AB003. Increased CD69+ tissue-resident memory T cells and STAT3 expression in cutaneous lupus erythematosus patients recalcitrant to antimalarials

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Background: Cutaneous lupus erythematosus (CLE) is an autoimmune disease involving T lymphocytes, plasmacytoid dendritic cells (pDCs), and myeloid dendritic cells (mDCs). While oral antimalarials, including hydroxychloroquine (HCQ) and quinacrine (QC) are first-line systemic therapy for all CLE subtypes, some patients remain refractory to both HCQ and HCQ + QC. To better understand reasons for refractoriness in CLE, we investigated the immunologic characteristics of patients who responded to antimalarials versus those who did not.

Methods: Biopsies from 65 CLE patients with well characterized treatment response to HCQ (n=22) and HCQ + QC (n=24), as well as treatment failure to HCQ + QC (n=19) were studied via immunohistochemistry and polymerase chain reaction. Lesional skin was biopsied prior to antimalarial treatment. The patient's CLASI score—a measure of disease activity—at the time of the biopsy was also determined.

Results: Immunohistochemistry showed CD69+ tissue-resident memory T (T_{RM}) cells were significantly higher in HCQ + QC-nonresponders compared to HCQ- and HCQ + QC-responders. mDCs were significantly higher in HCQ +QC-responders compared to HCQ-responders and HCQ + QC-nonresponders. There were significantly higher pDCs in the HCQ-responders compared to the nonresponders. CLASI scores of HCQ + QC-nonresponders correlated positively with the number of T_{RM} cells (r=0.6254, P=0.017) and macrophages (r=0.5726, P=0.041). mRNA expression demonstrated high STAT3 expression in HCQ + QC-nonresponders.

Conclusions: An increased number of CD69+ T_{RM} cells and correlation between CD69+ T_{RM} cells and macrophages with CLASI scores in the HCQ + QC-nonresponders, a finding not seen in either HCQ or HCQ + QC-responders, may suggest CD69+ T_{RM} cells and macrophages are involved in antimalarial-refractory skin disease.

Keywords: Cutaneous lupus erythematosus (CLE); antimalarials; tissue-resident memory T cell; myeloid dendritic cell (mDC)

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