INTRODUCTION
Levodopa therapy for Parkinson’s Disease (PD) becomes less effective over time, possibly due to the loss of the enzyme that converts dopamine into the presynaptic α-amino acid decarboxylase (AADC; Article 1A). Nigrostriatal autapses are the major source of AADC in the human brain, so as PD progresses and the cells die, AADC is lost. This prevents consistent, reliable synthesis and release of dopamine in response to levodopa, resulting in motor fluctuations.

Aim: Determine the safety of MRI-guided infusion of up to 900µL/putamen of VY-AADC01, an AAV gene therapy that replaces AADC.

Methods: Fifteen subjects with disabling motor fluctuations despite optimal medical management were recruited at the University of California- San Francisco (UCSF); University of Pittsburgh; and the University of California – Los Angeles. VY-AADC01 vector was co-infused with gadolinium to provide MRI guidance. MRI was used to monitor the infusions with MRI. Previous gene therapy trials used non-MRI-guided approaches.

Results: The infusions were well-tolerated with no vector-related SAEs. Of the 15 subjects, 4 had not reached 12-month follow-up. Data were available from 5/5 pts (Cohort 1) and 3/5 pts in Cohort 2. 2/5 pts in Cohort 2 had not reached 12-month follow-up.

Conclusion: VY-AADC01 is an AAV gene therapy that replaces AADC. Proof-of-concept results from an ongoing open-label, phase 1b study suggest that intraputaminal VY-AADC01 vector infusion is safe and may improve motor function in PD patients with disabling motor fluctuations.

INTRAPUTAMINAL AADC GENE THERAPY (VY-AAC01) FOR ADVANCED PARKINSON’S DISEASE: INTERIM RESULTS OF A PHASE 1b TRIAL

Levodopa is the gold standard of treatment for Parkinson’s disease (PD), but its effectiveness declines over time, a phenomenon known as levodopa-induced motor fluctuations. A potential solution is to use gene therapy to replace the enzyme aromatic L-amino acid decarboxylase (AADC), which converts dopamine into L-norepinephrine and L-epinephrine, thereby reducing fluctuations.

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