Combining Cell Therapy with Deep Brain Stimulation for the Treatment of Parkinson's Disease

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Objective: Determine the safety and feasibility of implanting autologous peripheral nerve grafts in subjects with Parkinson's disease undergoing deep brain stimulation (DBS) surgery and treatment. Introduction: DBS is FDA approved for the treatment of several conditions including Parkinson's disease (PD). However, many PD-related symptoms are not relieved through the use of DBS. We have coupled peripheral nerve graft delivery, to areas of the brain affected in PD, with DBS surgery. We recently completed a 1-year Phase I study (NCT01833364). Here we describe a follow-up, ongoing clinical trial examining the safety and feasibility of implanting autologous peripheral nerve grafts into an area of the brain affected by PD in patients undergoing DBS surgery.

Methods: Multi-stage, DBS surgery targeting the subthalamic nucleus or internal globus pallidus was performed using standard procedures. After the DBS electrodes were implanted, a section of sural nerve was unilaterally delivered into the substantia nigra or the nucleus basalis of Meynert (NBM). Adverse events were continuously monitored. Assessments include neurocognitive performance, quality of life, gait, (123I-ioflupane) SPECT imaging, and MR imaging at baseline and at the end of the study, 24 months after surgery. Participants also undergo a motor assessment (Unified Parkinson's Disease Rating Scale: UPDRS) evaluation before surgery and at 6, 12, 18 and 24 months after surgery.

Results: We have begun a follow-up, open-label two-year study of safety and feasibility (NCT02369003). Mean age for participants is 65.2 ± 7.6 (mean ± SD, N=24), Hoehn & Yahr score: 3.0 ± 0.7, motor scores (UPDRS part III) OFF medication: 37.1 ± 10.1, and ON medication: 18.5 ± 8.6. At baseline, participants showed a unilateral or bilateral decrease in 123I-ioflupane (DaTscan™) binding with SPECT imaging. In total, we have completed peripheral nerve graft delivery to the substania nigra in 25 participants and to the NBM in 7 participants. Immediate post- operative MRI scans did not indicate evidence of abnormal tissue disruption. Adverse event profiles were comparable to standard DBS surgery.

Conclusions: Initial results from two clinical trials indicate a potentially safe and feasible means of delivering biological therapy at the time of DBS surgery. On-going evaluations will further help assess the safety and feasibility of implanting peripheral nerve tissue in conjunction with DBS implant surgery for patients with PD and the potential benefits it may provide.