

AAN 69th ANNUAL MEETING ABSTRACT

Media Contacts:

Renee Tessman, rtessman@aan.com, (612) 928-6137

Michelle Uher, muher@aan.com, (612) 928-6120

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Abstract Title: Double-blind, randomized, placebo-controlled, Phase III study (TOLEDO) to evaluate the efficacy of apomorphine subcutaneous infusion in reducing OFF time in Parkinson's disease patients with motor fluctuations not well controlled on optimized medical treatment

Press Release Title: 150-year-old Drug May Provide 'Off' Time Relief for People with Advanced Parkinson's Disease

Objective: TOLEDO (NCT02006121) is the first prospective, randomized, multicenter, double-blind study to investigate the efficacy of apomorphine subcutaneous infusion (APO) versus placebo in Parkinson's disease (PD) patients with motor fluctuations not well controlled on optimized medical treatment.

Authors: Regina Katzenschlager, Werner Poewe, Olivier Rascol, Claudia Trenkwalder, Guenther Deuschl, Kallol Chaudhuri, Tove Henriksen, Teus Van Laar, Kevin Spivey, Senthil Vel, Andrew Lees

Background: Although extensive data from open-label studies with APO demonstrate its efficacy in reducing OFF time, dyskinesias and oral levodopa dose in patients with severe motor fluctuations that are poorly controlled by conventional therapy, evidence from randomized, blinded studies has been lacking.

Design/Methods: Patients from 23 centers in 7 countries were randomized to receive APO during their waking time (16±2 hours; ≤8 mg/hour), or placebo saline infusion using the same pump system. Based on efficacy and tolerability, the hourly flow rate of the infusion and dose of concomitant antiparkinsonian medication were adjusted during the first 4 weeks. The primary endpoint was the absolute change in OFF time from baseline to Week 12 based on patient diaries

Results: Compared with placebo (n=53), APO (n=53) provided significantly greater reduction (improvement) in OFF time between baseline and Week 12 (-0.58 hours versus -2.47 hours, respectively), a difference between treatment groups of -1.89 hours (95% CI: -3.16, -0.62; p=0.0025). The reduction in OFF time with APO was observed within the first week of treatment and sustained over 12 weeks, and was associated with a significantly greater increase in ON time without troublesome dyskinesia. The beneficial effects of APO were reflected in higher scores for Patient Global Impression of Change versus placebo at Week 12 (p<0.001). APO was generally well tolerated and no unexpected adverse events were observed.

Conclusions: These results show Level 1 evidence that APO provides a significant and clinically meaningful reduction in OFF time without increasing dyskinesias in patients whose motor fluctuations cannot be controlled with current standard of care, filling an important knowledge gap.

Study Supported By: Britannia Pharmaceuticals Ltd.