LEM5 and LEM10 were statistically significantly greater than those for PBO (all P<0.05).
Conclusion: Older adults with ISS achieved clinically meaningful improvement with LEM as assessed at the end of one month of treatment, with nearly 30% considered remitters and >50% considered treatment responders. LEM is a potential therapy for ISS patients who may have limited response to CBT-I.
Support (If Any): Eisai Inc.

0453

LEMBOREXANT EXPOSURE IS INDEPENDENT OF RACE

Sumit Rawal[1], Ishani Landry[1], Bojan Lalovic[1], Kenya Nakai[2], Naoki Kubota[2], Margaret Moline[1]
Eisai Inc. [1] Eisai Co., Ltd [2]

Introduction: Some hypnotic treatments for insomnia require dosing consideration due to exposure differences based on patient characteristics. Lemborexant (LEM) is a dual orexin receptor antagonist approved in multiple countries for the treatment of adult insomnia. LEM is not associated with exposure differences based on sex, age, or BMI that impact dosing. The potential impact of race on exposure was determined in two stand-alone pharmacokinetic (PK) studies and by modeling data from studies comprising the LEM clinical development program, which included healthy subjects and insomnia patients.
Methods: Study 003 (NCT02039089) was a single-center, multiple-dose, randomized, double-blind, placebo-controlled, parallel-group study in healthy Japanese and White subjects. Study 014 (NCT04555733) was a phase 1, single center, open-label, single and multiple oral dose study in healthy Chinese subjects. Additionally, effect of race on LEM exposure was independently examined as part of a population PK analysis incorporating LEM data from 9 Phase 1 studies (n=407), and Studies 201 (NCT01995838; n=235), 303 (NCT02952820; n=726) and 304 (NCT02783729; n=524) (Lalovic et al., 2020). Plasma concentrations of LEM were quantified from plasma by validated liquid chromatography with tandem mass spectrometry. Adverse events (AE) were recorded.
Results: Exposure of LEM increased in an approximately dose-proportional manner across the dose range (2.5 mg to 25 mg) in studies 003 and 014. There were no significant exposure differences between Japanese and White subjects following single LEM10 administration on Day 1 in Study 003 (maximum concentration [Cmax] mean[SD], ng/mL: Japanese, 46.5[25.8]; White, 47.3[28.1]; area under the curve from time zero to 24h [AUC0-24] mean[SD], ng·h/mL: Japanese, 231[40.2]; White, 208[83.4]) or when comparing PK data from Chinese subjects in Study 014 following single dose administration on Day 1 (Cmax mean[SD], ng/mL: LEM5, 29.8[12.8]; LEM10, 56.2[16.9]; LEM25, 116[46.8]; AUC0-24 mean[SD], ng·h/mL: LEM5, 106[29.9]; LEM10, 205[35.6]; LEM25, 549[116]) to Japanese and White subjects in Study 003. These results are supported by the cross-study, population PK model-based analysis, indicating no significant clinical or statistical differences in LEM PK attributable to the intrinsic factor race.
Conclusion: LEM exposure is not significantly affected by race. Therefore, dosing of LEM can be consistent across patient populations from different racial groups.
Support (If Any): Eisai Inc.

0454

RESPONSE TO LEMBOREXANT IN OLDER SUBJECTS WITH INSOMNIA DISORDER AND COMORBID PAIN AT BASELINE

Alan Kaplan[1], Jocelyn Cheng[2], Masahiro Suzuki[3], Dinesh Kumar[2], Manoj Malhotra[2], Margaret Moline[2], Elizabeth Pappadopulos[2]
Family Physician Airways Group of Canada [1] Eisai Inc. [2] Nihon University School of Medicine [3]

Introduction: The reciprocal relationship between pain and poor sleep has been well established. Pain interferes with sleep, and insomnia increases pain sensitivity, thus reducing quality of life. Therefore, it is of clinical importance to evaluate whether a sleep-promoting drug such as the dual orexin receptor antagonist, lemborexant (LEM; approved in multiple countries to treat adults with insomnia) can improve sleep in older patients, in whom both sleep and ongoing pain are prevalent.
Methods: Study 304 (NCT02783729), was a 1-month, double-blind, PBO- and active-controlled study in subjects age ≥55y with insomnia (full analysis set [FAS]=1006). Those who also endorsed some/severe pain at baseline on the pain/discomfort dimension of the EuroQual-5 Dimension-3 Level scale (EQ-5D-3L; no problems/some problems/extreme problems) at baseline were eligible for these post-hoc analyses. Medical history of pain conditions and/or ongoing therapy were not required for eligibility and were not evaluated. Subjects were randomized to bedtime doses of placebo, LEM 5mg (LEM5),10mg (LEM10) or zolpidem tartrate extended release (not reported here). Changes from baseline (CFB) in objective sleep parameters assessed by polysomnography (latency to persistent sleep [LPS]; wake after sleep onset [WASO]) were analyzed by mixed-effect repeated measures analyses adjusted for relevant factors.
Results: Approximately 18% of the FAS reported some or extreme pain at baseline (PBO=55; LEM5=78; LEM10=50). For LPS, baseline median values (minutes) were 31.0, 29.4 and 42.1 for PBO, LEM5 and LEM10, respectively. Median CFB for LPS were larger and statistically significantly different for both LEM doses compared with PBO at the beginning of treatment (mean of Nights 1/2: +2.5; -8.4, -15.8; P<0.005); and were (mean of Nights 29/30: -7.1,-9.9, -9.0) at the end of treatment LEM5 (P=0.031), LEM10 (P=0.054). For WASO, baseline median values (minutes) were 101.0, 103.6 and 111.1 for PBO, LEM5 and LEM10, respectively. Median CFB for WASO were larger and statistically significantly different (P<0.001) for both LEM doses compared with PBO at the beginning (Nights 1/2; -1.5; -41.5, -64.4) and end of treatment (Nights 29/30; -1.1, -37.9, -52.5).
Conclusion: These data suggest that lemborexant can effectively treat insomnia in older adults with concomitant painful conditions.
Support (If Any): Eisai Inc.

0455

THE INSOMNIA DAYTIME SYMPTOMS AND IMPACTS QUESTIONNAIRE: AN ANALYSIS OF CLINICALLY MEANINGFUL CHANGE USING PHASE 3 CLINICAL TRIAL DATA

Andrea Phillips-Beyer[1], Ariane Kawata[2], Leah Kleinman[2], Dalma Seboek Kinter[3]
Innovus Consulting Ltd [1] Evidera [2] Idorsia Pharmaceuticals Ltd [3]

Introduction: The Insomnia Daytime Symptoms and Impacts Questionnaire (IDSIQ) is a new validated patientreported outcome (PRO) instrument evaluating daytime functioning in people with