Selegiline Safe, Effective as Adjunct for Parkinson's

BY KERRI WACHTER
Senior Writer

WASHINGTON — An orally disintegrating formulation of selegiline appears to be a safe and effective adjunct for patients with Parkinson's disease who are experiencing a deterioration of levodopa response, according to data presented in a poster at the World Parkinson Congress.

Selegiline taken in the orally disintegrating form significantly decreased the amount of levodopa nonresponse time, compared with placebo in two phase III, randomized, double-blind trials, reported Dr. William G. Ondo of the department of neurology at Baylor University, Houston. Dr. Ondo performed a pooled analysis of data from the two trials.

The selective MAO type-B inhibitor selegiline is limited by low bioavailability, extensive first-pass hepatic metabolism, and the production of amphetamine metabolites.

However, orally disintegrating tablets dissolve on the first contact with saliva and undergo pregastric absorption, which minimizes first-pass metabolism while providing high plasma concentrations of the drug, Dr. Ondo wrote.

Until the development of an orally disintegrating form of the drug, selegiline—which was approved for use as an adjunct in the management of patients with Parkinson's disease who experience a deterioration in their response to treatment with levodopa/carbidopa—had been administered as a capsule or tablet to be swallowed.

He analyzed data from two trials of orally disintegrating selegiline versus placebo in patients experiencing an erosion of efficacy with optimized levodopa therapy. Patients were included in the trials if they were older than 30 years, had a confirmed diagnosis of Parkinson's disease, had a documented response to levodopa with a dopa-decarboxylase inhibitor, and experienced at least 3 hours daily when the beneficial effects of levodopa wore off.

Initially, patients in both trials were randomized to receive either 1.25 mg of orally disintegrating selegiline or placebo per day. At week 6, the dosage of orally disintegrating selegiline was increased to 2.5 mg per day. The average baseline number of "off" hours was determined using patient recordings for a 24-hour period for 2 days preceding the initial clinic visit. The average number of "off" hours throughout the trial were also determined using the diaries for the 2 days prior to clinic visits. Six visits were conducted throughout the 12-week trial.

Orally disintegrating selegiline decreased levodopa 'off' time at weeks 4-6.

DR. ONDO

In the first trial, 98 patients were randomized to selegiline and 50 to placebo; in the second, 94 patients were randomized to selegiline and 48 to placebo.

Combined results from both trials showed that orally disintegrating selegiline significantly decreased total levodopa "off" time at weeks 4-6. The treatment group had 5 hours per day during which efficacy wore off, compared with 6 hours per day for the placebo group (10% vs. 6% reductions from baseline, respectively).

Orally disintegrating selegiline also significantly decreased the percentage of levodopa "off" time at weeks 10-12. The treatment group had 4.5 hours per day during which efficacy wore off, compared with 6 hours per day for the placebo group (approximately 13% vs. 7% reductions from baseline, respectively).

Assessment of results from patients with the Clinical Global Impression of Severity and Improvement scales and the Patient Global Improvement scale significantly favored orally disintegrating selegiline as well at weeks 10-12.

Orally disintegrating selegiline was generally well tolerated in both trials. In the first trial, 8% of patients taking selegiline experienced serious adverse events, compared with 2% of patients given placebo. In the second trial, 3% of patients on selegiline experienced serious adverse events, compared with 4% of those on placebo. The most commonly reported adverse events were nausea, dry mouth, and dizziness. ■