Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

safety considerations in older adults. Lemborexant (LEM) is a dual orexin receptor antagonist approved in multiple countries, including the United States, Japan, Canada and Australia for the treatment of adults with insomnia. Study E2006-A001-312 (Study 312; NCT04009577) assessed prespecified dosing methods for directly transitioning from ZOL (immediate [IR] or extended release [ER]) to LEM (5mg [LEM5] or 10mg [LEM10]). Here, we report the findings from post hoc analyses that examined outcomes among subjects ≥60 years of age in Study 312.

Materials and Methods: Study 312 included a 3-week Screening Period during which subjects continued on ZOL, a 2-week Titration Period (TITR), a 12-week Extension Period (EXT), and a 4-week Follow-up Period. Subjects were adults (age ≥18 years) with insomnia and were intermittent (INT; 3-4 nights/week) or frequent (FREQ; ≥5 nights/week) users of ZOL-IR or ZOL-ER. The most common reason for wanting to transition was sleep maintenance difficulties. Cohort-1 comprised subjects with two weeks of INT ZOL or 1 week each of INT and FREQ ZOL use during the last 2 weeks of the Screening period. Subjects in Cohort-1 initiated TITR with LEM5. Cohort-2 comprised subjects who were FREQ ZOL users during the Screening Period. Subjects in Cohort-2 were randomized 1:1 to LEM5 (Cohort-2A) or LEM10 (Cohort-2B). Subjects who successfully transitioned to LEM had the option to enter EXT. Subjects could change LEM dose once during TITR and multiple times during EXT. The proportion of subjects who transitioned successfully to LEM at the completion of TITR was the primary endpoint. Treatment-emergent adverse events (TEAEs) were assessed.

Results: Of 53 subjects (Full Analysis Set), 30 (56.6%) were ≥60 years of age (Cohort-1, n=6; Cohort-2, n=24). In this subgroup of older adults, 23/30 (76.7%) subjects transitioned successfully to LEM after TITR. In Cohort-1: 5/6 (83.3%) subjects transitioned successfully with 3 subjects ending TITR on LEM5 and 2 on LEM10. In Cohort-2A: 7/8 (87.5%) subjects transitioned successfully with 3 subjects ending TITR on LEM5 and 4 on LEM10. In Cohort-2B: 11/16 (68.8%) subjects transitioned successfully with 1 subject ending TITR on LEM5 and 10 on LEM10. During TITR, 7 subjects discontinued; 6 discontinued due to TEAEs. All 23 subjects who transitioned successfully to LEM chose to continue in EXT, and 22/30 (73.3%) subjects completed the study. Across TITR and EXT, TEAEs occurred more frequently with LEM10 than LEM5, and all were mild or moderate in severity. Abnormal dreams (n=4) and somnolence (n=2) were the most commonly reported TEAEs.

Conclusion: Most (76.7%) of the older subjects from Study 312 successfully transitioned directly from INT or FREQ ZOL-IR or ZOL-ER use to LEM. LEM was generally well tolerated with a safety profile consistent with previously reported Phase 3 clinical studies. These results were generally consistent with those observed in the Full Analysis Set and suggest that older patients with insomnia, who have previously used ZOL could be offered an alternative treatment for insomnia.

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GROUP COGNITIVE BEHAVIORAL THERAPY FOR INSOMNIA: AN EXCELLENT ALTERNATIVE TREATMENT IN PUBLIC HEALTHCARE SYSTEM.

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Introduction: Cognitive behavioral therapy for insomnia (CBT-I) is highly recommended as first line treatment for chronic insomnia due to produce sustained benefits without the risk for tolerance or adverse effects associated with pharmacologic treatment.

Considering the high prevalence of insomnia and the overcrouding for medical consultation, Group CBT-I is considered as an alternative treatment in our public healthcare system.

To determine de efficacy of Group CBT-I in adults with chronic insomnia, a comparison of the Insomnia Severity Index (ISI) was made before and after the end of the therapy.

Materials and Methods: Single-size, observational study from March 2018 to December 2021 were performed. 92 participants with chronic insomnia started a 3 month therapy for insomnia.

Sleep diaries were used to determine sleep onset latency, total sleep time and sleep efficiency, and treatment effects were assessed by comparison ISI before and after therapy.

Descriptive statistical analysis was performed using frequency distributions for qualitative variables and mean and standard deviation for quantitative variables. The comparison of means had used Student's t testt for repeated measures and the relationship of qualitative variables was analyzed with Chi-square.

Results: 72 patients meet the inclusion criteria: 45.8 % were men with mean age of 51.8 ±10.1 years and a Body-mass index 25.1±4.5 Kg/m^2.

Group CBT-I produced a statistically significant ($p<0.05$) reduction on ISI from 17±3.7 to 14±4.1; and an improvement in sleep efficiency (from 64.6±25.2% to 81.2±11.7%) and in total sleep time (4.7±1.3 to 5.6±1.0 hours), $p<0.05$.

Furthermore, there was an increase in the % of patients with subjective sleep latency of less than 30 min, from 45.2 % at the beginning of therapy to 69.1 % at the end of therapy.

Conclusions: In our patient sample, this review demonstrated as in other published works, a clinically meaningful effect of Group CBT-I, wich represents an excellent alternative in our public healthcare system. Future research is needed to investigate the long term effect of Group CBT-I.

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GROUP COGNITIVE BEHAVIOURAL THERAPY FOR INSOMNIA ON-LINE IN THE TIME OF COVID-19

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Introduction: Cognitive behavioral therapy (CBT-I) is considered the first line of treatment for chronic insomnia. Group CBT-I has proven to be an effective therapeutic option in clinical practice. However, the COVI-19 pandemic made in-person meetings impossible, temporarily suspending group therapy. The multiple video call through Zoom® was the alternative to continue with this practice. But, is cognitive behavioral therapy for insomnia effective non-face-to-face? The aim was to assess the efficacy of online group CBT-I in our sleep unit.

Materials and methods: Prospective cohort study where patients who received online group CBT-I with Zoom® were included and compared with data collected from participants in face-to-face group therapy at Araba University Hospital from March 2018 to December 2021.

Anthropometric data, subjective total sleep time (TST), subjective sleep latency, subjective sleep efficiency (SE), as well as the insomnia severity index (ISI) were studied both at baseline and at the end of therapy.

Descriptive statistical analysis was performed using frequency distributions for qualitative variables and mean and standard deviation for quantitative variables. For the comparison of means had been used Student's t test for repeated measures and the relationship of qualitative variables was analyzed with Chi-square.

Results: Seventy-two patients were included, 44 on-line and 28 face-to-face. The mean age of the patients was 51.8 (SD=10.1) years, with a range of 20-71 years, 45.8% were men, and the mean body mass index was 25.1 (SD=4.5) Kg/m^2. No statistically significant differences were found between the characteristics of the samples, with the mean age in the online group being 51.4 years (SD=10.1) and in the face-to-face group 52.4 years (SD=10.3). The percentage of men was 50 % and 39.2 % and BMI of 24.6 (SD=6.1) and 24.9 (SD=4.1) resceptively.

A significant reduction ($p<0.001$) in ISI was observed after group CBT-I, showing no significant differences ($p=0.68$) between on-line (18.3 (SD=3.9) to 14.5 (SD=4.3) and face-to-face (17,5 (SD=3.3) to 13,3 (SD=3.7). In addition, there was an increase in subjective SE from 66.6% (SD=28.7) to 81.0% (SD=11.7) in the online group and from 59.4% (SD=12.4) to 81.5% (SD=12.2) in the face-to-face group ($p<0.001$) and increase in subjective TST from 4.9 hours (SD=1.4) to 5.7 hours (SD=1.0) in the online group and from 4.5 hours (SD=1.0) to 5.4 hours (SD=1.0) in the face-to-face group

(p<0.001).
Furthermore, there was an increase in the % of patients with subjective sleep latency of less than 30 min, from 34.1% (online) and 14.3% (face-to-face) at the beginning of therapy to 65.9% and 32.1% respectively at the end of therapy.
Conclusions: In our experience, the results of group CBT-I have a clear positive impact on the clinical improvement of the patient, both face-to-face and on-line. The group CBT-I on line is the first choice in times of pandemic and a good alternative for patients with difficulties in attending on-site therapy.
Acknowlegments: We would hereby like to express our gratitude to the staff of the sleep unit and the psychiatry service of the Araba University Hospital.

HEART RATE VARIABILITY IN NON-RAPID EYE MOVEMENT SLEEP STAGE 2 INDICATES INSOMNIA AND IS RELATED TO SUBJECTIVE DAYTIME PERFORMANCE

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Introduction: Insomnia disorder is characterized by subjectively perceived poor sleep and impaired daytime performance. However, objective findings of deficits in sleep continuity and cognitive functioning are often mild. The aim of this study was to examine whether objective markers of autonomous hyperarousal, specifically sleep stage related heart rate variability (HRV), would indicate insomnia more reliably than objective sleep continuity measures; and further, if such biomarkers would correlate with poor cognitive daytime performance.
Materials and Methods: Polysomnographic measures of 41 insomniacs (age: 37.9 ± 12.7 years, 56.1% females) were compared to a control group of 27 normal sleepers. Frequency domain measures of HRV (very low (VLF), low (LF) and high frequency (HF) power) were extracted from artefact-free 5-min ECG segments of non-rapid eye movement sleep stage 2 (NREM-S2). Daytime performance was assessed by subjective ratings with insomnia severity index (ISI; items "interference" and "noticeability") and objective testing of alertness (TAP: Testbatterie zur Aufmerksamkeitsüberprüfung).
Results: HRV measures in NREM-S2 distinguished between insomnia and normal sleep, with increased NREM-S2-VLF%-power (p = .012, g = .702) and decreased NREM-S2-HF%-power (p = .041, g = -.564) in insomnia. HRV findings in NREM-S2 sleep differed over the course of the night, with the largest contrast between insomnia and control group in NREM-S2-HF %-power in the first available NREM-S2-sleep segment (p = .019) and NREM-S2-VLF%-power in the last available NREM-S2-sleep segment (p = .006). Concerning objective sleep continuity parameters the two groups only differed by increased "sleep onset latency" (SOL) in insomniacs (p = .033). Concerning sleep architecture, insomnia was characterized by trend by decreased REM-sleep percentage (p = .055). However, there was no difference concerning NREM-S1- (p = .524), NREM-S2- (p = .302) or slow wave sleep percentage (p = .965). Furthermore, insomniacs presented with both, higher perceived impairment of daytime performance (ISI item "noticeability", p < .001, g = .80) and increased objective reaction time (p = .084, g = .435). Moreover, the above-mentioned NREM-S2-HRV-findings in insomnia correlated with both, poor subjective daytime performance ("noticeability"; VLF%-power: r = .334, p = .013 and HF%-power: r = -.316, p = .019, resp.) and prolonged objective reaction time (VLF%-power: r = .471, p < .001 and HF%-power: r = -.348, p = .008, resp.).
Conclusions: HRV in NREM-S2 sleep discriminates insomnia patients from healthy controls with moderate effect sizes, especially NREM-S2-HF %-power in the first and NREM-S2-VLF%-power in the last third of the night. The pattern of the results in NREM-S2 sleep suggests lower vagal activity in insomnia, which relates to the subjective complaints of hyperarousal and non-restoring sleep. We conclude that HRV analysis in NREM-S2 delivers more sensitive markers for insomnia than common sleep EEG variables and confirms previous evidence that insomnia is a disorder of hyperarousal. Moreover HRV-markers relate more closely to the subjective and objective complaints of non-restoring sleep and poor daytime functioning than sleep continuity measures.
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IMPACT OF LEMBOREXANT VERSUS PLACEBO AND ZOLPIDEM ON REM SLEEP DURATION BY QUARTER-OF-THE-NIGHT INTERVALS IN OLDER ADULTS WITH INSOMNIA DISORDER

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Introduction: Lemborexant (LEM) is a dual orexin receptor antagonist approved in multiple countries, including the United States, Japan, Canada and Australia for the treatment of adults with insomnia. The effects of LEM on sleep architecture in adults ≥55y with insomnia disorder were assessed in Study E2006-G000-304 (Study 304; SUNRISE-1; NCT02783729). These post hoc analyses examined the acute effect of LEM on REM pressure, as assessed by changes from baseline in REM latency and in REM sleep duration in 2-hour quarter-of-the-night (QoN) intervals.
Materials and Methods: Study 304 was a 1 month, randomized, double-blind, placebo (PBO)- and active-controlled (zolpidem tartrate extended-release 6.25mg [ZOL]) study of LEM (5mg, LEM5; 10mg, LEM10). Subjects received PBO (n=208), ZOL (n=263), LEM5 (n=266), or LEM10 (n=269). Paired polysomnographic assessments were conducted at baseline, the first 2 (N1/2), and the last 2 (N29/30) nights of treatment; mean values from the paired assessments are reported.
Results: Baseline REM latency (minutes) was similar across treatments (98.4-101.4). On N1/2, significant mean (SD) decreases from baseline in REM latency were observed for LEM5 (−42.6 [53.9]) and LEM10 (−49.6 [52.9]) vs PBO (−6.9[54.5]) and vs ZOL (0.2[54.2]) (all P<0.0001). On N29/30, REM latency was also significantly decreased from baseline with LEM5 (−30.7[55.7]) and LEM10 (−37.7[56.2]) vs PBO (−7.7[62.3]) and vs ZOL (−4.0[56.4]) (all P<0.0001). No difference was observed for ZOL vs PBO at either N1/2 or N29/30.
Within each QoN, baseline REM sleep duration (minutes) was similar across treatments. On N1/2, mean REM (minutes) across quarters ranged from 16.5-23.8 for LEM5, 19.7-26.1 for LEM10, 10.3-21.6 for PBO, and 8.5-22.8 for ZOL. On N29/30, mean REM values were 14.4-22.4 for LEM5, 16.9-24.1 for LEM10, 9.2-21.5 for PBO, and 8.3-22.3 for ZOL.
In each QoN during N1/2, REM sleep duration (minutes) significantly increased from baseline with LEM10 vs PBO (all P<0.0001) and vs ZOL (all P<0.001). With LEM5 during N1/2, REM sleep significantly increased from baseline vs PBO during Q1, Q3, and Q4 (all P<0.05) and vs ZOL in Q1 and Q2 (both P<0.01). With ZOL, REM was significantly decreased vs PBO during Q1 (P<0.05) and significantly increased vs PBO during Q3 (P<0.05).
On N29/30, REM sleep (minutes) significantly increased from baseline with LEM10 vs PBO in each QoN (all P<0.05) and vs ZOL in Q1, Q3, and Q4 (all P<0.05). With LEM5, REM sleep significantly increased from baseline vs PBO and vs ZOL in Q1 (both P<0.0001). No significant differences were observed for ZOL vs PBO in any QoN on N29/30. In each QoN, the increases in REM sleep were significantly greater on N1/2 than N29/30 with LEM5 (all P<0.05) and LEM10 (all P<0.0001).
Conclusion: LEM, but not ZOL, acutely increases REM pressure as evidenced by REM latency and REM duration per QoN. In each QoN, increases in REM sleep were greater with LEM5 and LEM10 than with ZOL or PBO. Decreases in REM latency and increases in REM sleep per QoN with LEM were greater during N1/2 than N29/30.
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IN-DEPTH CHARACTERIZATION OF SLEEP PATTERNS AMONG PEOPLE WITH INSOMNIA DURING THE PANDEMIC OF COVID-19

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