These results suggest that maintenance therapy with 1 session of rTMS per week may be able to prevent relapses in these patients, said Prof. Benadhira, who also emphasized the need for a larger study to confirm the result.

Higher Doses of Levomilnacipran May Benefit Patients With Severe Depression

Written by Nicola Parry

Gregory M. Asnis, MD, Albert Einstein College of Medicine, Montefiore Medical Center, Bronx, New York, USA, presented a poster with results of a Phase 3 trial to evaluate the efficacy and tolerability of levomilnacipran extended-release (ER) dose in adult patients with major depressive disorder (MDD) [APA 2014 (poster NR6-087); NCT00969709]. The results of the study indicated that higher doses of levomilnacipran ER may benefit some patients, including those with moderate to severe depression.

Levomilnacipran ER, a potent, selective serotonin and norepinephrine reuptake inhibitor (SNRI), is approved for use in the treatment of MDD in adults, with dose-proportional pharmacokinetic effects demonstrated in some studies [Chen L et al. APA 2013 (poster NR9-37)].

To be included in the 8-week, double-blind, multicenter, parallel-group, placebo-controlled study, patients were required to be 18 to 65 years and meet *DSM-IV-TR* criteria for MDD, with a current major depressive episode ≥8 weeks, and a score of ≥30 on the Montgomery-Asberg Depression Rating Scale (MADRS). Patients were randomized to placebo (n=179) or once-daily levomilnacipran ER 40 mg (n=181), 80 mg (n=181), or 120 mg (n=183); doses were initiated at 20 mg and titrated to the target dose over 7 days.

Exclusion criteria included patients with various psychiatric conditions, as well as nonpsychiatric conditions that may interfere with the study. Those with a history of nonresponse to ≥2 antidepressants were also excluded.

In the intention-to-treat (ITT) patient population, the primary outcome was the change in MADRS total score from baseline to the end of Week 8. Secondary outcome was Sheehan Disability Scale (SDS) total score.

Least squares mean difference (LSMD) was used to assess the relationship between levomilnacipran dose and efficacy. Compared with placebo, the LSMD for depressive symptoms (MADRS total score change) was significantly different (p=0.0186; p=0.0038; p=0.0005) for all levomilnacipran ER dose groups (40 mg, –3.23; 80 mg, –3.99; 120 mg, –4.86). The data also suggested a linear relationship between dose and efficacy.

In patients with more severe MDD (baseline MADRS ≥35), LSMD values demonstrated that improvements in depressive symptoms were significantly greater in the 80 mg (–5.14; p=0.0098) and 120 mg (–6.21; p=0.0016) groups, but not in the 40 mg group (–3.81; p=0.0558).

On the SDS, the LSMD was also significantly different for the levomilnacipran ER 80 mg (–2.51; p=0.0151) and 120 mg (–2.57; p=0.0141) groups but not for the 40 mg group (–1.41; p=0.1687).

Levomilnacipran ER was generally well-tolerated across the dosage groups. Serious adverse events (AEs) occurred in ≤2% of patients in all treatment groups, with no deaths reported. The incidence of treatment-emergent adverse events (TEAEs) was 63.6% in the placebo group, and was similar across all three levomilnacipran ER dosage groups (40 mg, 75.8%; 80 mg, 82.7%; 120 mg, 76.7%). However, a dose-related effect was observed for urinary hesitation and erectile dysfunction, which occurred in 6.1% and 9.5% of patients in the 120-mg group, respectively.

In summary, higher doses of levomilnacipran ER are associated with greater improvements in MADRS and SDS, with no overall increase in the incidence of TEAEs with higher doses. Higher doses of levomilnacipran ER may therefore benefit some patients with MDD, including those with more severe symptoms, concluded Dr. Asnis.

Potential Value of N-acetylcysteine in Reducing Cigarette Smoking

Written by Brian Hoyle

A randomized, double-blind, placebo-controlled study from researchers in Brazil and Australia has demonstrated the prowess of N-acetylcysteine (NAC) in reducing cigarette smoking for individuals previously refractory to smoking cessation efforts. Although the small number of patients precludes a definite conclusion, the potential of NAC in smoking cessation therapy is indicated. The study presenter was Eduardo Prado, MD, Londrina State University, Londrina, Brazil [APA 2014 (poster NR-8218)].

NAC is a cysteine prodrug that functions to restore glutamate homeostasis and promotes glutathione synthesis by virtue of its antioxidant activity. It has also been implicated in reducing the nicotine craving in cigarette smokers. However, the latter has not been rigorously assessed. Forty subjects were enrolled in the present 12-week study. Thirty-four subjects who had failed previous attempts to stop smoking were randomly assigned to receive 3000 mg/day of NAC (n=17) or placebo (n=17) for 12 weeks. Eleven subjects in the NAC group and 7 in the placebo group completed the study.

The primary outcome was smoking cessation as gauged by examination of the daily log of cigarette smoking maintained by each subject and objectively by