A Pilot Study of Adoptive Cellular Immunotherapy for Progressive Multifocal Leukoencephalopathy with Ex Vivo Generated Polyomavirus-Specific T-cells

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Objective: To determine safety of adoptive transfer of donor-derived anti-polyomavirus-specific T cells (PyVSTs) for treatment of patients with refractory progressive multifocal leukoencephalopathy (PML)(NCT02694783).

Background:
PML is an opportunistic infection of the central nervous system mediated by JC polyomavirus (JCV) occurring in immunosuppressed patients, including HIV/AIDS, primary immunodeficiency, hematological malignancies or following immunosuppressive therapy for transplant or autoimmunity. The disease is typically fatal unless adaptive immunity to JCV is restored.

Design/Methods: Using peptide libraries derived from BK Large T (LT) and Viral Protein 1 (VP1) that are highly cross-reactive with the structurally-homologous JC proteins, PyVSTs were generated from partially-matched 1st degree relatives of patients with PML with no other treatment options. Patients initially received 1x10⁶ PyVST cells/kg, followed by up to two additional infusions at 2x10⁶ PyVSTs/kg, a minimum of 28 days apart. Safety monitoring period was 28 days after each infusion. Serial MRI and lumbar punctures were performed to monitor response for 12 months following the last infusion.

Results: Twelve subjects received at least one infusion. No serious treatment-related adverse events were observed, including no overt immune reconstitution inflammatory syndrome (IRIS). One subject withdrew following his first infusion due to difficulty with travel. One subject clinically stabilized after 2 infusions. Six subjects received 3 infusions; of these, 3 died of refractory PML >30 days after last infusion. One subject completed one-year follow-up with stable PML. Two subjects whose had PML stabilized withdrew from study prior to completion of follow-up due to relapse of underlying disease. One patient remains in follow-up post 3 infusions; three subjects continue in the treatment phase.

Conclusions: PyVTs generated from healthy related donors can be safely used for adoptive immunotherapy of severely immunocompromised patients with PML. Our data suggest possible efficacy of this strategy as a life-saving therapy for patients who otherwise face a dismal prognosis.