A RANDOMIZED CLINICAL TRIAL OF FIPAMEZOLE IN THE TREATMENT OF DYSKINESIA IN ADVANCED PARKINSON’S DISEASE (FJORD STUDY)


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Objective: Fipamezole, a selective alpha-2 adrenergic antagonist, reduced LID in MPTP-lesioned monkeys. In 10 dyskinetic PD subjects, a proof-of-concept study showed similar effects at 60 and 90 mg/day. This study assessed efficacy of fipamezole (30, 60, 90 mg t.i.d.) versus placebo in suppressing levodopa-induced dyskinesias (LID) in advanced PD subjects.

Methods: This double-blind, randomized, placebo-controlled, dose-escalating 28-day study in levodopa-treated PD patients with LID was conducted at 25 U.S. centers (115 subjects) and at 7 in India (64 subjects). The primary endpoint was change from Baseline to Day 28 in a new LID rating scale, with 3 averaged assessments over 1 hr after subjects became ‘ON’ from levodopa. Outcome assessment used analysis of variance to evaluate fipamezole dose effects in a hierarchical stepwise manner, and Jonckheere’s test for dose-responsiveness.

Results: The total study population showed no statistically significant primary endpoint difference. However, because of inhomogeneity recognized between U.S., and Indian study populations, a pre-specified subgroup analysis of U.S. subjects was carried out, showing fipamezole at 90 mg reduced dyskinesia (mean LID rating improvement versus placebo: 3.7±1.0; p=0.047), with dose- responsiveness demonstrated (p=0.014 for placebo, 30, 60 and 90 mg). Fipamezole induced mild blood pressure elevation but was associated with an acceptable profile of adverse effects.

Conclusions: The evidence of efficacy in the U.S. study subgroup suggested that fipamezole may be useful to treat LID in PD without exacerbating parkinsonism.

Classification of evidence: This study provides Class I evidence that fipamezole is well-tolerated and can lessen LID with a 90 mg dose.