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A pilot study evaluating the efficacy of apremilast in the treatment of subjects with severe recurrent aphthous stomatitis

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Background: Recurrent aphthous stomatitis (RAS) affects both sexes with significant QoL impact. In severe disease (complex aphthosis), debilitating oral ulcers are recurrently present. Although no principal etiology has been established, immune up-regulation plays a role. Apremilast, a phosphodiesterase-4 inhibitor, down-regulates inflammatory response by modulating expression of TNF- α , interferon- γ , and interleukins 2, 12, 17, and 23. It is FDA approved for plaque psoriasis and was recently shown effective for Behçet disease aphthosis.

Objective: To evaluate efficacy of apremilast in RAS.

Methods: 15 RAS patients received apremilast 30 mg twice daily for 15 weeks after 1 week titration. Inclusion criteria were monthly oral ulcers in preceding 6 months; at least 2 ulcers in previous 4 weeks; 3 ulcers during flares; inadequate control with topical therapy. Exclusion criteria were immune-modulating therapy or systemic steroids, pregnant or breast-feeding women, systemic infection, celiac, depression, malignancy or vitamin deficiencies. Patients were assessed monthly, evaluating number of ulcers, visual analog pain scale, physician's global assessment and Chronic Oral Mucosal Disease Questionnaire (COMDQ).

Results: Within 4 weeks of therapy, there was complete clearance of lesions in majority of patients, remission was sustained during 16 weeks treatment. COMDQ responses improved considerably from baseline to week 8, and was continued until week 16. Commonest adverse effects were GI related, but were mild and tolerable, resolving by week 4.

Conclusions: Apremilast showed high efficacy in RAS, with rapid, impressive response and excellent safety profile. Given its efficacy in this pilot study, future larger studies are recommended to confirm efficacy and determine ideal dosing.

Commercial disclosure: None identified.



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Evolving resolution of clinical, cellular, and transcriptomic inflammatory markers during 1-year IL-17A inhibition by secukinumab

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Introduction: The objective was to determine the effect of 52-week secukinumab treatment on clinical and transcriptomic psoriasis markers. Materials and methods Biopsies of lesional and non-lesional skin from 24 patients receiving secukinumab 300 mg subcutaneously over 52 weeks (NCT01537432) were used for immunohistochemistry and gene expression analysis. The composition of the residual-disease genomic profile (RDGP; ie, molecular scar) after successful treatment with secukinumab was determined at week 12 and week 52.

Results: In patients achieving PASI75 or greater, psoriasis-transcriptome genes showed continued improvement, reaching non-lesional levels at week 52. Markers of keratinocyte and immune-cell infiltration, Ki67, KRT16, CD3, and CD83, were significantly ($P < .05$) lower and were similar to non-lesional levels by week 52. IL-17A and IL-22-dependent keratinocyte and reconstructive human epidermis genes improved beyond non-lesional levels in PASI75-responders at week 12 and week 52, as did IL-17-dependent feed-forward inflammatory mediators, TNF-dependent keratinocyte genes, and IL-23 pathway genes. The composition of week 12 and week 52 RDGP was significantly different ($P < .05$) yet overlapped, revealing genes with slow-resolving, persistently non-resolved, and decreasing-resolution dynamics. By week 12, the expression of the anti-inflammation genes SOCS1, CD207, and IL-37 were restored beyond non-lesional levels to a greater extent than with earlier psoriasis treatments and continued to improve up to week 52.

Conclusions: High efficacy of secukinumab was accompanied by sustained long-term (week 52) suppression of IL-17A and IL-23-dependent signaling, beyond nonlesional levels. The observed restoration of anti-inflammatory genes SOCS1, CD207, and IL-37 suggests activation of regulatory T-cells that continue to suppress inflammation.

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17707

Single-nucleotide polymorphisms predictive of response to a topical anti-aging product containing N-acetyl tyrosinamide, N-acetyl glucosamine, and maltobionic acid

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Making evidence-based recommendations for anti-aging products for patients is challenging. To address this problem, we explored the correlation between genetics and response to a topical anti-aging product. This IRB-approved study recruited 112 participants who applied a topical cream containing N-acetyl tyrosinamide, N-acetyl glucosamine, and maltobionic acid (a polyhydroxy acid) to the face twice daily for 6 weeks. Saliva samples were submitted by participants for single-nucleotide polymorphism (SNP) genotyping with the use of a commercially available genetic test. Participants were blinded to study product, provided baseline ratings of their skin, and rated their response to the product using a 5-point global esthetic improvement scale (GAIS). Univariate analysis of >600,000 SNPs from genotyping data identified 12 SNPs associated with participants' GAIS ratings (P values $< .004$). Only 1 baseline rating of skin/tone coloring was associated with GAIS ($P = .02$). No other demographic/baseline questions were associated with GAIS scores, including ethnicity, marital status, gender, or age. A further multivariate analysis identified 3 SNPs (P values $< .02$) as independently significant in predicting GAIS ratings of product response when controlling for the 12 SNPs significant in the univariate analysis and baseline skin tone/color ratings. All participants reporting "optimal response" had at least 1 of the 3 SNP genotypes shown to be predictive of higher GAIS ratings. In addition, the one participant reporting a negative response had all 3 SNP genotypes associated with lower GAIS ratings. Further studies correlating SNPs and anti-aging products may allow for more precise genetic-based skin care recommendations as well as product development.

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17743

Wound eversion versus planar closure for wounds on the face or neck: A randomized split-wound comparative effectiveness trial

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Background: While it has been shown that everted closure and planar closure of surgical wounds display similar overall esthetic outcomes, it has been hypothesized that wounds specifically of the face and neck may respond differently to the effects of eversion.

Objective: This study sought to determine whether wound edge eversion improves the cosmetic outcome of operative wounds on the face or neck, compared with planar closure.

Methods: In this prospective, split-scar, and evaluator-blinded comparison trial, cutaneous surgery patients were recruited from an outpatient dermatology clinic. This study was randomized so that one half of each wound received everted closure and the other half received planar closure. Patient Observer Scar Assessment Scale (POSAS) score, scar height, scar elevation, and occurrence of complications were assessed at 3-months after the procedure.

Results: Fifty patients were enrolled and 46 returned for follow-up. At a 3-month assessment, the total patient POSAS scores for everted (8.7) and planar (9.0) closures did not differ significantly. Similarly, there was no difference found in the observer POSAS scores for everted (11.8) and planar (12.1) closures. Finally, there was no difference in measurements of scar width, scar elevation or incidence of complications.

Limitations: This was a single-center study and the population studied was predominantly Caucasian, which may not reliably allow for broad application to diverse skin types.

Conclusions: There was no statistically significant difference found in cosmesis between planar and everted wound closure of common procedure areas of the face and neck.

Commercial disclosure: None identified.

