The Editor's Choice

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Apremilast Mechanism of Efficacy in Systemic-Naive Patients With Moderate Plaque Psoriasis: Pharmacodynamic Results From the UNVEIL Study

Pharmacodynamic (PD) subanalyses of clinical trials in patients with moderate to severe psoriasis demonstrated the efficacy of apremilast correlated with reductions in cytokines involved in the pathogenesis of psoriasis.

Strober et al evaluated the relationship between efficacy and changes in inflammatory biomarkers with apremilast versus placebo in PD subanalysis of a phase IV, randomized, controlled trial (UNVEIL) in systemic-naive patients with moderate plaque psoriasis. Of 221 randomized patients, 38 were included in PD analyses (placebo, n=12; apremilast, n=26). Median percentage reductions in plasma cytokine levels were significantly greater with apremilast versus placebo for IL-17A, IL -17F, and IL-22 at Week 4 and IL-22 at Week 16. At Week 16, in patients receiving apremilast, improvement in PGAxBSA significantly correlated with change in IL-17A. Adipokines, apolipoproteins, and T-cell population levels were largely unchanged. Clinical improvements in psoriasis correlated with apremilast-mediated decreases in IL-17A without significantly affecting systemic IL-23 levels, adipokines, or Th17 and regulatory T-cell numbers.

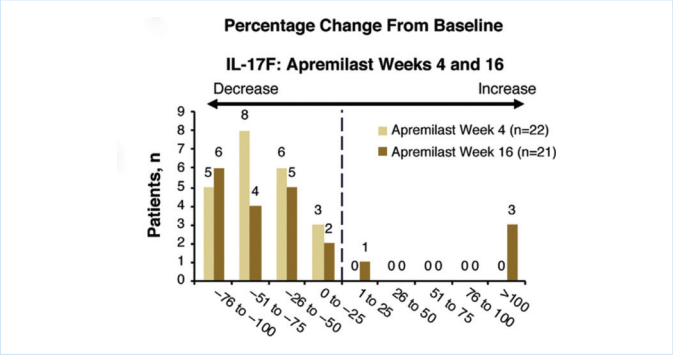

Fig. 1. a–h. Percentage Change From Baseline in Cytokine Levels at Week 4 and Week 16 IL = interleukin.

Possible therapeutic applicability of galectin-9 in cutaneous T-cell lymphoma

Galectin-9, a member of the galectin family, can promote tumor growth through inducing apoptosis in anti-tumor immune cells via T cell immunoglobulin and mucin domain 3 (TIM-3). On the other hand, galectin-9 also induces tumor cell apoptosis in many malignancies and thought to have potential as an anti-cancer agent. Nakajima R et examined the expression and therapeutic applicability of galectin-9 in cutaneous T-cell lymphoma (CTCL). Galectin-9 was expressed on tumor cells in lesional skin of CTCL and the expression levels were associated with decreased CD8+ T-cell infiltration. Serum galectin-9 levels were correlated with disease severity markers. High-dose galectin-9 induced cell death of CTCL cell lines through activation of caspase-3 and caspase-9, independently of TIM-3. High-dose galectin-9 suppressed the growth of CTCL cells and EL-4 cells *in vivo*. Galectin-9 expression on tumor cells may be associated with CTCL progression through attenuating anti-tumor immunity. On the other hand, exogenous high-dose galectin-9 administration can be a therapeutic strategy for CTCL.

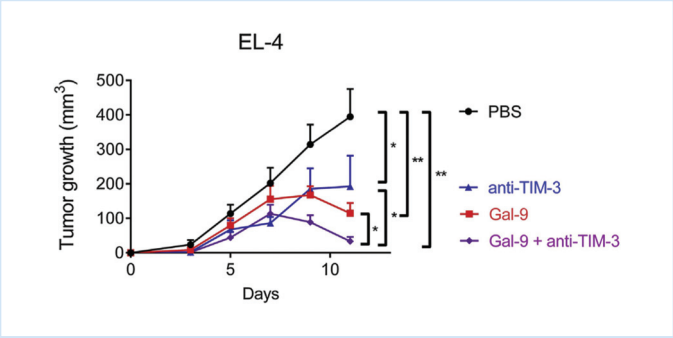

Fig. 6. Additional anti-TIM-3 blocking antibody administration augments galectin-9-induced inhibition of tumor growth of T-cell lymphoma cells *in vivo*.
(C) EL-4 cells were injected into WT mice. Mice were treated with PBS alone, recombinant human galectin-9, anti-TIM-3 blocking antibody, or combination of them. Recombinant human galectin-9 (1 μg/mouse) were injected subcutaneously on days 0, 4, and 7. Anti-TIM-3 blocking antibody (50 μg/mouse) were injected subcutaneously on days 4, and 7. The tumor volume was calculated using the equation: $V = \pi$ (length × width × height)/6, where V = volume (mm^3). n = 8-13.

Antioxidant cinnamaldehyde attenuates UVB-induced photoaging

Ultraviolet (UV) irradiation disrupts skin through several deleterious actions, such as induction of reactive oxygen species (ROS), DNA damage, and collagen degradation. Cinnamaldehyde (CIN) is a major constituent of the cinnamon and it possesses potent antioxidative activity. Tanaka Y et al investigated protective effects of CIN against UVB-induced photodamage. CIN significantly reduced the ROS production and accelerated the repair of DNA damage photoproducts in UVB-irradiated human keratinocytes *in vitro*. In the mouse model, topical application of CIN significantly inhibited wrinkle formation, epidermal hyperplasia, and dermal inflammatory cell infiltration. The antioxidative process was significantly promoted in the CINapplied site, as evidenced by upregulation of the antioxidative enzyme Hmox1 as well as the reduced accumulation of malondialdehyde. In addition, topical application of CIN normalized the UVB-induced collagen/*Col1a1* downregulation and the UVB-induced Mmp13 upregulation, implying the prevention of UVB-induced collagen degradation. CIN and CIN-containing herbal agents may exert potent protective effects against UVB exposure on skin.

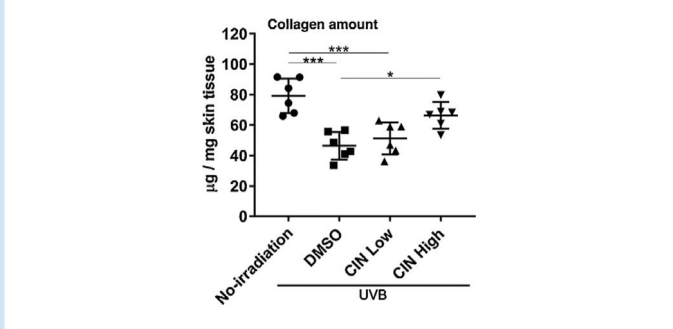

Fig. 5. UVB-induced collagenolysis is prevented by CIN.
(B) total collagen amount (μg per mg skin tissue) in the dorsal skin of mice were evaluated.