

ABSTRACT NUMBER: 2977

# Lenabasum, a Cannabinoid Type 2 Receptor Agonist, Reduces T-Cell Population and Downregulates Type 1 and 2 Interferon Activities in Lesional Dermatomyositis Skin

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**Meeting:** 2018 ACR/ARHP Annual Meeting

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## SESSION INFORMATION

**Date:** Wednesday, October 24, 2018

**Session Title:** 6W022 ACR Abstract: Muscle Biology, Myositis & Myopathies II: Clinical & Misc Topics (2976-2981)

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 11:00AM-12:30PM

**Background/Purpose:** Lenabasum is a synthetic, non-immunosuppressive, selective cannabinoid receptor type 2 (CB2) agonist that activates resolution of innate immune responses. CB2 is a G-protein coupled receptor found primarily on activated immune cells. Lenabasum has improved skin inflammation and fibrosis in systemic sclerosis patients. In-vitro, it has shown to affect T-cell activity, alter Th1 and Th2 cytokine production, and decrease type I interferon activity. We sought to characterize the in vivo effect of lenabasum on inflammatory cells and cytokines thought to be involved in the disease pathogenesis of dermatomyositis (DM).

**Methods:** 22 adult patients with refractory, skin-predominant DM on stable standard-of-care treatments were recruited for a double-blind, placebo-controlled, randomized trial. 86% percent of subjects were on stable immunosuppressive medications. Lenabasum was initially administered orally at a dose of 20 mg a day for 4 weeks, which was subsequently raised to 20 mg twice a day for an additional 8 weeks. In a subset of subjects, lesional skin biopsies were collected at baseline and at Week 12. Immunohistochemical staining of CD4, IFN-beta, IFN-gamma, IL-4, IL-31 and IL-31 RA and QRT-PCR for Type I IFN, IFN-gamma, and IL-4 were performed on RNA extracted from the tissue samples. Sections were analyzed using the Nikon Eclipse 80i microscope. The percentage of the dermis with positive staining was quantified using NIS Elements Software. Comparisons of percent area of protein staining in the dermis and mRNA levels of various cytokines between lenabasum and placebo groups were performed using the Wilcoxon signed-rank test.

**Results:** There was strong co-localization of CB2 with Th1 CD4+ T cells in baseline biopsies. CD4+ area in the skin biopsies from lenabasum-treated subjects were significantly decreased at Week 12 compared to the placebo group ( $p < 0.05$ ). There were significant reductions in type I IFN signature, IFN-beta protein staining, and IFN-gamma mRNA and protein staining at Week 12 in subjects on lenabasum compared to those on placebo ( $p < 0.05$  for all). IL-31 protein ( $p < 0.01$ ) was reduced at Week 12 in subjects who received lenabasum compared to those taking placebo, but IL-31 mRNA expression and IL-31RA+ protein staining did not change. There were no changes in IL-4 protein or mRNA expression.

**Conclusion:** Lenabasum reduces Type 1 and 2 interferon levels as well as T cell inflammation in dermatomyositis. These effects have the potential to inhibit underlying disease pathways in DM and thus contribute to any clinical benefit of lenabasum in DM.

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**Disclosure:** **N. Reddy**, None; **M. Zeidi**, None; **B. White**, Corbus Pharmaceuticals, Inc., 3; **V. P. Werth**, Corbus Pharmaceuticals, Inc., 5, 9.

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