## The epigenetic compound dihydromyricetin rejuvenates human skin cells and reactivates vitalityassociated genes

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## **Introduction & Objectives:**

Epigenetic changes have been reported to be a key hallmark of aged human skin. In particular, DNA methylation patterns are altered, resulting in increased biological age, deregulated gene expression and impaired tissue functionality, leading to the well-known skin aging phenotype. Active ingredients, which correct the aged methylation pattern represent a novel and attractive anti-aging approach. We identified dihydromyricetin (DHM) as natural active molecule and epigenetic compound, which can turn back the biological age of cells and rejuvenate the skin tissue. With this study we aimed to functionally analyze the reactivated age dependent silenced genes.

#### **Materials & Methods:**

In order to determine the anti-aging effect of DHM, primary keratinocytes were treated with 20  $\mu$ M DHM*in vitro* and the biological age was measured by methylation-based age clocks. Moreover, a vehicle-controlled study with 19 female volunteers was conducted, where a DHM containing formulation was topically applied on the inner forearm for 8 weeks. Epidermis samples from treated areas were obtained by suction blistering for mRNA expression analysis. To further characterize the genes changed upon DHM treatment, siRNA-mediated Knock down was performed in primary keratinocytes and cell viability assessed by fluorescein-diacetate staining. To assess phenotypic consequences of DHM treatment, supernatant of treated keratinocytes was used on fibroblasts to analyze how DHM influences the crosstalk between keratinocytes and fibroblasts. Finally, a 3-dimensional skin aging model using primary keratinocytes from a single donor and primary fibroblasts from two different age groups was established. After 6 weeks of culture, 20  $\mu$ M DHM was added to the medium. Epidermal thickness was compared after another 6 weeks.

#### Results:

DHM was able to reduce the biological age in keratinocytes by approx. 2 years. Moreover, DHM re-activated genes *in vivo* that are hypermethylated and downregulated upon aging, among them genes correlating with wrinkle development. Knock down experiments revealed that many of the re-activated genes were relevant for cell vitality *in vitro*. DHM-mediated cell rejuvenation translated into an improvement of crosstalk between keratinocytes and fibroblasts as determined by an increased proliferation of fibroblasts after incubation with DHM-conditioned medium from keratinocytes. Finally, in the 3-dimensional skin model, age-dependent thinning of the epidermis could be reversed by DHM.

#### **Conclusion:**

Our findings establish DHM as an epigenetic inhibitor with rejuvenating effects for aged human skin.

#### Deciphering the Code of hASC-EXO and Plant Stem Cell-derived EXO:Proteins, miRNAs, and Lipids

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#### **Introduction & Objectives:**

Adipose tissue-derived mesenchymal stem cell exosomes (ASC-EXO) and plant stem cell-derived exosome-like nanoparticles (PSC-EXO) have attracted significant interest for their therapeutic potential in regenerative medicine and aesthetics. This study explores the characteristics and biological functions of ASC-EXO and PSC-EXO, with an emphasis on their anti-inflammatory effects, enhanced cell proliferation, and promotion of collagen synthesis, highlighting their potential to improve skin health based on their 3 important molecular compositions of protein, lipids, and miRNAs.

To understand isolate and analyze the characteristics of ASC-EXO, and PSC-EXO in terms of the composition of protein, lipids, and miRNA

To evaluate the biological effects of ASC-EXO, and PSC-EXO on cell migration, proliferation, collagen synthesis, melanin inhibition, and anti-inflammatory activity in skin regenerative aesthetics.

#### **Materials & Methods:**

ASC-EXO and PSC-EXO were isolated using the ExoSCRTTM tangential flow filtration (TFF) method. ASC-EXO was applied to in vitro assay models such as cellular uptake, cell proliferation, and collagen synthesis in HDF, and anti-inflammation assay in LPS-macrophage. In addition, the contents of ASC-EXO were analyzed through protein, miRNA, and lipid profiling. PSC-EXO was applied to in vitro assay models such as cellular uptake, cell proliferation, and collagen synthesis in HDF in vitro model, anti-inflammation, and melanin synthesis. In addition, the contents of Plant-EXO were analyzed through protein and miRNA profiling.

#### **Results:**

ASC-EXO was analyzed using multi-omics (proteomics, lipidomics, and small RNA sequencing) and tested in vitro for its functionality. Multi-omics analysis (proteomics, lipidomics, small RNA sequencing) of ASC-EXO (30–200 nm) identified 777 proteins, 132 miRNAs (top 20 making up 78%, top 5 contributing 46%), and 373 lipid species (78% glycerophospholipids, 12% sphingolipids, >90% PE, PI, SM). ASC-EXO reduced IL-6 in LPS-stimulated macrophages and enhanced HDF proliferation and collagen synthesis.

The PSC-EXO was manufactured from the supernatant of plant stem cell cultures using ExoSCRTTM technology, similar to ASC-EXO. Manufactured from plant stem cell culture supernatants via ExoSCRTTM technology, PSC-EXO (30–200 nm) contained 206 peptides and over 1,000 miRNAs, including 30 matching human miRNAs (Let-7 family dominant). PSC-EXO reduced IL-6 in LPS-stimulated macrophages, promoted HDF migration and collagen synthesis, and inhibited melanin production. Notably, PSC-EXO contained specific miRNAs that enhance collagen expression, miRNA-122 that promotes hair growth, and miRNAs associated with anti-scarring and cellular proliferation.

#### **Conclusion:**

These findings suggest that both ASC-EXO and PSC-EXO have unique and beneficial properties for skin-related

applications, highlighting their potential for development into therapeutic agents in regenerative medicine and aesthetic uses. The OMICS analysis of ASC-EXO and PSC-EXO provides a comprehensive perspective on enhancing skin quality. These data collectively show that Exosomes containing microRNA and proteins have multiple biological functions in skin-related assays such as fibroblast growth and melanin content in melanocytes. Notably, this study highlights PSC-EXO's novel similarities to human-derived exosomes, making it a valuable candidate for aesthetic medicine.

## EVALUATING THE THERAPEUTIC EFFECT OF ORAL TRANEXAMIC ACID IN TREATMENT OF MELASMA AMONG COHORT of EGYPTIAN PATIENTS

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## **Introduction & Objectives:**

**Background:** Melasma, a chronic dermatological condition that significantly impairs patient quality of life, presents a persistent therapeutic challenge.

**Objectives:** To evaluate the therapeutic effect of oral Tranexamic Acid in treatment of Melasma among patients attended Al-Hussein university hospital, Cairo, Egypt

#### **Materials & Methods:**

It was a cross-sectional study. The study investigated 48 melasma patients presented to Al Hussain Teaching Hospital during December 2024 to March 2025. Total coverage technique employed. Fitzpatrick Skin Type test and dermatological examination were implemented twice before and after 12 weeks of treatment with oral tranexamic acid and anti-melasma medication to the selected patients as to calculate melasma area severity index. A case report form was filled in for each patient. Data was analyzed by SPSS program version 25.

#### **Results:**

Forty-eight patients were investigated. The study found 47.8% of patients had skin type III and 41.7% had skin type IV. Melasma distributed on the cheeks, nose, chin, frontal region, and upper lip subsequently. On examination After 12 weeks of treatment, patients with melasma showed significant improvement: patchy melasma decreased (p value = 0.031)., lesions lightened in color (p value = 0.000)., and larger patchy lesions were replaced with smaller specks (p value = 0.011). The study demonstrated a significant reduction in melasma severity over 12 weeks. Initially, 66.7% of patients presented with moderate melasma, while after treatment, 72.9% exhibited mild melasma. The mean MASI score decreased substantially from 19.3 to 9.5, a statistically significant improvement (p = 0.004). Oral Tranexamic Acid treatment significantly reduced melasma severity (MASI scores) and led to high patient satisfaction. The study found 58.3% of them reported being satisfied, and 18.8% reported being strongly satisfied. Patients with milder melasma post-treatment reported the greatest satisfaction

#### **Conclusion:**

Oral tranexamic acid presents a viable alternative treatment modality for melasma, relatively safe and cost effective with good patient compliance and may also serve as a beneficial adjunct to existing therapeutic regimens.

## Correlation between fungal load and response to treatment in cases of reaclcitrant superficial fungal infections.

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## **Introduction & Objectives:**

Treatment of superfical fungal infections (SFI) becomes a challenging issue. Most of conventional therapies show unsatisified results with frequent relapse and more observed is failure to response. The underlyiming factors for suc response included the virulance of the organism, the immune status of the patient and the efficacy of the therapeutic drugs. However, in this study we aimed to clarify the correlation between the therapeutic response and the quantity of fungal hyphae in the stratum corneum; known as fungal load.

#### **Materials & Methods:**

A total of 30 well-known patients with tinea corporis were enrolled in this study. All patients showed failure of response to systemic therapy for at least 12 weeks duration. Reassessment of the disease was performed by encounting the number of patches. For each patient, three skin biopsies were performed from different sites.

Routine H&E and special stains (PAS and GMS) was performed and fungal load was recoreded. Routine investigations were performed to exclude any underlying systemic diseases. Fungal load (FL) was considered high (all sections are positive), moderate (two sections are positive), mild (one section is positive) and negative (all sections are negative).

Patients were classified into three groups; each group included 10 patients. Group A treated with A combination of Itraconazole (200mg/d) and Isotretinoin (10-20mg/d). Group B treated with A combination of itraconazole (200mg/d) and terbinafin (250mg/d). Group C treated with voriconazole (200mg/d). After 6 weeks, clincial and histological reassesment was done and results were analyzed.

## **Results:**

Before treatment, all patients showed positive fungal load. In group A, patients showed 5 moderate and 5 high FL. In group B, patients showed one mild, 5 moderate and 4 high FL. In group C, patients showed 4 moderate and 6 high FL.

At the end of treatment period all patients achieved satisfied clinical improvement with significant decrease of symptoms. Histologically, out of 10 patients in group A, 3 patients (30%) were negative, 6 (60%) shifted to mild and only one patient (10%) showed moderate FL. In group B, out of 10 patients, one (10%) was negative, 6 (60%) shifted to mild while 3 patients (30%) showed moderate FL. In group C, no patients showed negative FL while 9 patients (90%) shifted to mild FL and only one patient (10%) showed moderate FL.

There was no significant correlation with the extent of lesions or the duration of the disease. Systemic diseases were encountered in 7 patients without significant correlation.

## **Conclusion:**

The results of this study suggested that the combination of itraconazole with isotretinoin has the best therapeutic

effect that can achieved clinical and histological cure. However, voriconazole has the advantage to control the disease but without significant cure. The combination of itraconazole with terbinafine has the least therapeutic effect. Further study to assess the relapse rate with these regimens are recommended to identify the most effective therapy in such resistant cases.

#### Botulinum Toxin Injection in the Treatment of Asymptomatic Fox-Fordyce Disease

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## **Introduction & Objectives:**

Fox-Fordyce disease (FFD) is a chronic disorder of apocrine sweat glands commonly presenting with pruritic follicular papules over axillae, anogenital and peri-areolar areas. Most patients suffer from intense pruritus affecting their quality of life. However, a subset of patients presents with asymptomatic disease. Commonly affecting young females between 15-35 years of age, treatment is sometimes aimed at improving the cosmetic appearance, especially at visible areas, e.g. the axillae. Botulinum toxin (BTX) injections have been used in multiple reports for refractory FFD to reduce itch and lesions severity.

#### **Materials & Methods:**

A 20-year-old lady presented to Dermatology clinic complaining of asymptomatic skin lesions over bilateral axillae and periumbilical area for 2 months. Lesions started abruptly, not preceded by laser hair removal or the use of any topicals. According to the patient, sweat production is normal. On examination, multiple skin-colored follicular papules measuring 1 mm were present over bilateral axillae and periumblical area. Lesions were surrounded by normal skin. On dermoscopy, folliculocentric papules with absence of dermatoglyphics were seen. Skin punch biopsy revealed mild perifollicular lymphohistiocytic infiltrate with dilated apocrine glands suggestive of FFD.

Patient was started on calcipotriene cream for 3 months with no improvement. Furthermore, tacrolimus 0.1% ointment was used but led similar results. Subsequently, treatment with intradermal botulinum toxin injections was given at a dose of 50 units for each axilla and 10 units at the periumblical region. A dilution of 2.5 ml of normal saline was used, and 2 units were injected at each papule. Clinical improvement in the number of papules over axillae was noted. Decreased sweating was also noticed. However, periumblical lesions remained the same. Improvement of axillary lesions were sustained at 3 months of follow up.

#### **Results:**

FFD is a rare disorder of apocrine sweat glands with no satisfactory cure. Treatment is usually aimed at decreasing pruritus rather than lesions resolution. Various topical treatments such as topical corticosteroids, topical calcineurin inhibitors and tretinoin have been tried and led contradictory results. Recently, BTX injections were used in refractory FFD to decrease pruritus. Although the mechanism of action is not fully understood, BTX is a known inhibitor of pruritogens such as acetylcholine, substance P and glutamate. Additionally, decreased sweat production and its contributory role in FFD pruritus is another possible mechanism. Surprisingly, Improvement in clinical appearance of the lesions with decreased number of papules has also been occasionally observed. This could be attributed to BTX inhibition of fibroblasts and the resultant alteration in the fibrotic pathways or possibly due to the reduced sweat production. Lack of improvement in the periumblical region in our case could be due to lower number of total units used. BTX injection is safe, well tolerated and has shown efficacy even in pediatric population with FFD.

## **Conclusion:**

Depending on the dose, Botulinum toxin injections are a valuable treatment option for Fox-Fordyce disease in

patients presenting with asymptomatic lesions.

#### Topical sirolimus in dermatology: a systematic review

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## **Introduction & Objectives:**

Topical sirolimus is increasingly utilised off-license to manage various dermatological conditions whilst avoiding typical adverse effects associated with systemic sirolimus. However, widespread use is limited by a highly heterogeneous evidence base of mixed quality.

Our aim was to evaluate the current evidence base for the indications, efficacy and safety profile for topical sirolimus in dermatology.

## **Materials & Methods:**

A literature search was conducted from 2005 to July 4th, 2023, of English language studies, with the following databases consulted: MEDLINE, PubMed, Embase, CENTRAL and EBSCO. Key words included 'topical', 'rapamycin', 'sirolimus' and 'dermatology'.

Data on drug efficacy, concentration, side effects, co-interventions and follow up were extracted.\*\*

#### **Results:**

The search identified 202 studies; 71 studies met the inclusion criteria. Efficacy of topical sirolimus was demonstrated in facial angiofibromas (799 patients) compared to placebo across multiple randomised controlled trials with a predominant concentration of 0.1%. Evidence was mixed for sirolimus use in port-wine stains (61 patients), with evidence of effectiveness in combined sirolimus and pulsed-dye laser. Multiple case reports demonstrated clinical improvement with topical sirolimus use in cutaneous vascular abnormalities (33 patients) at a higher concentration of 1%. Other applications of topical sirolimus were predominantly case reports demonstrating generally favourable outcomes. Topical sirolimus was generally well tolerated – most reported adverse effects were localised irritation and pruritus. Ointment-based preparations and once-daily dosing appeared to confer a better side effect profile.

#### **Conclusion:**

Most high-quality data pertain to the efficacy of topical sirolimus in treating facial angiofibromas in tuberous sclerosis. Outcomes are generally promising in other indications and good tolerability, but data quality is mixed.

Does oral isotretinoin therapy increase the risk of atherosclerosis in acne vulgaris patient? Effects of oral isotretinoin on plasma vitamin B12, folic acid, homocysteine, lectin-like low density lipoprotein receptor 1 (LOX-1) and oxided low density lipoprotein (ox-LDL) levels

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## **Introduction & Objectives:**

Isotretinoin is frequently used in the treatment of moderate to severe acne vulgaris. Although lipid-increasing effects of isotretinoin well demonstrated, there are few studies on isotretinoin treatment and the risk of atherosclerosis. The aim of this study was to determine the possible risk of atherosclerosis in acne vulgaris patients on systemic isotretinoin treatment by measuring the levels of vitamin B12, folic acid, homocysteine, ox-LDL and LOX-1.

#### **Materials & Methods:**

Eighty-one patients with acne vulgaris over the age of 18 who used oral isotretinoin at the dose of 0.5 mg/kg/day were included into the study. Venous blood samples were obtained at the baseline, the 1st and 3rd months of isotretinoin treatment. Vitamin B12, folic acid, homocysteine, ox-LDL and LOX-1 levels were measured. Serum levels of triglycerides (TG), total cholesterol (TC), HDL-cholesterol (HDL-C) and LDL-cholesterol (LDL-C) were also recorded.

**Results:** ### Sixty patients (49 female and 11 male) completed the study. The mean age was 21,9±3,3 (range 18-39). Acne severity was moderate in 43 (71.7%) and severe in 17 (28.3%) patients. The increase in ox-LDL levels was statistically significant between baseline and 1st month, between baseline and 3rd month, and between 1st month and 3rd month. The increases in TG, TC, LDL-C and VLDL levels between baseline and 1st month, and baseline and 3rd month were statistically significant. No significant change in folic acid and homocysteine levels with isotretinoin treatment was found compared to baseline. Increases in vitamin B12 and LOX-1 levels were not statistically significant. There was a positive correlation between lipid levels and age as well as body mass index.

#### **Conclusion:**

Increase in ox-LDL, LOX-1 and serum lipid levels at the 1st and 3rd month of oral isotretinoin treatment was observed in acne vulgaris patients suggesting an increased tendency to atherosclerosis. Studies in larger series and with long-term follow-up would clarify this issue.



Role of streptococcal infection in the etiopathogenesis of pityriasis lichenoides chronica and the therapeutic efficacy of azithromycin: a randomized controlled trial

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**Introduction & Objectives:** The exact aetiology of pityriasis lichenoides chronica (PLC) remains unknown. While phototherapy is the most investigated therapeutic modality, azithromycin has been used scarcely. The aim of this study is to evaluate the therapeutic efficacy of azithromycin in the treatment of PLC compared to NB-UVB and evaluating the presence of streptococcal infection as a possible etiological factor in PLC patients.

**Materials & Methods:** The study was designed as a randomised controlled trial. Twenty-four patients with PLC were randomly allocated into either azithromycin (n = 13, standard dose every 10 days) or NB-UVB (n = 11, thrice weekly) groups. End of study (EOS) was either complete clearance of lesions or a maximum of 8 weeks. Therapeutic efficacy was defined as percent reduction in lesions and was calculated for the rash as a whole, erythematous papules alone, and hypopigmented lesions alone and graded into complete, very-good, good, poor or no response. Anti-streptolysin O titre (ASOT), anti-deoxyribonuclease B titre (anti-DNaseB) and throat culture were evaluated at day 0.

**Results:** No significant difference existed between both groups as regards therapeutic efficacy. At EOS, NB-UVB achieved significantly more percent reduction in the extent of hypopigmented lesions and consequently in the rash as a whole (p = 0.001, p = 0.034, respectively). The extent of the rash as a whole was significantly less in the NB-UVB at EOS (p = 0.029, respectively). The effect of NB-UVB on hypopigmented lesions appeared early at week 4 of treatment. Only two patients, one from each group, relapsed during the 3 month follow-up. Evidence of recent streptococcal infection was present in 79% of the cases, mainly in the form of elevated ASOT (94.7%). It was significantly more encountered in young children (< 13 years) (p = 0.03) and was associated with more extent of erythematous papules and consequently with more extent of the rash as a whole (p = 0.05 and p = 0.01, respectively). It did not affect outcome of therapy at EOS.

**Conclusion:** Azithromycin did not show more favorable response in patients with recent streptococcal infection. Therapeutic efficacy of azithromycin is comparable to NB-UVB in treatment of PLC; however, NB-UVB is superior in management of hypopigmented lesions. It is highly suggested that PLC could be a post streptococcal immune mediated disorder.

# Novel method to visualize ex vivo skin barrier repair by ceramide complex using confocal Raman microscopy

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## **Introduction & Objectives:**

Ceramides are key molecules in the stratum corneum for the maintenance of skin barrier function. They comprise 30 – 40% of the stratum corneum by mass and thus have important function in structuring the skin barrier while preventing permeability. Confocal Raman microscopy (CRM) has emerged as a non-invasive imaging technique used to characterize molecular interactions with high spatial resolution. To visualize the effect of a normal and a damaged SC barrier, CRM was used in this study with salicylic acid (SA) being utilized as a model permeant. The SC barrier was chemically damaged using a lipid extraction solution. Subsequently, the damaged barrier was repaired by the topical application of ceramides. The repair of the barrier was measured by tracking the penetration of SA through the ex vivo skin using a CRM based method to elucidate the effectiveness of the treatment. The objective of the study was to analyze if the tropical application of ceramides helps in the repair of damaged stratum corneum barrier.

#### **Materials & Methods:**

In this study, CRM was used to visualise skin barrier disruption and recovery with SA as a model permeant. The skin barrier of *ex vivo* human skin was chemically damaged using a mixture of chloroform and methanol to disrupt the natural lipid barrier. Subsequently, the skin was pre-treated with a complex of ceramides to investigate if the damaged skin could be repaired. After a brief repair period on the Franz cell, barrier recovery was characterized by tracking the permeation of salicylic acid through the damaged skin using CRM.

### **Results:**

The results from the ceramide-treated skin were compared to disrupted-untreated skin to assess if the ceramides played a role in barrier repair. The obtained permeation profile of ceramide-treated skin was similar to that of undisrupted skin, where in both cases the salicylic acid remained closer to the skin surface as an indication of a strong intact barrier. Contrastingly, the profile of the disrupted-untreated skin showed that the majority of the salicylic acid had passed through the skin within the barrier recovery time.

## **Conclusion:**

This suggests that our approach to repair damaged skin with ceramides holds potential for the restoration of normal skin barrier function. Moreover, the Raman characterization via model permeant serves as a novel way to non-invasively examine skin barrier recovery.

Comparative study between topically applied irradiated human amniotic membrane and its extract in combination with tea tree oil versus topical tioconazole in pityriasis versicolor treatment

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**Introduction & Objectives:** Pityriasis versicolor (PV) is a chronic skin disease caused by virulence activities of Malassezia, a genus of skin-associated yeasts. Traditionally, Tioconazole is used as a topical antifungal for curing PV. Previous investigations cited that human amniotic membrane (HAM) and its extract, a placental tissue, has antimicrobial and anti-inflammatory activities and is useful as a dressing for healing skin lesions. Moreover, tea tree oil (TTO) has a potent antifungal efficacy. This clinical trial aims to achieve an alternative therapeutic treatment able to kill Malassezia and heal PV lesions using TTO-saturated HAM (TOSHAM), with little application times.

**Materials & Methods:** This study subjected 120 patients with hypopigmented or hyperpigmented PV lesions; half patients were treated weekly with TOSHAM compared with the others who applying 1% Tioconazole cream daily as a traditional treatment. Microbiological evaluation of in vitro fungicidal activity of TOSHAM versus Tioconazole was carried out against Malassezia furfur culture.

**Results:** The clinical outcomes of this study proved the superior activity of TOSHAM to heal PV lesions than Tioconazole; this was in harmony with microbiological findings.

Conclusion: This study approached a novel therapeutic treatment of PV with great outcomes by using TOSHAM.



Can the Glucocorticoid Toxicity Index Support Safer Steroid Use and Contribute to Treatment Planning in Dermatologic Care? Evidence from a 20-Year Real-World Cohort at a Tertiary Center

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**Introduction & Objectives:** Systemic glucocorticoids are a cornerstone of dermatological therapy due to their potent therapeutic effects in various types of inflammatory and autoimmune skin diseases. However, long-term exposure often results in clinically significant and cumulative toxicity. The Glucocorticoid Toxicity Index (GTI) is a validated multidimensional scoring system, designed to quantify glucocorticoid-induced toxicities across nine clinical domains. It was developed in 2017 by a multidisciplinary board and is currently used to assess steroid side effects, especially in rheumatology clinics. Nevertheless, its role in dermatology remains limited. In this study, we aimed to investigate the capacity of the GTI to reflect steroid-induced toxicities in dermatology patients and to evaluate its applicability to clinical practice.

**Materials & Methods:** This retrospective cohort study comprised 190 patients from all age groups, over a 20-year period at a tertiary dermatology center. All patients had received systemic corticosteroids for at least 3 months to manage a broad spectrum of dermatological conditions, such as autoimmune bullous diseases, alopecias, vasculitides, connective tissue diseases, neutrophilic dermatoses, chronic eczematous or psoriatic diseases. GTI-Cumulative Worsening Scores (CWS) were calculated by comparing each patient's pre-treatment status with their condition at the most recent follow-up visit, which was the latest time point that matched a 3-month interval. Multiple regression analyses, including stepwise linear and ordinal logistic models, were conducted to explore associations between independent clinical variables and both total GTI scores and nine individual subdomains.

**Results:** Gender distribution was balanced, with a wide age range. GTI scores ranged from 0 to 227 (mean: 50.54  $\pm$  52.80), displaying a positively skewed distribution. Toxicities were most prominent in metabolic, neuropsychiatric, and infectious domains. Higher GTI scores were significantly associated with age ≥45 years, female sex, treatment duration ≥9 months, higher cumulative and peak daily doses (all p < 0.05). Each 1000 mg increase in cumulative dose was found to be associated with a 34% increase in the risk of myopathy (p = 0.021) and an 18% increase in the risk of infection (p = 0.043). Age and sex were also independently associated with toxicities related to blood pressure (p = 0.014), body mass index (p = 0.003), and blood glucose levels (p = 0.017). Diagnosis-specific associations were particularly observed in patients with graft versus host disease (p = 0.009) and autoimmune blistering diseases (p = 0.026). This summary presents the key findings; additional significant relationships were also identified in subgroups.

**Conclusion:** This is the first comprehensive study to interpret GTI scores in a large, real-world dermatology population across major disease categories. Based on advanced statistical modeling and multidomain evaluation, GTI-CSD provides an effective, novel approach to quantify cumulative glucocorticoid toxicity. We suggest that its incorporation into routine dermatologic practice will promote safer and more individualized treatment modalities for patients by supporting strategies that reduce long-term toxicity without compromising therapeutic goals.

# Protective Effects of Lactiplantibacillus plantarum IS-10506 Against Ultraviolet B (UVB)-Induced Photoaging in Wistar Rats: An Animal Study

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## **Introduction & Objectives:**

Photoaging is an extrinsic aging process, mainly influenced by ultraviolet B (UVB) exposure. The treatment and prevention of skin aging have been studied extensively. This is a novel study aiming to explore the protective effects of *Lactiplantibacillus plantarum* IS-10506 lysate (LIS) against UVB-induced photoaging in Wistar rats. The role of LIS in transepidermal water loss (TEWL), collagen type 1, matrix metalloproteinase (MMP)-1, and tyrosine-related protein (TRP)-1 will be described in this report.

#### **Materials & Methods:**

An animal study was carried out with a post-test-only control group design. A total of 48 male Wistar rats were included in the study and divided into four groups: normal control, UVB control, treatment group 1, and treatment group 2. Treatment group 1 received a topical application of 50% LIS gel twice daily on the days of UVB exposure, while treatment group 2 received a topical application of 5% LIS gel twice daily continuously for 5 weeks. UVB exposure was administered at a dose of 3100 mJ/cm2 for five weeks (thrice weekly for 3 weeks and twice weekly for 2 weeks) for UVB control, treatment group 1, and treatment group 2. An immunohistochemistry examination was performed to analyze the expression of collagen type 1, MMP-1, and TRP-1. TEWL was assessed using TewameterÒ (Courage+Khazaka Electronic, Koln, Germany).

#### Results:

While the UVB control group experienced a significant increase in TEWL (p = 0.002), the treatment groups 1 and 2 experienced a substantial decrease in TEWL (p < 0.001 and p = 0.022, respectively), indicating that the treatment improved the skin barrier. The immunohistochemistry examination showed that treatment groups 1 and 2 had the highest collagen type 1 expression (6.10  $\pm$  1.65 and 5.58  $\pm$  2.74; p < 0.001), suggesting the promotion of collagenesis. The UVB control group showed the significantly lowest collagen type 1 expression compared to other groups (2.42  $\pm$  1.33; p = 0.002). MMP-1 expression was significantly higher in the UVB control group (8.67  $\pm$  1.56; p < 0.001), suggesting the induction of the collagen degradation process. On the other hand, both treatment groups 1 and 2 showed significantly lower MMP-1 expression (3.67  $\pm$  2.25 and 3.07  $\pm$  2.26; p < 0.001). Both treatment groups 1 and 2 showed significantly low TRP-1 expression compared to UVB control group (2.70  $\pm$  1.23 and 3.82  $\pm$  1.81 vs 3.75  $\pm$  2.59; p < 0.001), indicating reduced melanogenesis in the treatment group.

## **Conclusion:**

This study proved that LIS could effectively protect Wistar rats' skin from UVB-induced photoaging by improving TEWL, collagenesis, MMP-1 expression, and melanogenesis. This study emphasizes the potency of LIS as a novel anti-aging agent.

A randomized trial comparing simulated daylight and conventional photodynamic therapy for the treatment of actinic keratoses.

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## **Introduction & Objectives:**

While conventional photodynamic therapy (C-PDT) using red light is effective in treating actinic keratoses (AKs), it is often associated with considerable pain. Simulated daylight photodynamic therapy (SDL-PDT) may offer a less painful alternative, although its effectiveness remains insufficiently explored.\*\* This study aimed to determine whether SDL-PDT is non-inferior to C-PDT in treating mild to moderate AKs. Secondary objectives included evaluating patient-reported pain, post-procedural skin responses, and treatment preferences.

#### **Materials & Methods:**

A randomized, controlled, single-center, non-inferiority trial was conducted, enrolling adult patients with bilaterally or symmetrically distributed mild to moderate AKs at one or more body sites. Each treatment area was split so that one side received a single session of C-PDT and the other SDL-PDT, both using 5-aminolevulinic acid hydrochloride as the photosensitizing agent. Pain experienced during light exposure was recorded on a numeric rating scale (0–10). Patient preferences were collected using self-administered questionnaires. Follow-up was performed at 12 months to assess overall lesion clearance rates.

#### **Results:**

A total of 69 patients with 1,458 AKs identified through clinical and dermoscopic assessment were included with the majority of lesions located on the face or scalp (89.9%). After one year, lesion clearance reached 71.0% with SDL-PDT compared to 85.3% with C-PDT (p<0.001), indicating that SDL-PDT did not meet the criteria for non-inferiority. Pain scores were significantly higher with C-PDT (mean 6.6) than with SDL-PDT (mean 0.8) (p<0.001). On the day after the treatment, 98.3% of participants indicated a preference for SDL-PDT.

#### **Conclusion:**

Although SDL-PDT was associated with significantly less discomfort, its lower effectiveness in clearing AKs suggests it may not be suitable as a first-line treatment option.

Efficacy and tolerability of a moisturizer containing a synergistic blend of bioactive ingredients in treating hyperpigmentation including post-inflammatory hyperpigmentation.

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<sup>2</sup>The Estee Lauder Companies, Melville, United States

## **Introduction & Objectives:**

Hyperpigmentation is the darkening of skin that occurs when excess melanin forms deposits, leading to uneven skin color and a photo-aged appearance. Facial hyperpigmentation results from conditions such as melasma, dermatosis nigra, age spots and post-inflammatory hyperpigmentation (PIH); causes include genetics, disease, chemical or drug exposure, UV exposure, and hormones. PIH manifests at sites of previous inflammation and can vary in darkness and size. Facial hyperpigmentation has a prolonged course and affects individuals with light and dark skin tones. Clinical and *in vitro* testing are used to elucidate the efficacy of a topical moisturizer and a blend of key ingredients on skin parameters including pigmentation.

#### **Materials & Methods:**

*In vitro* - Testing was conducted using melanocyte containing skin models (Mattel, MelanoDerm B) treated with a prototype cassette emulsion containing 8 uniquely chosen bioactive ingredients including (AA2G, *Trametes versicolor* extract). The model was topically dosed over 7 days, after which melanin content and tissue viability were quantified.

Clinical - This single-center clinical trial to assess the efficacy of the facial treatment when applied twice daily was conducted on 36 Chinese female subjects, with mild to moderate mottled pigmentation and at least 3 pigmented spots on the face. Clinical grading for Radiance, Translucency, Smoothness and Texture, was conducted at 1, 4, 8 and 12 weeks, while Pigmentation (Mottled pigmentation, PIH intensity and contrast), Skin Tone Evenness and Sallowness were measured starting at 4, 8 and 12 weeks, using a modified Griffiths 10-point scale. Moisturization changes were measured in triplicate on the cheek at 1 and 4 weeks using a Corneometer CM 825 (Courage + Khazaka electronic GmbH, Köln, Germany) and Barrier function at 4 weeks in duplicate with a Tewameter TM Hex (Courage + Khazaka electronic GmbH, Köln, Germany).

## Results:

In vitro - the blend significantly reduced normalized melanin by 31% vs untreated (p = 0.0123) and by 27% vs vehicle (p = 0.0426), while also increasing tissue viability by 88% compared to controls (p = 0.0041)

Clinical - Results of the clinical grading of efficacy parameters showed a statistically significant improvement in Radiance on the global face at Week 1 through Week 12; Translucency on the global face and Texture (smooth appearance) (visual) on the cheeks at Week 4 through 12; Smoothness (tactile) on the cheeks at Week 1 through12; Sallowness (tactile) on the cheeks, Mottled hyperpigmentation (brown patches) and Skin tone evenness on the global face, and the target post-acne mark/ PIH Intensity and Contrast at Week 4 through 12 when compared to Baseline (**Figure 1**).

Results for both Corneometer (Week 1 (8.65 + 6.2) and 4 (14.15 + 8.39)) and Tewameter (Week 4 (-2.16 + 2.98)) showed a statistically significant improvement from baseline.

#### **Conclusion:**

*In vitro* evaluation of the eight-ingredient blend demonstrated significant modulation of melanogenesis. The results from the clinical study demonstrated that incorporating the Trametes Versicolor blend into a moisturizer formulation was effective in improving skin conditions when used over the course of 12 weeks by Chinese women with lack of radiance, textural roughness, mottled hyperpigmentation, acnes marks/PIH, when used twice daily.

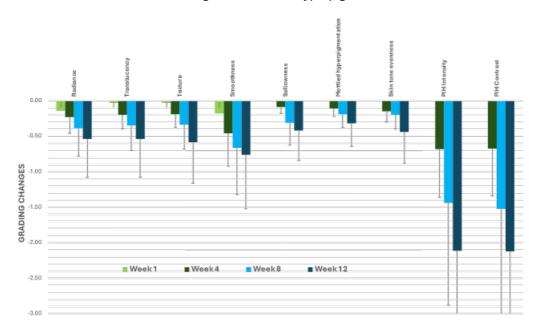


Figure 1. Skin Improvements over 12 Weeks

#### Investigation of sunscreen utilization and label comprehension proficiency in society

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## **Introduction & Objectives:**

It has been proven that sunscreens protect against skin aging and skin cancer when used appropriately. Today, ingredients that provide UVA and UVB protection are included in sunscreens in different amounts and combinations. Although efforts are made to inform people to choose appropriate ingredients according to their age and needs and to use them correctly, it is thought that there is a lack of competence in reading sunscreen labels in society and that sunscreen selection is made according to different criteria. This study aims to investigate sunscreen orientation and usage habits in society, better define sunscreen awareness and labeling deficiencies, and contribute to the literature for public information studies and further research.

## **Materials & Methods:**

Our study was planned as a prospective survey study. A 27-question Google Forms survey link was shared with participants online to be answered by non-dermatologists. Questions included demographic information, physical characteristics, frequency of sunscreen use, affecting factors in sunscreen purchase, participants' level of sun protection knowledge, and their familiarity with sunscreen labeling terminology according to FDA's final rule. The participants were asked to evaluate their knowledge about sunscreen labeling and sun protection before and after the sun protection knowledge-related questions and after the informative text, which was shared at the end of the survey, comprising the correct answers. Descriptive frequencies were used to characterize the responses. Ethics committee approval was received.

## **Results:**

Of the 1056 individuals who agreed to fill out the survey, 81,1% (n=854) were female and 18,9% (n=199) were male. 51,5% (n=542) were non-dermatologist physicians, 9,3% (n=98) were non-physician health care workers, and 39,2% (n=413) were of other proficiencies. 64.4% (n=680) of the participants apply sunscreen at least several times a week. The most influencing factors were the physician's advice (66,4%, n=693) and a friend's advice (46,3%, n=483). The most important factors in using sunscreen were protection from hyperpigmentation (69.5%, n=725), delaying skin aging (64.1%, n=669), and protection from skin cancer (56.0%, n=584). 46.9% (n=492) knew that the SPF value only indicates protection against UVB. 73.8% (n=779) knew that broad-spectrum sunscreens protect against UVA+UVB. 61.1% (n=638) did not know that broad-spectrum products were needed to protect against skin cancer and photoaging. Before answering the sunscreen knowledge-related questions, 28,5% (n=300) of participants claimed their sunscreen knowledge as very good/good. After answering the questions, 17.7% (n=186) rated their knowledge level as very good/good. 84.2% (n=887) agreed to read the informational text at the end of the survey. After reading the text, 88.3% (n=783) of them evaluated their level as very good/good.

#### **Conclusion:**

Our study demonstrated that participants are motivated to use sunscreen, but their ability to interpret sunscreen labels remains limited, resulting in product choices that do not align with their intended purpose. These results

were similar to previous studies. Additionally, our results indicate that educational interventions of this nature are well-received and can significantly enhance public knowledge. These outcomes underscore the need for further educational efforts to support informed decision-making in sunscreen selection.

A new extended-release Topical Formulation of Brimonidine Tartrate - First Clinical Evaluation and Perspectives.

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<sup>1</sup>Tarian Pharma, Grasse, France

## **Introduction & Objectives:**

TAR-0520 gel is a patent-protected topical formulation of brimonidine tartrate, designed for improved efficacy and 24-hour extended-release of this specific alpha-2 agonist. Applied to the skin, TAR-0520 gel induces local and reversible vasoconstriction of the superficial cutaneous vessels. The phase 1 program evaluated the local tolerance, the PK profile as well as the primary (skin blanching) and secondary (anti-inflammatory) pharmacodynamic activities when TAR-0520 gel was applied to the skin of healthy volunteers (HV).

#### **Materials & Methods:**

**Local tolerance** was assessed in a classical 21-day irritation assay with 4 increasing concentrations of TAR-0520 gel (ranging from 0.5% to 1.5%) applied daily to the skin of 20 HV.

**For pharmacokinetic evaluation**, 2.0 g of TAR-0520 gel 1% were applied daily to the chest, face and back (1000cm<sup>2</sup>), of 8 HV for 5 days. Brimonidine level determinations were performed in blood samples collected on day 1 and day 5 using a validated and sensitive analytical method (LOQ 12pg/ml).

**The primary pharmacodynamic effect** was assessed over 24 h by measuring skin blanching resulting from the superficial vasoconstriction induced by TAR-0520 gel 1.5% in 12 healthy volunteers. A Minolta colorimeter was used to monitor the decrease in the a\* value corresponding to the skin blanching intensity.

**The secondary pharmacodynamic effect** was evaluated in a UV-induced erythema model. After evaluation of the individual minimal erythemal dose (MED), 6 skin areas were exposed to increasing UV doses (1 MED, 2 MED and 3 MED) with 3 areas pretreated (24h and 2h before UV exposure) with TAR-0520 gel and 3 areas pretreated with the same formulation without active. Twenty-four hours after UV exposure, the erythemal response was measured on the 6 areas by clinical observation and by chromametry.

#### **Results:**

No adverse reactions and no SAE were reported during these studies. TAR-0520 gel was shown to be well tolerated with no sign or symptom of irritation when applied at concentrations up to 1.5%.

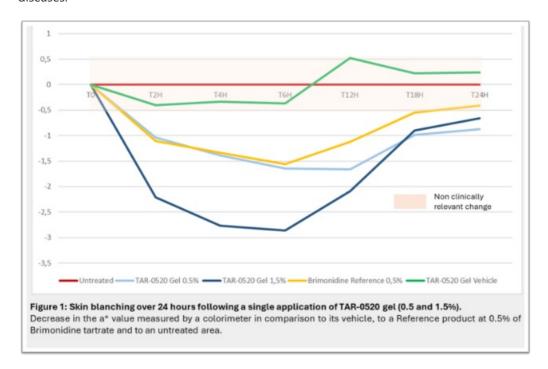
**The PK assessment** conducted under maximized conditions confirmed a slow and extended release of the active with the systemic exposures similar to those reported with marketed products that contain lower brimonidine concentrations.

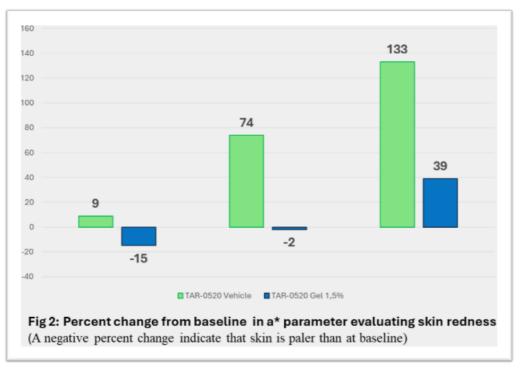
**The primary pharmacodynamic effect** confirmed a dose dependent and long-lasting TAR-0520 gel activity, with the highest concentrations\*\* showing vasoconstriction (skin blanching) over a period of 24 hours (Figure 1).

**The secondary pharmacodynamic effect** was demonstrated with a significant erythema reduction in the area treated with TAR-0520 gel: 100% erythema reduction observed at MED x 1 and at MED x 2 and 70% erythema reduction at MED x 3, (Figure 2).

#### **Conclusion:**

In a clinical evaluation involving healthy volunteers, TAR-0520 gel demonstrated excellent local tolerability and minimal systemic absorption, underscoring a favourable safety profile. The sustained vasoconstrictive response, in combination with potent anti-inflammatory activity, positions TAR-0520 gel as a promising topical intervention for the prevention of chemotherapy-induced skin toxicities and the management of chronic inflammatory skin diseases.





Split-face case series of tirbanibulin 1% ointment versus photolyase-based repair cream in actinic keratosis: clinical outcomes and cosmetic field improvements

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## **Introduction & Objectives:**

Tirbanibulin 1% ointment is approved for the topical treatment of actinic keratosis (AK). While its efficacy is well-established, potential cosmetic effects in photodamaged skin remain underexplored. This study aimed to evaluate the clinical and cosmetic outcomes of tirbanibulin using a split-face design, comparing it with a photolyase-based repair cream applied to the contralateral side.

#### **Materials & Methods:**

Five patients with bilaterally distributed, non-hyperkeratotic facial AKs were included. Tirbanibulin 1% ointment was applied once daily for 5 consecutive days to one hemiface. On the opposite side, a commercially available photolyase-based topical repair cream was applied daily for 8 weeks. Standardized photographs were taken at baseline and at 8 weeks. Outcomes included AK clearance, skin reactions, and cosmetic changes such as lentigo fading and skin texture improvement. Clinical and cosmetic changes were assessed using photographic comparison.

#### **Results:**

The tirbanibulin-treated side achieved complete or near-complete clearance of AKs in 4 of 5 patients (80%). The photolyase-treated side showed partial improvement in lesion count. Local skin reactions on the tirbanibulin side were mild and self-limited. Cosmetic improvement, including lentigo fading and smoother skin texture, was observed in 3 patients on the tirbanibulin side, with minimal or no changes on the control side.

#### **Conclusion:**

This split-face case series suggests that tirbanibulin 1% ointment is not only effective in clearing AKs but may also confer additional cosmetic benefits in photodamaged skin when compared to a repair cream with photolyase. These findings support further investigation into tirbanibulin's broader field-directed potential.

## Efficacy of Cryopeel and Targeted Cryotherapy in the Treatment of Multiple Actinic Keratosis: A Case Series of 8 Patients

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#### **Introduction & Objectives:**

Actinic keratoses (AKs) are precancerous skin lesions caused by chronic sun exposure, with a potential risk of progression to squamous cell carcinoma, if untreated. Effective treatment strategies should not only target individual lesions but also address field cancerization. Cryopeel along with targeted cryotherapy, offers a promising, non-invasive solution to treat AKs.

The objective is to evaluate the efficacy and safety of cryopeel combined with targeted cryotherapy in patients with multiple AKs.

#### **Materials & Methods:**

Patients with multiple AKs on the face and without any prior treatment were included for Cryopeel and targeted cryotherapy. The treatment, conducted at intervals of 3 to 12 weeks, included between 1 and 6 sessions of Cryopeel combined with targeted cryotherapy. Treatment was applied by a qualified medical professional. The Actinic Keratosis Area and Severity Index (AKASI) was used to assess treatment efficacy. The safety was assessed by collecting all side effects using an unstructured questionnaire conducted by the medical team. The normally distributed variables were compared using paired samples t-test, while non-normally distributed variables were compared using Wilcoxon signed-rank test.

## **Results:**

A total of eight female patients (six with Fitzpatrick skin type II and two with Fitzpatrick skin type III) were included in this study. Patients in the study had a mean age of  $73.5 \pm 5.45$  years. Three patients had a history of skin cancer (1 melanoma and 2 non-melanoma skin cancer). In all patients, the treatment led to a notable reduction in AKASI scores. The mean AKASI score decreased from an initial score of  $3.75 \pm 1.01$  to a final score of  $1.77 \pm 0.52$ . In addition to AKASI mean score improvement of 52.8% ( $\Delta$ AKASI = -1.98; 95%CI = -1.34 to -2.21, p = 0.003), patients also reported an improvement in overall skin texture and appearance, with a rejuvenated, more youthful look. The treatment was well tolerated, with no significant side effects.

## **Conclusion:**

Cryopeel combined with targeted cryotherapy proves to be an effective and well-tolerated approach for the treatment of multiple AKs. Administered by a qualified medical professional, the treatment ensured not only efficacy and safety but also provided unexpected aesthetic benefits.

## Topical PI3K/mTOR inhibitor bimiralisib (PQR309) in Actinic Keratoses and Cutaneous Squamous Cell Carcinoma

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## **Introduction & Objectives:**

Actinic keratoses (AKs) are prevalent precancerous skin lesions associated with increased risk of cutaneous squamous cell carcinoma (cSCC). Treatment options for AKs include topical drugs, destructive modalities and surgical removal. However, all of these agents induce skin inflammation of varying severity and their clinical efficacies are sub-optimal.

The PI3K/mTOR signaling is hyperactivated in cSCC, squamous cell carcinoma in situ (SCCIS) and AKs, making this pathway a potential therapeutic target. This study evaluated the application of topical bimiralisib (PQR309), a dual PI3K/mTOR inhibitor, as a potential therapy for AK/SCCIS/cSCCs in 2 preclinical *in vivo* models with the aim to develop a topical formulation for clinical use.

## **Materials & Methods:**

We have tested *in vivo* a topical gel containing 1-3 % bimiralisib on K14-Fyn-Y528F transgenic mice, which produce spontaneous skin lesions that mimic human AK, SCCIS and cSCC as well as in the SKH-1 immune-competent hairless mice that developed AK/SCC like lesions after 14 weeks of daily UV-B-irradiation.

To develop a topical non-aqueous formulation 2% of bimiralisib (NA03-2% bimiralisib) for clinical use a range of formulations were tested on human and porcine skin ex-vivo or in-vivo. This allowed to develop the topical non-aqueous 2% bimiralisib formulation was developed for clinical use and tested in clinical studies to evaluate the efficacy and safety (Windt et al. 2022) as well as in patients suffering from AK (NCT06319794; 2024).

#### Results:

Experimental topical formulation of 1% showed marked regression of treated cSCCs in K14-Fyn-Y528F transgenic mice by 99% which correlated with inhibition of PI3K/mTOR signaling. In the SKH-1 immune-competent hairless mice that developed AK/SCC like lesions after 14 weeks of daily UV-B-irradiation application of topical bimiralisib gel for four weeks clearly prevented the progression of AK lesion as quantified by a global macroscopic score using three masks and relative weighting. Although no statistical significance could be assessed, these data demonstrate that the topical treatment of UVB-induced cutaneous lesions in SKH-1 mice with PQR309 was very

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well tolerated with no weight loss or any detectable skin irritation compared to Zyclara. Topical PQR309 decreased the lesion progression from AK to SCC although the protective effects of PQR309 is lost when the treatment is ceased. Topical bimiralisib in both K14-Fyn-Y528F and UV-B-irradiated SKH-1 mice was well tolerated and did not induce skin erythema, crusting or ulceration.

A topical non-aqueous 2% bimiralisib formulation for clinical use showed that the concentrations of PQR309 achieved in the epidermis and dermis of pig skin following a single exposure was sufficient to significantly inhibit the PI3K/mTOR pathway, The excellent penetration of bimiralisib could be confirmed in by MALDI imaging into the epidermis of human patients (Windt et al. 2022).

## **Conclusion:**

Overall, topical bimiralisib combines high efficacy in animal models with AK/SCCIS/cSCC lesions, with low detectable adverse effects and high skin penetration properties. A topical formulation of 2% bimiralisib for clinical use was developed and has been tested in healthy volunteers without significant safety issues (Windt et al. 2022) and is currently in a clinical trial to evaluate the efficacy and safety in patients suffering from AK (NCT06319794; 2024).

#### Tirbanibulin treatment for Actinic Keratosis: LC-OCT with AI-based algorithm evaluation

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## **Introduction & Objectives:**

Actinic keratosis (AK) is a prevalent precancerous skin condition primarily caused by prolonged exposure to ultraviolet (UV) radiation, most commonly affecting individuals with fair skin. It typically presents as rough, scaly patches on areas frequently exposed to the sun and carries a risk of progressing to invasive squamous cell carcinoma (SCC). Early identification and timely intervention are crucial to preventing malignant transformation. In recent years, non-invasive imaging technologies such as Line-field Confocal Optical Coherence Tomography (LC-OCT) have become valuable tools for real-time, in vivo assessment of skin lesions. LC-OCT combines the cellular resolution of confocal microscopy with the depth penetration of optical coherence tomography, allowing for high-resolution visualization of both the epidermis and dermis. This enables accurate diagnosis and monitoring of AK without the need for invasive biopsies. Tirbanibulin, a novel topical agent approved for the treatment of AK, works by inhibiting tubulin polymerization.

**Materials & Methods:** Study images were acquired using LC-OCT devices (DAMAE Medical, Paris), which enable painless and non-invasive imaging. These devices generate vertically oriented (histology-like) and horizontally oriented (similar to Reflectance Confocal Microscopy, RCM) sectional images, as well as full 3D volume reconstructions. LC-OCT technology operates through a two-beam interference microscope equipped with a supercontinuum laser (class 1 light source, central wavelength of 800 nm) and a line-scan camera as the detector. It measures both the time of flight and the amplitude of light backscattered from tissue microstructures illuminated by a focused line of light. This innovative technique integrates the interferometric principles of Optical Coherence Tomography (OCT) with the spatial filtering capabilities of RCM. Once the images were acquired, they were processed using an artificial intelligence algorithm to obtain data on keratinocyte atypia.

**Results:** Tirbanibulin has been found to be effective in the treatment of AK. Additionally, the implementation of AI-based algorithms for keratinocyte segmentation offers a cutting-edge method for detecting and quantifying keratinocyte atypia before and after treatment. These systems employ user-friendly colorimetric scales to enhance interpretability

**Conclusion:** The integration of advanced imaging techniques with targeted topical therapies marks a significant step forward in the personalized management of actinic keratosis, improving precision in diagnosis, treatment planning, and non-invasive follow-up care.

# Systemic SMO-Hedgehog inhibition with Sonidegib: real-life experience of the Dermatology Unit of University of Pisa

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## **Introduction & Objectives:**

Basal Cell Carcinoma (BCC) is a skin malignancy originating from keratinocytes in the basal layer of the epidermis. It is the most prevalent malignant neoplasm in humans. It generally occurs on sun-exposed areas of individuals with pale skin, with the head and neck being the most prevalent locations. The intervention typically relies on surgical excision. If not feasible, alternative methods encompass radiotherapy, cryotherapy, topical agents (such as imiquimod cream), and systemic therapy. SMO-Hedgehog-inhibitor drugs, sonidegib and vismodegib, are used for difficult-to-treat basal cell carcinomas (locally advanced, multiple, or metastatic variants).

#### Materials & Methods:

This is a case series detailing our experience with sonidegib. We included five patients: three with locally advanced basal cell carcinomas (BCCs) located in the right malar region, right lower eyelid, and right ear, and two who had multiple BCCs, including fifteen lesions distributed across the body and two locally advanced BCCs on the neck. Our team has monitored patients with biopsy for initial diagnosis, conducted screening blood tests, and performed monthly clinical and biochemical evaluations until the clearance of lesions, utilizing a neoadjuvant approach or in combination with cryotherapy.

#### **Results:**

Each case demonstrated significant efficacy of this medical treatment, exhibiting either a partial or complete response during the initial months. We achieved partial responses by integrating systemic therapy with surgery or cryotherapy, consistently attaining total disease remission. Sonidegib was administered to each patient for a maximum duration of 7 months, resulting in no adverse events (aside from mild and reversible dysgeusia), and an enhancement in their quality of life was observed (the patient depicted in Fig. 1 previously experienced a partial obstruction of his visual field, while the patient in Fig. 2 had an obstruction of the external auditory canal and reported deafness).

#### **Conclusion:**

Sonidegib is an oral SMO-Hedgehog inhibitor approved for the treatment of locally advanced basal cell carcinomas (BCCs). Based on our expertise, it is a secure and effectively administered medication that provides patients with a comprehensive response or the opportunity to opt for a less invasive surgical intervention. Its application in patients with multiple BCCs may minimize surgical interventions, hence decreasing expenses and enhancing quality of life.

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## Efficacy and tolerability of a hydroxy acid combination formula in sensitive skin syndrome

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**Introduction & Objectives:** Sensitive skin syndrome (SSS), a common dermatosis characterized by stinging, burning, and erythema in response to innocuous stimuli, is proposed to occur secondary to alterations in epidermal barrier function, stratum corneum integrity, and neurogenic inflammation. The underlying mechanisms causing SSS may manifest as uneven skin tone and texture. Hydroxy acids (HAs) are commonly used exfoliants that promote epidermal turnover and barrier renewal to improve skin tone and texture, however, their tolerability in individuals with SSS is limited, with over 50% of this demographic reporting adverse reactions to topical skincare products. In this study, the efficacy and tolerability of a combination HA lotion containing mandelic acid, salicylic acid, gluconolactone was investigated in a cohort including individuals with SSS.

Materials & Methods: A total of 389 participants, including 116 with clinically diagnosed SSS (SensiScale score ≥ 13), applied the combination HA lotion daily for up to 56 days. Instrumental assessments were performed using dansyl chloride staining and fluorescence measurement for evaluation of skin cell exfoliation and turnover, and corneometry and VapoMeter analyses for evaluation of skin hydration and transepidermal water loss (TEWL), respectively. Clinical evaluations of skin appearance and texture were performed by trained investigators, and participant-reported outcomes were collected via self-assessment questionnaires.

**Results:** Exfoliation was observed as early as day 3 of daily application (p=0.0010), and acceleration (+8%) in epidermal turnover was observed at day 21 (p<0.05) compared to control sites. Within 24 hours of first application, TEWL decreased by 15% and electrical capacity increased by 25%, indicating enhanced barrier function and increased moisturization, respectively (p<0.05). Visual and tactile improvements in skin texture occurred by day 2, with an overall 31% reduction in roughness compared to baseline by day 28 (p<0.05). Clinical improvements in skin tone evenness were noted after the first application and sustained through day 28 (p<0.05). Self-assessments corroborated these findings, with 94-96% of participants reporting visible improvements in skin texture and appearance by day 28. Global skin sensitivity scores decreased by over 75% by day 28 in individuals with SSS (p<0.0001). The lotion had a favorable tolerability profile among all subjects, and no AEs were reported throughout the course of the study.

**Conclusion:** The investigated combination HA formulation enhanced epidermal turnover, barrier function, and skin texture and tone without compromising tolerability in individuals with SSS. Its favorable efficacy profile highlights its potential as an accessible over-the-counter solution to help address a gap in skincare options for SSS.

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#### Management of Hailey-Hailey Disease with ruxolitinib 1.5% cream

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## **Introduction & Objectives:**

Benign Familial Pemphigus (Hailey-Hailey Disease) is a rare chronic condition for which there is no cure, therefore, treatments consist of managing disease symptoms as effectively as possible.

Clinical presentation of Hailey-Hailey Disease (HHD) encompasses blisters that become erythematous plaques and fissures within flexural areas on a relapsing/ "flaring" basis. Therapeutic management of disease "flare-up" and symptoms commonly includes the utilization of topical corticosteroids and antibiotics.

Ruxolitinib is a janus kinase (JAK) inhibitor indicated for treatment of mild to moderate eczema and nonsegmental vitiligo and has not been used for treatment of HHD in the past. However, there have been cases of successful use of other JAK inhibitors in the management of HHD. Ruxolitinib provides a localized anti-inflammatory treatment option for HHD. Additionally, part of the consideration for utilizing ruxolitinib for treatment of HHD, was the aim to prevent and minimize the recurrence of lesions that allow bacterial colonization.

## **Materials & Methods:**

We present a case of a 72 year old female with refractory HHD.

#### **Results:**

Despite management with standard HHD treatments, such as antibiotics and corticosteroids, the patient's "flare-ups" of erythematous plaques and blistering persisted. The patient was then started on ruxolitinib 1.5% cream which has since then proven effective.

## Conclusion:

This case demonstrates the difficulties a patient with refractory HHD may experience, and the significance of exploring novel treatment options to improve disease response and patient quality of life. Ruxolitinib may be an effective treatment option for HHD management, however, further investigation is necessary at this time.

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A randomized trial comparing simulated daylight and conventional photodynamic therapy in the treatment of clinically diagnosed superficial basal cell carcinoma

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## **Introduction & Objectives:**

Simulated daylight photodynamic therapy (SDL-PDT) has been suggested as a potentially less painful alternative to conventional photodynamic therapy (C-PDT). This study aimed to determine whether SDL-PDT is as effective as C-PDT in treating superficial basal cell carcinoma (sBCC).

#### **Materials & Methods:**

This single-center, randomized controlled trial assessed the non-inferiority of SDL-PDT compared to C-PDT for adult patients with clinically diagnosed sBCCs in areas appropriate for PDT. Included lesions were randomly assigned to receive two sessions with either SDL-PDT or C-PDT with 5-aminolevulinic acid used as the photosensitizer. Pain was measured during illumination using a numeric rating scale (NRS, 0–10). Treatment outcomes were assessed at 1 year to determine overall clearance rates.

#### **Results:**

Seventy-eight participants with 193 sBCCs were treated. The majority were located on the trunk (47.2%), and 64.2% were diagnosed based solely on dermoscopy. At the 1-year follow-up, clearance rates were 62.4% for SDL-PDT and 91.8% for C-PDT (p<0.001), rejecting the non-inferiority hypothesis. Pain levels were significantly lower with SDL-PDT (mean NRS 0.1 for both sessions) compared to C-PDT (mean NRS 3.5 and 3.7; p<0.001). Immediately following treatment, 87.5% of patients preferred SDL-PDT for future treatments.

#### **Conclusion:**

While SDL-PDT offers a considerable reduction in pain compared to C-PDT, its lower clearance rate makes it less suitable as a primary treatment for sBCC. Future studies could investigate the role of SDL-PDT in situations where managing pain is more important than treatment effectiveness.

#### Clinical response to topical tirbanibulin in actinic keratoses of the scalp: potential predictive factors

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## **Introduction & Objectives:**

Actinic keratoses (AKs) and field cancerization are commonly treated with therapies associated with high rates of local skin reactions, which can compromise adherence and efficacy. Tirbanibulin 1% ointment is a novel topical treatment with antiproliferative and antitumor activity that is generally better tolerated. However, predictive clinical factors for treatment response remain unclear.

Our objective was to evaluate the clinical efficacy of tirbanibulin in treating AKs on the scalp and to identify clinical variables potentially associated with treatment response.

#### **Materials & Methods:**

We conducted a retrospective study of patients treated with tirbanibulin 1% ointment for AKs located on a single contiguous area of <25 cm² between June 2023 and June 2024. Inclusion criteria required ≥10 non-hyperkeratotic, clinically typical AKs. Treatment consisted of once-daily application for five consecutive days. Response was independently evaluated by two dermatologists and categorized as complete (>80% clearance), partial (40–80% clearance), or no response (<40% clearance). Clinical and demographic data were collected. A descriptive and bivariate analysis was performed to identify potential associations with treatment outcomes.

## **Results:**

Fifty patients were included (mean age: 72 years; sex ratio 1:1). The most common locations were scalp and cheeks (34%). Complete response was observed in 64% of patients, partial response in 18%, and no response in 14%. No significant associations were found between treatment response and age, sex, or history of non-melanoma skin cancer. While no statistically significant differences were identified regarding lesion location, a trend toward better outcomes was noted in scalp lesions.

#### **Conclusion:**

Topical tirbanibulin is effective in treating AKs, particularly those located on the scalp. Although no clinical variables reached statistical significance as predictors of response, the anatomical site may influence treatment outcomes. Multicenter studies with larger cohorts are needed to better characterize the clinical profile of responders.



The AhR agonist tapinarof suppresses human skin inflammation by inducing metabolic reprogramming and reducing production of mitochondrial pro-inflammatory DAMPs

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**Introduction & Objectives:** The aryl hydrocarbon receptor (AhR) plays a key role in skin homeostasis and immune regulation. The topical AhR agonist tapinarof effectively treats both psoriasis and atopic dermatitis but there are no mechanistic studies of its effects in human skin. We aimed to dissect tapinarof's impact on immune activation and cellular metabolism using translational models of human skin inflammation.

**Materials & Methods:** We used a xenograft model of human skin inflammation by grafting healthy skin onto immunodeficient NSG mice, followed by injection of allogeneic PBMCs. Mice were treated topically for 3 weeks with tapinarof or vehicle. Skin biopsies were analyzed by histology, immunostaining, and bulk RNA-sequencing. In parallel, *in vitro* assays were conducted on activated human T cells and 3D psoriatic skin constructs to explore metabolic and inflammatory changes upon AhR activation.

**Results:** Tapinarof treatment significantly reduced epidermal thickness and skin immune cell infiltration. It suppressed T cell, macrophage, dendritic cell and NK cell activation. Upstream damage-associated molecular pattern (DAMP) sensing via cytoplasmic nucleic acid sensing was downregulated, leading to reduced cGAS/STING, and inflammasome activation, and decreased type I, II, and III IFN and type 1, type 2 and type 17 cytokine production.

In vitro, in human T cells, tapinarof reduced mitochondrial ROS production and release of mitochondrial DNA into the cytoplasm, thereby impairing type I IFN signaling and reducing T cell activation and proliferation. Treatment of psoriatic skin constructs led to metabolic reprogramming, including inhibition of hypoxia sensing, glycolysis, fatty-acid (FA)  $\beta$ -oxidation, and glutamate influx. Tapinarof-induced AhR signaling reduced HIF1 $\alpha$  and mTOR expression in T cells, limiting glucose uptake, glycolytic capacity, and FA metabolism, while also impairing mitochondrial respiration and ATP production, inducing marked metabolic dysfunction.

**Conclusion:** In summary, tapinarof acts at the level of the mitochondria to reduce DAMP sensing via reduced ROS production and mtDNA release, thus markedly reducing inflammatory tone, and by blocking multiple metabolic pathways, thus blocking the cells' ability to use and generate energy in the hypoxic skin microenvironment. These findings provide mechanistic insights into the therapeutic efficacy of tapinarof and highlight the relevance of targeting immunometabolism in chronic inflammatory skin diseases.

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# Treatment pathway for actinic keratosis in the French general population: an insurance claims database study (EPIKA)

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## **Introduction & Objectives:**

Actinic keratosis (AK) is a common chronic, recurrent skin disease generally affecting older individuals caused by cumulative sun exposure, which is a risk factor for the development of squamous cell carcinoma (SCC). Although AK is common, awareness in the general population is low and the condition is probably underdiagnosed and under treated. For this reason, general population epidemiological studies of AK are challenging to perform. The availability of insurance claims databases provides an opportunity to collect information on large numbers of patients with AK. The objective of this study in the French national health insurance claims database was to describe the characteristics of patients treated for AK and their treatments at the national level.

#### **Materials & Methods:**

This study was performed in random sample of ~50% of all French residents in the Système National des Données de Santé (SNDS, French national health insurance claims database). All patients aged >40 years with claims for a specific AK treatment between 1st January 2014 and 31st December 2019 were identified and followed from the date of the first claim until the end of the study on 31st December 2021, or until they died. A subset of these patients with no AK-related claims in the two years prior to the index date were identified for the determination of incidence.

#### **Results:**

A total of 286,085 prevalent patients (Population 1), and 211,714 incident patients (Population 2) with an initial AK-related claim were identified. In 2019, the 12-month prevalence of AK was 15,184 cases/100,000 individuals and the incidence 1,328 cases/100,000 per year. In Population 1, the mean age was  $71.9 \pm 12.5$  years and 56.5% were men. The highest prevalence was observed in coastal regions of France. At least one AK-specific treatment was identified for 207,031 incident patients (97.8%). 107,418 of these incident patients started therapy with a topical AK treatment (51.9%). Cryotherapy was performed in 32,900 patients (15.9%) and surgery in 31,574 (15.3%), whereas photodynamic therapy was less frequently used (3.9%). The mean duration of the first treatment episode was 35.5 days (median 30 days) with 8.5 months average between episodes (median 4.6 months). After the first episode, 31,081 (14.7%) received no further therapy. For the 107,418 patients initially receiving topical treatment, 35.7% received a subsequent topical therapy, 20.4% underwent cryotherapy and 20.1% underwent skin surgery. 10,709 patients undergoing cryotherapy (35.4%) relayed to a topical treatment, as did 15,478 patients undergoing skin surgery (53.4%).

#### **Conclusion:**

The EPIKA study identified >250,000 patients receiving a specific treatment for AK in the SNDS database. This is the largest sample of patients with AK to have been studied in France. The estimated prevalence is consistent with recent population-based studies from dermatology clinics, but is likely to underestimate the actual prevalence of AK, since untreated patients will not have been identified. The principal treatment modalities were topical therapy and cryotherapy, although the use of cryotherapy is probably underestimated as patients treated with cryotherapy alone were not included as this treatment is not specific for AK. Around one-third of patients undergoing cryotherapy and one-half of those undergoing skin surgery received a relay topical therapy to prevent recurrence, which is consistent with current practice standards.

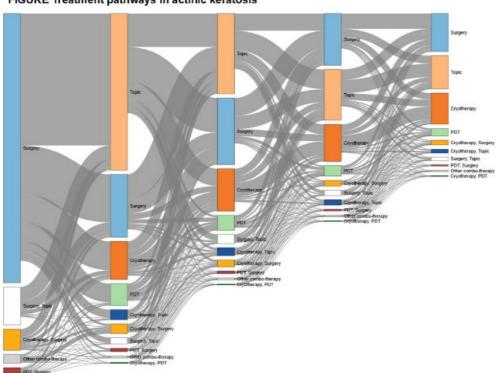


FIGURE Treatment pathways in actinic keratosis

### A potent combo can reverse the age-dependent decline of NAD+ in Men regulated by AMPK pathway

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# **Introduction & Objectives:**

NAD is an essential cofactor that plays a critical role in cellular bioenergetics. It is an energy precursor, that is constantly synthesized, metabolized, and recycled in the cell to maintain stable intracellular NAD levels through various pathways, enzymes, and precursors. As we age, NAD levels decline leading to a drop of energy production, mitochondrial dysfunction and overall, a plethora of metabolic dysfunctions. It was shown that NAD levels decline with aging in men skin. AMPK, an evolutionary conserved master regulator of cellular homeostasis and metabolism, is activated to rescue cell's energy demands. As we age, AMPK machinery decays, leaving skin deprived of energy to perform its cellular housekeeping functions, therefore, we specifically tested the effects of two potent active ingredients in activating AMPK levels in two male cells from 28- and 68-year-old donors. The aim of this study is to show the stimulating activity of a potent combo in increasing the levels of NAD further to boost ATP production and mitochondrial function in male Normal Human Dermal Fibroblasts.

### **Materials & Methods:**

Combo of Niacinamide and Resveratrol-Salicylate were evaluated for their efficacy in increasing NAD+/NADH levels, ATP production and mitochondrial function. Male fibroblast from different age donor were cultured in medium, treated with various dosage of Niacinamide and Resveratrol-Salicylate. NAD/NADH was performed using the NAD/NADH-Glo™ Assay kit (Promega, #G9071) according to the manufacturer's instruction. And ATP production and mitochondrial oxygen consumption (OCR) were conducted using Agilent Seahorse XF Analyzers.

# **Results:**

We observed an up to 26% decline of total NAD+/NADH level in aged cells compared to the young one. And the treatment of Niacinamide and Resveratrol-Salicylate was found to be effective at increasing NAD levels by 15.6% in only four hours. Resveratrol-Salicylate and Niacinamide combo can significantly increase phosphor-AMPK levels in male skin cells. We also demonstrated the decline of ATP production in aged male cells, with treatment of the potent combo the ATP/energy levels were significantly increased. In the meanwhile, we investigated the steady-state levels of mitochondrial oxygen consumption in both young and old male skin cells, the data showed the OCR was significantly increase in both cell lines.

## **Conclusion:**

Our results show that the powerful combination of these two compounds aids in producing optimal levels of energy by increasing healthy levels of NADH, increases mitochondrial oxygen consumption by supplying mitochondria with newly produced molecules of ATP while activating in concert the nutrient-sensing salvage pathway of AMPK to support skin in rescuing a faster recovery and optimal repair.

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#### Dietary supplements in dermatology: Safety versus toxicity

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# **Introduction & Objectives:**

Dietary supplements, popular since the 1980s, include vitamins, minerals, plants, and other substances with physiological effects. Although their consumption is increasing, particularly in dermatology, their regulation remains complex. While controls exist for imported products, local manufacturing is not subject to strict regulation, raising concerns about their composition, compliance with recommended dosages, and potential adverse effects. Thus, the aim of this project was to conduct a market study in order to determine the composition of dietary supplements used in dermatology and their toxicity versus safety.

#### Materials & Methods:

Between June and December 2023, a selection of 20 pharmacies and 13 parapharmacies, geographically distributed across several regions, were visited. Ingredient lists for all available dietary supplements used in dermatology were photographed and entered into a database. Statistical analysis was performed using SPSS for Windows v25. Products were evaluated according to the safe upper levels of National Agency for Food, Environmental and Occupational Health Safety (NAFEOHS) of France, and in the absence of safe upper levels, the population's nutritional references (PNR) were used. Children were excluded from the study due to the absence of well-defined toxic thresholds for this population.

#### **Results:**

Of the 155 dietary supplements studied, 71.6% were available in both pharmacies and parapharmacies, 20.6% were exclusively sold in parapharmacies, and 7.7% were only available in pharmacies. The majority (79.4%) did not specify an age group, while 11.6% were intended for adults. The most common pharmaceutical forms were capsules (59.4%), followed by tablets (18.1%) and soft capsules (9.7%). Regarding safety of use, 82.6% of products did not provide information for pregnancy, and 89.7% lacked information for breastfeeding. Only 8.4% were suitable for pregnant women, and 1.9% for breastfeeding women. Significant disparities were observed in nutrient concentrations, with 74.1% of products containing excessive doses of vitamin B3, 64.9% of vitamin B5, and 76.2% of vitamin E. Compliance with recommendations was observed for vitamin B6, selenium, calcium, and iodine. Finally, 9% of products lacked labeling.

## **Conclusion:**

The study reveals that many dietary supplements in dermatology on the market exceed recommended dosages, endangering consumer safety. It is crucial to improve labeling, strengthen controls, and raise awareness of the risks associated with unregulated consumption. A strict legislative framework is necessary to ensure their safety.

### Study assessing biotin effectiveness for treatment of seborrheic dermatitis

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# **Introduction & Objectives:**

Seborrheic dermatitis is a chronic inflammatory skin disease highly resistant to therapy. Biotin shows positive effect on sebum production and normalization of keratinization in the pilosebaceous unit, which may possibly be effective for seborrheic dermatitis treatment. Objective of the study: to evaluate the biotin effectiveness for the treatment of seborrheic dermatitis.

#### **Materials & Methods:**

150 patients with seborrheic dermatitis were enrolled in the study. The severity seborrheic dermatitis severity score was worked out. The scoring scale included assessment of erythema, edema, vesiculation, excoriations, scaling and skin oiliness. In addition, itching and sleep disturbances were assessed. Patients with seborrheic dermatitis were randomized into 2 groups: Group I - 100 patients who received biotin at a dose of 5 mg per day orally for 3 months; Group II - 50 patients who used traditional therapy without the use of biotin. Clinical examination of patients was performed before treatment, after 1 and 3 months of treatment.

#### **Results:**

The clinical evaluation of the results of 1 month treatment is presented in Table 1. Patients from both groups significantly improved in seborrheic dermatitis severity score within 1 month of treatment. The indicators were statistically significantly better in the group of patients who received biotin comparing with group of patients receiving only standard therapy. 93% of patients in the group that additionally received biotin during 1 month did not have any clinical manifestations of seborrheic dermatitis. A positive effect was obtained in patients with different localization of the process.

Table 1. Seborrheic dermatitis severity score and subjective symptoms in patients with seborrheic dermatitis after 1 month treatment ( $\underline{M}\pm\underline{m}$ )

| Indexes                       | Patients before | Patients after 1 month of treatment |   |  |  |
|-------------------------------|-----------------|-------------------------------------|---|--|--|
|                               | treatment       | Standard<br>treatment               | Treatment with<br>additional biotin<br>prescription |  |  |
| Erythema score                | 2,3±0,2         | 1,4±0,2●                            | 0,6±0,1•◊   |  |  |
| Edema score                   | 2,1±0,3         | 1,3±0,3                             | 0,6±0,1●  |  |  |
| Vesiculation score            | 1,5±0,2         | 1,0±0,2                             | 0,2±0,04•   |  |  |
| Excoriation score             | 1,5±0,1         | 1,0±0,1●                            | 0,3±0,05•◊  |  |  |
| Scaling score                 | 2,4±0,2         | 1,6±0,1●                            | 0,4±0,1•◊   |  |  |
| Skin greasiness               | 2,3±0,3         | 1,7±0,3                             | 0,3±0,07•◊  |  |  |
| Seborrheic dermatitis scoring | 2,0±0,2         | 1,3±0,1●                            | 0,4±0,1•◊   |  |  |
| Itching                       | 5,0±0,9         | 3,1±0,7                             | 1,5±0,4◆  |  |  |
| Sleep disorders               | 1,7±0,3         | 1,0±0,2                             | 0,1±0,02•◊  |  |  |
|                               | 1               |                                     |   |  |  |

Notes: • – significant difference (P<0.05) before and after treatment; ◊ - significant difference (P<0.05) after treatment between groups with different treatment regimens.

In order to ensure complete recovery of patients and long-term remission, use of biotin was extended up to 3 months. The clinical results are presented in Table 2. Patients from both clinical groups had a positive clinical result in 3 months after the start of treatment. The additional use of biotin led to the recovery of 98% of patients with localization of the pathological process on the scalp and face. Only 5.3% of patients with localization of seborrheic dermatitis on the scalp and face had mild scaling and 4.7% of patients with localization of seborrheic dermatitis on the trunk had mild scaling and changes in skin oiliness.

Table 2. Seborrheic dermatitis severity score and subjective symptoms in patients with seborrheic dermatitis after 3 months treatment ( $M\pm m$ )

| Indexes                       | Patients before | Patients after 1 month of treatment |                      |  |  |
|-------------------------------|-----------------|-------------------------------------|----------------------|--|--|
|                               | treatment       | Standard<br>treatment               | з включенням біотину |  |  |
| Erythema score                | 2,3±0,2         | 0,6±0,1●                            | 0,0±0,0•◊            |  |  |
| Edema score                   | 2,1±0,3         | 0,7±0,2●                            | 0,0±0,0●             |  |  |
| Vesiculation score            | 1,5±0,2         | 0,2±0,1•                            | 0,0±0,0•◊            |  |  |
| Excoriation score             | 1,5±0,1         | 0,4±0,1•                            | 0,0±0,0•◊            |  |  |
| Scaling score                 | 2,4±0,2         | 0,9±0,2●                            | 0,1±0,04•◊           |  |  |
| Skin greasiness               | 2,3±0,3         | 1,1±0,2●                            | 0,1±0,03•◊           |  |  |
| Seborrheic dermatitis scoring | 2,0±0,2         | 0,65±0,1●                           | 0,03±0,01•◊          |  |  |
| Itching                       | 5,0±0,9         | 1,5±0,3●                            | 0,0±0,0•◊            |  |  |
| Sleep disorders               | 1,7±0,3         | 0,5±0,1•                            | 0,0±0,0•◊            |  |  |

Notes: ● – significant difference (P<0.05) before and after treatment; ◊ - significant difference (P<0.05) after treatment between groups with different treatment regimens.

The seborrheic dermatitis severity score was statistically significantly better in patient who used biotin than in the group receiving standard therapy. Itching and sleep disturbances were statistically significantly lower after biotin

**Conclusion:** Treatment of seborrheic dermatitis with biotin is justified as it provides a rapid and long-lasting clinical effect.

#### Impact of long-term topical treatment on patient outcomes in patients with psoriasis

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**Introduction & Objectives:** The aim of the study was to evaluate the efficacy of long-term (>12 weeks) topical treatments in reducing the severity of psoriasis.

**Materials & Methods:** We conducted a systematic literature search for English-language peer-reviewed articles in PubMed, Web of Science, Medline, and CINAHL from 1994 to 2023. We assessed percentage reduction in mean psoriasis severity and improvement in quality of life from baseline to final study visit.

**Results:** Eighteen studies conducted in Western Europe, North America, and Asia were included. The study designs included prospective studies, single- and multicenter randomized controlled trials, and retrospective observational studies. Participants included both adults and children with mild-to-severe psoriasis. Severity of psoriasis was measured using different psoriasis severity scores (PSS), including the Psoriasis Area Severity Index (PASI), Lattice System Physician's Global Assessment (LS-PGA), Psoriasis Global Assessment (PGA), and Body Surface Area (BSA).

Topical calcipotriol used for 26–52 weeks led to up to 67% reduction in mean PSS. Tacalcitol ointment used over 26–78 weeks led to up to 75% reduction in mean PSS. Calcipotriol/betamethasone dipropionate (various formulations) used for up to 56 weeks reduced mean PSS by up to 64%. Proactive maintenance therapy following disease clearance was associated with reduced recurrence rates (Fig. 1). Only four studies reported quality-of-life outcomes, showing improvements of up to 78%. Additional adherence support further improved the efficacy of topical drugs. Most studies were of medium quality and reported no severe adverse events.

Few studies reported SD, and original data were often unavailable due to study age, limiting quantitative synthesis. Results were therefore summarized narratively and graphed without SD. Low baseline disease severity may have inflated percentage changes.

**Conclusion:** Long-term use of topical treatments provides clinically meaningful improvements in psoriasis severity and quality of life. Proactive therapy reduces relapse rates, and adherence support enhances outcomes. Topical agents containing corticosteroids and/or vitamin D analogues are effective and well tolerated for extended use in patients with mild-to-severe psoriasis.

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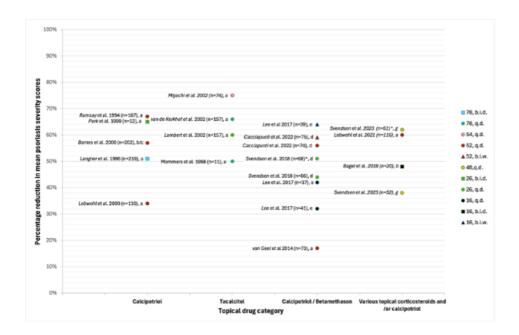


Figure 1: Percentage reduction in mean psoriasis severity scores, following different long-term topical treatments in 1867 mild-to-severe psoriasis cases. The 21 plotted points reflect split datasets originating from 16 studies, due to multiple clinical endpoints reported per study. The various topical drug categories are grouped on the X-axis as calcipotriol, tacalcitol, calcipotriol/betamethasone and different topical corticosteroids. The Y-axis indicates percentage reduction in mean psoriasis severity scores (PASI (14), PGA (2), LS-PGA (4) and BSA (2)) from baseline to final visit. Symbol shape reflects application frequency: ● = once daily (q.d.), ■ = twice daily (b.i.d.), ▲ = twice weekly (b.i.w.). Color indicates treatment duration in weeks: black = 16 weeks, green = 26 weeks, yellow = 48 weeks, red = 52 weeks, pink = 54 weeks, blue = 78 weeks. Mean PSS reductions ranged from 17% to 75%, with the greatest effects observed for tacalcitol and calcipotriol monotherapy. n = included cases. a = ungventum, b = solution, c = cream, d = foam, e = gel, f = lotion and g = various formulations.

# Investigation of the Turmeric (Curcuma longa) Fermentation Process by Lactobacillus plantarum and Saccharomyces cerevisiae for Cosmetic Applications

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# **Introduction & Objectives:**

Turmeric is a widely used herb in both medicine and food preparation. Recently, fermented turmeric has emerged as a promising material, attracting significant research attention in the pharmaceutical and food industries. However, its application in cosmetics remains largely unexplored. To address this gap, our research group investigated the fermentation of turmeric using *Lactobacillus plantarum* (L. plantarum) and *Saccharomyces cerevisiae* (S. cerevisiae), to evaluate its potential for cosmetic use.

#### Materials & Methods:

Turmeric was fermented separately with the bacterial strain *L. plantarum*, the yeast strain *S. cerevisiae*, and through co-fermentation with both. The biological activities of the fermented turmeric were then assessed, including antibacterial properties, tyrosinase enzyme inhibition, and antioxidant activity, and compared with those of non-fermented turmeric.

#### **Results:**

Both fermented and non-fermented turmeric samples exhibited strong antibacterial activity against pathogenic bacteria including *Escherichia coli* (E. coli), methicillin-susceptible *Staphylococcus aureus* (MSSA), methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa* (P. aeruginosa), and *Cutibacterium acnes* (C. acnes). The minimum inhibitory concentration (MIC) values for fermented turmeric were reduced by half compared to non-fermented samples (Table 1). Notably, turmeric co-fermented for 72 hours showed the highest tyrosinase inhibitory activity, increasing by 2.03 times (Fig 1), and the greatest DPPH radical-scavenging activity, increasing by 1.38 times (Fig 2), relative to non-fermented turmeric.

#### **Conclusion:**

Fermented turmeric demonstrates strong biological activities relevant to cosmetic applications, including antibacterial, antioxidant, and tyrosinase-inhibiting effects, supporting its potential use in skin care products.

<sup>&</sup>lt;sup>2</sup>University of Medicine and Pharmacy at Ho Chi Minh City, Dermatology, Ho Chi Minh, Viet Nam

| Turmeric extract samples | MIC<br>(mg/ml) |  |  |
|--------------------------|----------------|--|--|
|                          | MSSA           |  |  |
| LP24                     | 5              |  |  |
| LP48                     | 2,5            |  |  |
| LP72                     | 2,5            |  |  |
| LPSC24                   | 5              |  |  |
| LPSC48                   | 2,5            |  |  |
| LPSC72                   | 2,5            |  |  |
| SC24                     | 5              |  |  |
| SC48                     | 5              |  |  |
| SC72                     | 2,5            |  |  |
| N                        | 5              |  |  |

Table 1. MIC values (mg/ml) of turmeric extract samples. (*L. plantarum* for 24 hours: LP24, *L. plantarum* for 48 hours: LP48, *L. plantarum* for 72 hours: LP72, *L. plantarum* and *S. cerevisiae* for 24 hours: LPSC24, *L. plantarum* and *S. cerevisiae* for 72 hours: LPSC72, *S. cerevisiae* for 24 hours: SC24, *S. cerevisiae* for 48 hours: SC48, *S. cerevisiae* for 72 hours: SC72, Non-fermented: N)

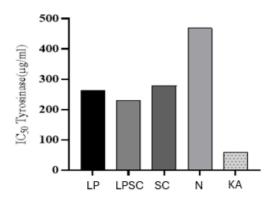


Figure 1. Comparison of the IC50 values (µg/ml) for tyrosinase enzyme inhibition between turmeric extracts fermented for 72 hours, non-fermented turmeric extract, and kojic acid. (LP: *L. Plantarum*, LPSC: *L. plantarum* and *S. Cerevisiae*, SC: *S. Cerevisiae*, N: Non-fermented, KA: kojic acid)

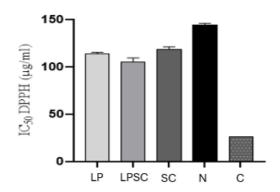


Figure 2. Comparison of the IC50 values (μg/ml) for DPPH radical scavenging activity between turmeric extracts fermented for 72 hours, non-fermented turmeric extract, and vitamin C. (LP: *L. Plantarum*, LPSC: *L. plantarum* and *S. Cerevisiae*, SC: *S. Cerevisiae*, N: Non-fermented, C: vitamin C)

### STAR Particles: A Breakthrough solution for safe and effective siRNA skin Delivery

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# **Introduction & Objectives:**

The small interfering RNA (siRNA) drug class holds great promise as a targeted therapy for chronic inflammatory skin conditions, offering specificity, selectivity, safety, and long-lasting effect with infrequent dosing. However, the effective topical delivery of these macromolecules is hindered by the stratum corneum. To address this, star-shaped ceramic sub-millimetric particles, termed STAR particles, have been engineered to create microscopic pores in the skin,~~ enabling transepidermal drug delivery. This study aimed to deliver functional siRNA into the skin both *ex vivo* and *in vivo* using STAR particles. Additionally, separate studies were conducted to evaluate the tolerability of these particles in healthy individuals and patients with atopic dermatitis, a prevalent and burdensome chronic skin disease.

#### **Materials & Methods:**

Human and porcine skin *ex vivo* were used to assess *siRNA delivery and potency at silencing JAK1 mRNA (ALD-102 & minipig surrogate ALD-105). STAR particles were formulated in a gel with ALD-105 and tested* in vivo\* in Gottingen minipigs; safety, tolerability, skin pharmacokinetics (PK) and pharmacodynamics (PD) were assessed. In addition, the safety and tolerability of STAR particles in a gel, without an active ingredient, were evaluated in healthy individuals and atopic dermatitis patients.

# **Results:**

STAR particles effectively facilitated the delivery of JAK1-targeting siRNA in both human and porcine *ex vivo* skin models. The INF-g-induced chemokine CXCL10 was also suppressed by STAR particles-ALD102 treatment. *In vivo* studies with Göttingen minipigs demonstrated that STAR particles successfully delivered siRNA to the skin with accumulation above efficacy level observed for at least 3 weeks after last application. This resulted in long-term JAK1 silencing as well as suppression of downstream inflammatory signaling pathways. Both the long-lasting efficacy of siRNA and skin PK/PD modeling support application frequency once every 2 to 3 weeks. Finally, we demonstrated that STAR particles are well tolerated in healthy and atopic dermatitis subjects. \*\*

# **Conclusion:**

Collectively, these findings underscore the groundbreaking potential of STAR particle-facilitated siRNA delivery as a transformative approach for non-invasive, well-tolerated, and infrequent local treatment of dermatological conditions.

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### Efficacy and tolerability of tirbanibulin 1% ointment in basal cell carcinoma: real-life experience in Italy

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**Introduction & Objectives:** Tirbanibulin 1% ointment is approved for treating actinic keratosis on the face or scalp over a field up to 25 cm2 in Europe and up to 100 cm2 in the United States. Tirbanibulin inhibits tubulin polymerization and Src kinase signalling, resulting in antiproliferative and pro-apoptotic activity. Its efficacy and safety were demonstrated by two phase III clinical trials [1]. Its mechanism of action, together with its favourable tolerability, has prompted the exploration of its possible extension to new therapeutic applications. Therefore, here we present our clinical experience with tirbanibulin for basal cell carcinoma (BCC).

**Materials & Methods:** Efficacy and tolerability of tirbanibulin 1% ointment were evaluated in adult patients with BCC at one centre in Italy. Tirbanibulin was applied for one or two cycles of 5 or 10 consecutive days with a variable break between 1 and 3 weeks. Effectiveness was assessed by the percentage of patients who achieved complete resolution or improvement of lesions and by percentage of patients with persistent BCC. Both clinical and dermoscopic assessments were performed at 1, 3, 6, 9 and 12 months after application. Local skin reactions were evaluated during treatment course, and were scored as 0 (absent), 1 (mild), or 2 (moderate-severe).

**Results:** A total of 36 patients (mean age: 68.0 years; women: 52.8%) with BCC (superficial: 50.0%; nodular: 38.9%; pigmented: 11.1%) were included. BCC was located mainly on face (33.3%) or trunk (41.7%). Patients applied tirbanibulin for 5 consecutive days (in occlusion; 5.7%); for 10 consecutive days (40.0%), for two 5-day cycles (25.7%), or for two 10-day cycles (28.6%). A month after treatment with tirbanibulin, resolution of lesions was achieved by 58.3% of patients (patients with superficial BCC: 71.4%); and an improvement was achieved by 22.2% of patients (patients with nodular BCC: 62.5%). In 19.4% of patients BCC persisted (patients with nodular BCC: 71.4%). Regarding tolerability, 66.7% of patients experienced moderate-severe erythema and 25.0% of patients experienced mild erythema.

**Conclusion:** Tirbanibulin 1% ointment was effective and well tolerated in patients with BCC. Tirbanibulin could represent a potential new therapeutic option in BCC with promising outcomes.

[1] Blauvelt A et al. N Engl J Med. 2021;384(6):512-20.

### Back to life: transcriptomic and metabolomic signatures of revived skin probiotics

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<sup>3</sup>Universitat Pompeu Fabra, Faculty of Medecine and Life Sciences, Barcelona, Spain

# **Introduction & Objectives:**

The efficacy of probiotics relies on the ability of freeze-dried bacterial strains to revive and regain metabolic activity upon skin application. Ideally, bacterial revival should be rapid and efficient to maximize therapeutic impact, either by re-colonizing disbalanced skin microbiota or by ensuring active delivery of beneficial compounds. Yet, these biological mechanisms remain unclear, limiting precision in product efficacy. This study aims to dissect the early "back-to-life" dynamics of distinct *Cutibacterium acnes* (*C. acnes*) phylotypes, exploring the biological requirements for successful reactivation. By reviving different *C. acnes* phylotypes in skin-mimicking media, we generate extensive multi-omics datasets, including growth kinetics, metabolic profiling, and gene expression, supported by robust biological replicates. Our objective is to decode the revival trajectories of freeze-dried probiotics, uncover key drivers of reactivation, and identify strains or conditions with faster and stronger skin revival potential.

# **Materials & Methods:**

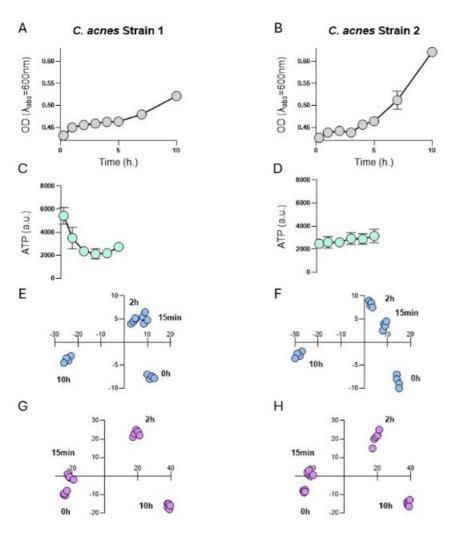
Freeze-dried *C. acnes* strains were revived alone or in combination in skin-mimicking media (KSFM, KSFM+lactate, and keratinocyte-conditioned KSFM). Revival was monitored by optical density and ATP measurements across five biological replicates per strain and medium over ten hours, generating 195 samples. Secretome analysis by UHPLC-Orbitrap-MS and Trace element analysis by ICP-MS was used for untargeted metabolomics. Over 30 OPLS-DA models captured comparisons across strains, timepoints, replicates, and media types. For transcriptomics, total RNA was extracted, rRNA depleted, and used for directional RNA-seq library prep. Sequencing was done with 2×150 bp paired-end reads on the Illumina NovaSeq 6000. Reads were quality filtered, mapped to reference genomes, and analyzed for differential gene expression with DESeq2.

#### **Results:**

We observed that one *C. acnes* strain showed early growth driven by usage of stored ATP, the other *C. acnes* strain displayed very slow growth in the early revival phase during ATP-generation (Fig. 1 A to D). Multi-omics analysis at several timepoints revealed over 500 significantly different chemical/biological compounds across strains, timepoints, and media. OPLS-DA showed clear metabolic shifts over time, mapping the transition from dormancy to active life (Fig. 1 E, F). A similar distribution pattern was observed in the PCAs of the transcriptomic profiles, underscoring the reproducibility of the results (Fig 1 G, H). Remarkably, metabolic activity surged within just 15 minutes for both strains and confirmed the distinct revival strategies between strains. Interestingly, significant differences between the media types were noticed, emphasizing the influence of host/microbes crosstalk molecules on bacterial revival. By correlating the transcriptome and the metabolome during the first minutes of probiotic revival, we mapped the biological transitioning of bacterial revival including the specificity of this biological process and the biological needs according to strain.

#### **Conclusion:**

These insights highlight strain-specific revival behaviors and early metabolic needs of topical probiotics. Our findings also emphasize the complex interplay between probiotic strains, their environment, and the host-derived crosstalk molecules.



**Figure 1** | Freeze-dried *C. acnes* growth in KSFM: optical density 0-10hours (A, B); ATP measurement 0-5hours (C, D). Muli-omics in KSFM: OPLS-DA of secretome (E, F); PCA of transcriptome (G, H).

# Apremilast Improves Patient-reported Pain Regardless of Sex and Age in Early Oligoarticular Psoriatic Arthritis: A Post-hoc Analysis From FOREMOST

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**Introduction & Objectives:** Psoriatic arthritis (PsA) is characterized by pain, fatigue, stiffness, and swelling, with pain reported as a prominent symptom negatively impacting patient quality of life.1 Females report greater pain severity and disease burden than males, highlighting the need for sex-specific analyses in clinical studies.2 Additionally, little is known about how age affects pain in PsA, and if pain in older patients may be recalcitrant to treatment. This post hoc analysis of the FOREMOST study assessed changes in patient-reported pain outcomes across sex and age subgroups through 48 weeks of apremilast (APR) treatment in patients with early oligoarticular (oligo) PsA and the impact of APR on pain.

Materials & Methods: FOREMOST (NCT03747939) enrolled 308 patients with early oligo (>1-≤4 swollen and >1-≤4 tender joints; 66-68 joints assessed) PsA.3 Patients were randomized 2:1 to APR or placebo (PBO) for 24 weeks (early escape at week 16), after which all patients received APR through Week 48. We report changes in patient-reported pain outcomes through Week 48 by sex and age (<40, 40-55, and >55 years): pain visual analogue scale (VAS; 0 to 100 mm, higher scores indicate more pain), PsA Impact of Disease 12-item questionnaire (PsAID-12) pain score (0 [best] to 10 [worst]), and 36-item Short Form Survey (SF-36) bodily pain domain score (norm-based, higher scores indicate less pain). Week-16, PBO-controlled data are reported for the full analysis set (N=308); up to Week-48, extension-phase data are reported as observed for N=291 patients who received ≥1 dose of APR during the study.\*\*

**Results:** Of 308 patients (PBO n=105, APR n=203), 169 (54.9%) were females, with uneven distribution between arms: PBO, n=51 (49%) and APR, n=118 (58%). By age, 67 (21.8%) patients were <40 years (PBO, n=25; APR, n=42), 124 (40.2%) 40–55 years (PBO, n=41; APR, n=83), and 117 (38.0%) >55 years (PBO, n=39; APR, n=78). Baseline pain was higher in females than males (**Figure 1**) and generally similar across age groups (**Figure 2**); patients <40 years randomized to PBO reported lower baseline Pain VAS.

At Week 16 and across sex and age groups, patients reported greater improvements in all pain scores with APR vs PBO, with patients <40 years generally reporting the numerically largest differences (**Figure 1-2**). At Week 16, improvements in pain scores in PBO were greater in patients aged >55 years compared with other age groups (**Figure 2**). Patients continuing or switching to APR in the extension phase continued to report improvements in pain scores through Week 48, regardless of sex or age (**Figures 1-2**).

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<sup>&</sup>lt;sup>5</sup>Sorbonne Université, Paris, France

<sup>&</sup>lt;sup>6</sup>Krembil Research Institute, Toronto, Canada

<sup>&</sup>lt;sup>7</sup>UC San Diego School of Medicine, San Diego, United States

<sup>&</sup>lt;sup>8</sup>Amgen Inc., Thousand Oaks, United States

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Conclusion: In the FOREMOST study, APR improved patient-reported pain in patients with early oligo PsA regardless of sex or age, with sustained benefits through Week 48. Females reported greater baseline burden of PsA-related pain vs males. Younger patients showed the numerically largest improvements in pain with APR vs PBO; however, in the PBO group, older patients experienced greater improvements in pain than younger patients, potentially due to baseline imbalances in patient characteristics affecting pain outcomes, other causes of pain, or comorbidities. These findings highlight the need to better understand factors contributing to pain in PsA to improve patient care.

#### **References:**

- \1. Gudu and Gossec. Expert Rev Clin Immunol. 2018;14(5):405-417
- \2. Passia et al. Arthritis Res Ther. 2022;24(22)

\3. Gossec et al. Ann Rheum Dis. 2024;83(11):1480-1488 Figure 1. Change From Baseline in Patient-Reported Pain at Weeks 16 and 48 By Sex ■ PBO ■ PBO/APR APR a. Pain VAS (mm) 73 60 5.0 Mean (SE) change from baseli Patient's Assessment of Pain VAS (mm) 0.0 -5.0 -2.5 -10.0 -15.0 -7.5 -20.0 -16.1 -17.6 -17.2 -25.0-20.8-30.0 -26.1 -35.0 Week 16 Week 48 Week 16 Week 48 Baseline Values: Patient's Assessment of Pain VAS (mm) Placebo APR Sex Mean ± SE (n) Mean ± SE (n) Male 47.9 ± 3.4 (54) 49.8 ± 2.4 (82) 54.5 ± 2.7 (51) 54.1 ± 2.0 (116) Female b. PsAID-12 Pain Score Male 50 72 43 59 99 34 71 0.0 (SE) change from baseline PsAID-12 Pain Score -0.5-1.0-0.6 -0.5 -1.5-2.0-1.8 -2.5-3.0 Week 48 Week 16 Week 16 Week 48 Baseline Values: PsAID-12 Pain Score Placebo APR Mean ± SE (n) Sex Mean ± SE (n) Male  $5.5 \pm 0.3 (54)$ 5.3 ± 0.2 (81) Female  $5.9 \pm 0.3$  (51) 5.8 ± 0.2 (116) c. SF-36 Bodily Pain Domain Score 46 63 110 36 9.0 (SE) change from baseline: PsAID-12 Pain Score 7.0 5.0 3.0 1.0 -1.0 Week 16 Week 48 Week 16 Week 48 Baseline Values: SF-36 Bodily Pain Domain Score APR Placebo Sex Mean ± SE (n) Mean ± SE (n) Male 41.0 ± 1.1 (54) 40.6 ± 0.8 (81)

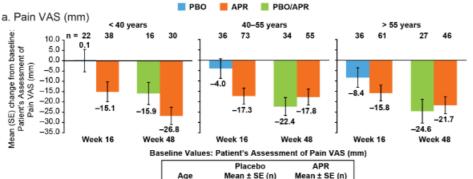
N = Number of subjects in the analysis set; n = Number of subjects with observed data. Week 16 data are reported as least squares means for the Full Analysis Set (all randomized patients: PBO, N = 105; APR, N = 203); Week 48 data are reported as arithmetic means as observed for patients who receive teast one dose of apremilast at any time in the study, as randomized or transitioned from PBO to APR at Week 16 or 24 (PBO, N = 88; APR, N = 203). PsAID-12: PsA Impact of Disease 12-item; SE: standard error; SF-36: 36-item Short Form Survey; VAS: visual analog scale

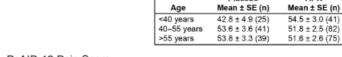
38.0 ± 1.0 (51)

38.8 ± 0.7 (116)

Female

Figure 2. Change From Baseline in Patient-Reported Pain at Weeks 16 and 48 By Age





#### b. PsAID-12 Pain Score < 40 years 7 16 40–55 years 73 34 > 55 years 61 27 Mean (SE) change from baseline: PsAID-12 Pain Score 0.5 n = 22 37 29 36 73 66 36 0.0 -0.5-1.0 -0.2 -0.5 -1.5 -0.9 -2.0 -2.5 -2.0 -2.0 -3.0 -2.5-3.5-3.1 -4.0 · Week 16 Week 48 Week 16 Week 48 Week 48

Baseline Values: Patient's Assessment of Pain VAS (mm) Placebo APR Mean ± SE (n) Mean ± SE (n) Age  $4.8 \pm 0.5 (25)$ 6.0 ± 0.3 (40)

#### < 40 years 40-55 years 5.8 ± 0.3 (41) > 55 years $6.2 \pm 0.3 (39)$ 5.5 ± 0.3 (75)

#### c. SF-36 Bodily Pain Domain Score Mean (SE) change from baseline: SF-36 Bodily Pain Domain Score < 40 years 40-55 years > 55 years 8.0 -7.0 -6.0 -5.0 -4.0 -3.0 -2.0 -1.0 --1.0 --2.0 0.2 17 n = 23 39 32 40 78 34 58 37 72 31 52

Week 16

Week 16

Week 48

Baseline Values: SF-36 Bodily Pain Domain Score

Week 48

Week 16

Week 48

|             |                 | APR   |
|-------------|-----------------|---|
| Age         | Mean ± SE (n)   | Mean ± SE (n)   |
| < 40 years  | 42.2 ± 1.9 (25) | 38.3 ± 1.0 (40)   |
| 40-55 years | 40.2 ± 1.1 (41) | 40.2 ± 0.9 (82)   |
|             | 37.1 ± 1.1 (39) | 39.4 ± 0.9 (75)   |
|             | < 40 years      | < 40 years 42.2 ± 1.9 (25)<br>40–55 years 40.2 ± 1.1 (41) |

N = Number of subjects in the analysis set; n = Number of subjects with observed data. Week 16 data are reported as least squares means for the Full Analysis Set (all randomized patients: PBO, N = 105; APR, N = 203); Week 48 data are reported as arithmetic means as observed for patients who received at least one dose of apremiliast at any time in the study, as randomized or transitioned from PBO to APR at Week 16 or 24 (PBO, N = 88; APR, N = 203). PsAID-12: PsA Impact of Disease 12-item; SE: standard error; SF-36: 36-item Short Form Survey; VAS: visual analog scale

### **Improving Oral Aperture with Perioral Hyaluronidase in Systemic Sclerosis**

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# **Introduction & Objectives:**

Systemic sclerosis (SSc) is a chronic autoimmune connective tissue disease characterized by excessive extracellular matrix production, fibrosis, and vascular damage, often leading to multisystem complications.

Among the common clinical manifestations of SSc is microstomia, defined as an abnormally reduced oral aperture with an interincisal distance (IID) of less than 50 mm. This condition, which affects approximately 52% to 80% of patients, results from perioral soft tissue fibrosis and is associated with progressive functional impairment. Microstomia significantly impacts patients' quality of life by interfering with essential functions such as eating, speaking, and maintaining oral hygiene.

Despite its high prevalence, there is currently no standardized treatment for microstomia, and the available therapeutic approaches offer limited evidence. In this context, we present a clinical case to evaluate the use of intradermal hyaluronidase as a therapeutic intervention.

## Materials & Methods:

We report the case of a 62-year-old woman diagnosed with diffuse systemic sclerosis for 17 years, under stable systemic treatment.

At baseline, the interincisal distance (IID) was measured in maximal forced opening, yielding a value of 35 mm. Oral circumference was assessed using a mobile application, and the Mouth Handicap in Systemic Sclerosis Scale (MHISS) questionnaire was administered to evaluate the functional impact of microstomia. This tool ranges from 0 (no disability) to 48 (maximum disability).

The treatment consisted of intradermal hyaluronidase injections administered in the perioral region: 200 units distributed across six injection sites per session. A total of four sessions were performed at monthly intervals. Follow-up continued for three additional months, with monthly evaluations including clinical photography, and reassessment of IID, oral circumference, and MHISS scores.

# **Results:**

After 4 sessions of intradermal hyaluronidase and 3 months of follow-up, the following clinical outcomes were observed:

- **Interincisal distance (IID):** increased from 35 mm to 39 mm, showing a 4 mm gain from baseline, corresponding to an **11.4% improvement**.
- **Oral circumference:** increased from 16.5 cm to 16.6 cm, a 0.1 cm difference, which represents a**0.6% improvement**, suggesting a mild enhancement in perioral tissue extensibility.
- Quality of life (MHISS): a 30-point reduction was observed in the MHISS score, with the most notable improvement in the eating domain, indicating a significant functional benefit.

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**Adverse effects:** no serious adverse events were reported. The most frequent side effect was**mild pain at the injection site**, present in all sessions and well tolerated with the use of**topical anesthetic** applied beforehand.

#### **Conclusion:**

This case suggests that intradermal hyaluronidase may enhance perioral tissue elasticity and facilitate an increase in oral aperture in patients with microstomia secondary to systemic sclerosis. The objective improvement in interincisal distance and oral circumference, along with the subjective enhancement in quality of life (MHISS), supports its potential clinical benefit.

Although the results are promising, they should be interpreted with caution due to the limitations of a single-case report. Further prospective studies with larger patient cohorts and long-term follow-up are essential to confirm these findings and determine the duration and consistency of the therapeutic effect.



# Access to systemic dermatologic treatments worldwide: insights from the SkinObservatory study

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**Introduction & Objectives:** Prior studies evaluating access to dermatologic medications have focused on a limited number of countries and conditions but have illustrated substantial disparities. Although access to systemic agents for conditions like psoriasis and atopic dermatitis is well established in North America and Europe, studies have shown that low- to middle-income countries, especially in Africa and South America, have little to no access to these potentially transformative therapies. For instance, one study on systemic psoriasis treatments in Brazil and Chile found that only one-third of patients were able to obtain prescribed biologics due to insurance or regulatory challenges. Despite these data, there has been no assessment of access to commonly prescribed systemic dermatologic treatments on a global scale.

**Materials & Methods:** The ILDS Global Access to Skin Health Observatory Study (SkinObservatory) is a cross-sectional, Delphi-developed, online survey of national-level dermatologic leaders in all 194 WHO member states. Participants reported the availability of thirteen systemic medications, with responses compared across World Bank income (WBI) levels using Chi-squared and Fisher's exact tests.

**Results:** The SkinObservatory survey launched in August 2024, and data has been collected for 128 countries distributed across the four World Bank income groups: low (13% of countries), lower-middle (32%), upper-middle (26%), and high (29%). Antibiotics and antifungals were among the most widely available systemic medications, without significant variation based on WBI level (**Table 1**). Antibiotics were generally available (>50% of settings) in 93.0% of countries, and antifungals were similarly available in 85.2% of countries. Corticosteroids (89.8%) and methotrexate (68.0%) were also generally available in most countries, but the availability of corticosteroids (p=0.011) and methotrexate (p=0.001) was significantly associated with WBI level, with limited access in lower-income countries.

We found a significant (p<0.001) association between WBI level and the availability of newer systemic agents, including TNF-alpha inhibitors (TNFi), PDE4 inhibitors (PDE4i), IL4/IL13 inhibitors, IL23 inhibitors, CD20 inhibitors, and JAK inhibitors (JAKi) (**Table 2**). These medications were generally available in 56.8% (PDE4i) to 72.9% (TNFi) of high-income countries. Conversely, availability of these newer systemic agents ranged from generally not available (<50% of settings) to not available in 81.3% (PDE4i) to 93.8% (JAKi) of low-income countries.

**Conclusion:** This study represents the first systematic global assessment of access across a wide range of dermatologic medications. The advent of targeted therapies has revolutionized dermatology's ability to safely and effectively treat diseases with significant morbidity and mortality. Although patients in most countries are able to access oral antibiotics and antifungals, a significant discrepancy in access was apparent for newer systemic therapies across WBI income groups. Our data highlight stark disparities in access to advanced therapies between higher- and lower-resourced settings, underscoring the need for global transparency and advocacy to improve access to therapeutics among under-resourced populations.

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Table 1. Reported availability of systemic medications across all countries

| Medication           | Generally<br>available (>50%<br>of settings)<br>(n, %) | Theoretically<br>available but<br>significant barriers<br>(n, %) | Generally not<br>available (<50%<br>of settings)<br>(n, %) | Not available<br>in the country<br>(n, %) | Unsure<br>(n, %) |
|----------------------|--|--|--|---|------------------|
| Oral antibiotics     | 119 (93.0%)  | 7 (5.5%)   | 2 (1.6%)   | 0 (0.0%)                                  | 0 (0.0%)         |
| Oral antifungals     | 109 (85.2%)  | 12 (9.4%)  | 7 (5.5%)   | 0 (0.0%)                                  | 0 (0.0%)         |
| Oral steroids        | 114 (89.8%)  | 9 (7.1%)   | 4 (3.2%)   | 0 (0.0%)                                  | 0 (0.0%)         |
| Oral retinoids       | 66 (51.6%)   | 30 (23.4%)   | 25 (19.5%)   | 5 (3.9%)                                  | 2 (1.6%)         |
| Methotrexate         | 87 (68.0%)   | 24 (18.8%)   | 16 (12.5%)   | 1 (0.8%)                                  | 0 (0.0%)         |
| Azathioprine         | 67 (52.3%)   | 30 (23.4%)   | 25 (19.5%)   | 5 (3.9%)                                  | 1 (0.8%)         |
| Cyclosporine         | 61 (48.4%)   | 29 (23.0%)   | 28 (22.2%)   | 7 (5.6%)                                  | 1 (0.8%)         |
| TNF-alpha inhibitors | 36 (28.6%)   | 32 (25.4%)   | 25 (19.8%)   | 30 (23.8%)                                | 3 (2.4%)         |
| PDE4 inhibitors      | 23 (18.7%)   | 15 (12.2%)   | 26 (21.1%)   | 54 (43.9%)                                | 5 (4.1%)         |
| IL4/IL13 inhibitors  | 25 (20.0%)   | 24 (19.2%)   | 24 (19.2%)   | 49 (39.2%)                                | 3 (2.4%)         |
| IL23 inhibitors      | 27 (21.6%)   | 17 (13.6%)   | 21 (16.8%)   | 56 (44.8%)                                | 4 (3.2%)         |
| CD20 inhibitors      | 28 (22.6%)   | 29 (23.4%)   | 33 (26.6%)   | 31 (25.0%)                                | 3 (2.4%)         |
| JAK inhibitors       | 27 (21.8%)   | 22 (17.7%)   | 23 (18.6%)   | 49 (39.5%)                                | 3 (2.4%)         |

Table 2. Reported availability of newer systemic agents by World Bank Income level

|   | Low-income  | Low-middle-      | Middle-high-      | High-income |
|---|---|------------------|-------------------|-------------|
| Medication (p-value based on Chi-squared test)            | (n, %)  | income<br>(n, %) | income<br>(n, %)  | (n, %)      |
| TNF-alpha inhibitors (p<0.001)                            |   |                  |                   |             |
| Generally available (>50% of settings)                    | 0 (0.0%)  | 2 (5.3%)         | 6 (18.2%)         | 27 (73.0%)  |
| Theoretically available but significant<br>barriers exist | 0 (0.0%)  | 14 (36.8%)       | 9 (27.3%)         | 8 (21.6%)   |
| Generally not available (<50% of settings)                | 4 (25.0%)   | 8 (21.1%)        | 13 (39.4%)        | 0 (0.0%)    |
| Not available in the country                              | 10 (62.5%)  | 14 (36.8%)       | 4 (12.1%)         | 2 (5.4%)    |
| Unsure  | 2 (12.5%)   | 0 (0.0%)         | 1 (3.0%)          | 0 (0.0%)    |
| PDE4 inhibitors (p<0.001)                                 |   |                  |                   |             |
| Generally available (>50% of settings)                    | 0 (0.0%)  | 0 (0.0%)         | 2 (6.3%)          | 21 (56.8%)  |
| Theoretically available but significant<br>barriers exist | 2 (12.5%)   | 7 (19.4%)        | 2 (6.3%)          | 4 (10.8%)   |
| Generally not available (<50% of settings)                | 1 (6.3%)  | 7 (19.4%)        | 15 (46.9%)        | 3 (8.1%)    |
| Not available in the country                              | 12 (75.0%)  | 21 (58.3%)       | 11 (34.4%)        | 9 (24.3%)   |
| Unsure  | 1 (6.3%)  | 1 (2.8%)         | 2 (6.3%)          | 0 (0.0%)    |
| IL4/IL13 inhibitors (p<0.001)                             |   |                  |                   |             |
| Generally available (>50% of settings)                    | 0 (0.0%)  | 0 (0.0%)         | 2 (6.3%)          | 23 (62.2%)  |
| Theoretically available but significant<br>barriers exist | 1 (6.3%)  | 7 (18.4%)        | 9 (28.1%)         | 7 (18.9%)   |
| Generally not available (<50% of settings)                | 2 (12.5%)   | 7 (18.4%)        | 11 (34.4%)        | 4 (10.8%)   |
| Not available in the country                              | 12 (75.0%)  | 24 (63.2%)       | 9 (28.1%)         | 3 (8.1%)    |
| Unsure  | 1 (6.3%)  | 0 (0.0%)         | 1 (3.1%)          | 0 (0.0%)    |
| IL23 inhibitors (p<0.001)                                 |   |                  |                   |             |
| Generally available (>50% of settings)                    | 0 (0.0%)  | 0 (0.0%)         | 3 (9.4%)          | 24 (64.9%)  |
| Theoretically available but significant<br>barriers exist | 1 (6.3%)  | 5 (13.2%)        | 5 (15.6%)         | 6 (16.2%)   |
| Generally not available (<50% of settings)                | 1 (6.3%)  | 3 (7.9%)         | 14 (43.8%)        | 3 (8.1%)    |
| Not available in the country                              | 13 (81.3%)  | 30 (78.9%)       | 8 (25.0%)         | 4 (10.8%)   |
| Unsure  | 1 (6.3%)  | 0 (0.0%)         | 2 (6.3%)          | 0 (0.0%)    |
| CD20 inhibitors (p<0.001)                                 |   | 1 - Inc 1 - 1    |                   |             |
| Generally available (>50% of settings)                    | 0 (0.0%)  | 2 (5.3%)         | 2 (6.3%)          | 24 (66.7%)  |
| Theoretically available but significant<br>barriers exist | 1 (6.3%)  | 10 (26.3%)       | 8 (25.0%)         | 8 (22.2%)   |
| Generally not available (<50% of settings)                | 3 (18.8%)   | 14 (36.8%)       | 15 (46.9%)        | 1 (2.8%)    |
| Not available in the country                              | 11 (68.8%)  | 12 (31.6%)       | 5 (15.6%)         | 3 (8.3%)    |
| Unsure  | 1 (6.3%)  | 0 (0.0%)         | 2 (6.3%)          | 0 (0.0%)    |
| JAK inhibitors (p<0.001)                                  | 7.1<br>19.00 (19.00 |                  | N2-1/46070-0540-0 | 2200220000  |
| Generally available (>50% of settings)                    | 0 (0.0%)  | 2 (5.3%)         | 3 (9.7%)          | 22 (59.5%)  |
| Theoretically available but significant<br>barriers exist | 0 (0.0%)  | 7 (18.4%)        | 7 (22.6%)         | 8 (21.6%)   |
| Generally not available (<50% of settings)                | 2 (12.5%)   | 5 (13.2%)        | 12 (38.7%)        | 4 (10.8%)   |
| Not available in the country                              | 13 (81.3%)  | 24 (63.2%)       | 8 (25.8%)         | 3 (8.1%)    |
| Unsure  | 1 (6.3%)  | 0 (0.0%)         | 1 (3.2%)          | 0 (0.0%)    |

# Tirbanibulin Ointment 1% over a Treatment Field up to 100 cm2 in Actinic Keratosis: A Phase 3 Study

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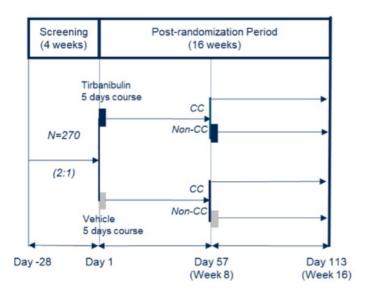
**Introduction & Objectives:** Actinic keratosis (AK) is a pre-cancerous skin disease resulting from the atypical proliferation of keratinocytes that may progress to invasive squamous cell carcinoma. Tirbanibulin 1% ointment is approved for treating AK on the face or scalp in Europe over a field up to 25 cm2, and in the United States over a field up to 100 cm2.

Materials & Methods: This is a Phase 3, multicentre, randomised, double-blind, vehicle-controlled, parallel-group study (EudraCT: 2023-505487-11-00) to evaluate the efficacy and safety of tirbanibulin 10 mg/g ointment applied to a treatment field (TF) larger than 25 cm2 and up to 100 cm2, containing ≥4 to ≤12 clinically typical, visible, and discrete AK lesions, in adult patients with AK on the face or the balding scalp. At baseline, eligible patients were randomized in a 2:1 ratio to either tirbanibulin 10 mg/g ointment or vehicle; the randomisation was stratified by the number of lesions at baseline (≥4 to ≤8, >8 to ≤12), treatment location (face or scalp), and country. Patients applied tirbanibulin 10 mg/g ointment or vehicle once daily for 5 days. All patients were evaluated for efficacy, safety, and tolerability at Days 8, 15, 29, and 57. Those patients who did not achieve complete clearance (CC) at Day 57 received a second 5-day course of the randomised treatment. Patients receiving a second treatment course were also evaluated for efficacy, safety, and tolerability at Days 64, 71, 85 and 113.

**Results:** Primary endpoint is percent change from baseline (CFB) in lesion count at Day 57. Moreover, proportion of patients with partial clearance (PC), defined as ≥75% clearance in the TF, proportion of patients with CC, defined as 100% clearance in the TF, CFB in Skindex-16, cosmetic outcome assessed by patient and by the investigator, and Treatment Satisfaction Questionnaire for Medications (TSQM-1.4) transformed score at Day 57 and, for patient who received 2 treatment courses were assessed, at Day 113 as well. Tolerability assessments include local tolerability score (0-3), maximum (max) local tolerability score, local tolerability signs (LTS) composite score (0-18), and changes in pigmentation and scarring by treatment course and visit. Safety assessments include adverse events (AEs), serious AEs, AEs of special interest, abnormalities in clinical laboratory results and vital signs. Results to be disclosed in the poster.

**Conclusion:** The aim of this study is to evaluate the efficacy, safety, and tolerability of tirbanibulin 10 mg/g ointment, compared to vehicle, in adult patients with AK on the face or scalp in a field larger than 25 cm2 and up to approximately 100 cm2, as well as examining the effects of up to two 5-day treatment courses.

Figure 1 Study Design



CC, complete clearance; PC, partial clearance.

Sun exposure monitoring by ultraviolet sensor in patients with actinic keratosis treated with tirbanibulin 10 mg/g ointment or diclofenac sodium 3% gel: a Phase IV randomized study

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**Introduction & Objectives:** Patients with actinic keratoses (AK) were monitored for sun exposure by wearing an ultraviolet (UV) sensor device fully integrated with a validated data capture platform1. The system captures the intensity of UV radiation and measures it as UV Index (UVI) allowing to generate personalised alerts based on the skin type about the daily maximum UV dose reached. The study aims to determine whether the UV sensor and mobile app help patients become aware about daily solar radiation and its impact on health, and whether they have an impact on overall exposure, promote sun protection habits and engage patients into a long-term safety study.

Materials & Methods: This is a Phase IV multi-centre, randomized, evaluator-blinded, active-controlled, parallel group study (EudraCT: 2024-514394-22-00) to determine the incidence of invasive squamous cell carcinoma after treatment with tirbanibulin and to evaluate the long-term safety of tirbanibulin administered on the face or scalp in patients with AK. Adults with a contiguous field measuring 25 cm2 that contains 2-8 clinically typical, non-hypertrophic, non-hyperkeratotic, visible, discrete, AK lesions were included in the study. Patients were randomized 1:1 to receive tirbanibulin 10 mg/g for 5 days or diclofenac sodium 3% for 60-90 days. UV sensor use was optional. Patients that accepted to wear the UV sensor were monitored for sun exposure from baseline up to day 57 (short-term use). These patients were monitored from March 1st to September 30th of each year (long-term use). The UV sensor is paired with a mobile app, and the smartphones display a real-time UVI, real-time cumulative UV exposure, as well as historical data of daily UV exposure during the week. Patients were instructed to wear the sensor on the wrist during the day regardless of whether they were indoors or outdoors. Collection of UV exposure was performed in both treatment arms.

**Results:** A total of 197 patients (average age: 70 years; male: 86.8%) from France, Germany, Italy, Poland, Spain and United Kingdom accepted to wear the UV sensor and use the App in 2023 (N=161) and 2024 (N=97), which is 44% of the overall patients in the study (64% used both; 29% only the app; 7% only the sensor). Overall retention rate for the study is 84%, but for patients who have been wearing the sensor is 91.3%. Most patients (83.6%) used it for a long-term period (>57 days). Average overall UVI exposure was 0.82 (based on WHO UVI scale 1-11+). This average decreased in 2024 in comparison with 2023 (reduction rate: 13%). Additionally, it was observed that UVI average was higher during spring (April and May) than during summer (July and August) in both 2023 and 2024. The sensor was used on average 115 days. Overall, average number of days with a UVI exposure higher than recommended (UVI<2)2 was 46 days. Short-term users (N=23 [16.4%]) used the sensor an average of 10 days, and for 4 days the sensor registered an UV higher than the recommended. Long-term users (N=117 [83.6%]), used it on average 135 days and had UV above recommended for 52 days on average (38.5%).

**Conclusion:** UV sensor might be a potential tool to visualize the risks associated with sun overexposure. In spring the UVI average was higher than in summer. Moreover, patients were exposed to UVI higher than recommended

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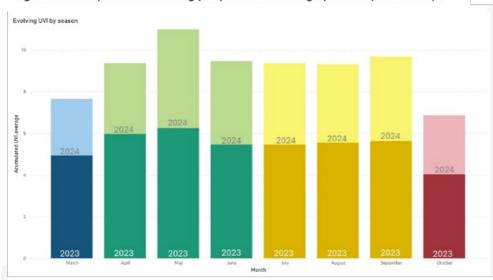
<sup>&</sup>lt;sup>4</sup>Hospital Clinic of Barcelona, Barcelona, Spain

but improving habits from one year to another.

1Replior: Data Collection Solutions for Clinical Trials

2World Health Organization. Radiation: The ultraviolet (UV) index. 2022

Figure 1: Sun exposure monitoring (UVI). Overall evolving by season (2023-2024).



# Safety and tolerability of tirbanibulin for the treatment of actinic keratosis: Results from clinical trials and post-registration

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**Introduction & Objectives:** Broadening the understanding of the safety for medications, including those employed for actinic keratosis (AK) treatment, requires information from large cohorts [1]. Comparing safety and tolerability from clinical trials vs those in clinical practice is important because of restrictive entry criteria and limitations on concomitant medications in controlled clinical trials [2].

**Materials & Methods:** Information regarding safety and tolerability of tirbanibulin 1% ointment has been obtained in (i) three phase III trials, in two tirbanibulin was applied to an area of 25 cm2 (NCT03285477, NCT03285490) [3] and in one, to an area of 100 cm2 (NCT05279131) [4] (N=458 total patients), (ii) one open phase IV multicenter, single-cohort, low-interventional study (TirbaSkin [EU2022-001251-16] [5], N=334) and (iii) two real-world/low interventional studies, KLIR (DRKS00027120) [6] (N=543) and PROAK (NCT05260073) [7] (N=300), in which tirbanibulin was applied to an area of 25 cm2. In all studies, tirbanibulin was applied once daily for 5 days according to the prescribing information.

**Results:** Combined results for 1,635 tirbanibulin-treated patients indicated that 19.6% had adverse events (AEs, all causality, application site and systemic) and 12.8% had AEs possibly related to tirbanibulin. Serious AEs were reported for 0.8% and severe AEs for 0.4%. AEs leading to drug or study discontinuation were reported for 0.4%. The most common individual AEs were pain (2.9%) and pruritus (8.3%) at the application site. Local skin reactions (LSRs) were evaluated in 1,320 patients and were generally mild-to-moderate. Erythema was reported for 89.8% (7.9% severe) of patients, flaking/scaling for 73.8% (5.4% severe), crusting for 46.4% (3.4% severe), swelling for 25.3% (0.3% severe), vesiculation/pustulation for 6.4% (0.4% severe), and erosion/ulceration for 11.1% (0.6% severe).

**Conclusion:** These combined results indicate that tirbanibulin has low occurrence for serious or severe AEs, and severe LSRs were uncommon. The safety/tolerability profile for tirbanibulin in real-world clinical practice was comparable to the one reported in clinical trials.

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# Clearance of actinic keratosis with tirbanibulin: Comparing results from controlled trials with real-world/low interventional clinical studies

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**Introduction & Objectives:** Randomized controlled trials (RCTs) are known to provide information about the efficacy of treatments under highly controlled conditions and in carefully selected homogeneous patient groups [1,2]. It is important to examine how efficacy achieved in such trials compares with that obtained in a broader spectrum of patients in real-world clinical practice.

Materials & Methods: Efficacy of tirbanibulin 1% ointment in the treatment of actinic keratosis (AK) has been evaluated in three phase III clinical trials; two [NCT03285477, NCT03285490] [3] in which tirbanibulin was applied to an area of 25 cm2 and one to an area of 100 cm2 [NCT05279131] [4] (N=458 total patients). Tirbanibulin efficacy has also been assessed in an open-label phase IV trial (TirbaSkin [EU2022-001251-16] [5], N=334) and two real-world studies (KLIR [DRKS00027120] [6] N=543, and PROAK [7] [NCT05260073] N=300). These phase IV studies were low-interventional and in all of them tirbanibulin was applied to an area up to 25 cm2 once daily for 5 days according to prescribing information. Complete and partial clearance were defined as clearance of 100% and ≥75% to <100% of lesions, respectively.

**Results:** Combined results from two phase III studies (N=353 patients, 25 cm2 application) reported a clearance ≥75% in 72.2% of patients. Combined results from real-world/low interventional studies PROAK, KLIR (assessed in SmPC time window), and TirbaSkin (N=1,123 patients) showed a clearance ≥75% in 66.1%. Reported percent reduction in AK lesions from three phase III trials (N=458) was 78.4% and from two post-registration studies (TirbaSkin and KLIR, N=832) was 74.4%.

**Conclusion:** These results indicate that clearance rates and reductions in AK lesion counts achieved with tirbanibulin in RCTs approximated results achieved in an open-label phase IV study and in real-world clinical practice.

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# Relating patient-reported treatment satisfaction and clinical outcomes in post-registration studies of tirbanibulin for actinic keratosis

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**Introduction & Objectives:** Expert guidance on the treatment of AKs acknowledges the importance of patient satisfaction and its impact on adherence to therapy [1-3]. However, there is little information relating physicians' evaluations of actinic keratosis (AK) treatment success with patient-reported outcomes (PROs).

Materials & Methods: Clinician assessments of complete (100%) and partial (≥75% to <100%) clearance of lesions and PROs were collected in two post-registration studies of tirbanibulin in patients with AK on the face or scalp. PROAK (NCT05260073) [4] was a single-arm multicenter, prospective cohort study that included adult patients (N=278 evaluable) with AK on the face or scalp treated with tirbanibulin in community practices in the United States as part of usual care. TirbaSkin (EU2022-001251-16) was an open phase IV multicenter, single-cohort, low-interventional clinical trial of tirbanibulin in adult patients (N=328 evaluable) with AK on the face or scalp from Spain or Italy [5]. In both PROAK and TirbaSkin, patients applied tirbanibulin once daily for 5 days to an area of up to 25 cm2 according to instructions in the prescribing information. Patients also completed the Treatment Satisfaction Questionnaire for Medication-9 (TSQM-9) at 8 weeks.

**Results:** Results from the two studies were combined (N=606 evaluable) for the current analysis. ≥75% of clearance was achieved in 75.1% of patients. Pooled TSQM-9 scores for Effectiveness, Convenience, and Global Satisfaction domains at week 8 (score range = 0-100) were 74.9, 83.9, and 78.8, respectively.

**Conclusion:** Results from this combined analysis of results from PROAK and TirbaSkin indicated that the high AK clearance rate achieved with tirbanibulin was associated with corresponding high scores for all domains of the TSQM-9.

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### Successful Treatment of Pyoderma Vegetans with Lymecycline: First Case Report

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# **Introduction & Objectives:**

Pyoderma vegetans (PV) is a rare inflammatory dermatosis with unclear etiology, lacking standardized treatment protocols, which may be attributable to its infrequency. This case report aims to present a patient with facial pyoderma vegetans who responded favorably to lymecycline, highlighting its potential as a novel therapeutic option.

# **Case Report:**

A 69-year-old man with a history of asthma and well-controlled type 2 diabetes presented with an atypical facial dermatosis. Clinical examination revealed a well-defined infiltrating vegetating plaque covering the nose and left cheek, with complete erosion of the left upper eyelid.

A skin biopsy from the left cheek, examined microscopically, showed pseudoepitheliomatous hyperplasia and a neutrophilic inflammatory infiltrate.

Treatment with lymecycline was initiated at 300 mg/day for 4 months, followed by a reduction to 150 mg/day, then stopped at 6 months.

#### **Discussion:**

Pyoderma vegetans manifests as a vegetating inflammatory reaction, primarily in immunocompromised patients, although it can occur in immunocompetent individuals.

The skin lesions, typically vesiculopustular, exudative, and vegetating, are often located on the face, scalp, axillae, genital organs.

Histologically, PV is characterized by pseudoepitheliomatous hyperplasia and intra- or subepidermal microabscesses with neutrophils or eosinophils.

There are no standardized treatment recommendations for PV, probably due to its rarity. Systemic corticosteroids are generally the first-line treatment, sometimes associated with steroid-sparing agents. Two cases reported in the literature showed a good response to doxycycline.

In our case, lymecycline, used for the first time in the literature for PV, led to a remarkable clinical response. Initial regression of the lesion was observed at 2 months, followed by complete resolution at 6 months. Six months after discontinuing treatment, no recurrence was observed.

# **Conclusion:**

This case report highlights the potential of lymecycline in the treatment of pyoderma vegetans, constituting, to our knowledge, the first documented case of successful treatment with this antibiotic. Further studies are needed to validate these results.

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# Topical Calcineurin Inhibitors versus Topical Antifungals for the Treatment of Seborrheic Dermatitis: A Systematic Review and Meta-Analysis

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# **Introduction & Objectives:**

Seborrheic Dermatitis is an inflammatory skin condition of sebaceous-rich areas, afflicting 5% of the U.S. population and significantly impacting quality of life. Topical calcineurin inhibitors, such as pimecrolimus and tacrolimus, have emerged as potential alternatives to conventional therapies. This Meta-analysis of Randomized Controlled Trials aims to assess their effectiveness and tolerability in patients with Seborrheic Dermatitis.

#### Materials & Methods:

A systematic review and meta-analysis was conducted in PubMed, Web of Science, Cochrane, and Scopus to identify Randomized Controlled Trials (RCT) comparing Topical Calcineurin Inhibitors with Topical Antifungals. Outcomes included reduction in clinical severity score (Scoring Index – SI). A random-effects model with 95% confidence intervals were implemented and heterogeneity was assessed with the I<sup>2</sup>. Statistical analysis was performed using R software (version 4.4.3).

## Results:

567 studies were included in the initial search. Of these, 4 articles qualified based on the eligibility criteria. A total of 282 patients were included for this analysis, 140 received 1% Pimecrolimus or 0.03% to 0.1% Tacrolimus were compared with 142 patients that underwent antifungal therapies, such as 2% Ketoconazole/Sertaconazole or 1% Ciclopirox Olamine. The RCT's follow-up range varied from 4 to 24 weeks. There was no statistically significant difference between Topical Calcineurin Inhibitors and topical antifungals in the Scoring Index for reducing clinical severity for seborrheic dermatitis (OR: 0.80; 95% CI: 0.32-2.02;  $I^2=0\%$ , p=0.637).

#### **Conclusion:**

This meta-analysis investigated the effectiveness of topical calcineurin inhibitors compared to topical antifungals in reducing clinical severity scores (Scoring Index – SI) in patients with seborrheic dermatitis. Based on our results, no statistically significant difference was observed between the two treatments, suggesting similar clinical efficacy. These findings underscore the need for further large-scale, high-quality studies to confirm and expand upon these results.

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|                       |                | CD         | No       | n-CD          |        |      |              | Odds Ratio             |
|-----------------------|----------------|------------|----------|---------------|--------|------|--------------|------------------------|
| Study                 | events.e       | Total      | events.c | Total         | Weight | OR   | 95% CI       | MH, Random, 95% CI     |
| Goldust, 2013a        | 24             | 30         | 25       | 30            | 50.0%  | 0.80 | [0.22; 2.97] | <u>i</u>               |
| Goldust, 2013b        | 24             | 30         | 25       | 30            | 50.0%  | 0.80 | [0.22; 2.97] |                        |
| Koc, 2009             | 18             | 18         | 20       | 20            | 0.0%   |      |              |                        |
| Total (95% CI)        |                | 78         |          | 80            | 100.0% | 0.80 | [0.32; 2.02] |                        |
| Heterogeneity: Tai    |                |            |          | $0); I^2 = 0$ | .0%    |      |              | 1 1 1                  |
| Test for overall effe | ect: Z = -0.47 | (P = 0.63) | 37425)   |               |        |      |              | 0.5 1 2                |
|                       |                |            |          |               |        |      |              | Favors CD Favors Non-C |

**Figure 1.** Forest plot of the mean difference in final clinical severity scores comparing topical calcineurin inhibitors (CD: calcineurin derivatives – tacrolimus or pimecrolimus) to topical antifungals (Non-CD: ketoconazole or ciclopirox) in seborrheic dermatitis.

# Evaluation of the Effects of Disease and Treatment on Quality of Life in Individuals with Autoimmune Bullous Disease

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**Introduction & Objectives:** In this study, we used bullous disease quality of life (abqol) and the effect of autoimmune bullosis disease treatment on quality of life (tabqol) questionnaires to investigate how autoimmune bullosis disease and treatment affect the quality of life of patients. The questionnaires were developed and approved in 2013-2014). We used the Turkish version of these questionnaires. Each of these questionnaires consists of 17 items scored between 4 (always, sometimes, sometimes, and never) 0-3, with a final maximum score of 51. A score above 20 represents poor quality of life. ABQOL's questions focus on pain, itching, recovery, depression and anxiety. TABQOL's questions focus on medication count, financial difficulties, lethargy, clear thinking, and fear of relapse.

**Materials & Methods:** The study included 119 patients who were followed up with a diagnosis of bullous disease at Istanbul University-Cerrahpaşa, Cerrahpaşa Medical Faculty, Department of Dermatology and Venereal Diseases. The patients were asked to fill in the ABQOL and TABQOL questionnaires, each consisting of 17 questions. Based on these data, the dermographic characteristics of the patients, how much their disease and treatments affect their quality of life were investigated.

## **Results:**

Of the 119 patients included in the study, 63 (52.9%) were men and 56 (47.1%) were women. The ages of the patients ranged from 20 to 88, and the mean age was  $49.9 \pm 14.9$ . Subtype pemphigus vulgaris (n = 63, 52.9%), followed by bullous pemphigoid (n = 32, 26.9%), pemphigus foliaceus (n = 11, 9.2%), Linear IgA dermatosis (n = 4, 3 4%), cicatricial pemphigoid (n = 3, 2.5%), pemphigus vegetans (n = 2, 1.7%), acquired epidermolysis bullosa (n = 1, 0.8%), other (n = 3, 2.5%).

The mean score for ABQOL was 27.6  $\pm$  10.4, and the mean score for TABQOL was 32.6  $\pm$  9.4. ABQOL and TABQOL are scored on 51 points. A score above 20 is considered a high score and indicates a worse quality of life, and a score below 7 is considered low.3

The average age of the Bullous pemphigoid patients who completed the questionnaire was higher than the average age of patients with pemphigus vulgaris and other diseases (p < 0.001).

When the gender and scale scores of the patients were compared, no statistically significant difference was found (p = 0.320, p = 0.694, respectively)

When patients with and without mucosal involvement were compared, 57 (31.9  $\pm$  8.9) with mucosal involvement and 62 (23.4  $\pm$  10.3) without mucosal involvement were found. As a result, the quality of life was higher in patients without mucosal involvement. p <0.001

We also evaluated the patients by dividing them into active, partial remission and complete remission groups according to disease activity. 66 patients were active (35.5  $\pm$  5.9), 39 patients were in partial remission (21.1  $\pm$  3.2), 14 patients were in complete remission (10.6  $\pm$  6.4). Among these patients, the quality of life was found to be lower in patients with active disease. p <0.001

# **Conclusion:**

We think that objective and valuable measures such as ABQOL and TABQOL should be used in every patient with AIBD to help physicians understand patients' distress. We found that disease activities and mucosal involvement seriously affect patients' quality of life.

# Benefit/risk Ratio of Low-dose Methotrexate in Cutaneous Lesions of Mycosis Fungoides and Sézary Syndrome

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# **Introduction & Objectives:**

Low-dose methotrexate (LD-MTX) is frequently used for mycosis fungoides (MF) and Sézary syndrome (SS), but data on long-term outcomes remain limited. This study aimed to assess the benefit-risk profile of LD-MTX in these conditions.

#### **Materials & Methods:**

A retrospective review was conducted on 48 patients with MF or SS treated with LD-MTX and followed for ≥12 months. Clinical responses and adverse events were analyzed.

#### **Results:**

Complete and partial responses were achieved in 10 (21%) and 25 (52%) patients, respectively, with similar response rates between MF and SS. Of responders, 57% relapsed after a median of 11 months. LD-MTX was discontinued in 44 patients due to failure or toxicity (n=9).

### **Conclusion:**

LD-MTX remains a valid treatment for MF and SS, offering good initial response, though duration is limited and some patients may experience significant toxicity.

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## Therapeutic approach to Granulomatous Cheilitis: A Case Series

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**Introduction** Granulomatous cheilitis (GC) is a rare, chronic inflammatory disorder characterized by persistent, non-tender swelling of the lips due to non-caseating granuloma formation. With an estimated incidence of 0.08%, GC presents diagnostic and therapeutic challenges. It may occur idiopathically or in association with systemic conditions such as Crohn's disease or sarcoidosis. The clinical course is often unpredictable, and responses to therapy vary. This case series highlights three patients with histologically confirmed GC, each with a distinct presentation and treatment response, contributing to the limited literature on this condition.

**Materials and Methods** Three patients with persistent, progressive lip swelling were evaluated. Detailed histories and physical examinations were performed to exclude systemic diseases, infections, trauma, and relevant family history. Investigations included chest radiographs and Mantoux tests to rule out tuberculosis and sarcoidosis, all of which were unremarkable. Lip biopsies confirmed the presence of non-caseating granulomatous inflammation. Based on individual presentations and drug responses, patients were managed with various combinations of oral metronidazole, clofazimine, minocycline, dapsone, and intralesional triamcinolone acetonide.

Results All three patients had no identifiable systemic disease and did not respond to initial empirical treatments.

- **Case 1**: The patient showed partial improvement with oral metronidazole. Clofazimine was introduced, leading to notable reduction in lip swelling, but was discontinued due to hyperpigmentation. Subsequent therapy with oral minocycline and intralesional triamcinolone resulted in further improvement.
- Case 2: Initial treatment with clofazimine provided mild benefit. Addition of intralesional triamcinolone led to a marked decrease in swelling.
- Case 3: The patient had a prior diagnosis of borderline tuberculoid Hansen's disease and was treated with multidrug therapy including clofazimine and dapsone. Lip swelling improved gradually; however, the patient was lost to follow-up.

**Discussion** GC remains a diagnostic challenge requiring histopathological confirmation. All cases demonstrated non-caseating granulomas in the absence of systemic disease. Clofazimine, used in all three cases, was effective in reducing inflammation but limited by cosmetic side effects and potential relapse. Intralesional triamcinolone acetonide proved beneficial as a localized immunosuppressant. Metronidazole offered minimal standalone benefit. The therapeutic outcomes underscore the importance of individualized, multi-modal treatment approaches. Given the lack of standardized guidelines and limited high-quality data, future research should aim to establish uniform treatment protocols and explore targeted biologic options for refractory or recurrent GC.

|                                  | CASE 1  | CASE 2   | CASE 3  |
|----------------------------------|---|--|---|
| GENDER                           | Male  | Female   | Male  |
| AGE                              | 53 <u>year</u>  | 48 <u>year</u>   | 60 year   |
| CHIEF COMPLAINTS                 | Upper lip swelling gradually worsened despite multiple prior treatments, including antihistamines and topical corticosteroids | Upper lip swelling<br>and redness  | Lower lip swelling  |
| DURATION                         | 12 month  | 8 month  | 36 month  |
| CLINICAL                         | diffuse, firm, non-   | diffuse,   | firm, non-tender, diffuse swelling of   |
| EXAMINATION                      | tender swelling of<br>the upper lip   | erythematous, firm,<br>non-tender swelling<br>of the upper lip   | the lower lip   |
| ASSOCIATED                       | none  | none   | none  |
| DISEASE                          |   |  |   |
| HISTOPATHOLOGY                   | Acanthosis, upper<br>dermis- ill formed<br>granulomas with<br>mononuclear<br>infiltrate                                       | Acanthosis, mild focal hyperkeratosis, mild local hypergranulosis. Dermis shows perivascular, periadnexal mild to moderate mononuclear inflammatory infiltrate. Few epitheloid cell granulomas, with minimal lymphocytic cuffing in few of them identified | Mild acanthosis, hyperkeratosis,<br>perivascular mononuclear infiltrate,<br>upper dermis- ill formed granulomas |
| OTHER REVELANT<br>INVESTIGATIONS | FNAC- smears are<br>paucicellular showing<br>occasional<br>granulomas in a<br>haemorrhagic<br>background.                     | NA   | NA  |

# When the Cream Becomes the Curse: A Rare Case of Iatrogenic Cushing's Syndrome Following Chronic Topical Corticosteroid Use in Extensive Psoriasis

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# **Introduction & Objectives:**

Topical corticosteroids remain the cornerstone of treatment in inflammatory skin diseases, including psoriasis. However, chronic use on large body surface areas, especially with potent molecules like clobetasol propionate, may lead to significant systemic adverse effects, among which iatrogenic Cushing's syndrome is rare but potentially life-threatening. We present a striking case of severe iatrogenic Cushing's syndrome secondary to prolonged topical corticosteroid use in a patient with generalized pustular and plaque psoriasis.

This case aims to illustrate the clinical and hormonal manifestations of systemic corticosteroid overload induced by topical administration, highlight diagnostic challenges, and reinforce the need for multidisciplinary management and vigilant long-term monitoring in dermatologic chronic therapy.

## **Materials & Methods:**

We present the case of a 45-year-old female with a 6-year history of generalized pustular and plaque psoriasis, treated continuously since 2019 with topical clobetasol propionate 0.05%, applied once daily over approximately 70% of her body surface. In April 2025, she presented to our dermatology clinic following an endocrinological consultation prompted by clinical signs of adrenal suppression and Cushingoid features.

The patient reported recent exacerbation of psoriatic lesions after interrupting clobetasol for a short period (March 28 to April 4), which prompted the resumption of therapy. At presentation, she exhibited linear violaceous striae, parchment-like atrophic skin, and numerous erythematous scaly plaques covered with silvery-white scales on the scalp and limbs. Additionally, multiple pinpoint sterile pustules and large flaccid bullae with purulent content were observed on the dorsal thighs, lower back, and hypogastric region.

#### **Results:**

Endocrine investigations revealed suppressed serum cortisol (2.49  $\mu$ g/dL), low DHEA-S (11  $\mu$ g/dL; reference: 35.4–256  $\mu$ g/dL), undetectable total testosterone (<0.087 nmol/L), and ACTH within normal range (15.7 pg/mL). The profile was compatible with iatrogenic Cushing's syndrome due to exogenous corticosteroid exposure and hypothalamic-pituitary-adrenal (HPA) axis suppression.

The topical corticosteroid was immediately discontinued, and systemic treatment was initiated with oral Acitretin 20 mg/day and oral Prednisone 20 mg/day, followed by a tapering regimen to prevent acute adrenal insufficiency.

### **Conclusion:**

This case underscores the serious systemic risks of chronic potent topical corticosteroid use, especially on large body areas, and calls for routine endocrine surveillance in patients on long-term dermatologic therapies.

It emphasizes the value of interdisciplinary collaboration between dermatologists and endocrinologists to ensure

early recognition and appropriate management of iatrogenic complications.

Patient education and pharmacovigilance remain vital to preventing such outcomes.

## A Balancing Act - Optimizing Efficacy vs. Safety with Time-Resolved Tissue-Level PK Data

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# **Introduction & Objectives:**

Topical soft drugs for dermatology indications can significantly reduce systemic exposure hence toxicological liabilities. However, optimizing drug metabolism in tissues while achieving the desired clinical efficacy can be challenging. In addition, using animal models to evaluate drug absorption can be costly and time-consuming, with uncertain translatability to human. We present a case study in which time-resolved, cutaneous pharmacokinetic (PK) data in human skin, obtained by the novel Open Flow Microperfusion (OFM) technology, was used to effectively assess a topical Janus kinase inhibitor (JAKi) soft drug candidate for its PK performance and hence development potential.

#### **Materials & Methods:**

An ex-vivo OFM study involving fresh (< 3 h) human skin explants was carried out to benchmark the PK performance of the soft drug candidate against the reference drug product (Opzelura®, ruxolitinib cream 1.5%). For 24 hours OFM probes, implanted in the dermis, were used to continuously sample interstitial fluid (ISF) after topical drug applications (drug candidate and Opzelura®). The ISF and skin biopsy samples, the latter collected at the end of the OFM sampling from the drug application sites, were analyzed for the concentrations of the parent/metabolite of the soft drug candidate, as well as ruxolitinib for Opzelura®.

#### **Results:**

The JAKi, or the parent compound, was detected at a consistent low level in the ISF samples collected via OFM. In contrast, the concentration of the inactive JAKi metabolite increased steadily and became greater than that of the parent compound after 8 hours. The results confirmed an effective degradation of the soft drug candidate as intended. However, the low JAKi concentration in the dermis, particularly in comparison to the reference drug, raised a concern of its potential clinical efficacy.

#### Conclusion:

The ex vivo OFM study outcome was decisive in determining the development priority for the soft drug candidate. The time-resolved, free drug concentration data generated by OFM can further support PBPK prediction, for example via Simcyp™ PBPK Simulator, to assess drug bioavailability and to support dosing strategy development and other IND-enabling activities. Last but not least, the ex vivo human tissue model used is align with the current regulatory priority to reduce animal testing and qualified as a New Approach Methodology (NAM) under the recently announced US FDA roadmap.

<sup>&</sup>lt;sup>2</sup>Certara, Drug Development Solutions, Durham, United States



## Clinical improvement of generalized mophea in a pediatric patient with tofacitinib: a case report

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<sup>1</sup>Policlinica geral do Rio de Janeiro , Rio de janeiro, Brazil

# **Introduction & Objectives:**

Scleroderma, or localized scleroderma (morphea), is a chronic autoimmune connective tissue disease characterized by vascular dysfunction, immune dysregulation, and progressive fibrosis of the skin. In generalized morphea, multiple plaques affect different anatomical areas, often leading to significant physical and psychosocial impact. From a dermatologic perspective, early manifestations include edema, pruritus, and skin tightness, evolving into induration, atrophy, pigmentary changes, and in some cases, functional limitation. As there is no curative treatment, current management is symptom-driven including topical therapies and systemic immunosuppressants. This case report aims to

describe a successful therapeutic approach using tofacitinib, a Janus kinase (JAK) inhibitor, in a pediatric patient with with extensive cutaneous involvement.

#### **Materials & Methods:**

A comprehensive review of the literature was carried out for this case report

## **Results:**

A 15-year-old male presented with multiple plaques with atrophic centers and hyperpigmented borders, predominantly affecting the upper and lower limbs, retrosternal region and gluteal region.

The lesions had developed progressively since early childhood, with significant esthetic and emotional impact. Skin biopsy confirmed the diagnosis.

The patient was treated with oral tofacitinib in a dose of 5 mg per day, administered five days per week, in a one-year period.

Throughout follow-up, there was no development of new lesions. Clinical improvements included enhanced skin texture and partial repigmentation of affected areas. The patient reported high satisfaction with the outcome and demonstrated good tolerance to tofacitinib, with no significant adverse events reported. The treatment led to both symptomatic relief and improved quality of life, which translated into improved self-esteem and emotional well-being.

## **Conclusion:**

Tofacitinib may represent an effective, safe, and innovative therapeutic option in the management of generalized scleroderma, particularly in refractory or pediatric cases. This case highlights its potential to induce lesion remission, reduce aesthetic concerns, and improve long-term outcomes for patients with extensive cutaneous involvement.

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# Study of Efficacy And Safety Of Oral Minoxidil (2.5mg) V/S Oral Finasteride (1mg) In Male Androgenic Alopecia- A Double Blind Study

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Study of Efficacy And Safety Of Oral Minoxidil (2.5mg) V/S Oral Finasteride (1mg) In Male Androgenic Alopecia- A Double Blind Study

#### INTRODUCTION-

Androgenic alopecia is a common form of hair loss in both men and women. In men, this condition is also known as male-pattern baldness. Hair is lost in a well-defined pattern, beginning at the frontal area and vertex. Hair also thins at the crown often progressing to partial or complete baldness.

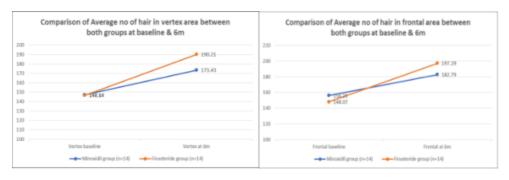
## Aim and objectives -

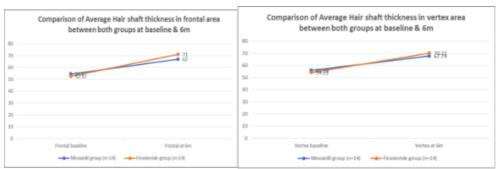
- To study the effectiveness of oral minoxidil vs oral finasteride in androgenic alopecia.
- To establish the results and tolerability of oral minoxidil and oral finasteride in male androgenic alopecia.

#### Material and methods-

- All those willing to participate will be explained the procedure. Detailed history and thorough dermatological, physical and systemic examination will be conducted.
- This study will be a double blind randomization study.
- Total 28 patients are planned to enroll. There will be 28\*6 bottled packs which will be labeled as-
- A, B, C up to Z and a and b. (Total 28). 6 Bottles of each letter will be prepared.
- These packs will be in air tight container and sealed packed, prepared and labeled by the dispenser.
- 14 packs of each drug will be dispensed.
- This Random number will be stored with dispenser and investigator will only know the letter assigned to each patient.
- After completion of the study the dispenser will open and reveal the random distribution of both drugs.
- Trichoscopic evaluation was done with help of Tricholab Software.
- Assessment will be done with help of clinical photographs, norward hamilton scale trichoscopic evaluation, PGA scale and visual analog scale.

# Result





Results of both groups were comparable and statistically significant. Although more improvement was seen in terms of norwood Hamilton scale, increase in number of hairs and increase in hair shaft thickness in finasteride group over minoxidil group.

## Conclusion-

- In this comparative study of systemic finasteride and oral minoxidil, it was concluded that both drugs were effective and safe in the treatment of mild to severe AGA
- Oral Minoxidil was found to be efficacious and tolerable in treating androgenic alopecia .
- Finasteride was found to be efficacious and tolerable in treating androgenic alopecia
- The efficacy and tolerability of minoxidil was found to be comparable that of finasteride

**Cutis Verticis Gyrata: Hyaluronidase Injection as a Treatment Option** 

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## **Introduction & Objectives:**

Cutis verticis gyrata (CVG) is a rare disease characterised by thickening of the scalp, giving it a brain-like appearance. This condition, may be an isolated condition, is divided into 3 subgroups as primary-essential, primary-nonessential and secondary according to whether there are accompanying findings or other underlying diseases. Treatment options for this rare disease are limited and success rates are low. Here, we aimed to present a case of primary-nonessential CVG in which we performed intralesional hyaluronidase injection.

## **Materials & Methods:**

A 33-year-old woman admitted to the dermatology department 2 years ago with the complaint of thickening of the scalp. In dermatological examination, grooves and ridges resembling brain appearance were observed on the entire scalp, the ridges were soft on palpation. It was learnt that the patient had previously applied to the neurology department because of the accompanying headache. The headache did not improve despite multiple drug use. Apart from the patient's known fibromyalgia, no additional disease was detected in the physical examination, laboratory tests and imaging of the patient. The patient received 150 IU intralesional hyaluronidase injection once a month between September and December 2024.

## **Results:**

The response to treatment was evaluated by comparing the brain magnetic resonance imaging taken at the patient's first application with the brain MRI taken after 4 sessions of intralesional hyaluronidase injection. The distance between the scalp external tachula and the number of scalp folds were examined. All measurements were performed by the same experienced radiologist. These two scans have limitations in evaluating the effectiveness of the treatment due to long time period between them due to the patient's course. The patient states that the headache decreased after the injections. Clinically, a decrease in the thickness of the ridges was observed.

## **Conclusion:**

To date, there is no consensus on a treatment modality for primary CVG disease. In the treatment, topical antiseptic and antifungal treatments are used to prevent dirt accumulation in the recesses and fungal infection, and systemic retinoid treatments are tried to prevent progression of the disease. Surgical procedures are applied to treat the scalp deformity. With our case, we wanted to draw attention to intralesional hyaluronidase injection, which is a less invasive treatment option compared to surgical interventions, as a treatment option. Further and comprehensive studies are needed to determine the dose and duration of hyaluronidase injection treatment.

# Unlocking siRNA's Promise in Dermatology: Achieving Long-Term Gene Silencing via Intradermal Delivery of siRNA

Fakih Hassan<sup>1</sup>, Abideen Mohammad Zain<sup>1</sup>, Rachid Mohamad<sup>1</sup>, Gross Katherine<sup>1</sup>, Thomas Ormsby<sup>1</sup>, Ross Vella<sup>1</sup>, Gagnon Rosemary<sup>1</sup>, Christopher Dalhke<sup>1</sup>, Furgal Raymond<sup>1</sup>, Lochmann Clemens<sup>1</sup>, Summers Ashley<sup>1</sup>, Claire Bouix-Peter<sup>1</sup>, Juliana Gordilho<sup>2</sup>, Thibaud Portal<sup>2</sup>, Sleiman Hanadi<sup>3</sup>, Tang Qi<sup>1</sup>, John E. Harris<sup>1</sup>, Khvorova Anastasia<sup>1</sup>, Carine Blanchard<sup>2</sup>, Lars E. French\*<sup>4</sup>, Julia Alterman<sup>1</sup>

**Introduction & Objectives:** Small interfering RNAs (siRNAs) offer significant therapeutic potential. Where dermatological conditions affect over one-third of the population worldwide, extrahepatic applications, particularly to the skin, remain a challenge.

**Materials & Methods:** Here, we developed and tested a skin-specific siRNA targeting JAK1 ex vivo in human and porcine skin. We investigated in vivo in minipigs, the skin exposure up to 2 months after injection, and the duration of effect in vivo 28 days after injection.

**Results:** We demonstrated that increased hydrophobicity significantly enhances skin retention and efficacy of siRNAs ex vivo and in vivo. Using a validated JAK1-targeting compound, ALD-102, we demonstrate that local delivery of siRNA enables accumulation across multiple skin cell types and suppression of JAK1-dependent inflammatory pathway in human skin *ex vivo*. In porcine in vivo models, intradermal injections with ALD-102, or its minipig surrogate ALD-105, resulted in a prolonged skin siRNA retention (more than 8 weeks) and a limited systemic tissue exposure. The JAK1 siRNA led to sustained target gene silencing, as well as a downregulation of the IFN-g-induced downstream-signaling pathway (CXCL10, CXCL11, CXCL9) for at least one month.

**Conclusion:** These results underscore the importance of tailored siRNA conjugate design for achieving optimal skin bioavailability and therapeutic efficacy, thereby providing a foundation for infrequent siRNA-based treatments for a broad range of dermatological conditions. ALD-102 is currently being investigated in a Phase 1b/2a clinical trial for alopecia areata.

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<sup>&</sup>lt;sup>2</sup>Aldena Therapeutics/Alys Pharmaceuticals, London, United Kingdom

<sup>&</sup>lt;sup>3</sup>McGill University, Montreal, Canada

<sup>&</sup>lt;sup>4</sup>Ludwig Maximilian University , Munich, Germany

**Topical Oxytocin: A Gentle Hormonal Touch for Ageless Skin** 

Amr Ghareeb\*1

<sup>1</sup>AL-Azhar university - faculty of medicine, Giza, Egypt

# **Introduction & Objectives:**

As Oxytocin functions as a stress-coping molecule with anti- inflammatory, antioxidant, protective and anti-ageing functions (as proven in an in-vitro studies).

Epidermal keratinocytes synthesize and secrete OT and its carrier protein neurophysin-1, moreover Oxytocin receptors are expressed on human fibroblasts.

Previous studies demonstrated that Oxytocin levels inversely correlated with skin age score and solar damage and prevented the induction of ageing in dermal fibroblasts.

A clinical study for the effects of topical oxytocin (with microneedling assisted delivery) was conducted.

#### Materials & Methods:

The presentation is based on a randomized, placebo-controlled, comparative, split-face study evaluated the safety and efficacy of topical Oxytocin in the treatment of facial skin ageing.

As no topical preparations for Oxytocin are available, we used micro-needling as a method for the delivery of Oxytocin solution into the skin.

Seventeen female participants, aged 35–59 years (mean  $\pm$  SD=47.41 $\pm$ 7.46), with signs of facial skin ageing, were consecutively recruited from the dermatology clinic, Al-Hussein

University Hospital (Al-Azhar University, Faculty of Medicine, Cairo, Egypt)

Exclusion criteria included: pregnancy, lactation, facial inflammatory or infectious conditions.

## **Results:**

A significant difference in improvement is noted in the Oxytocin treated site in terms of pigmentation, fine lines, and skin texture.

## Conclusion:

This is the first reported study emphisizing the efficacy of topical Oxytocin adminstration in skin rejuvenation providing a novel treatment method to reverse the fibroblast sensecence.

## Clinical improvement of generalized mophea in a pediatric patient with tofacitinib: a case report

Maria Jose Mancero Rodríguez<sup>1</sup>, Ana Amelia Bezerra Milfont<sup>1</sup>, Fabricio Lamy<sup>1</sup>, Ana Julia Geraige Nunes<sup>1</sup>, Paola Aparecida de Campos Elache<sup>1</sup>, Antonio Corrêa Villela Neto<sup>1</sup>, Omar Lupi da Rosa Santos<sup>1</sup>, Thayner Lacerda Lima<sup>1</sup>, Amanda De Freitas Sampaio Periquito<sup>1</sup>, Eduarda Gregório Arnaut Lima<sup>1</sup>, Maurício Romero Uribe<sup>1</sup>, Veronica Malta Franco<sup>1</sup>, Dayra Mercedes Moronta Calderón<sup>1</sup>

<sup>1</sup>Policlinica geral do Rio de Janeiro, Rio de Janeiro, Brazil

# **Introduction & Objectives:**

Scleroderma, or localized scleroderma (morphea), is a chronic autoimmune connective tissue disease characterized by vascular dysfunction, immune dysregulation, and progressive fibrosis of the skin. In generalized morphea, multiple plaques affect different anatomical areas, often leading to significant physical and psychosocial impact. From a dermatologic perspective, early manifestations include edema, pruritus, and skin tightness, evolving into induration, atrophy, pigmentary changes, and in some cases, functional limitation. As there is no curative treatment, current management is symptom-driven including topical therapies and systemic immunosuppressants. This case report aims to

describe a successful therapeutic approach using tofacitinib, a Janus kinase (JAK) inhibitor, in a pediatric patient with with extensive cutaneous involvement.

## **Materials & Methods:**

A comprehensive review of the literature was carried out for this case report

#### **Results:**

A 15-year-old male presented with multiple plaques with atrophic centers and hyperpigmented borders, predominantly affecting the upper and lower limbs, retrosternal region and gluteal region.

The lesions had developed progressively since early childhood, with significant esthetic and emotional impact. Skin biopsy confirmed the diagnosis.

The patient was treated with oral tofacitinib in a dose of 5 mg per day, administered five days per week, in a one-year period.

Throughout follow-up, there was no development of new lesions. Clinical improvements included enhanced skin texture and partial repigmentation of affected areas. The patient reported high satisfaction with the outcome and demonstrated good tolerance to tofacitinib, with no significant adverse events reported. The treatment led to both symptomatic relief and improved quality of life, which translated into improved self-esteem and emotional well-being.

#### **Conclusion:**

Tofacitinib may represent an effective, safe, and innovative therapeutic option in the management of generalized scleroderma, particularly in refractory or pediatric cases. This case highlights its potential to induce lesion remission, reduce aesthetic concerns, and improve long-term outcomes for patients with extensive cutaneous involvement.

## Factors influencing the decision over systemic therapy and goals of therapy for atopic dermatitis

Liborija Lugovic Mihic<sup>1</sup>, Renata Tomašević<sup>2</sup>, Ema Barac<sup>2, 3</sup>, Ena Parać<sup>4</sup>, Lucija Zanze<sup>3, 4</sup>, Ana Ljevar<sup>4</sup>, Lorena Dolački<sup>2</sup>

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- <sup>2</sup>1Department of Dermatovenereology, University Hospital Center Sestre Milosrdnice,, Zagreb, Croatia
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**Introduction & Objectives:** Atopic dermatitis (AD) impacts various aspects of patients' lives including personal life, psychological aspects/disturbances (e.g., depression, anxiety, or even suicidal thoughts), school, and work-related activities, including career advancement. The quality of life for patients with AD is significantly affected by the disease, with the extent of the impact largely dependent on its severity. The aim of this review is to to identify and present the latest available information on AD patients' problems related to their disease in daily life, goals of therapy, and deciding factors regarding standard/advanced systemic therapy.

**Materials & Methods:** We analysed literature data on factors influencing the decision over systemic therapy and goals of therapy for AD, and took into account data published in prominent medical databases during the period between 2013 and 2024. in the PubMed, Web of Science (WOS) and Scopus databases.

**Results:** Current guidelines and systematic reviews support the safety and efficacy of systemic therapy including conventional drugs (cyclosporine, methotrexate, and azathioprine), biologics (dupilumab and tralokinumab), and JAK inhibitors (baricitinib, upadacitinib, and abrocitinib) recommended for treating moderate and severe AD. Recently, additional biologics have been evaluated in clinical trials, including lebrikizumab, nemolizumab, eblasakimab, and OX40/OX40L, among others. Thus, AD patient management and decisions regarding advanced/systemic therapy are complex-requiring the consideration of multiple disease-related factors: disease severity, patient medical history and comorbidities, previous topical therapy use, patient preferences, expectations and fears, pregnancy planning, impact on related risks and any associated psychological or psychiatric issues.

**Conclusion:** Available data indicate the importance of a personalized, stepwise, and multidisciplinary approach which promotes patient compliance, satisfaction with therapy, and increased engagement, leading to a better patient outcomes. In addition, the most recently suggested approach to treating AD patients suggests focusing on therapy that targets and achieves minimal disease activity (MDA), where therapy decisions are informed by both the patient and the clinician.

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Between Indications and Hesitations: Topical Corticosteroid Prescribing by General Practitioners and Medical Interns

Yasmina El Bouhali<sup>1</sup>, ouiame el jouari<sup>1</sup>, salim gallouj<sup>1</sup>

<sup>1</sup>Mohammed VI University Hospital Center, dermatology, TANGIER

# **Introduction & Objectives:**

Topical corticosteroids (TCS) are a key antiinflammatory and immunomodulatory treatment for eczema, psoriasis, and contact dermatitis. Despite their proven efficacy, many general practitioners and trainees hesitate to prescribe them because of concerns about side effects and uncertainty around potency classes and dosing regimens. In primary care, TCS prescribing varies widely—shaped by clinicians' training, experience, and access to specialists—and the absence of clear, standardized guidelines further fuels these inconsistencies. This study aims to assess the prescribing practices, knowledge, and challenges encountered by general practitioners and medical interns regarding topical corticosteroids. It also explores their collaboration with dermatologists and perceptions of their training in this area.

#### Materials & Methods:

An online questionnaire was distributed via Google Forms to general practitioners and interns. The survey was shared through social media platforms (WhatsApp, Instagram, Facebook). Data were collected on prescribing habits, familiarity with TCS potency classes, and perceptions of training and specialist support.

## **Results:**

A survey of 600 physicians (450 general practitioners and 150 medical interns), predominantly aged 30-50 with an average of 10 years' clinical experience, revealed that most regularly prescribe moderate to highpotency topical corticosteroids (TCS) in ointment or cream form for conditions such as eczema, psoriasis, contact dermatitis, and pruritus. However, only a minority adjust the choice of formulation to lesion type or location, and 60% admitted unfamiliarity with TCS potency classifications; many were also uncertain about appropriate treatment durations and tapering strategies. When faced with treatment failure, relapse, or atypical presentations, most practitioners refer patients to dermatology specialists, yet 20% avoid TCS altogether due to concerns over adverse effects, diagnostic uncertainty, sensitive sites, or patient age. All respondents expressed a strong desire for specialized training in TCS prescribing and closer collaboration with dermatologists to improve their daily practice.

## **Conclusion:**

This study reveals that while general practitioners and medical interns frequently prescribe topical corticosteroids for common dermatoses, their use is marked by inconsistent knowledge of potency classes, treatment regimens, and tapering strategies. Providers tend to prescribe cautiously—often due to safety concerns or diagnostic uncertainty—and seek specialist input when needed. A strong demand for targeted education and closer collaboration with dermatologists offers a clear pathway to standardize prescribing practices and enhance the quality of dermatologic care in primary settings.

# Preventing pigmentary visible light damage in dark skin by topical application of a vitamin c, vitamin e and ferulic acid containing antioxidant mix

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<sup>1</sup>Plants for Human Health Institute, Animal Science Dept., NC Research Campus, NC State University, NC, USA;, Kannapolis, United States

<sup>2</sup>Plants for Human Health Institute, Dept. of Food, Bioprocessing and Nutrition Sciences, NC Research Campus, NC State University, NC, USA;, Kannapolis, United States

<sup>3</sup>Ten Bio Technologies Inc, Kannapolis, United States

## **Introduction & Objectives:**

In recent years, increasing evidence has demonstrated that visible light exposure (VL), previously considered without photodamage effects on the skin, is instead able to alter the redox homeostasis, inducing an increase in cutaneous oxidative bioactive molecules, metalloproteinase activation, and the release of inflammatory mediators. Moreover, dark skin phototype (IV-VI) has been demonstrated to be more susceptible to visible light exposure, showing pigmentary alteration. The lack of a standardized method to protect against VL exposure on dark skin prompts us to evaluate the protective effect of an antioxidant mix (AO MIX) compose of vitamin C, vitamin E and Ferrulic acid on dark skin (phototype V), exposed up to 7 days to VL radiation.

# **Materials & Methods:**

Human skin explants were cultured under physiological tension to retain in vivo skin physiology (TenBio model) and pretreated every day, before VL exposure, with an AO MIX.

# **Results:**

First, an analysis of protein expression levels of a well-known marker of oxidative stress, 4-hydroxynonenal (4-HNE), demonstrated a significant increase after 7 days of VL exposure, together with the ability of AO MIX to prevent the increase at the time points analyzed. Moreover, the analysis of Heme oxygenase-1 (HO-1), one of the principal target genes involved in the antioxidant response, demonstrates a similar trend in the mRNA levels with an increased expression after VL exposure compared to the untreated condition at a longer time point. At the same time, the ability of AO MIX pre-treatment to maintain the expression levels similar to the untreated condition was confirmed. Furthermore, as expected, VL was able to significantly increase the protein expression of MMP2, an important matrix metalloproteinase involved in the degradation of the extracellular matrix, especially after 7 days of exposure. Instead, the pre-treatment with AO MIX exhibited a significant reduction of MMP2 expression after VL exposure at both day 2 and 7. These data were also confirmed by the analysis of Collagen 1, one of the most important components of the extracellular matrix responsible for the strength and resilience that characterize the skin. The expression was in fact significantly reduced in VL-exposed skin biopsies in all the time points analyzed. Instead, the pretreatment with AO MIX formulations displayed significant Collagen 1 protection, more evident at day 2.

#### **Conclusion:**

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Our results confirmed the ability of VL exposure to induce an alteration in redox homeostasis and skin structure and suggest the beneficial effects of AO MIX to prevent the pigmentary photodamage effects of VL exposure in darker skin types.

Disclosures: This study was funded by L'Oreal SkinCeuticals.

AG, JI, RH, MC, AP, and GV are researchers at NCSU

PB and HC are employees of SkinCeuticals

# Re-evaluating Methotrexate-Induced Liver Fibrosis Monitoring in Dermatology: Overestimated Risk and the Emerging Role of FIB-4

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# **Introduction & Objectives:**

Methotrexate (MTX) is a well-established and widely utilised systemic treatment for many skin conditions, including psoriasis and atopic dermatitis. However, historic concerns regarding MTX-induced liver fibrosis have prompted intensive monitoring practices, most notably three-monthly procollagen III N-terminal peptide (P3NP) testing. Emerging evidence challenges previous assumptions about the true incidence of MTX-induced fibrosis, suggesting current surveillance practices may be excessive and insufficiently evidence-based.

By critically examining the prevailing understanding, we advocate for a more evidence-based, risk-adapted monitoring approach.

### **Materials & Methods:**

A literature review of recent publications in dermatology and hepatology, along with relevant clinical guidelines, was conducted. The review also examined current understanding of fibrosis progression and non-invasive markers of liver fibrosis employed in dermatology research to date.

#### **Results:**

The risk of methotrexate-induced hepatic fibrosis appears low, with some evidence suggesting methotrexate may not cause fibrosis at all, particularly at the doses used in dermatological practice. Methotrexate may have been incorrectly implicated in cases where fibrosis was more likely attributable to underlying metabolic dysfunction-associated steatohepatitis (MASH).

Comorbidities such as obesity and diabetes are more strongly associated with hepatic fibrosis than Methotrexate and warrant proactive management, particularly in patients with psoriasis, among whom the prevalence of metabolic syndrome is increased. However, it remains uncertain whether methotrexate contributes to fibrosis progression in individuals with pre-existing MASH.

Utilising FIB-4 aligns with monitoring recommendations in hepatology guidelines for the non-invasive assessment of liver fibrosis. Retrospective analyses in psoriasis patients demonstrated FIB-4 may reduce unnecessary investigations triggered by procollagen III N-terminal peptide (P3NP). In contrast, P3NP lacks specificity, is infrequently used outside of dermatology, and offers limited clinical utility. The Enhanced Liver Fibrosis (ELF) test may be more appropriately reserved for second-line assessment within hepatology services rather than as a first-line screening modality in dermatology patients.

Although rates of fibrosis progression vary depending on the underlying aetiology, the process is typically indolent, often requiring several years to reach advanced stages. Studies analysing patients with MASH demonstrated even rapid progressors, which represent a minority of patients, took a mean of 5.9 years to progress to advanced fibrosis (F3/F4). Accordingly, three-monthly monitoring may not align with the slow progression of hepatic fibrosis.

## **Conclusion:**

The risk of MTX-induced liver fibrosis is likely overstated, resulting in unnecessarily intensive monitoring protocols.

There is compelling justification to revise guidelines to reflect current evidence. Adopting FIB-4 as the primary test for fibrosis will streamline monitoring practices while preserving vigilance for rare but serious hepatic adverse events. Reducing monitoring frequency, particularly in low-risk individuals, aligns better with the slow progression of fibrosis and may enhance clinical efficiency, lower costs, and improve patient experience, without compromising quality of care.

# A rare case of infantile gluteal granuloma and tinea incognita in a toddler: diagnostic pitfalls and clinical relevance

Millena de Freitas Ribeiro<sup>1</sup>, Aline Almeida<sup>1</sup>, Ariana Mendonca<sup>1</sup>, Thaina Moreira Costa<sup>1</sup>, Caroline Fattori Assed Saad<sup>1</sup>, Dávson Aguilar Guimarães<sup>1</sup>, Leninha Valerio do Nascimento<sup>1</sup>, Heloisa Taboada<sup>1</sup>, Paula Sá<sup>1</sup>, Hugo M. Faver<sup>1</sup>

<sup>1</sup>Hospital Central do Exército, Dermatologia Tropical, Rio de Janeiro

# **Introduction & Objectives:**

Infantile gluteal granuloma (IGG) is a rare pediatric inflammatory dermatosis that typically presents as erythematous-infiltrated papules or plaques on the gluteal or perianal region. Its multifactorial pathogenesis involves chronic diaper use, exposure to topical irritants, and particularly the inappropriate application of corticosteroids. These factors may obscure concomitant fungal infections and contribute to the emergence of tinea incognita. This case aims to highlight the diagnostic challenges posed by the clinical overlap between inflammatory dermatoses and corticosteroid-modified fungal infections.

## **Materials & Methods:**

A 2-year-5-month-old male toddler presented with a 3 cm, well-demarcated, erythematous-squamous lesion on the right gluteal region. The lesion worsened after unsupervised topical use of mometasone furoate and fusidic acid. A clinical diagnosis of IGG was proposed, while tinea incognita was considered as a differential. A direct mycological examination (DME) was performed, yielding negative results. Corticosteroids were promptly withdrawn, and serial photographic follow-up with clinical reassessment was undertaken.

## **Results:**

Despite the negative DME, clinical suspicion of corticosteroid-masked dermatophytosis persisted. Clinical improvement was observed following discontinuation of corticosteroids and initiation of empirical antifungal therapy. Literature review reveals fewer than 50 well-documented cases of IGG in English by 2020, with even fewer reports from Brazil, particularly those associated with fungal co-infection. IGG is frequently misdiagnosed as candidiasis, irritant contact dermatitis, or atopic dermatitis. Recent studies emphasize the importance of considering fungal investigations in persistent lesions affecting occluded areas in infants.

#### Conclusion:

This case reinforces the importance of early clinical recognition and fungal investigation in persistent inflammatory lesions in infants, especially those previously exposed to topical corticosteroids. It contributes meaningful insight to the limited national literature on IGG and underscores the diagnostic complexity introduced by tinea incognita. The case advocates greater clinical awareness within the fields of pediatric dermatology and clinical mycology.

## Successful cases of multimodal therapy in recalcitrant warts

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<sup>1</sup>Universidad Pontificia Bolivariana, Medellín, Colombia

<sup>2</sup>Aurora Specialized Skin Cancer Center, Medellin, Colombia

<sup>3</sup>Únula, Medellín, Colombia

# **Introduction & Objectives:**

Warts related to the nail unit represent therapeutic challenges due to high recurrence rates and resistance to conventional treatments (1). Various treatment modalities have been explored, including topical agents, cryotherapy, laser therapy, and surgical interventions, each with varying degrees of recovery and different mechanisms of action (2). The persistent nature of these warts and the limitations of existing treatments emphasize the need for alternative therapeutic strategies, including multimodal therapies.

**Objectives:** To present a case series of 10 patients with acral warts treated with two different methods in a dermatology clinic in Medellín, Colombia, highlighting the therapeutic outcomes of the 2 different treatment modalities.

# **Materials & Methods:**

Ten patients diagnosed with acral viral warts were included in this case series, they were managed with one of two different combined therapies:

- **Method 1:** After lesion shaving and hemostasis with 30% trichloroacetic acid (TCA), neutralized with bicarbonate or water, three cycles of cryotherapy were performed. During the final cycle, multiple punctures were made using an 18G needle, followed by the application of bleomycin. Occlusion was done, and patients continued daily bleomycin application for 3–5 days. Topical treatment began after two weeks.
- **Method 2:** Following lesion shaving and hemostasis, 40% TCA was applied and neutralized. A 40% salicylic acid dressing was applied and occluded using a glove. After 3–4 days, the dressing was removed, macerated tissue was curetted, and a topical healing agent was applied.

### **Results:**

Among the included participants, the mean age was 49.7 years (21–81 years), with a predominance of female patients (80%, n=8). Occupations varied, including housewives (n=3), cashiers (n=2), and individual cases of a pilot, model, dentist, architect, and student.

Lesions were most commonly located on the hands (70%) and feet (50%), with some patients presenting involvement in both regions. Subungual involvement was noted in 70% of cases (n=7), and lesions greater than 1 cm were observed in the same proportion. Nine patients underwent biopsy, all confirming the diagnosis of viral wart. All individuals had received prior treatments before inclusion in this therapeutic protocol.

Each patient received one treatment session, except for three cases that required two sessions due to resistant lesions. All patients achieved complete clinical and dermoscopic resolution, yielding a 100% response rate.

The mean time to full response was 5.5 months (2–12 months). Shorter response times were observed in patients treated with Method 2 (4–6 months, mean 4.75 months), whereas the average for those treated with Method 1 was slightly longer (mean 6 months), with one patient experiencing delayed resolution up to 12 months.

## **Conclusion:**

Viral warts in acral locations remain a therapeutic challenge, specially those near the nail unit due to their frequent recurrence. Our case series highlights that a multimodal approach can improve clinical outcomes. Close follow-up and individualized treatment selection are essential for successful management.

| Patient | Age<br>(years) | Sex | Occupation | Disease<br>Duration | Compromised digit  | Subungual<br>involvement | Lesion>1<br>cm | Biopsy<br>performed | Histopathology results | Prior treatments  | Management<br>method | Number of sessions   | Topical treament<br>after/between<br>sessions                    | Time to full<br>clinical an<br>dermoscopi<br>response<br>(months) |
|---------|----------------|-----|------------|---------------------|--|--------------------------|----------------|---------------------|------------------------|---|----------------------|--|--|---|
| 1       | 81             | F   | Housewife  | 4 years             | Right hallux   | Yes                      | Yes            | Yes                 | Viral wart             | Cryotherapy   | Method 2             | 1.   | Tazarotene 0.05%   | 5   |
| 2       | 57             | м   | Pilot      | 2 years             | Second finger<br>left foot   | Yes                      | Yes            | Yes                 | Viral wart             | Cryotherapy,<br>topical salicylic<br>acid, 5-<br>fluorouracil | Method 2             | 1  | Wound healing<br>cream   | 4   |
| 3       | 29             | F   | Model      | 18 months           | Second finger<br>left hand   | Yes                      | Yes            | No                  |                        | Cryotherapy,<br>imiquimod                                     | Method 2             | 1  | Wound healing<br>cream   | 4   |
| 4       | 43             | F   | Dentist    | 12 years            | Right thumb  | Yes                      | Yes            | Yes                 | Viral wart             | Cryotherapy,<br>5-fluorouracil,<br>imiquimod,<br>cantharidin  | Method 2             | 1  | 30-dilution hydrogen<br>peroxide                                 | 6   |
| 5       | 63             | F   | Housewife  | 3 years             | Second and<br>third fingers right<br>hand /Third,<br>fourth and fifth<br>fingers left hand | Yes                      | No             | Yes                 | Viral wart             | Cryotherapy,<br>diphenylcyprone                               | Method 1             | 1 except in<br>right hand<br>fourth finger (2<br>sessions) | 5-fluorouracil +<br>hydrogen peroxide+<br>wound healing<br>cream | 12  |
| 6       | 26             | F   | Architect  | 18 months           | Second finger<br>right foot  | Yes                      | Yes            | Yes                 | Viral wart             | Cryotherapy   | Method 1             | 1  | 5-fluorouracil +<br>hydrogen peroxide+<br>wound healing<br>cream | 6   |
| 7       | 57             | F   | Cashier    | 6 years             | Second finger<br>left hand   | Yes                      | Yes            | Yes                 | Viral wart             | Cryotherapy   | Method 1             | 1  | 5-fluorouracil +<br>hydrogen peroxide+<br>wound healing<br>cream | 6   |
| 8       | 77             | F   | Housewife  | 5 years             | Second and<br>third fingers left<br>foot   | No                       | No             | Yes                 | Viral wart             | Cryotherapy   | Method 1             | 1  | 5-fluorouracil +<br>hydrogen peroxide+<br>wound healing<br>cream | 2   |
| 9       | 43             | F   | Cashier    | 2 years             | Fifth finger left hand   | No                       | No             | Yes                 | Viral wart             | Cryotherapy   | Method 1             | 2  | 5-fluorouracil +<br>hydrogen peroxide+<br>wound healing<br>cream | 7   |
| 10      | 21             | м   | Student    | 3 years             | Plantar region of<br>the right forefoot  | No                       | Yes            | Yes                 | Viral wart             | Cryotherapy   | Method 1             | 2  | 5-fluorouracii +<br>hydrogen peroxide                            | 3   |

No Pain, No Gain: Patients Need to Trust the Process — 5-FU for Actinic Keratosis

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# **Introduction & Objectives:**

Actinic keratosis (AK) represents a spectrum of keratinocyte dysplasia with potential progression to invasive squamous cell carcinoma (SCC), particularly when multiple lesions coexist in the context of field cancerization (1). While several new treatments are available, topical 5-fluorouracil (5-FU) remains a cornerstone for field-directed therapy, especially on sun-exposed areas like the face and scalp (2). This case illustrates the efficacy of 5-FU and the importance of documenting its expected inflammatory evolution to guide patient education and adherence.

## **Materials & Methods:**

An 81-year-old male with extensive chronic sun damage presented with two hyperkeratotic plaques (6 cm and 3 cm) on the scalp. Clinical and dermoscopic features were consistent with AK, without signs suggestive of invasive SCC, such as milky-red areas or atypical vascular patterns (3). Treatment with topical 5-FU 5% cream once daily for four weeks was initiated, applied under occlusion with petroleum jelly.

### **Results:**

A pronounced inflammatory reaction—erythema, erosions, and crusting—was observed by week two, consistent with the expected cytotoxic activity of 5-FU. Complete re-epithelialization occurred within two weeks after discontinuation of therapy. At six weeks, a near-complete clinical response was achieved, with no recurrence at 3-month follow-up. The visual documentation of treatment evolution was used to educate and reassure the patient, emphasizing that inflammation represented a therapeutic response rather than an adverse effect.

# **Conclusion:**

This case reinforces the enduring relevance of 5-FU in the treatment of field cancerization. Its predictable inflammatory course can be leveraged as a visual tool to improve patient compliance and satisfaction. Occlusion may enhance absorption in hyperkeratotic lesions without increasing systemic exposure. Far from outdated, 5-FU remains a strategic, effective, and patient-centered therapy when appropriately framed and monitored (1,2).

# **References:**

- 1. Stockfleth E, Terhorst D, Braathen LR. Field cancerization: From molecular evidence to select management *J Eur Acad Dermatol Venereol.* 2020;34(Suppl 1):17–24.
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## How Should Topical Corticosteroids be Reduced Once an Eczema Flare has Improved?

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## **Introduction & Objectives:**

Atopic eczema/dermatitis (eczema) is very common, affecting 20% of children and 5% of adults. Eczema typically has episodes where it is worse, often referred to as a flare, and times when it is better. Topical corticosteroids (TCS) are one of the main treatments used to treat flares, and they are frequently used alongside emollients and topical calcineurin inhibitors (TCI). TCS can be used reactively (to treat a flare) and/ or proactively (to prevent a flare). However, there is a lack of consensus and guidance on how they should be reduced once a flare has improved, often referred to as tapering or weaning. This can lead to confusion and frustration for patients.

### Materials & Methods:

A systematic review was performed, we searched eight databases on the 19th December 2024: Medline, Embase, Cochrane Specialist Register, Cochrane Central, CINAHL, Web of Science, Epistemonikos and Proquest. We included anyone with eczema, of any age, whereby TCS were used and stopped in any method. All study types were included.

#### **Results:**

10846 abstracts were found, of which 4787 were duplicates. 6058 abstracts were screened independently by two reviewers. 263 were included for full text screening, with 83 excluded from the full text review. An additional 3 abstracts were found from Lax et al's 2022 Cochrane review, and an additional 6 abstracts were added from citation searching, thus 177 abstracts were included. All trial abstracts included an element of TCS use reactively, with some either stopping the treatment and following up after a defined time, or using a proactive or reducing regime. 23 abstracts include more than 2 stages of reducing/ tapering the TCS after reactive use.

The main categories of papers that were included are shown in table 1. We plan to perform a meta-analysis, if possible, from the available quantitative data, and summarise key themes and quotes from qualitative literature.

| Type of study   | n   |  |  |
|---|-----|--|--|
| Non-randomised controlled study                               | 18  |  |  |
| RCT   | 109 |  |  |
| Retrospective cohort study                                    | 4   |  |  |
| Single arm controlled study                                   | 9   |  |  |
| Case report   | 11  |  |  |
| Case series   | 6   |  |  |
| Cross sectional study   | 1   |  |  |
| Health care professional Questionnaire                        | 3   |  |  |
| Observational cohort study with embedded RCT                  |     |  |  |
| Patient Questionnaire   | 9   |  |  |
| Prospective cohort  | 1   |  |  |
| Prospective observational study with retrospective comparison | 1   |  |  |
| Qualitiative study  | 4   |  |  |
| Total   | 177 |  |  |

Table 1 - Types of study within each abstract

# **Conclusion:**

Tapering regimes of topical steroids in eczema vary in clinical practice, and there is a lack of guidance for both clinicians and patients. The existing evidence for the most effective and safe tapering regime is not well understood and has not been systematically reviewed before. The next stage of this research will be to conduct interviews and surveys to help us understand the tapering regimes advised by HCPs, and why.

## Efficacy of Rituximab in prolonged pemphigoid gravidarum

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## **Introduction & Objectives:**

Pemphigoid gravidarum (PG) is a very rare autoimmune bullous dermatosis that usually has a self-limited course in the post-partum period. We report an unusual case of a persistent form that was resistant to CLASSICAL treatment, requiring the initiation of another treatment. Rituximab is an exceptional therapeutic option that can yield results.

# Materials & Methods (Cas report):

A 25-year-old primiparous patient presented at 35 weeks of gestation with a very pruritic urticarial rash, starting in the peri-umbilical area and extending to the abdomen and extremities; the diagnosis of pemphigoid gravidarum (PG) was clinically suspected. A skin biopsy was performed, revealing a subepidermal blister guiding the diagnosis towards pemphigoid gravidarum (PG). She was started on topical treatment with clobetasol propionate. In the immediate post-partum period, the condition evolved into an exacerbation of lesions with the appearance of tense bullae on the trunk and limbs, necessitating a switch to systemic corticosteroid therapy at a dose of 1mg/kg/day. However, the bullous eruption and debilitating pruritus recurred during dose tapering. Various treatments were tried without notable results, treatment with methotrexate was initiated, then replaced by dapsone. After 6 weeks, the disease was still active, and it was decided to treat the patient with Rituximab (2 infusions of 1g at a 15-day interval) while continuing systemic corticosteroids at a dose of 0.5mg/kg/day. This led to a spectacular clinical remission after 01 month."

## **Result and Discussion:**

Regarding the request for references, authors, and long-term follow-up of the two previously reported cases of Rituximab response in pemphigoid gravidarum: While the medical literature indicates that Rituximab has been used in severe and refractory cases of pemphigoid gravidarum, and persistence of the condition beyond six months postpartum is a known bien que rare phenomenon (sometimes leading to consideration as pregnancy-triggered bullous pemphigoid), a specific identification of "only two" universally acknowledged prior individual case reports with their complete references, author details, and published long-term follow-up was not definitively yielded by a general literature search. The user may be referring to specific cases from particular sources. Further detailed review of specialized dermatological and obstetric journals would be necessary to attempt to pinpoint the exact two cases referenced.

# Conclusion

Rituximab constitutes an interesting therapeutic alternative with better tolerability. Further studies are necessary in the future to better evaluate the efficacy of this treatment and to include it in the therapeutic protocol for resistant PG