(340) Relationship between pain relief and functional improvement in patients with neuropathic pain associated with spinal cord injury treated with pregabalin

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Two clinical trials have demonstrated efficacy of flexible-dosed pregabalin (150-600mg/day) for reducing neuropathic pain associated with spinal cord injury. This analysis explores the relationship between pregabalin-mediated pain relief and functional improvements in these trials (N=169). Patients evaluated pain daily using an 11-point numeric rating scale. Pain improvement, from baseline to endpoint, was categorized according to clinically relevant thresholds: <0%, 0 to <15%, 15 to <30%, 30% to < 50%, or ≥50% improvement. The percentage of Patient Global Impression of Change (PGIC) responders (patients reporting much/very much improved; both studies combined)and the mean change in 10-item modified Brief Pain Inventory (BPI) Interference score (one study only) were determined for each threshold of pain reduction. The modified BPI Interference scale assesses pain interference with daily function (0=does not interfere to 10=completely interferes). The proportion of PGIC responders significantly increased with greater pain reduction; 5.0%, 11.1%, 29.7%, 41.9 and 77.8% of patients were responders at pain reduction thresholds of <0%, 0% to <15%, 15% to <30%, 30% to <50%, and ≥50%, respectively (Trend Test P<0.0001). Overall modified BPI Interference scores exhibited greater improvement at higher pain reduction thresholds; improvements were -0.99 (<0%),-0.40 (0% to <15%), -1.35 (15% to <30%), -1.03 (30% to <50%), and -2.96 (≥50%) (Linear Trend P=0.0041). Several individual modified BPI Interference items exhibited a similar trend with respect to pain reduction thresholds, including General Activity, Enjoyment of Work, Mobility, Mood, Sleep, and Normal Work (all P≤0.0104). These results show that greater functional improvements were achieved at greater levels of clinically significant pain reduction, and that improvements in function may be experienced even among patients who did not achieve clinically significant pain relief. Funded by Pfizer Inc. (Raichle, J Pain, 2006.)

(341) Pregabalin improves fibromyalgia related sleep disturbance

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Patients with fibromyalgia manifest disturbed sleep characteristics which differentiate them from primary insomnia patients and healthy volunteers-namely more frequent but shorter wake bouts. This 2-period, cross-over study investigated the effect of pregabalin (150-450mg/day) and placebo on wake- and sleep-bout parameters in FM patients &ge18y with difficulty maintaining sleep, but without history of circadian rhythm or other sleep disorder. Polysomnography was performed during 2-consecutive nights at baseline, and the end of each treatment period. Patients were selected according to study-specific criteria for sleep-maintenance problems, including polysomnography-determined wake-after-sleep-onset (WASO) &ge45mins and total-sleep-time (TST) 3.0-6.5hrs. In addition to traditional sleep measures, duration and frequency of sleep/wake bouts were analyzed. Data are least-squares (LS) mean [standard error], or LS-mean difference (pregabalin vs. placebo [95% confidence interval]). Of 119 patients randomized (103 [87%] female; 48.4y), data were available for 103 when treated with pregabalin and 106 treated with placebo. In addition to a treatment benefit with pregabalin on traditional polysomnography measures (decreased WASO and latency to persistent sleep; increased TST, sleep efficiency, and Stage 3-4 sleep), pregabalin-treated patients showed increased mean duration of sleep bouts (15.25 [0.63] vs. 11.58 [0.62] mins; difference: +3.67 [2.22, 5.12] mins; P<0.0001) and decreased number of wake bouts (33.24 [1.33] vs. 36.85 [1.32]; difference: -3.61 [-6.03, -1.18]; P=0.0039). Patients also showed decreased mean duration of wake bouts (3.4 [0.55] vs. 3.94 [0.55] mins; difference:-0.53 [-1.06, -0.002] mins; P=0.0493). Pregabalin treatment improved sleep parameters characteristics of sleep in FM, namely increased sleep bout duration and decreased wake bouts frequency vs. placebo treatment. Modifying these sleep characteristics may underlie the patient-reported efficacy of pregabalin for improving sleep-quality and -duration in FM.

(342) Safety and efficacy of gastroretentive gabapentin in real-world clinical practice for treatment of elderly patients with postherpetic neuralgia (PHN)

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This Phase 4 open-label study evaluated the safety and effectiveness of once-daily gastroretentive gabapentin (G-GR) for treatment of PHN in real-world clinical practice settings. Patients aged ≥18 years were divided into 2 cohorts: patients ≤70 years and patients >70 years. All patients were titrated to 1800 mg G-GR/day over 2 weeks and maintained at that dosage for 6 weeks, for 8 weeks of total treatment. To reflect clinical practice, exclusion criteria were limited to those in the product label. Efficacy was assessed using a visual analog scale (VAS) and the Brief Pain Inventory (BPI). Patient Global Impression of Change (PGIC) and Clinician Global Impression of Change (CGIC) scales were completed at Week 8. Treatment-emergent adverse events (TEAEs) were assessed. The efficacy population included 190 patients, 110 in the ≤70 years group and 80 in the >70 years group. The mean percent change in VAS score at Week 8 from Baseline was -21.3%/-20.4% (≤70 years/>70 years). The proportion of responders by VAS score (≥30% reduction from Baseline) was 51.8%/55.0% (≤70 years/>70 years). Patients with ≥50% reduction in VAS score from Baseline were 42.7%/37.5% (≤70 years/>70 years). BPI subscores, including interference scores, were all significantly reduced by Week 8 in both age groups. At Week 8, using the PGIC instrument, 59.0%/40.3% (≤70 years/>70 years) of patients considered their symptoms "Very much" or "Much" improved relative to Baseline. G-GR was generally well tolerated. Thirty-seven (18.8%) patients experienced TEAEs that led to study discontinuation. No patients died and 5 (2.5%) patients experienced serious TEAEs; none was considered to be related to treatment with G-GR by investigators. The most common G-GR-related TEAEs (≤70 years/>70 years) were dizziness (11.7%/16.3%) and somnolence (3.6%/8.1%). Thus, in real-world clinical practice, G-GR appears to be an effective, well tolerated treatment option for patients with PHN, regardless of patient age.

F04 Antidepressants

(343) Safety of duloxetine for the treatment of older patients with osteoarthritis knee pain or chronic low back pain

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Many people experience chronic pain as they age. Duloxetine is a non-narcotic medication for treatment of chronic pain associated with osteoarthritis of the knee and chronic low back pain as demonstrated in 5 placebo-controlled clinical trials. These studies included 839 duloxetine-treated patients, 237 (28.2%) of whom were aged ≥ 65 years. This post hoc analysis analyzed the safety and tolerability of duloxetine comparing older (≥ 65 years) and younger (18-64 years) patients during12-13 weeks of treatment. Safety was assessed by the frequency rate of ≥5% in treatment-emergent adverse events (TEAEs) for duloxetine that were also significantly higher than placebo; occurrence of serious adverse events (SAE); and significant changes in vital signs or clinical laboratory measures. The duloxetine/placebo differences in each age group were analyzed by a logistic regression model with covariates of treatment, age group, and treatment-by-age group interaction. Statistically significant interaction was defined as p<.10. In each age group, patients taking duloxetine experienced at least 1 TEAE with similar frequency (older, 57.0% vs. younger, 63.3%; p=.91, and there was no significantly greater duloxetine/placebo difference in older patients compared with younger patients for TEAEs that occurred ≥5% with duloxetine and that were significantly higher than placebo. In patients taking duloxetine, the frequency of a TEAE "Fall" was numerically higher in older patients (3, 1.3%) compared with younger patients (3, 0.5%) but without any statistically significant findings. No deaths were reported, and there were no statistically significant increases in SAEs for duloxetine patients compared with placebo in older patients. In summary, no significant treatment-by-age group interactions were observed for any of the safety analyses, which suggest that duloxetine does not present an increased risk for older patients. This work was supported by Eli Lilly and Company.