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A 3-in-1 night facial serum containing melatonin, bakuchiol, and vitamin C restores the homeostatic properties of photoaged skin by activating hypoxia-inducible factor 1 signaling

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Skin aging is principally driven by solar ultraviolet (UV) radiation that elicits changes to skin's homeostasis and alters its structure and physical appearance. To counter these effects, ISDIN have developed a novel night facial serum (3-in-1 NFS) containing three ingredients with known anti-aging properties; melatonin, bakuchiol and the vitamin C derivative ascorbyl tetraisopalmitate. To better define its mechanism of action, a whole genome expression profiling of photoaged skin explants treated with 3-in-1 NFS was performed. Human skin obtained from 2 healthy Caucasian women undergoing abdominoplasty was treated with 3-in-1 NFS 1 hour after irradiation (12.5 J/cm^2 UVA + 50 mJ/cm^2 UVB) on 4 consecutive days. Following the final UV-treatment cycle, gene expression levels were determined by RNA-Seq analysis and differentially expressed genes (DEGs) identified by comparing gene expression levels in treated skin explants to those in untreated UV-exposed skin explants. Functional enrichment analysis of these DEGs suggested 3-in-1 NFS acted principally through the Hypoxia-Inducible Factor 1 (HIF-1) signalling pathway. Indeed, almost half (43 of 96) of the genes up-regulated by 3-in-1 NFS were predicted to be HIF-1 targets, including genes that regulate collagen biosynthesis, stimulate angiogenesis, improve skin's barrier properties and its metabolic function. Levels of HIF-1α mRNA and protein were increased following 3-IN-1 NFS treatment, suggesting that 3-in-1 NFS modulates HIF-1α mRNA and protein turnover. Together these data demonstrate that 3-in-1 NFS improves the homeostasis of photoaged skin by modulating HIF-1 signaling. To our knowledge, 3-in-1 NFS is the first cosmetic to have such a mechanism of action.

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Tildrakizumab provides early predictability of response in patients with moderate to severe psoriasis: Results from reSURFACE 1 and reSURFACE 2 phase 3 trials

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Introduction: Tildrakizumab (TIL) is an anti−IL-23p19 monoclonal antibody for psoriasis. Response-guided therapy, particularly at early time points, is clinically relevant in psoriasis treatment with biologics.

Objective: To evaluate whether an early improvement in PASI could predict PASI response at week (W) 28.

Methods: Data on observed adult patients with moderate to severe plaque psoriasis continuously treated with TIL 100 mg or 200 mg from reSURFACE1/reSURFACE2 trials. PASI50 response (≥50% improvement in PASI) at W4, W8, W16 was used to predict PASI response at W28, defined as PASI90 (≥90% improvement in PASI) or PASI <3.

Results: 593/597 patients on TIL100 mg/200 mg were analyzed. Among PASI50 responders at W4: 66.7% (TIL100 mg), 74.4% (TIL200 mg) achieved PASI90 at W28; 77.1% (TIL100 mg), 84.8% (TIL200 mg) PASI<3. Among PASI50 responders at W8: 64.4% (TIL100 mg), 70.2% (TIL200 mg) achieved PASI90 at W28; 77.1% (TIL100 mg), 80.9% (TIL200 mg) PASI<3. Among PASI50 nonresponders at W4: 55.1% (TIL100 mg), 52.1% (TIL200 mg) did not achieve PASI90 at W28; 42.9% (TIL100 mg), 40.5% (TIL200 mg) did not achieve PASI<3. Among PASI50 nonresponders at W8: 78.2% (TIL100 mg), 78.4% (TIL200 mg) did not achieve PASI90 at W28; 70.1% (TIL100 mg), 66.4% (TIL200 mg) did not achieve PASI<3. Among PASI50 nonresponders at W16: 100% (TIL100 mg), 100% (TIL200 mg) did not achieve PASI90 at W28; 95.5% (TIL100 mg), 96.2% (TIL200 mg) did not achieve PASI<3.

Conclusions: Response to TIL, graded as PASI50, showed an early and high predictability to achieve long-term success: at W8, PASI50 responders showed a high predictability to achieve PASI90 at W28. These results can be used in cost-effective models and clinical practice to help guide better treatment decisions for psoriasis patients.

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A case of multiple aggressive granular cell tumors

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A thirty-eight-year-old African-American woman presented with a 6-year history of asymptomatic growths of the tongue, back and axilla. She had been treated previously with surgical excisions with no recurrence. Her sister has similar symptoms and review of symptoms revealed hemoptysis and dyspnea on exertion. Physical exam demonstrated papular and nodular lesions on the dorsum of the tongue and a right axillary mass. Biopsy of a tongue lesion demonstrated granular cells positive for CD68 and S-100, negative for pankeratin, muscle-specific actin and myogenin, consistent with granular cell tumor (GCT). Blood tests were normal. Biopsy of the right axillary mass confirmed a benign GCT. A left lung nodule was identified on imaging. Biopsy of the lung nodule was also consistent with GCT. Pazopanib was recommended due to the patient's aggressive course and history of one malignant GCT treated by surgical excision. After a failed trial of pazopanib the patient opted for close monitoring. GCTs are rare tumors of neural origin more commonly found in women aged 20-40 years. Lesions are typically found in the tongue but can occur on any skin or mucosal surface. GCTs are usually benign however up to 2% are malignant, which are distinguished by histologic examination. Benign GCTs are cured by excision and rarely recur after negative-margin excision. Malignant GCTs have metastatic potential and often recur with a 40% mortality rate. Common sites of metastasis are the lung, lymph nodes, and bones. Due to unpredictable sites of involvement, GCTs are best managed with a multidisciplinary approach.

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Improvement in specific locations, quality of life, and pruritus after 24 weeks of apremilast in bio-naïve moderate plaque psoriasis patients who failed to achieve a PASI-75 response: Interim results of a real-world prospective study in Greece (APRAISAL)

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Introduction: Psoriasis is a multifaceted disease for which a patient-centered approach that goes beyond Psoriasis Area Severity Index (PASI) improvement, evaluating the treatment effect on the patients' disease burden and well-being, is recommended. Under this perspective, it was of interest to examine outcomes in specific locations, pruritus and quality of life after 24 weeks of apremilast treatment in patients that did not achieve a PASI-75 response.

Methods: This 52-week, noninterventional, prospective study conducted in 23 hospital sites of Greece enrolled bio-naïve moderate psoriasis patients who were newly initiated on apremilast as per the approved label. Interim data from the first 100 eligible consented patients who completed 24 weeks of observation are presented.

Results: Patients (mean age: 49.9 years; 71.0% males; 41.0% obese) had a median psoriasis duration of 8.0 years; 67.0% were previously treated with systemic therapy. Week 24: the DLQI ≤5 and PASI-75 rates were 70.4% and 52.4%, respectively (as-observed data); the overall clinical response rate (PASI-75 and 50 ≤ PASI <75 combined with DLQI ≤5) was 70.4%. The 24-week adherence rate (no missed tablets) was 69.2%. The 24-week apremilast retention rate was 86.9%. Week 24: 43.6% of PASI-75 non-responders attained a DLQI ≤5; 44.7% improved their pruritus severity state; 41.7% and 80.0% of those with baseline Scalp and Palmoplantar Physician's Global Assessment ≥3, respectively, attained scores of 0/1; and 64.0% of those with baseline Nail Psoriasis Severity Index (NAPSI) ≥1 achieved NAPSI-50 response.

Conclusions: Apremilast treatment offered benefits in specific locations, quality of life, and pruritus in a clinically meaningful proportion of PASI-75 non-responders.