Abstract Title: #006 - A placebo controlled, randomized, double-blind study to assess the safety and clinical benefit of rasagiline as an add-on therapy to dopamine agonist monotherapy in early Parkinson’s disease (PD): The ANDANTE study

Press Release Title: New Drugs May Improve Quality of Life for People with Parkinson’s Disease

Objective: Determine the efficacy and safety of rasagiline add-on therapy for early-PD patients sub-optimally controlled by dopamine agonist (DA) monotherapy.

Author(s): Robert Hauser, MD, MBA, FAAN; Dee Silver, MD; Azhar Choudhry, MD; Stuart Isaacson, MD

Background: DAs are often used as initial symptomatic therapy for early PD. With disease progression, DA monotherapy can become suboptimal, requiring increasing dose to maintain efficacy. However, increasing DA dose is associated with a higher risk of adverse events (AEs) (Antonini et al PMID:19709931). Rasagiline is a selective, irreversible MAO-B inhibitor that reduces striatal dopamine catabolism, and this distinct mode of action provides a rationale for add-on therapy to DAs for additional symptomatic benefit.

Design/Methods: ANDANTE is a Phase-IV, 18-week study of PD patients (Hoehn&Yahr 1-3) aged ≥30 years taking stable DA dosages of ≥6 mg/day ropinirole or ≥1.0 mg/day pramipexole with suboptimal symptom control. Patients were randomized to rasagiline 1mg or placebo; DA dosage remained stable throughout. Primary outcome: change from baseline in total-UPDRS score. Secondary outcomes: changes from baseline in UPDRS activities of daily living (ADL) and motor scores, and CGI-I. Safety was assessed by AE frequency and severity, and discontinuation due to AEs. 328 patients were randomized, and 321 patients (mean age 62.6; duration PD 2.13 years) were included in the efficacy analysis.

Results: Treatment with add-on rasagiline resulted in a significant improvement in total-UPDRS score vs. placebo (Primary endpoint: treatment effect±SE -2.4±0.95 (95% CI -4.3,-0.5, p=0.012). Rasagiline also significantly improved UPDRS-motor scores (p=0.007). There were no significant differences between groups for UPDRS-ADL (p=0.301) or CGI-I scores. Rasagiline was well-tolerated, with no significant difference in percentage of patients with AEs (64.2% vs. 61.0%) or serious AEs (4.9% vs. 3.0%) vs. placebo. Only 11 patients required rescue with levodopa during the study.
**Conclusions:** Addition of rasagiline significantly improved motor symptoms in patients suboptimally controlled with DA monotherapy, and was safe and well-tolerated with an AE profile similar to placebo.

**Study Supported By:** Teva Pharmaceuticals Inc.