

Dermatology

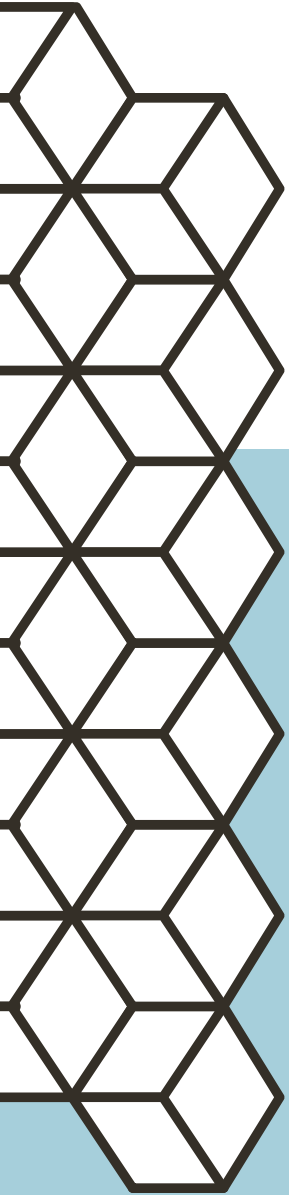
INSIDE

ACTINIC KERATOSIS 2

RX IDEA #2 3

RX IDEA #3 4

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ACTINIC KERATOSIS

Actinic keratosis is a precursor to cutaneous squamous cell carcinoma. Long treatment durations and severe side effects have limited the efficacy of current actinic keratosis treatments. Thymic stromal lymphopoietin (TSLP) is an epithelium-derived cytokine that induces a robust antitumor immunity in barrier-defective skin. Here, we investigated the efficacy of calcipotriol, a topical TSLP inducer, in combination with 5-fluorouracil (5-FU) as an immunotherapy for actinic keratosis.

The mechanism of calcipotriol action against skin carcinogenesis was examined in genetically engineered mouse models. The efficacy and safety of 0.005% calcipotriol ointment combined with 5% 5-FU cream were compared with Vaseline plus 5-FU for the field treatment of actinic keratosis in a randomized, double-blind clinical trial involving 131 participants. The assigned treatment was self-applied to the entirety of the qualified anatomical sites (face, scalp, and upper extremities) twice daily for 4 consecutive days. The percentage of reduction in the number of actinic keratoses (primary outcome), local skin reactions, and immune activation parameters were assessed.

Calcipotriol suppressed skin cancer development in mice in a TSLP-dependent manner. Four-day application of calcipotriol plus 5-FU versus Vaseline plus 5-FU led to an 87.8% versus 26.3% mean reduction in the number of actinic keratoses in participants (P <0.0001).

Importantly, calcipotriol plus 5-FU treatment induced TSLP, HLA class II, and natural killer cell group 2D (NKG2D) ligand expression in the lesionall keratinocytes associated with a marked CD4+ T cell infiltration, which peaked on days 10-11 after treatment, without pain, crusting, or ulceration.

The authors findings demonstrate the synergistic effects of calcipotriol and 5-FU treatment in optimally activating a CD4+ T cell-mediated immunity against actinic keratoses and, potentially cancers of the skin. (J Clin Invest. 2017;127(1):106-116.)

Compounded Medication

5-FU 5% / Calcipotriene 0.005%

Topical Cream

15gm or 30gm

Apply a thin layer to AA BID