bound S1P does not suppress lymphocyte egress suggesting that its large size prevents it from entering secondary lymphoid organs and acting as a functional antagonist to down-regulate lymphocyte S1PR1. Studies on chaperone bound S1P action on ECs during pathological changes will be presented. These mechanistic studies have deepened our understanding of S1P biology thus allows rational design of new therapeutic approaches to not only tame the immune system but also enhance vascular endothelial functions.

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Lupus Clinical Trials

1207 UPDATE ON PROGRESS OF THE MESENCHYMAL STEM CELL TRIAL IN REFRACTORY LUPUS

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Body There is a growing interest and use of cellular therapies in almost all fields of medicine. Mesenchymal stromal cells (MSCs) are pluripotent in their ability to differentiate in chondrocytes, adipocytes and osteoblasts. They more recently were reported to have significant immune activity, primarily by producing anti-inflammatory molecules. They can be derived from umbilical cords, adipose tissue and bone marrow primarily. Recent studies have tested their safety and efficacy in immune mediated diseases including graft versus host disease, inflammatory bowel disease and Type 1 diabetes among others. Reports of uncontrolled trials of MSCs in China suggest safety and efficacy of MSCs as treatment for refractory lupus. Based on encouraging results of a Phase I trial of 6 patients with lupus treated with MSCs, we initiated the first placebo-controlled trial of MSCs to treat lupus patients refractory to standard of care medications. There are nine participating centers across the US. The trial has two cohorts, one receiving low dose MSCs (one million cells/kg) and a high dose cohort of five million cells per kg, given as a one-time infusion. Patients then attend 10 follow-up visits over a year. Primary outcome is a decrease in the SRI of 4 at week 24. Inclusion criteria are patients with confirmed lupus refractory to 6 months of standard of care therapy. The first patient was screened in November of 2018. Patients are randomized with a 2/1 ratio of MSCs/placebo. Cohort 1 consisting of 41 patients was completed in May of 2021. We have infused 10 out of 40 patients in Cohort 2 to this point. Extensive studies of B cell, T cell, monocyte, dendritic cell and PMN number, function and phenotype are being performed. To this point there are no safety signals or concerns with DSMB reviews quarterly. There have been no SAEs.