

TITLE: ASPIRO Trial – Twelve-month safety, tolerability, and efficacy of intracranial delivery of autologous iPSC-derived dopaminergic precursors (*Sasineprocel*) in moderate to advanced Parkinson's Disease

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AIMS: The study's primary aim is to assess safety and tolerability of bilateral administration of autologous induced pluripotent stem cell (iPSC) derived dopaminergic neuron precursors (DANPCs) into the post-commissural putamen. The study's secondary aim is to evaluate clinical efficacy of the therapy as measured by mean change from baseline in multiple patient- and clinician-reported PD-specific outcomes.

METHODS: A first-in-human, open-label phase 1/2a trial evaluating safety, tolerability, and efficacy of intracranial implantation of two doses of autologous iPSC-derived DANPCs in subjects with moderate to advanced PD. The product was derived from skin fibroblasts which were converted into iPSCs and then differentiated into DANPCs. Four patients received 5 million cells/hemisphere, and four patients received 5 to 10 million cells/hemisphere under MRI guidance via occipital surgical approach. Top-level clinical outcomes were assessed every six months after transplantation.

RESULTS: At twelve months, no serious surgical adverse events nor any graft induced dyskinesia were observed. No symptomatic hemorrhages or infarctions were observed. Real time intraoperative MRI confirmed accurate placement of the DANPCs into the post-commissural putamen. Both dosing cohorts showed improvements in mean Good ON time (2 hours in low dose (LD), 2.4 hours in high dose (HD)), mean MDS-UPDRS III OFF scores (15.5 points in LD, 13.5 points in HD), mean MDS-UPDRS II scores (5.3 points in LD, 2.3 points in HD), and mean PDQ-39 scores (51.6% in LD, 28.5% in HD).

CONCLUSIONS: Twelve-month data show that the surgical procedure and cell product were safe and well tolerated. MRI confirmed accurate cell placement. At one year, improvements were seen in Good ON time, MDS-UPDRS III OFF scores, MDS-UPDRS II scores, and PDQ-39 scores across both dosing cohorts. Collection of longer-term safety and efficacy data is ongoing.