minutes on the Maintenance of Wakefulness Test (MWT), and ≥15 cataplexy attacks per week.
Results: The analysis populations included 108 patients for the ESS (pitolisant, n=54; placebo, n=54), 105 for the MWT (pitolisant, n=59; placebo, n=46), and 31 for cataplexy (pitolisant, n=20; placebo, n=11). Mean change in ESS from baseline was significantly greater for pitolisant (-6.1) compared with placebo (-2.6; P=0.0002). A significantly greater percentage of pitolisant-treated patients were classified as treatment responders: for ESS score reduction ≥3, 68.5% in the pitolisant group versus 35.2% in the placebo group (P=0.0006); for final ESS score ≤10, 35.2% versus 9.3%, respectively (P=0.0026). Mean increase in sleep latency on the MWT was significantly greater for pitolisant (7.0 minutes) compared with placebo (3.4 minutes; P=0.0089). Decrease in mean weekly rate of cataplexy was significantly greater for pitolisant (baseline, 21.8; final, 3.9) compared with placebo (baseline, 20.9; final, 18.2); the rate ratio was 0.35 (95% CI, 0.26–0.47; P<0.001). The adverse event profile in the analysis populations was consistent with the known safety profile for pitolisant; headache was the most common adverse event in pitolisant-treated patients (10.0%-20.4%).
Conclusion: In patients with severe symptom burden, pitolisant produced significantly greater improvements in excessive daytime sleepiness and cataplexy compared with placebo, highlighting the important role of histamine in narcolepsy.
Support: Bioprojet Pharma and Harmony Biosciences, LLC.

0763

EFFECTS OF SOLRIAMFETOL ON DRIVING PERFORMANCE IN PARTICIPANTS WITH NARCOLEPSY

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Introduction: Patients with narcolepsy have an increased risk of automobile accidents. Solriamfetol, a dopamine/norepinephrine reuptake inhibitor, is approved in the US (Sunosi®) for adults with excessive daytime sleepiness (EDS) associated with narcolepsy (75-150 mg/day). This study evaluated the effects of solriamfetol on on-road driving performance in participants with narcolepsy.
Methods: In each period of this randomized, double-blind, placebo-controlled, crossover study (NCT 02806908; EudraCT 2015-003931-36), driving performance during an on-road driving test (a 1-hour drive on a public highway) was assessed at 2 hours and 6 hours postdose following 7 days of treatment with solriamfetol (150 mg/day × 3, then 300 mg/day × 4) or placebo. For assessment of driving performance, the primary endpoint was standard deviation of lateral position (SDLP), a measure of "weaving," at 2 hours postdose. Comparisons (solriamfetol vs placebo) used a Wilcoxon signed-rank test.
Results: The study included 24 participants (54% male; mean age, 40 years); 22 were included in the analyses of SDLP data. At 2 hours postdose, SDLP for solriamfetol (median, 19.08 cm) was statistically significantly lower than that for placebo (median, 20.46 cm; P=0.0022; incomplete driving tests: solriamfetol, n=4; placebo, n=7), indicating a better performance with solriamfetol. At 6 hours postdose, SDLP for solriamfetol (median, 19.59 cm) was not statistically significantly different from that for placebo (median, 19.78 cm; P=0.1245; incomplete driving tests: solriamfetol, n=3; placebo, n=10). Common adverse events (≥5%) were headache, decreased appetite, somnolence, sleep disorder, agitation, nausea, and palpitations.
Conclusion: Solriamfetol (300 mg/day) improved SDLP, an important measure of driving performance, at 2 hours after administration in participants with narcolepsy.
Support: Jazz Pharmaceuticals

0764

PITOLISANT IN THE TREATMENT OF PATIENTS WITH NARCOLEPSY: A 2-YEAR, PROSPECTIVE, OBSERVATIONAL, SINGLE-CENTER STUDY

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Introduction: Pitolisant, a selective histamine H_3 receptor antagonist/inverse agonist, increases histamine release in the brain. The efficacy of pitolisant in adults with narcolepsy was demonstrated in randomized, placebo-controlled trials. This study evaluated long-term use of pitolisant in clinical practice.
Methods: This prospective, open-label, 2-year, observational study was conducted at a major narcolepsy center in Germany and enrolled adults with a diagnosis of narcolepsy who had no prior treatment with pitolisant. Assessments included excessive daytime sleepiness (Epworth Sleepiness Scale [ESS]), weekly rate of cataplexy (WRC), and health-related quality of life (Short-Form Veterans RAND [VR-36]).
Results: The study enrolled 147 patients: mean age, 29.9 years; 57.1% female, 65.3% with cataplexy, and 66.7% with disrupted nighttime sleep. In patients who were tested, CSF hypocretin-1 was <110 pg/mL in 70.8% (51/72), and 79.4 % (77/97) were HLA-DQB1*0602 positive. The pitolisant dose was 35.6 mg/d in 38.1% of patients at Month 3, and 73.5% at Month 24. Most patients received concomitant narcolepsy medications (63.3% at baseline; 79.6% at month 24). Mean ESS score decreased from 16.2 at baseline to 12.4 at Month 12 and 12.6 at Month 24. Mean WRC was reduced by 31% at Month 24. Significant improvement in quality of life was noted at Months 12 and 24 on VR-36 subscales that assess general health perception, vitality, and social function. In all, 38 patients (25.8%) discontinued from the study before Month 24: 15.0% for lack of efficacy and 10.8% due to adverse events. The most common adverse events were disrupted nighttime sleep (29.3% of patients), headache (15.5%), and nausea (12.2%).
Conclusion: These real-world data show that long-term treatment with pitolisant (usually with 35.6 mg/d) was efficacious for reducing EDS and cataplexy and improving quality of life in patients with narcolepsy. Treatment was generally well tolerated.
Support: Writing support funded by Harmony Biosciences, LLC.

0765

RELIABILITY AND VALIDITY STUDY OF THE CHINESE VERSION OF NARCOLEPSY SEVERITY SCALE FOR ADULT PATIENTS WITH NARCOLEPSY TYPE 1

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Introduction: Narcolepsy is a chronic sleep disorder that can affects significantly patient functioning, involving social, work, and affective life. At present, many drugs have been developed to treat narcolepsy efficiently. But there is no Chinese version of Narcolepsy

Severity Scale (NSS) available yet, for that the aim of this study is to translate the NSS into Chinese and evaluate reliability and validity of the NSS in adult patients with narcolepsy type 1 (NT1).
Methods: NSS was translated according to the standard procedures of double-back translation and cross-cultural adaptation steps. The NSS was administered to 62 adult patients (42 males, 20 females; mean age 34 years; range 19 to 67 years) with NT1 from April 2019 to December 2019. The validity of the scale was assessed by the exploratory factor analysis, discriminant validity and convergent validity. The reliability was assessed by the Cronbach's α coefficient and test-retest reliability.
Results: Three common factors were extracted and 15 items explained 57.4% of the total variance. Cronbach's α coefficient for total scale was 0.767 and Cronbach's α for three dimensions ranged from 0.729 to 0.787. Scores were significant difference between treated and untreated group in dependent samples (p=0.036), but no differences in the independent samples (p>0.05). The NSS had good correlations with Epworth Sleepiness Scale (r=0.302, p=0.017) and Insomnia Severity Index (r=0.526, p=0.000). The NSS showed good test-retest reliability (r=0.72, p=0.029).
Conclusion: The Chinese version of NSS was proved to be valid and reliable and can be used to evaluate the severity and consequences of symptoms in Chinese adult patients with NT1.
Support:

0766

SAFETY AND TOLERABILITY OF PITOLISANT IN THE TREATMENT OF ADULT PATIENTS WITH NARCOLEPSY: FINAL ANALYSIS OF AN OPEN-LABEL, EXPANDED ACCESS PROGRAM IN THE UNITED STATES

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Introduction: Pitolisant Expanded Access Clinical Evaluation (PEACE) provided adult patients with narcolepsy access to treatment with pitolisant while it was an investigational medication in the United States.
Methods: Pitolisant was titrated to 35.6 mg/day (or the highest tolerable dose) over a 3-week period. Dose adjustments were permitted at the discretion of the treating physician based on patient response. Treating physicians followed their standard of care and were required to report adverse events (AEs). Demographic and baseline information for all enrolled patients, and safety results available through October 30, 2019, are reported here (presentation will include final data from the PEACE program).
Results: In all, 623 patients (67.9% female; 84.6% white; mean age, 40.0 years; narcolepsy type 1, 51.5%) were treated with pitolisant in the PEACE program. Nearly all patients (98.4%) had been previously treated with other narcolepsy medications (88.1% with ≥2 narcolepsy medications). Overall, 35.2% of patients discontinued from the program; 16.7% due to an AE and 12.2% for lack of effect. At Month 1, 97.3% of patients remained in the study, 88.2% at Month 3, 76.5% at Month 6, 66.9% at Month 9, and 55.0% at Month 12. In all, 256 (41.1%) patients experienced ≥1 AE; majority (52.5%) of these AEs occurred early in treatment (by Week 3). The most commonly reported AEs were headache (9.8% of AEs), nausea (6.6%), anxiety (5.6%), and insomnia (4.7%).
Conclusion: In the PEACE program, patient characteristics were generally reflective of the US narcolepsy patient population. The safety and tolerability profile of pitolisant was similar to that seen in the clinical development program, with no new safety signals identified. The program ceased enrollment in August 2019 after the US approval of pitolisant for the treatment of excessive daytime sleepiness in adult patients with narcolepsy.
Support: Harmony Biosciences, LLC.

0767

ANALYSIS OF THE EFFECT ON BLOOD PRESSURE AND HEART RATE WHEN ADDING SOLRIAMFETOL (SUNOSI) TO STIMULANT THERAPY

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Introduction: Solriamfetol is a non-stimulant wakefulness-promoting agent (WPA) indicated for the treatment of excessive daytime sleepiness in adult patients with obstructive sleep apnea or narcolepsy. It acts by inhibiting reuptake of dopamine and norepinephrine. Since many patients with excessive daytime sleepiness take stimulants, clinicians commonly ponder the safety of adding solriamfetol in this population due to concern of increased blood pressure and/or heart rate (HR).
Methods: We conducted a retrospective chart review and identified 18 patients who had solriamfetol added to their stimulant therapy. Of those, 7 to date have had a follow-up appointment after the addition of solriamfetol (6 on 150mg, 1 on 75mg). We collected the blood pressure and HR readings at the appointment immediately prior to and following the addition of solriamfetol and conducted a paired t-test.
Results: The systolic blood pressure (SBP) had a mean difference of -0.57 (95% CI -9.6 to 8.5, p=0.88), diastolic blood pressure (DBP) 1.7 (95% CI -4.4 to 7.9, p=0.52), mean arterial pressure (MAP) 0.95 (95% CI -5.6 to 7.5, p=0.73), and HR 6.6 (95% CI -0.07 to 13.2, p=0.052).
Conclusion: The addition of solriamfetol to stimulant therapy did not lead to a significant increase in SBP, DBP, MAP, or HR.
Support: none

0768

TIME COURSE OF IMPROVEMENT IN EXCESSIVE DAYTIME SLEEPINESS AND CATAPLEXY DURING TREATMENT WITH PITOLISANT IN PATIENTS WITH NARCOLEPSY

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Introduction: This analysis evaluated the efficacy of pitolisant over time in three 7- to 8-week, randomized, placebo-controlled studies of adults with narcolepsy.
Methods: Patients in all 3 studies (HARMONY-1, HARMONY-1bis, HARMONY-CTP) experienced excessive daytime sleepiness (EDS) at study baseline; patients in HARMONY-CTP also experienced ≥3 cataplexy attacks/week. Pitolisant was titrated to a maximum dose of 35.6 mg/day (HARMONY-1, HARMONY-CTP) or 17.8 mg/day (HARMONY-1bis). Change from baseline in mean Epworth Sleepiness Scale (ESS) score (3 studies) and mean weekly rate of cataplexy (WRC; 1 study) was compared for pitolisant versus placebo.