Pramipexole Acts as Antidepressant in PD

BY SUSAN LONDON

SEATTLE — Pramipexole reduces depressive symptoms in patients with Parkinson's disease, largely independent of its effect on motor symptoms, according to the results of a randomized trial.

An estimated 45% of patients with Parkinson's disease (PD) have a depressive disorder, said lead investigator Dr. Paolo Barone, a neurologist at the University of Naples "Federico II" in Italy. Recent evidence suggests that depression is not simply reactive in this population, but occurs independently of motor symptoms and may be related to dysfunction in limbic dopaminergic circuits.

"Generally speaking, there are very few placebo-controlled studies of depression in Parkinson's disease," he noted. "We have several open-label studies showing that dopaminergic agents, pramipexole [Mirapex] in particular, are able to reduce [or] improve depressive symptoms in Parkinson's disease." Pramipexole is approved by the Food and Drug Administration for the treatment of the signs and symptoms of idiopathic Parkinson's disease and moderate to severe primary restless legs syndrome.

Patients in the trial were 30 years or older and had idiopathic PD with stable motor function; a score of 5 or greater on the Geriatric Depression Scale score; a score of 2 or greater on part I, question 3 (depression) of the Unified Parkinson's Disease Rating Scale (UPDRS); and a score of 24 or greater on the Mini-Mental State Examination, Dr. Barone reported at the annual meeting of the American Academy of Neurology

They were allowed to continue on other medications for PD, depression, and comorbidities at constant doses.

In the 12-week study, 152 patients were randomly assigned to placebo and 144 were assigned to pramipexole, with optional titration up to a dose of 1.0 mg three times a day. Rates of trial completion were 88% and 86%, respectively.

The patients were 67 years old on average, and 53% were female. The mean duration of PD was 4 years, and 77% of patients had a modified Hoehn and Yahr stage of 2 or 3. Ninety percent were receiving concomitant therapy for their PD.

Compared with Parkinson's patients on placebo, those taking pramipexole saw improvements in their Geriatric Depression Scale, UPDRS II, and UPDRS III scores.

The baseline total score on the Beck Depression Inventory (BDI) was 19.2 in the placebo group and 18.7 in the pramipexole group, corresponding to moderate depression, he said. By week 12, the respective scores were 15.0 and 13.1. The adjusted mean difference in the change in scores between groups—the trial's primary end point—was 1.9, significantly favoring the active treatment.

Compared with placebo, pramipexole was also associated with significantly greater improvements in Geriatric Depression Scale score (adjusted mean difference, 0.8), UPDRS II score (adjusted mean difference, 1.2), and UPDRS III score (adjusted mean difference, 2.2).

Control of depression and control of PD motor symptoms were only poorly correlated, Dr. Barone reported, with a correlation coefficient between the BDI score and UPDRS III score of 0.088 for placebo-treated patients and 0.215 for pramipexole-treated patients.

In addition, a path analysis showed that 80% of the treatment effect on depressive symptoms was accounted for directly by BDI score, whereas only 20% was accounted for by the indirect effect of UPDRS III score.

Adverse event profiles showed that patients in the pramipexole group had higher rates of certain types of events, compared with the control group, such as dizziness (11% vs. 6%, respectively), somnolence (10% vs. 8%), and dyskinesia (7% vs. 3%), he observed.

Dr. Barone reported that he has received research support and personal compensation for consulting activities from Boehringer Ingelheim Pharmaceuticals Inc., the manufacturer of Mirapex. ■

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