AUBURN UNIVERSITY
MRI Research Center

HUDSONALPHA
INSTITUTE FOR BIOTECHNOLOGY

A COMPREHENSIVE ANALYSIS OF RELAPSE IN MULTIPLE SCLEROSIS

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BACKGROUND

The Neurosciences have ushered in an era of astounding discovery. Yet there is still much to learn about the complexities of neurological diseases, especially Multiple Sclerosis. Therefore the Tanner Center for MS formed an alliance with the HudsonAlpha Institute of Biotechnology, and Auburn University utilizing 7T Imaging. Our specific purpose was to apply immunogenomic analysis, and advanced imaging of documented clinical MS relapses treated with 14 days of Acthar gel.

OBJECTIVES

The purpose of the study is to better understand the immunology, imaging metrics and clinical outcomes of subjects treated with Acthar Gel administered for 14 days rather than the current 5 day treatment.

METHOD

This is an observational cohort study comprised of 20 subjects with Relapsing Forms of MS, seen within 72 hours of relapse onset. Baseline labs for immunogenomic analysis, and 7T Imaging are performed followed by 14 days of Acthar gel. Additional labs are drawn at Days 5,14, 30. For immune repertoire analysis, peripheral blood mononuclear cells are purified using a Ficoll density gradient, and are then sorted into panB, panT, monocytes, T helper, regulatory T and T cytotoxic cell populations. Cell-specific TCR beta and IgH variable region genes are amplified from extracted cellular RNA using amplicon-rescued-multiplex-PCR (arm-PCR) and are sequenced using Illumina next generation sequencing platforms. 7T imaging is performed at baseline and at Day30 utilizing T2 FLAIR, T1 MPRAGE, SWI, and T1 post contrast at 8,14, and 20 minutes.

RESULTS

Immunogenomic analysis has been completed with VDJ rearrangements for 6 cell subsets covering 4 timepoints of 5 subjects (120 libraries) have been generated. The distribution of CDR3 sequences, corresponding to the T cell and B cell receptors were examined for changes in overall diversity levels (D50 measurements), CDR3 length distribution, V- and J- usage frequencies, and N-addition and trimming to assess the effect of treatment on different cell subsets for the first 5 subjects. The qualitative MRI analysis confirms that 7T imaging utilizing T2 FLAIR, T1 MPRAGE, and delayed contrast is robust in confirming both inflammation and axonal degeneration.

CONCLUSION

Initial immunogenomic analysis and 7T MRI data of subjects who received Acthar gel for up to 14 days are presented. Notably, the regulatory T cell subset shows a statistically significant decrease in D50 values after initial treatment and persisting through D14, indicating a clonal expansion in this important cellular subset. In addition the initial MRI analysis indicates improved metrics in confirming an inflammatory response as well as secondary axonal degeneration. Identified trends will be reevaluated as more subject data becomes available.

Grant provided by Mallinckrodt Pharmaceuticals