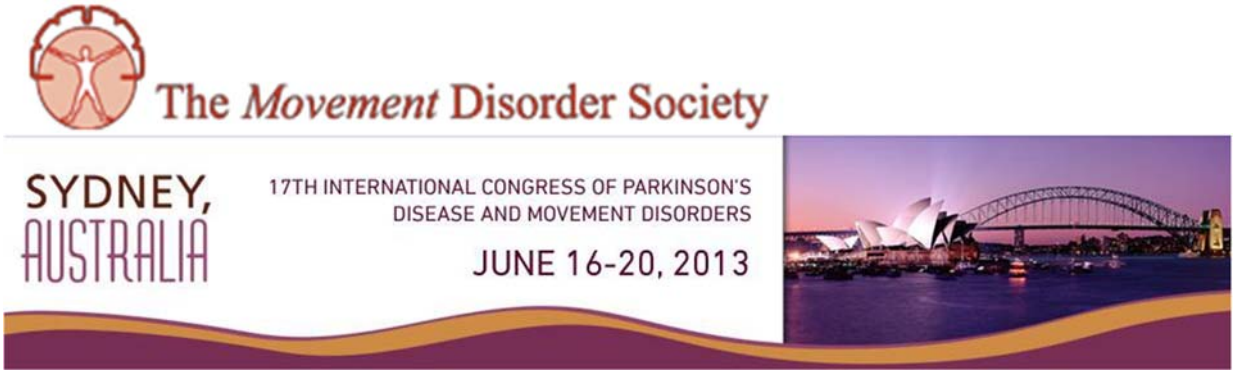

Safety and efficacy of recombinant human platelet derived growth factor BB (rhPDGF-BB) in Parkinson's Disease

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Objective: To evaluate safety, tolerability and exploratory efficacy of intracerebroventricular (ICV) administration of rhPDGF-BB (PDGF) in patients with Parkinson's disease (PD).

Background: ICV infusion of PDGF significantly and long-lastingly reduces PD-like behavior and increases dopamine-transporter (DAT) binding in animal models of PD. This effect is dependent on PDGF-induced stem/progenitor cell proliferation in the lateral ventricular wall. These findings have prompted a clinical study in patients with moderate/severe PD.

Methods: Twelve patients with idiopathic PD were implanted with a drug pump and an investigational catheter (Medtronic Inc) leading into the lateral ventricle. Patients were divided into 3 dose cohorts (0.2, 1.5 or 5 µg PDGF/day) and received either PDGF or placebo (buffer, 1 patient/cohort) for 12 days, after which all patients received buffer and were followed up to Day 85. Study objectives included continuous safety and tolerability assessments and UPDRS, MADRS, MMT, EQ5-D and DAT-binding (PET) assessments pre-treatment and at the end-of study.

Results: There were no unresolved adverse events related to the drug, the infusion system or implant procedure. Most patients improved in motor symptoms with no significant differences between dose cohorts. There were no significant therapeutic effects as assessed with MADRS, MMT or EQ5-D. Placebo patients displayed an expected reduction in DAT-binding over time. Patients in the highest dose group showed not only stabilization, but an increase in DAT-binding in regions of dopaminergic denervation with a maximum in the putamen (P=0.002).

Conclusions: ICV delivery of PDGF was safe and well tolerated and resulted in a significant dose-dependent positive effect on DAT-binding. The data support further clinical studies as PDGF may potentially slow down or reverse the nigrostriatal degeneration in PD.