Once-Daily Opicapone Increases ON-Time in Patients with Parkinson’s Disease: Results from Two Phase 3 Studies
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Objective: To evaluate changes with once-daily opicapone in ON-time in Parkinson’s disease (PD).

Background: Catechol-O-methyltransferase (COMT) inhibitors were developed to prolong the clinical actions of levodopa. Opicapone is a novel, highly-selective, peripheral COMT inhibitor under development in the U.S. as an adjunct to levodopa for PD with motor fluctuations. The efficacy of opicapone has been evaluated in two international Phase 3 studies (BIPARK-1 [NCT01568073], BIPARK-2 [NCT01227655]).

Design/Methods: Participants received double-blind (DB) treatment with opicapone (5mg [BIPARK-1 only], 25mg, 50mg), entacapone 200mg (BIPARK-1 only), or placebo for 14-15 weeks added to levodopa. Participants completing DB treatment were eligible to enroll in the 1-year open-label (OL) phase of each study. Efficacy analyses included mean changes from baseline in absolute ON-time without troublesome dyskinesia (defined as either no dyskinesia or non-troublesome dyskinesia). Results for the 50mg opicapone dose are presented, along with dyskinesia as a treatment-emergent adverse event (TEAE).

Results: In BIPARK-1 (opicapone at 5mg=119, 25mg=116, 50mg=115; entacapone=120; placebo=120), a significant increase from baseline to Week 14/15 in absolute ON-time without troublesome dyskinesia was found for opicapone 50mg versus placebo (least-squares mean change [±standard error], hours): 50mg, 1.9±0.2; placebo, 0.9±0.2; P=0.002. Similar results arose from BIPARK-2 (25mg=125, 50mg=147, placebo=135): 50mg, 1.7±0.3; placebo, 0.9±0.3; P=0.025. Improvements in ON-time without troublesome dyskinesia were sustained in long-term extension studies, with mean changes from DB baseline to OL endpoint (±standard deviation) in all opicapone-treated participants of 2.0±2.6 hours for BIPARK-1 (N=494) and 1.8±3.2 hours for BIPARK-2 (N=339). In the pooled DB safety population (N=631), a TEAE of dyskinesia was reported in 17.4% of all opicapone-treated (versus 6.2% for placebo). Few subjects had dyskinesia TEAE leading to discontinuation (opicapone, 1.9%; placebo, 0.4%) or serious dyskinesia (opicapone, 0.3%, placebo, 0%).

Conclusions: Once-daily opicapone increased ON-time without troublesome dyskinesia in PD patients with motor fluctuations.