (3.0) | 1 (0.4) | 2 (0.7) |
| **Serious TEAE** | 0 | 4 (1.5) | 2 (0.7) | 0 |
| **Leading to study discontinuation** | 2 (1.0) | 7 (2.6) | 2 (0.7) | 3 (1.1) |
| **Leading to interruption of study drug** | 1 (0.5) | 2 (0.8) | 1 (0.4) | 0 |
| **Death** | 0 | 0 | 0 | 0 |
| **TEAEs reported in >2% of participants in any active treatment group** | | | | |
| Headache | 13 (6.2) | 14 (5.3) | 17 (6.4) | 13 (4.9) |
| Somnolence | 4 (1.9) | 4 (1.5) | 11 (4.1) | 19 (7.1) |
| Urinary tract infection | 2 (1.0) | 2 (0.8) | 3 (1.1) | 9 (3.4) |
| Nasopharyngitis | 3 (1.4) | 1 (0.4) | 7 (2.6) | 1 (0.4) |
| Upper respiratory tract infection | 4 (1.9) | 2 (0.8) | 6 (2.2) | 1 (0.4) |
| Dizziness | 4 (1.9) | 8 (3.0) | 3 (1.1) | 2 (0.7) |

Table 4 presents the safety results of the 1010 randomly selected participants who were treated with placebo, zolpidem extended-release (ER) 6.25 mg, lemborexant 5 mg, or lemborexant 10mg during the treatment and follow periods. As expected in pharmacologic insomnia trials, treatment-emerging adverse events (TEAEs) were observed in all the groups with higher rates in the active arms of treatment than in the placebo. The percentage of those having any TEAE was 25.7 in the placebo arm and 35.8 in the zolpidem ER arm and the intermediate rates of lemborexant 5 mg and 10mg were 28.1 percent and 31.0 percent, respectively.

TEAEs were also found to be more common with treatment-related in the zolpidem ER (15.8%) compared with lemborexant 5mg (11.2%), lemborexant 10mg (14.6%), and placebo (7.6%). Notably,

severe and serious adverse events were not common in all groups of treatments. There were ≤3.0 percent severe TEAEs in each group, and serious TEAEs were uncommon, only being reported in zolpidem ER (1.5) and lemborexant 5 mg (0.7) groups. The study did not give any deaths. There were few instances when study drug was discontinued on adverse events (1.0 to 2.6% across groups) which pointed to high overall tolerability. Equally, there were less than 1 percent instances in each group of interruption of the study medication, which was temporary.

Headache was the most frequently reported of individual adverse events in individuals having care in over 2% in all active groups undergoing treatment (both placebo and active). The increase with dose was dose-related with lemborexant and the highest prevalence as per pharmacodynamic profile was shown in the 10 mg group (7.1%). Additional events that were most frequently reported were urinary tract infection, nasopharyngitis, upper respiratory tract infection, and dizziness which were usually mild and proportionately distributed across arms. In general, the results show that lemborexant at 5 mg and 10 mg was usually safe and well tolerated and its safety profile was favorable, similar to zolpidem ER and there were no significant safety concerns.

## DISCUSSION

This paper will show that lemborexant is both a useful and well-desirable intervention in the treatment of insomnia disorder in senior citizens. The insomnia of the elderly is often marked by a lack of sleep initiation and sleep maintenance and the current pharmacologic treatment options do not provide sufficient coverage of these areas but offer serious safety risks, including falls, impaired cognitive functions, and residual sedation. The current results prove the importance of lemborexant as a potentially promising alternative whose mechanism has a direct effect on the orexin-mediated system of wake promotion [1,2].

The two doses of lemborexant showed statistically and clinically significant changes in latency to persistent sleep, wake-after-sleep onset, and sleep efficiency. Interestingly, the effects of these showed up in the first few as well as days of therapy and continued up to the close of the therapy session, which showed long-term efficacy without signs of tolerance [3,4]. The effects were most significant with the 10 mg dose implying the existence of a dose-dependent effect. Lemborexant was observed to have better effect on objective sleep parameters than zolpidem extended-release especially on sleep maintenance and second-half-of-the-night awakenings, typical complaints of the elderly patients [5].

In addition to objective sleep changes, lemborexant also had a strong effect of decreasing the severity of insomnia and enhancing daytime functioning, as assessed by the Insomnia Severity Index. These are clinically significant improvements, which are manifested in a better quality of life and alertness as well as performance in everyday life. Notably, both lemborexant and zolpidem showed comparable improvement in the severity of insomnia, which implies that they were equally perceived as beneficial by the patient [6-9].

On the safety side, lemborexant was well tolerated in general and the rates of adverse events were similar or lower with lemborexant than with zolpidem. The increased dose resulted in increased somnolence but the events were manageable and serious adverse events were infrequent. It is tolerable as well due to low discontinuation rates. In general, the findings indicate that lemborexant has a good efficacy-safety profile to be used in the pharmacologic treatment of insomnia in elderly people.

## CONCLUSION

The results of this randomized controlled trial show that lemborexant is a useful and safe treatment agent in the management of insomnia disorder among elderly patients. Lemborexant is a GABA agonist that inhibits orexin receptors involved in body wakefulness and, therefore, prevents sleep initiation and sleep disturbance as well as sleep maintenance disturbances, especially in the elderly population. Both the 5 mg and 10 mg dosages resulted in considerable objective improvements in the polysomnography of the participants, the subjective measures of sleep, the severity of insomnia and

the functioning of the day, and the long-term effect of the treatment lasted one month. Zolpidem extended-release and placebo were found to be less effective compared to lemborexant in achieving the optimal effect on the key parameters of sleep and in having a good safety profile. Its tolerability is demonstrated by the low rates of severe adverse events and discontinuation of the treatment in a population that is highly susceptible to drug-related adverse events. These findings endorse the clinical use of lemborexant as an effective supplement to conventional hypnotics especially in patients who cannot withstand or cannot sufficiently react to the current therapy. To sum up, lemborexant is a valuable contribution to pharmacologic treatment of insomnia disorder among geriatric patients providing good symptom control and safety performance.

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