**First long-term (2-year) controlled study to evaluate treatment with safinamide as add-on to levodopa in patients with Parkinson's disease and motor fluctuations**

Anand R,[1] Borgohain R,[2] Szasz J,[3] Stanzione P,[4] Meshram C,[5] Bhatt M,[6] Lucini V[7]

*[1]APC AG, St Moritz, Switzerland; [2]Nizam's Institute of Medical Sciences, Hyderabad, India; [3]Emergency County Hospital Targu Mures, Targu Mures, Romania; [4]Clinica Neurologica, Policlinico Tor Vergata, Rome, Italy; [5]Brain and Mind Institute, Nagpur, India; [6]Jaslok Hospital & Research Centre, Mumbai, India; [7]Newron Pharmaceuticals SpA, Bresso, Italy*

**Objective:** To evaluate long-term use of safinamide as add-on to levodopa.

**Background:** In Study 016, six months' treatment with safinamide (50 and 100 mg/day) added to levodopa in Parkinson's disease (PD) with motor fluctuations significantly increased ON time with no/minor dyskinesia.

**Methods:** Study 016 and its double-blind, placebo-controlled, 18-month extension (018) assessed change over 24 months in dyskinesia, motor fluctuations, parkinsonism, UPDRS scores, and non-motor symptoms in patients with PD and motor fluctuations despite optimized antiparkinsonian treatment. Analysis was hierarchical; if the primary endpoint was not significant, subsequent endpoints were exploratory.

**Results:** 440 of 669 randomized patients completed 24 months' treatment. Baseline dyskinesia rating scale (DRS) scores were 3.4 (placebo), 3.9 (safinamide 50 mg/day), and 3.7 (100 mg/day). At Month 24, there were no significant treatment differences for DRS scores (018 primary endpoint). In post-hoc analysis of patients with baseline DRS >4, safinamide 100 mg/day improved DRS scores vs. placebo ($p<0.05$). For secondary endpoints, safinamide 50 and 100 mg/day improved ON time with no/minor dyskinesia vs. placebo, by 0.67 ($p=0.0031$) and 0.83 ($p=0.0002$) hours, respectively, i.e. the benefits in Study 016 were still present after 2 years. Improvements in OFF time, UPDRS II, III and IV, CGI-S, GRID-HAMD, and PDQ-39 were also shown for safinamide 100 mg/day vs. placebo ($p<0.05$). Incidence of adverse events and clinically-notable values were similar among groups.

**Discussion:** This is the first 2-year, prospective, placebo-controlled study in patients with mid-late PD and motor fluctuations despite optimized antiparkinsonian treatment. Safinamide improved nominal motor fluctuations, parkinsonism, activities of daily living, depressive symptoms, and quality of life without worsening dyskinesia. Lack of improvement in DRS in the overall population may reflect the low incidence of troublesome dyskinesia at baseline (32%). In patients with more severe dyskinesia, safinamide 100 mg/day improved DRS scores. Acknowledgements: On behalf of Study 018 Investigators.

Study supported by: Newron/Merck Serono S.A.–Geneva