

Pathological findings from two Parkinson disease patients after intraputamina

Vanessa Smith, MD¹ • Tritia Yamasaki, MD, PhD² • Yi Ai, PhD³ • Don Gash, PhD³ • Peter Nelson, MD, PhD¹ • Gerhardt Greg, PhD³ • John Slevin, MD²

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¹Pathology, University of Kentucky • ²Neurology, University of Kentucky • ³Anatomy and Neurobiology, University of Kentucky

Objective: To describe the postmortem findings from two patients who underwent intraputamina

Background: GDNF has been shown to have neuroprotective and neuroregenerative effects in vitro, and antiparkinsonian effects in animal models. Intraputamina

Methods: These patients were part of a ten patient cohort for an FDA-approved Phase I trial conducted in 2003. In this study, GDNF was continuously infused with dose-escalation through a unilateral intraputamina

Results: Here we report the pathological findings of two patients approximately one decade post intraputamina

infusion. Clinically, both patients had a significant improvement in motor scores by 6 months and 1 year of treatment, which was lost within 9 months of GDNF withdrawal. Unilateral administration of GDNF in the two patients did not demonstrate detectable long-term effects in terms of significant gliosis at the infusion site. There was no evidence of cerebellar lesions or Purkinje cell loss similar to what was seen in a preclinical primate toxicology study, which also supports the results of a prior MRI study of these patients. As expected, Lewy body pathology consistent with advanced PD was seen in both cases. One patient had a post-study course complicated by metastatic melanoma.

Conclusions: This is the first post-mortem study of GDNF intraputamina