AB018. Myeloid dendritic cells (mDCs) are major producers of interferon-beta in dermatomyositis and increased numbers of mDCs are found in hydroxychloroquine nonresponders

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Background: Dermatomyositis (DM) is an autoimmune disease affecting skin, skeletal muscle, and lungs. Pathogenesis is considered largely driven by interferon-beta (IFN-beta) and involves CD4+ cells and dendritic cells (DCs). (I) Quantify inflammatory cells and IFN-beta in skin; correlate with Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) scores. (II) Identify DC type contributing to refractoriness to hydroxychloroquine (HCQ). (III) Compare IFN-beta production by mDCs *vs.* pDCs in DM.

Methods: (I) DM skin biopsies evaluated for cells and cytokines using IHC from 12 patients with moderate-severe skin disease at baseline and after 12 weeks of therapy. (II) IHC performed on skin biopsies to compare myeloid DC (mDC) and pDC expression in HCQ-responders *vs.* -nonresponders. (III) Flow cytometry performed on PBMCs from 5 healthy controls and 5 DM patients.

Results: (I) CD4+ cells, macrophages, mDCs, and TRM cells were the most populous in DM skin, followed by CD8+ cells, mast cells, and pDCs. Change in CD4+ and CD8+ cells/HPF significantly correlated with change in CDASI scores (r=0.82, P<0.05; r=0.81, P<0.05). Changes in IFN-beta protein expression correlated with change in CDASI scores (r=0.63, P<0.05). (II) Significantly increased mDCs/HPF found in skin of HCQ nonresponders (P<0.05). (III) mDCs and pDCs both produced IFN-beta in DM patients; pDCs were dominant producers of IFN-beta in healthy controls.

Conclusions: mDCs are major producers of IFN-beta in DM patients and may play an important role in DM pathogenesis.

Keywords: Dermatomyositis (DM); interferon-beta (IFN-beta); dendritic cells (DCs)

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