THE PLASMA FOR ALZHEIMER SYMPTOM AMELIORATION (PLASMA) STUDY.

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Background : Plasma obtained from young mice has been demonstrated in aged mice to restore memory and to stimulate synaptic plasticity in the hippocampus. Whether these findings translate to man is unknown as the effects of plasma on cognitive function have not yet been studied in aged humans or in patients with Alzheimer's disease (AD). The primary objective of this study was to assess the safety, tolerability and feasibility of infusions of plasma from 18-30-year-old donors in patients with mild to moderate AD. Secondary objectives were to determine the effect of plasma infusions on cognition, functional ability, and mood. Evaluation of potential effects on functional connectivity in the default mode network and the identification of plasma components associated with aging and Alzheimer's disease were exploratory endpoints.

Methods : Patients with mild to moderate AD were recruited for a safety, tolerability and feasibility study of infusions of young plasma in humans. Nine subjects were enrolled and randomized to treatment under a double-blind crossover protocol with four once-weekly infusions of either ~250mL of plasma from 18 to 30-year-old male donors or saline, followed by a 6-week washout and then crossover to four once-weekly infusions of the alternate treatment. An additional 9 subjects were enrolled and treated under an open label amendment with four once-weekly infusions of ~250mL of plasma from male donors aged 18-30. As part of this study, patients and/or informants were administered the ADAS-Cog 13-item version, Trail Making Test Part A (TMTA) and Part B (TMTB), Geriatric Depression Scale (GDS), Neuropsychiatric Inventory (NPI-Q), Clinical Dementia Rating Scale Sum of Boxes (CDR-SB), the Functional Activities Questionnaire (FAQ) and the Alzheimer's Disease Cooperative Study Activities of Daily Living Inventory (ADCS-ADL) prior to infusions, after the fourth infusion, and after the eighth infusion (when applicable). All analyses were carried out in the R programing language and environment. Safety measures were compared between baseline and 4-week post-treatment timepoints using paired nonparametric rank tests. For each cognitive and functional measure, we performed a linear mixed-effects regression analysis of both the crossover and open-label patients. The linear mixed-effect regression model also takes into account performance at baseline, repeated measures, and missing data.

Results : Results describing the primary endpoints of safety, tolerability and feasibility will be presented and analyzed. Results describing the secondary and exploratory endpoints will be presented and analyzed.

Conclusion : Conclusions will be presented.