Other Adult Neurology

P.047

Effect of lemborexant on sleep architecture in subjects with comorbid insomnia and mild obstructive sleep apnea from a phase 3 trial

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doi: 10.1017/cjn.2023.151

Background: Lemborexant (LEM), a dual-orexin-receptor-antagonist approved to treat adults with insomnia, increases total sleep time (TST) and rapid eye movement (REM) sleep. Patients with obstructive sleep apnea (OSA) or co-morbid insomnia and OSA (COMISA) report sleeping difficulties and reduced REM, therefore sleep architecture was analyzed during LEM treatment. Methods: Study E2006-G000-304 (NCT02783729) was a 1-month, randomized, double-blind, placebo (PBO)- and active-comparator zolpidem-ER 6.25mg (ZOL)-controlled study in adults ≥55y with insomnia disorder. Subjects received PBO, LEM 5mg (LEM5), 10mg (LEM10), or ZOL. Least-square-mean duration of each sleep stage (minutes) was compared from pooled data on Nights (NT)1/2 and NT29/30 for mild OSA subjects (apnea hypopnea index ≥5 to <15 events/h). Treatment-emergent adverse events (TEAEs) were recorded. Results: Of 409 subjects with mild OSA (LEM5=114/LEM10=105/ZOL=112/PBO=78) change from baseline (CFB) in TST and REM sleep was significantly larger with both LEM doses versus ZOL/PBO on both nights. CFB for total nonREM sleep was significantly higher ($P<0.0001$) with both LEM doses versus PBO on both nights. LEM5 showed significantly higher ($P<0.05$) nonREM sleep versus ZOL at NT29/30. Most TEAEs were mild/moderate. Conclusions: LEM significantly increased TST, REM, and nonREM sleep versus PBO in subjects with insomnia and mild OSA. Data support LEM treatment in the COMISA population.

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Monitoring and managing gastrointestinal events with sodium phenylbutyrate and ursodoxicoltaurine for the treatment of Amyotrophic Lateral Sclerosis

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doi: 10.1017/cjn.2023.152

Background: Sodium phenylbutyrate and ursodoxicoltaurine/taurursodiol (PB&TURSO) is indicated for the treatment of amyotrophic lateral sclerosis (ALS) in Canada and the U.S. In the CENTAUR trial, a phase 2 U.S. multicenter trial in ALS, PB&TURSO was generally well-tolerated. The most common adverse reactions were gastrointestinal (GI) and occurred most often during the first three weeks of therapy. Although the occurrence of GI events in people living with ALS (PLWALS) and treated with PB&TURSO are recognisable and generally manageable, many of the symptoms are often not managed proactively. We sought to develop an evidence-based tool to help guide clinicians on managing diarrhea and abdominal pain in PLWALS and treated with PB&TURSO. Methods: Three ALS specialized neurologists and one gastroenterologist combined their clinical experience, research, and each Medications respective product monograph, to develop a patient-centric GI tool. Results: A guide to monitoring and managing potential GI events with PB&TURSO was developed. The tool provides clinicians a proactive, step-by-step guide to help manage diarrhea and abdominal pain in PLWALS treated with PB&TURSO. Conclusions: The GI tool has the potential to improve monitoring, recognition, and treatment of GI events in PLWALS treated with PB&TURSO. Proactively managing GI events may aid medication adherence and improve patient quality of life.

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Neurologists' attitudes and perceptions on palliative care: a Canadian perspective

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doi: 10.1017/cjn.2023.153

Background: Despite significant advances in the treatment of neurological disorders, many conditions remain palliative. Neurologists are in a unique position as they are integral in providing patient centered care, understanding neurologic disease and illness trajectory, and how disease can affect patients' sense of self and values. Currently, little is known about neurologists' perceptions and challenges in care planning and palliative care for their patients. Methods: A qualitative approach was utilized with semi-structured interviews of ten neurologists. Data was analyzed using a constant comparative method (constructivist grounded theory). Results: Participants represented a broad spectrum of neurologist experience and subspecialties. Four theories were identified: (1) care planning and palliative care are high priorities, (2) neurologic diseases uniquely affect patients and require a dynamic, patient-centered care plan, (3) a care gap exists in providing palliative care for neurologic patients with multifactorial barriers, and (4) opportunities to improve care exist with continuing education, collaboration, and health system support. Conclusions: Neurologists have a key role in care planning and palliative care for patients with chronic neurological diseases. Our findings show that there is a gap in the provision of palliative care. Future directions may include exploring educational opportunities and dedicated health systems to improve care management.

P.050

Effect of lemborexant on sleep architecture in adult and elderly subjects with mild to severe obstructive sleep apnea

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doi: 10.1017/cjn.2023.154

Background: Obstructive sleep apnea (OSA) may be associated with sleep difficulties and decreased rapid eye movement

(REM) sleep. Lemborexant (LEM), a dual-orexin-receptor-antagonist approved to treat adults with insomnia, increases total sleep time (TST) and REM sleep, and demonstrated respiratory safety in subjects with mild through severe OSA. Sleep architecture was thus analyzed after LEM treatment in those subjects. Methods: Studies E2006-A001-102 and E2006-A001-113 enrolled adults with mild (apnea-hypopnea index [AHI] ≥5 – <15) or moderate (AHI ≥15 – <30)/severe (AHI ≥30) OSA without insomnia. Subjects received LEM 10mg (LEM10) or placebo (PBO) in 2 treatment periods, Days 1 (D1) and 8 (D8), separated by ≥14 days. Least-squares-mean (minutes) for each sleep stage was compared. Treatment-emergent adverse events (TEAEs) were recorded. Results: Thirty-nine subjects with mild and 33 with moderate/severe OSA were randomized. On both days, TST was significantly higher in the LEM period for these subjects. Total non-REM on D1 in subjects with mild OSA and on both days in subjects with moderate/severe OSA were higher with LEM than PBO; REM also significantly increased in subjects with mild and moderate/severe OSA. Most TEAEs were mild. Conclusions: In OSA subjects without insomnia, LEM was associated with higher TST, non-REM, and REM versus PBO.

P.051

Effect of lemborexant on cognition in patients with comorbid insomnia disorder and mild obstructive sleep apnea

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doi: 10.1017/cjn.2023.155

Background: Some sleep-promoting medications are associated with cognitive impairment, making treatment of comorbid obstructive-sleep-apnea (OSA) and insomnia (COMISA) challenging. Lemborexant is a dual-orexin-receptor-antagonist approved for insomnia treatment. This post-hoc analysis evaluated cognition in the subgroup of subjects with mild-OSA (apnea-hypopnea-index ≥5–<15 events/h-of-sleep). Methods: Study E2006-G000-304 was a 1-month, randomized, double-blind, placebo (PBO)- and active-comparator (zolpidem-ER 6.25mg [ZOL])-controlled study of lemborexant 5/10mg (LEM5/LEM10). Subjects ≥55y with insomnia disorder/sleep maintenance problems were enrolled (N=1006). A cognitive-performance assessment battery (CPAB) was performed at morning waketime of Days(D)2/3 and D30/31. Change-from-baseline (CFB) for mean power-of-attention (PoA), continuity-of-attention (CoA), quality-of-memory (QoM), and speed-of-memory-retrieval (SoMR) for CPAB tasks was analyzed. Results: The mild-OSA subgroup comprised 410 (40.8%) subjects. On D2/3 and D30/31, CFB for PoA, CoA, QoM, and SoMR for LEM5/LEM10 were not significantly different than PBO. On D2/3, PoA and QoM were significantly worse with ZOL vs PBO; QoM was significantly better with LEM5/LEM10 vs ZOL. On D30/31, SoMR was significantly worse with ZOL vs PBO and significantly better with LEM5/LEM10 vs ZOL. LEM safety in the subgroup was consistent with the overall study population. Conclusions: Memory and attention domains in subjects with COMISA characterized by mild-OSA were not impacted by LEM, unlike ZOL.

Support: Eisai Inc.

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Trazodone for treating insomnia: abuse and safety risks

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doi: 10.1017/cjn.2023.156

Background: Although unapproved by the FDA for treating insomnia, trazodone is commonly prescribed in the US partly due to lack of scheduling, hence it's perceived as safer than z-drugs and benzodiazepines. This study investigated trazodone abuse/dependence potential and safety risks. Methods: Cases involving trazodone or benzodiazepines (temazepam, triazolam, estazolam) frequently prescribed for insomnia were identified from the FDA Adverse Events Reporting System (FAERS), National Forensic Laboratory Information System (NFLIS) for confiscation data, and the American Association of Poison Control Centers'-National Poison Data System (AAPCC-NPDS). Drug-related falls risk was assessed from claims databases. Results: FAERS included 11,228 trazodone and 5120 benzodiazepine reports. Of these, drug-abuse and drug-dependence cases with trazodone were lower than benzodiazepines (drug-abuse: 6.4%/12.6%; drug-dependence: 1.1%/3.6%). Serious cases (81.8%/83.9%) and deaths (35.4%/36.0%), were similar between trazodone and benzodiazepines. NFLIS reported 612/1,575,874 (0.04%) drug-seizure cases that included trazodone. AAPCC-NPDS reported 22,225/1,446,011 (1.54%) total case mentions of trazodone/all pharmaceuticals and 8445 trazodone-related single-exposure cases. Falls risk (1year-period) in Medicare beneficiaries ≥65y and commercially-insured enrollees ≥18y was reported for trazodone and benzodiazepines: Medicare, 9.5%/11.3%; Commercially-insured: 4.6%/3.7%. Conclusions: Trazodone has abuse/dependence potential and important safety risks. Given limited data from well-controlled studies and off-label use, re-evaluation of trazodone prescribing rates in patients with insomnia is warranted.

P.053

Efficacy of lemborexant in adults with insomnia is supported by improvements in both objective and subjective measures

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doi: 10.1017/cjn.2023.157

Background: Improvements in sleep-onset, maintenance, and daytime functioning, are all important outcomes for the treatment of insomnia. These improvements are usually assessed by objective or patient-reported (subjective) measures or both. Some sleep-promoting drugs do not report consistently aligned subjective and objective outcomes. Therefore, we examined concordance in change from baseline (CFB) in sleep parameters (objective/subjective measures) and daytime functioning (subjective measures) in the clinical program of lemborexant (LEM), a dual-orexin receptor antagonist. Methods: Study E2006-G000-304 (NCT02783729),