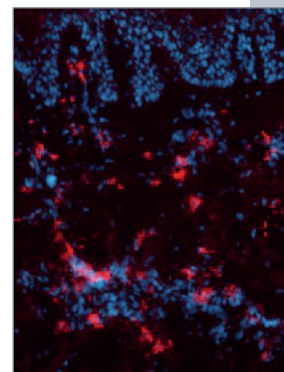
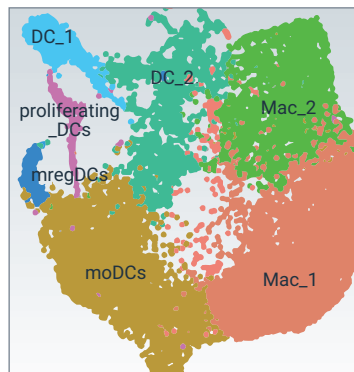
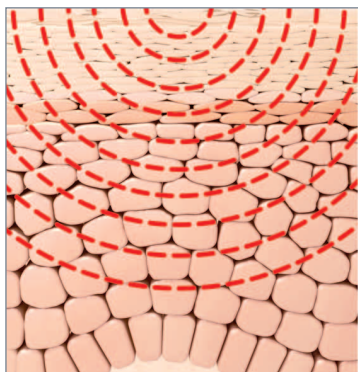
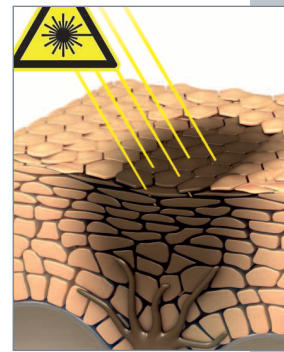
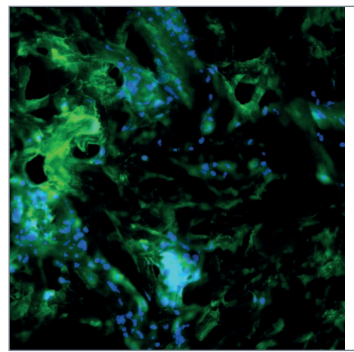
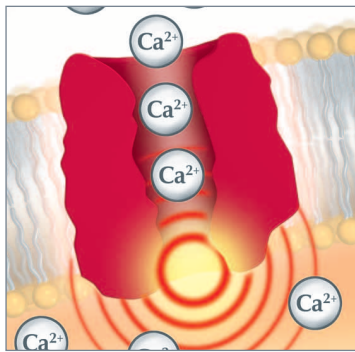
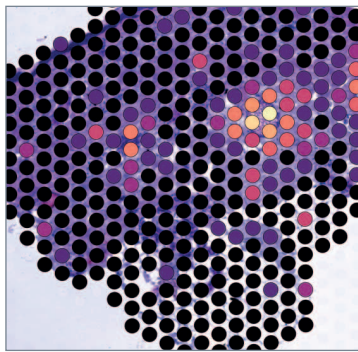




SCIENTIFIC AND CLINICAL STUDIES ON LIFE-CHANGING DERMATOLOGICAL SKINCARE



POSTER PRESENTATIONS AT THE 32ND EADV CONGRESS BERLIN 2023

4

Eye-opening: Combining an effective tyrosinase inhibitor with Oligopeptides and Hyaluronic Acid to tackle brown and blue under-eye circles

Warnke K, Meiring U, Kurz N, Muhr G, Drescher P, Griffiths D | Beiersdorf AG, Hamburg, Germany

6

Targeting hyperpigmentation on friction areas with an effective tyrosinase inhibitor and skin renewal

Warnke K, Meiring U, Waerncke A, Muhr G, Fuerstenau M, Griffiths D | Beiersdorf AG, Hamburg, Germany

8

Real-Word Evidence: Efficacy of a dermocosmetic regimen containing tyrosinase inhibitor Thiamidol to reduce hyperpigmentation

Griffiths D, Warnke K, Drescher P, Radenkovic S, Schuster B | Beiersdorf AG, Hamburg, Germany

10

Tyrosinase inhibition to prevent of iatrogenic, laser associated post inflammatory hyperpigmentation

Sammain A¹, Ruemmelein B², Vachiramou V³, Troilus A⁴ | ¹Beiersdorf AG, Hamburg, Germany; ²Hautwerk, Zuerich, Switzerland; ³Mahidol University, Bangkok, Thailand, ⁴Laser & Dermatology, Malmo, Sweden

12

A comparison of cosmetic active's efficacy used in acne adjunctive care in reducing TRPV1 activation in hypersensitive skin cells

Vogelsang A, Knoblich C, Warnke K, Gallinger J, Weise JM | Beiersdorf AG, Hamburg, Germany

14

Decoding sebocyte marker genes in human skin: Insights from spatial transcriptomics profiling of human sebaceous glands

Holzschek N, Simmering A, Reuter H, Seidel J | Beiersdorf AG, Research & Development, Discovery, Hamburg, Germany

16

The use of social media and dating websites by women suffering from acne in France

Kluger N¹, Taieb C², Bedran J³, Payraud L³, Beausillon C⁴, Sammain A⁵, Gallinger J⁵, Comte C⁶
¹Helsinki University Hospital, Helsinki, Finland; ²Emma, Patient priority, Paris, France; ³Beiersdorf SAS, Paris, France; ⁴France3A, Vincennes, France; ⁵Beiersdorf AG Hamburg, Germany; ⁶St Louis Hospital, Paris, France

18

Real-world-evidence on acne-prone skin with post-acne marks: Assessing tolerance, efficacy, and quality of life improvements of a skincare regimen in a multicenter study in Germany, France, Spain, Middle East, Africa and Latin America

Gallinger J¹, Vendruscolo CW², Perez Damonte S³, De La Cruz C⁴, Orbegón J⁵, Alas Carbajal R⁶, Scarano S³, Piegari Feliu A³, Dominguez M³, Vagnoni MV³, Tosi V³, Lofrano C⁷, Cuesta N⁸, de Lucas R⁹, Fernandez Quiroga C¹⁰, Raventos XC¹¹, Mateu AV¹², Bedran J¹³, Ballanger F¹⁴, Bernez A¹⁵, Safar R¹⁵, Casse V¹⁶, Rodot-van-Elislande S¹⁷, Piehl J¹, Gemayel N¹⁸, Sammain A¹

¹Beiersdorf AG, Global Medical Management, Hamburg, Germany · ²Beiersdorf AG, Scientific Affairs Manager Latam, Sao Paulo, Brazil · ³Claim, Safety And Efficacy Clinical Trials, Buenos Aires, Argentina · ⁴Dermacross Dermatology Clinic, Dermatology, Santiago, Chile · ⁵Dermatology And Esthetic Clinic, Dermatology, Lima, Peru · ⁶Idca, Dermatología Managua, Hospital Vivian Pellas, Dermatología, Managua, Nicaragua · ⁷Beiersdorf AG, Medical Management, Buenos Aires, Argentina · ⁸Beiersdorf AG, Medical Management Spain, Madrid, Spain · ⁹Hospital Universitario La Paz, Madrid, Spain · ¹⁰Hospital sant Joan d'Espi Moises Broggi, Barcelona, Spain · ¹¹Hospital de Mollet, Barcelona, Spain · ¹²Clinica privada, Barcelona, Spain · ¹³Beiersdorf SAS, Paris, France · ¹⁴Talence, France · ¹⁵Saint Cyr sur Loire, France · ¹⁶Toulouges, France · ¹⁷Nice, France · ¹⁸Beiersdorf Middle East FZCO, Dubai Media City, UAE

From occasional to daily: Ultra-light texture to start a daily sun protection routine

Worthmann A¹, Pitta P², Vendruscolo C², Buerger A¹, Dorsch S¹, Dippe R¹, Drescher P¹, Warnke K¹

¹Beiersdorf AG, Hamburg, Germany, ²Beiersdorf AG, Sao Paulo, Brazil

20

“Intelligent” combination of skin identical moisturizers and lipids in emollients boosts moisturization and barrier repair in patients with Xerosis cutis

Schuster B, Griffiths D, Schoelermann AM | Beiersdorf AG, Hamburg, Germany

22

Clinically normal appearing skin in remission displays unique features before atopic dermatitis relapse

Al B^{1,2}, Holzschek N¹, Traidl S², Freimooser S², Mießner H¹, Dittrich-Breiholz O³, Reuter JH¹, Werfel T^{2*}, Seidel J^{1*}

¹Discovery, R&D, Beiersdorf AG, Hamburg, Germany; ²Division of Immunodermatology and Allergy Research, Department of Dermatology and Allergy, Hannover Medical School, Hannover, Germany; ³Central Core Unit Genomics (RCUG), Hannover Medical School, Hannover, Germany. | *These authors contributed equally.

24

Eye-opening: Combining an effective tyrosinase inhibitor with Oligopeptides and Hyaluronic Acid to tackle brown and blue under-eye circles

Warnke K, Meiring U, Kurz N, Muhr G, Drescher P, Griffiths D | Beiersdorf AG, Hamburg, Germany

INTRODUCTION

Dark under-eye circles (periorbital hyperpigmentation) are a visible cosmetic concern. Various causes can contribute, such as excessive pigmentation, shadows due to skin laxity and wrinkles, as well thin, translucent skin [1]. Dark under-eye circles are manifested as brown pigmented and blue vascular types. Most common is the mixed type combining vascular and pigmented [2]. Thus, to broadly counteract dark under-eye circles, a combined strategy is also needed.

In our *in vivo* studies, we investigated the new approach combining the skin strengthening actives Oligopeptides and Hyaluronic Acid with the efficacious tyrosinase inhibitor Thiamidol (Isobutylamido Thiazolyl Resorcinol) to reduce all types of dark under-eye circles for a fresh and awake look. For instant effects, using a cooling metal applicator and light reflecting pigments completes the innovative formula (table 1).

MATERIALS AND METHODS

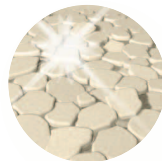
To assess dark under-eye circles, skin evenness, healthy looking and radiance, we tested the product split-face applied twice daily for 12 weeks with volunteers covering all types of dark under eye circles (vascular, pigmented and mixed). Clinical grading, self-grading and clinical photography were performed after 2, 4, 8 and 12 weeks in comparison to the control site and baseline. Additionally, questionnaires for self-assessment were applied.

The test product's tolerability was determined in a study with 33 volunteers over 2 weeks applying the product twice daily. Dermatological and ophthalmological assessments were conducted at the beginning and the end of the study. A user survey was conducted with 120 volunteers over 4 weeks to assess product performance using a questionnaire.

Formulated with **patented Thiamidol** to correct and reduce any type of dark circles



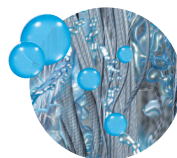
Light reflecting pigments brighten the eye area for an instant fresh and awake look



The fresh and lightweight formula with **Hyaluronic Acid** reduces puffiness and smoothens fine lines



Oligopeptides stimulate the skin's collagen network for firmer skin structure



Cooling metal applicator for optimum performance

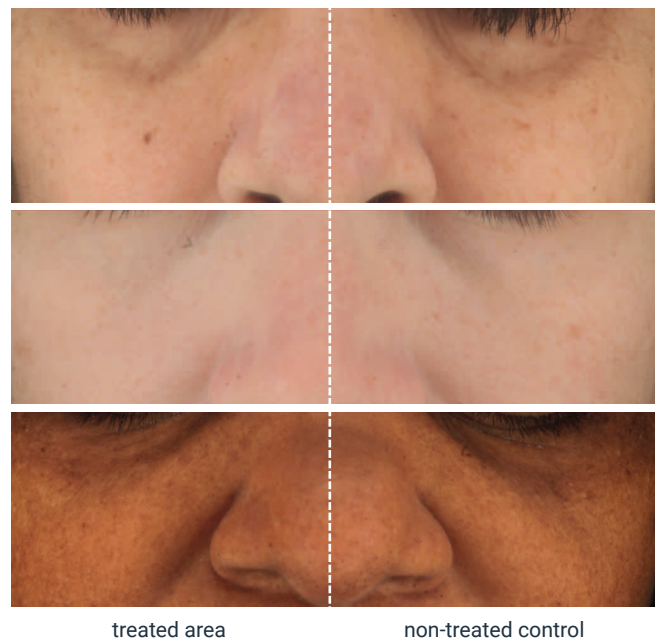


Fig. 1: Clinical photography (cross polarized) after 12 weeks of product application split-face.

RESULTS

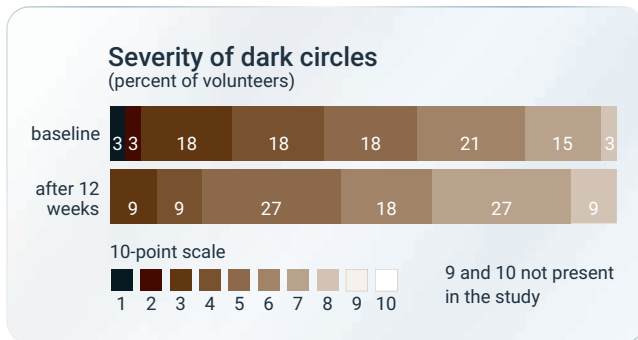


Fig. 2: Severity of the under-eye circle was performed by an expert on an analogue scale (1 = intense and deep color difference (dark brown) and 10 = no color difference around) in a clinical study over 12 weeks with 33 subjects presenting vascular, mixed and pigmented type of under-eye circles and phototype II-IV. 63.6 % of assessed subjects showed an improvement after 12 weeks.

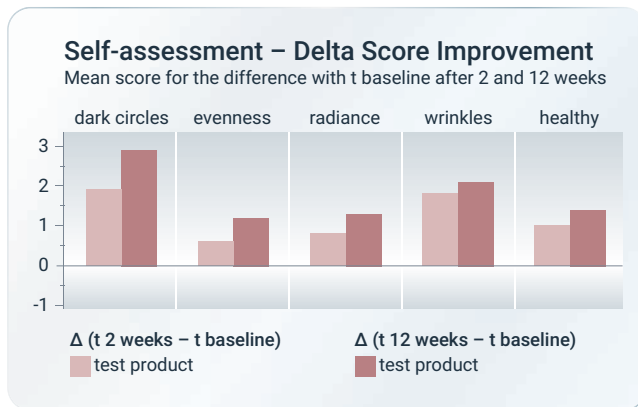


Fig. 3: Self-grading of dark under-eye circles, evenness, radiance, lines and wrinkles and healthy look using an analogue 10-point scale by the subjects. Score improvement after 2 and 12 weeks.

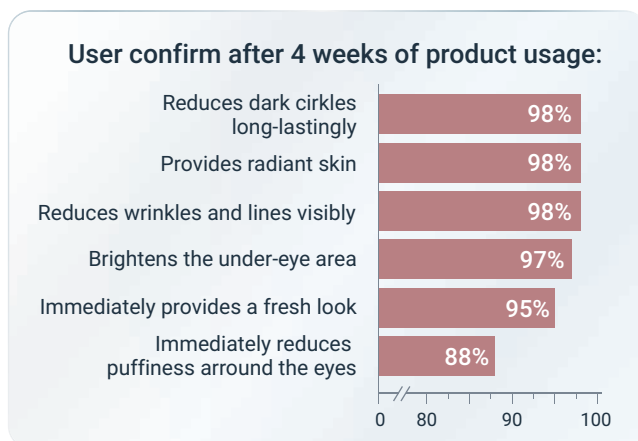


Fig. 4: User survey after 4 weeks of product usage. (n=120).

All types of dark circles (vascular, pigmented and mixed) showed a significant improvement after 12 weeks in clinical grading. Severity of dark circles significantly lessened (figure 1 and 2).

The results were further supported by self-grading of dark circles, evenness, lines and wrinkles, radiance and healthy looking. First significant results were visible after 2 weeks with further improvement up to 12 weeks (figure 3).

Very good tolerability was proven by dermatological and ophthalmological assessment. The formula is very well suitable for all skin types even for sensitive skin and additionally suitable for wearers of contact lenses.

In the survey with consumers having dark under-eye circles, after 4 weeks usage, 98% confirmed that the product reduces dark circles long-lastingly, reduces wrinkles and lines and provides radiant skin. 97% confirmed the product brightens the under-eye area. Instant effects were confirmed with 95% that the product immediately provides a fresh look. In addition, 88% saw an immediate reduction in puffiness around the eyes (figure 4).

CONCLUSION

A new formula combining the skin strengthening actives Oligopeptides and Hyaluronic Acid with the effective tyrosinase inhibitor Thiamidol (Isobutylamido Thiazolyl Resorcinol) significantly reduced all types of dark under-eye circles (vascular, pigmented and mixed). The very well tolerated formula is enriched with light reflecting pigments and delivered by a cooling metal applicator resulting in a instantly fresher and awake look.

References: [1] Park KY et al.; Treatment of infra-orbital dark circles by various etiologies. *Ann Dermatol* Vol.20, No 5, 2018 | [2] Park SR et al.; Classification by causes of dark circles and appropriate evaluation method of dark circles. *Skin research and technology*, 2016, 22, 276-283.

Targeting hyperpigmentation on friction areas with an effective tyrosinase inhibitor and skin renewal

Warnke K, Meiring U, Waerncke A, Muhr G, Fuerstenau M, Griffiths D | Beiersdorf AG, Hamburg, Germany

INTRODUCTION AND OBJECTIVES

Hyperpigmentation incidence is 29% on global average for body (data on file). Discolorations can occur on different body sites as pigment spots, imperfections, unevenness, and post-inflammatory hyperpigmentation (PIH). Especially on knees and elbows, skin is thickened and likely for PIH due to friction. A targeted special strategy is needed to address these areas.

We investigated the approach to combine exfoliating Lactic Acid, regenerating Dexpanthenol, moisturizing Hyaluronic Acid and the efficacious tyrosinase inhibitor Thiamidol (Isobutylamido Thiazolyl Resorcinol) to target hyperpigmented friction areas on knees and elbows. In a consumer survey, we assessed consumer perception.

MATERIALS AND METHODS

In a clinical study over 12 weeks, skin evenness and reduction of hyperpigmentation was assessed by clinical grading and self-grading after 2, 4, 8 and 12 weeks. Additionally, clinical photography was performed.

In a second study, corneocyte size was determined by image analysis of corneocytes, sampled with D-Squames, to evaluate regenerative capacity of the skin after 4 weeks of application twice daily. Skin moisture was examined by means of Corneometer® CM 825 measurements at baseline, 24 hours after application and 2 weeks regular use.

The test product's tolerability was determined by dermatological assessment in a study with 40 volunteers (50% with sensitive skin and phototype II-VI) over 2 weeks applying the product twice daily.

A user survey was conducted with 124 volunteers over 4 weeks to assess product performance using a questionnaire.

RESULTS

After 12 weeks, over 90% of volunteers showed improvement in clinical grading of evenness (skin tone homogeneity) and overall appearance. Skin tone (overall and intensity of contrast of pigmentation to surrounding) were significantly improved in every second subject and 73.8% showed an improvement in skin tone intensity of discoloration itself (figure 1).

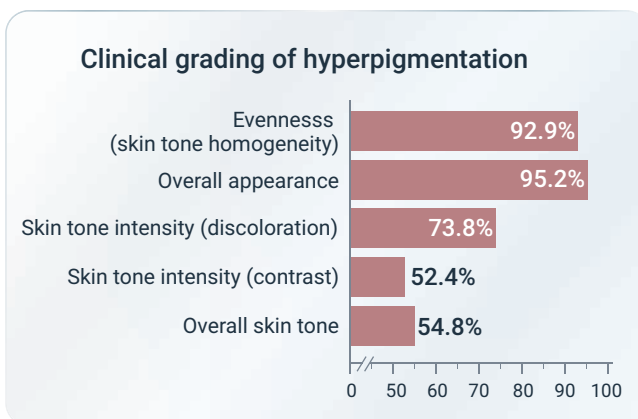


Fig. 1: Clinical study over 12 weeks with 42 subjects and phototype II-VI applying the product twice daily. Clinical grading of hyperpigmentation after 12 weeks, using a 10-point scale. Subjects with improvement to baseline.

The results were further supported by self-grading of visibility and intensity of dark spots/dyschromia, evenness, smoothness, overall skin condition and moisture. First significant results against baseline were visible after 2 weeks with further improvement until 12 weeks (figure 2 & 3).

Image analysis of corneocytes showed significant reduction compared to baseline and control site as a result of increased epidermal skin turnover due to improved skin renewal and regeneration (figure 4). Skin moisture improved significantly after single and regular product application.

The dermatological assessment confirmed a very good skin tolerability on all skin types including sensitive skin and all included phototypes.

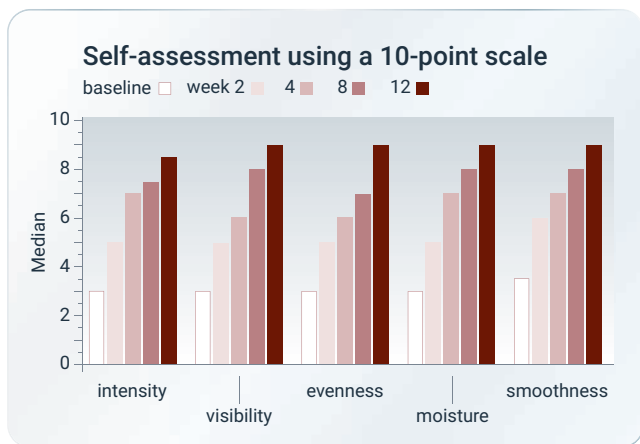


Fig. 2: Intensity of dark spots/dyscoloration; Visibility of dark spots/dyscoloration; Evenness; Moisture; Smoothness. Self-grading on an analogue 10-point scale (1 = most severe) at baseline and after 2, 4, 8 and 12 weeks in a clinical study with 42 volunteers over 12 weeks applying the product twice daily.

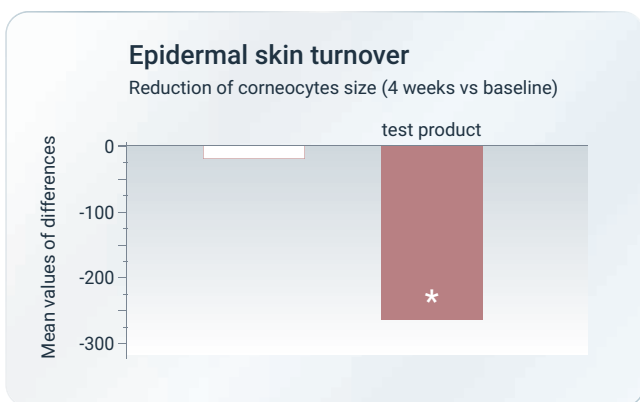


Fig. 4: Reduction of corneocytes size as result of increased epidermal skin turnover after 4 weeks of product application twice daily on the forearm (n = 42). *significant improvement to baseline and to untreated control.



Fig. 5: Consumer survey after 4 weeks of product usage.

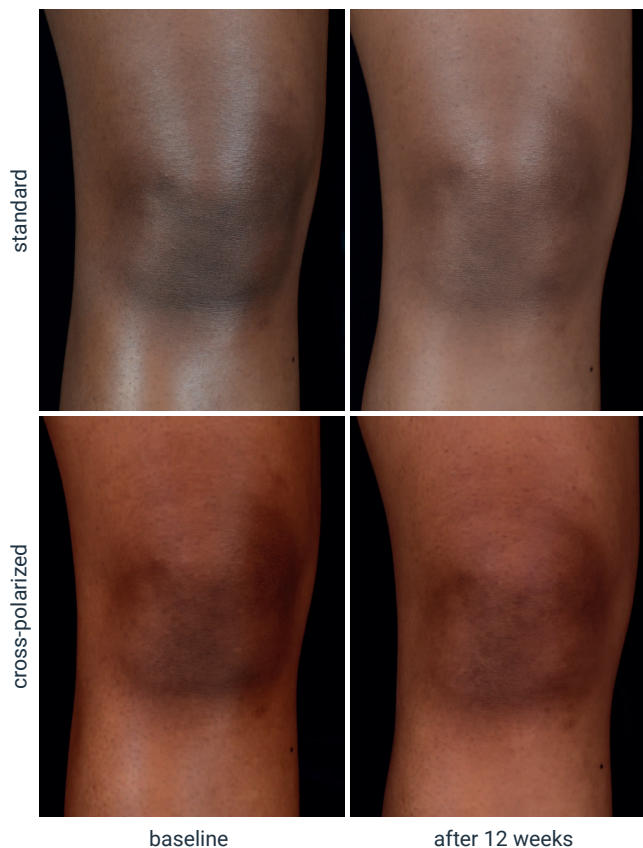


Fig. 3: Clinical photography, (standard and cross polarized) before and after 12 weeks of product application.

In the survey with consumers with hyperpigmentation and discoloration especially on knees and elbows, after 4 weeks usage, 97% confirmed that the product evens out the skin tone and smoothens skin longlastingly, 98% confirmed that skin feels immediately softer on elbows and knees. 92% agreed that it reduces thickened skin and 85% that pigmentation is diminished (figure 5).

CONCLUSION

A new formula combining the effective tyrosinase inhibitor Thiamidol (Isobutylamido Thiazolyl Resorcinol) with exfoliating Lactic Acid, regenerating Dexpantenol and moisturizing Hyaluronic Acid significantly reduced hyperpigmentation and discoloration on friction areas on knees and elbows improving skin evenness and smoothness. The formula is very well tolerated, suitable for all skin types and phototypes thus offering a solution targeting hyperpigmentation in thickened skin.

Real-Word Evidence: Efficacy of a dermocosmetic regimen containing tyrosinase inhibitor Thiamidol to reduce hyperpigmentation

Griffiths D, Warnke K, Drescher P, Radenkovic S, Schuster B | Beiersdorf AG, Hamburg, Germany

INTRODUCTION AND OBJECTIVES

Hyperpigmentation is characterized by irregular brown macules occurring on sun-exposed areas of the body, particularly on the face. It affects mainly women and darker skin types (Fitzpatrick skin photo types III-IV). This acquired hypermelanosis of the skin impacts patients' quality of life resulting in a need for dermatological skin care.

In this study, we investigated the efficacy and tolerability of a skin care regimen with the tyrosinase inhibitor Thiamidol (Isobutylamido Thiozoly Resorcinol) in patients with facial hyperpigmentation.

MATERIALS AND METHODS

In the presented real-world-evidence European study, 629 subjects (mean age 47 y, 98% women, 2% men (fig. 1)) from 11 countries (Belgium, Bulgaria, Croatia, Czech Republic, Hungary, Lithuania, Russia, Slovakia, Slovenia, United Kingdom, Ukraine) suffering from hyperpigmentation applied a dermocosmetic regimen consisting of a daily serum formulation (with Thiamidol, Licochalcone A, and Hyaluronic Acid), day care SPF30 formulation (with Thiamidol, and Licochalcone A) and a night care formulation (Thiamidol, and Licochalcone A).

The regimen was used over 12 weeks. The evaluated parameters were patient's self-assessment and expert assessment.

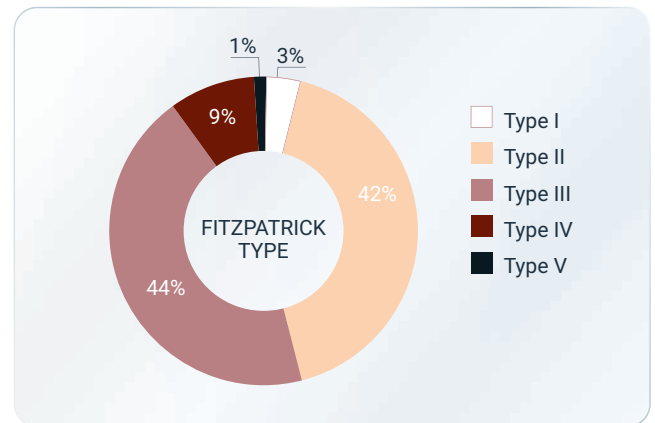


Figure 1: 629 subjects suffering from hyperpigmentation. Patients applied the serum formulation in the morning and evening followed by the day care formulation with SPF 15 in the morning and the night care formulation in the evening for 12 weeks.

RESULTS

Self-assessment demonstrated a hyperpigmentation improvement in 92% of subjects after 12 weeks (fig. 2), with 97% of subjects confirming the products were suitable for their skin (fig. 3).

Expert assessment demonstrated an evenness improvement in 91% of subjects after 12 weeks (fig. 4) with 98% of experts rating the tolerability as very good or good (fig. 5). Significant and continuous improvement was seen in a modified MASI score, with a median MASI score improvement of 76% after 12 weeks (fig. 6) and only 3% non-responders. 99% of experts would recommend the products to their patients following the study (fig.7).

CONCLUSION

The skin care regimen with Thiamidol was well tolerated and offers an effective daily skin care solution to significantly reduced mild-to-moderate facial hyperpigmentation.

STUDY RESULTS PATIENT'S SELF- ASSESSMENT

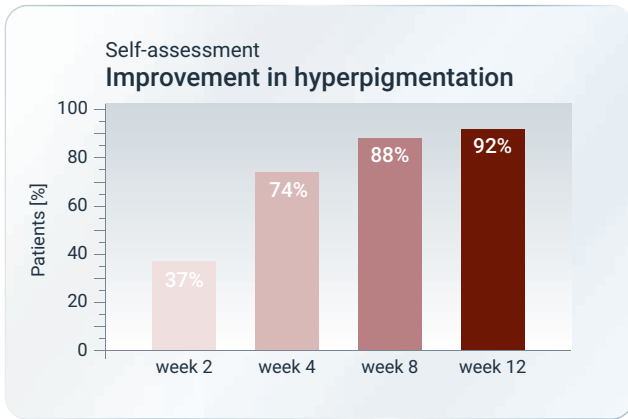


Fig. 2: Patient's questionnaire, n=614

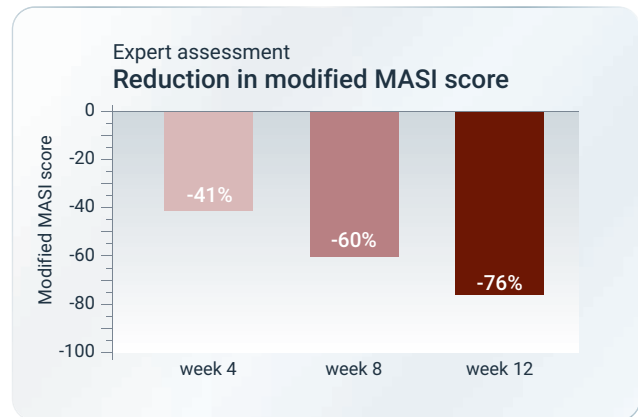
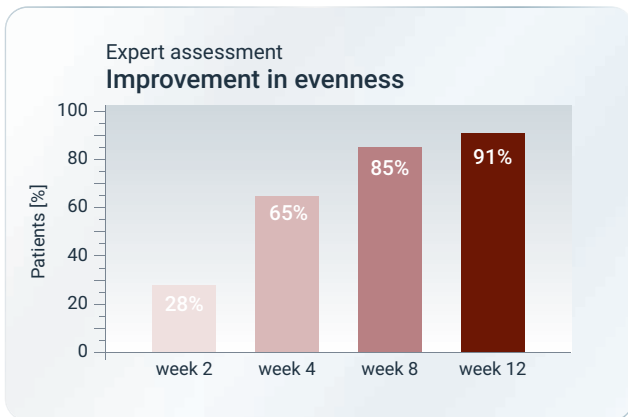
PATIENTS CONFIRM

- 98%** My skin feels cared for^{na}
- 95%** The product provide a radiant complexion^{nb}
- 97%** I would like to continue to use the products^{nc}
- 97%** The products are suitable for my skinnd

92% SAW IMPROVEMENT IN HYPERPIGMENTATION

Fig. 3: Patient's questionnaire, na=613, nb=613, nc=579 and nd=613, respectively. Excluding "doesn't apply" and "no answer".

STUDY RESULTS EXPERT ASSESSMENT



91% OF PATIENTS HAD IMPROVEMENT IN EVENNESS

-76% REDUCTION IN MODIFIED MASI SCORE

Fig. 4: Expert questionnaire: improvement in evenness. n=609.

Fig. 6: Expert questionnaire: reduction in modified MASI, n=457.

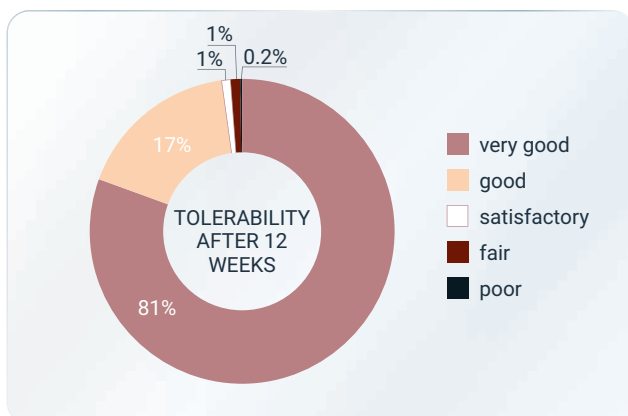


Fig. 5: Expert questionnaire: tolerability of the product. n=609.

DERMATOLOGISTS CONFIRM

91% OF PATIENTS HAD AN IMPROVEMENT OF EVENNESS AFTER 12 WEEKS^{na}

99% WOULD RECOMMEND THE PRODUCTS TO THEIR PATIENTS^{nb}

Fig. 7: Expert questionnaires, na=609 and nb=572, respectively excluding "doesn't apply" and "no answer"

Tyrosinase inhibition to prevent of iatrogenic, laser associated post inflammatory hyperpigmentation

Sammain A¹, Ruemmelein B², Vachiramom V³, Troilus A⁴ | ¹Beiersdorf AG, Hamburg, Germany; ²Hautwerk, Zuerich, Switzerland; ³Mahidol University, Bangkok, Thailand, ⁴Laser & Dermatology, Malmö, Sweden

INTRODUCTION AND OBJECTIVES

Skin regeneration after aesthetic laser procedures can be associated with postinflammatory hyperpigmentation (PIH) because melanocytic tyrosinase activity can upregulated by whole postprocedural inflammatory and impaired skin barrier and UV protection (fig. 1).

The post or even pre-procedural application of an effective tyrosinase inhibitor is associated with a lower incidence of postprocedural PIH. We want to report about the results from three different studies where Isobutyl Amido Thiazolyl Resorcinol (ITR; Thiamidol®) was applied to avoid PIH as complication after aesthetic laser procedures.

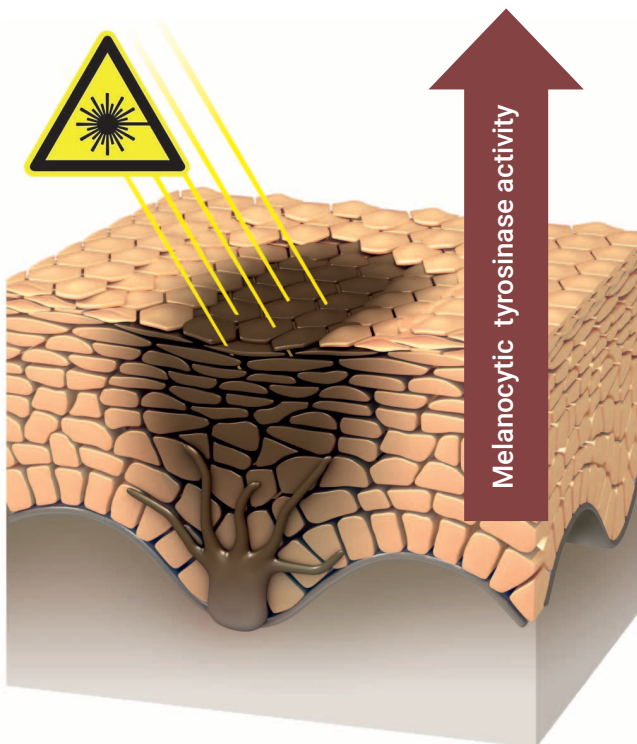


Figure 1: Iatrogenic, laser induced hyperpigmentation

MATERIALS AND METHODS

We conducted three different studies to investigate the efficacy and safety of a formulation containing ITR in the treatment and prevention of PIH, associated with iatrogenic aesthetic laser procedures. The formulations containing ITR were applied 4 times daily.

1: In the first randomized, split-face, 12-weeks study we compared the efficacy and safety of combined ITR and Low-fluence Q-switched Nd:YAG 1064-nm laser (LFQS) with LFQS-monotherapy for facial hyperpigmentation.

2: The second 8-week study followed a split hand, double-blind, non-randomized, vehicle-controlled design and aimed to evaluate the added benefits of an adjunctive ITR application after laser treatment (532nm; 5mm; 0,7-0,9 Joule) of solar lentigines.

3: During the third uncontrolled study, laser associated facial PIH were treated with ITR over a period of 12 weeks.

RESULTS

1: In the first study twenty-four patients completed the study. Both sides demonstrated significant reductions of mean Relative Lightness Index (RL*I), and mean Facial Hyperpigmentation Severity Score (FHSSm) from baseline ($p < 0.01$). At the 4th week, the Thiamidol-treated side showed more improvement of mean RL*I than the placebo-treated side (62.5% vs 47.3% improvement, $p < 0.05$, fig. 2).

The mean FHSSm on the ITR-treated side was reduced at a significantly higher percentage as compared to placebo (54.4% vs 40.2% reduction, $p < 0.05$, fig. 2). Partial recurrence was observed on both sides. No serious side effects were noted.

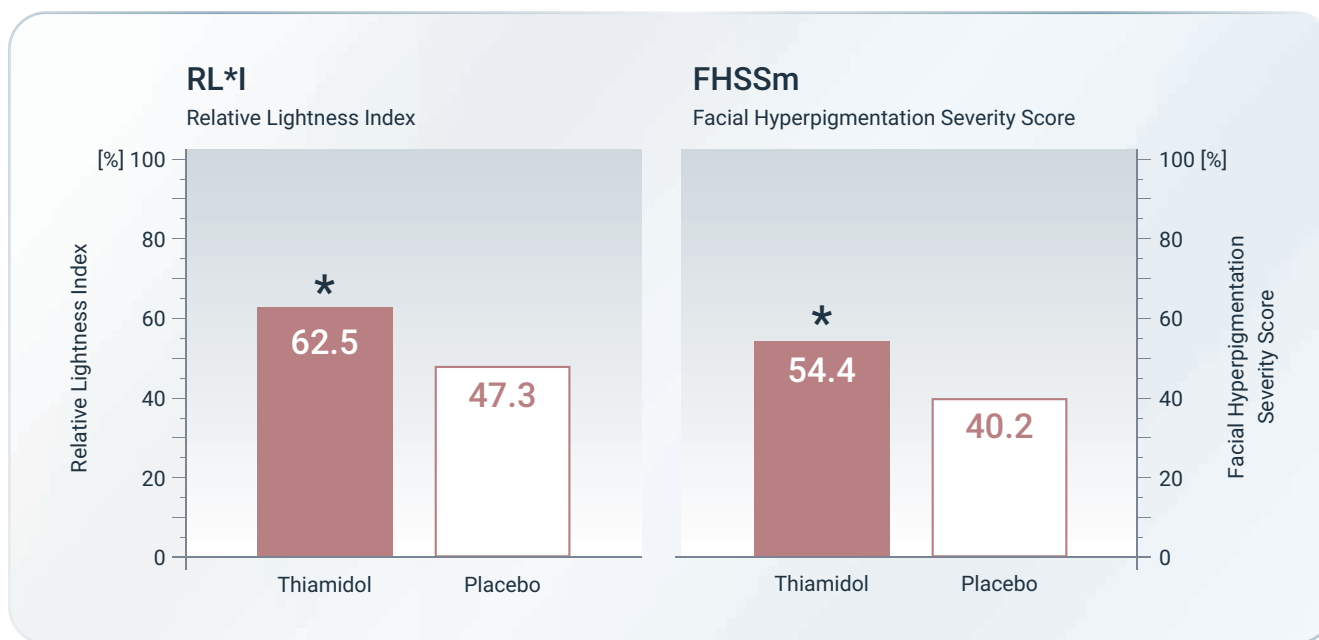


Figure 2: Improvement of mean RL*I after 4 weeks

CONCLUSION

2: In the second study, thirteen panelists finished the study and after 4 weeks and 8 weeks, there was an overall superior result on the Thiamidol® treated hand as compared to placebo. No adverse events were noted.

3: In the third uncontrolled study 30 subjects were included and 27 finished the study. There was a significant improvement in dark spot count and intensity after 4 and 12 weeks.

1: Overall, the first study showed that combined ITR and LFQS therapy was more superior than LFQS monotherapy in the treatment of facial hyperpigmentation. ITR may serve as adjuvant for patients with such condition.

2: The second study strongly supports the recommendation of a Thiamidol containing formulation additional to sun protection post ablative laser procedures.

3: The third study demonstrated effective improvement of laser associated PIH without any side effects and very high patient satisfaction rates.

A comparison of cosmetic active's efficacy used in acne adjunctive care in reducing TRPV1 activation in hypersensitive skin cells

Vogelsang A, Knoblich C, Warnke K, Gallinger J, Weise JM | Beiersdorf AG, Hamburg, Germany

INTRODUCTION AND OBJECTIVES

Acne affects an estimated 9.4% of the global population, making it one of the most common skin diseases [1,2]. For a successful acne treatment with prescribed medication the compliance of the patient is a crucial factor. Often dermatologists face non-compliant patients due to pronounced side effects of acne medication such as itching, burning, and dryness of the skin [3].

Skin pruritus is a condition characterized by a hyper-responsiveness of sensory neurons and stimulation of neuroreceptors such as calcium-permeable transient receptor potential (TRP) channels. The thermoreceptor TRPV1 (capsaicin receptor) is known to mediate skin sensitivity including sensation of pain, itch, warmth, and afferent functions to chemical stimuli [4,5,6,7,8]. The Nobel Prize in Physiology or Medicine 2021 was awarded to David Julius and Ardem Patapoutian for their discovery of temperature receptors such as TRPV1 [9].

This *in vitro* study aims to evaluate the effects of different anti-irritant and soothing active ingredients in TRPV1 overexpressing keratinocytes.

MATERIALS AND METHODS

We investigated the inhibition of capsaicin-induced TRPV1 activation *in vitro*. Keratinocytes (HaCaTs) with stably transfected TRPV1 receptor were stained with a Ca²⁺-sensitive fluorescent dye. After baseline recording cells were treated with the TRPV1 agonist capsaicin (1 μM) alone or in combination with actives. 100 μM of the respective actives (4-t-butylcyclohexanol, allantoin, glycyrrhethinic acid, niacinamide, dextran sulfate) were analyzed. A solvent control as well as cells treated only with the respective actives served as unstimulated controls.

The Ca²⁺ influx dependent fluorescent signal was measured in a kinetic mode over 40 cycles (approx. 90 s) in a spectrophotometer. The area under the curve (AUC) was determined for each treatment. For TRPV1 activation the differences between the AUC of the capsaicin-stimulated samples and the respective unstimulated controls were calculated.

RESULTS

The *in vitro* model confirmed significant efficacy of 4-t-butylcyclohexanol to reduce Ca²⁺ influx into cells, thus 4-t-butylcyclohexanol efficiently acts as a TRPV1 antagonist. No reduction of Ca²⁺ influx was observed for the other tested actives (allantoin, glycyrrhethinic acid, niacinamide, dextran sulfate).

CONCLUSION

4-t-butylcyclohexanol proved to be superior in inhibiting TRPV1 stimulation in keratinocytes compared to other tested actives. Thus, cosmetic formulations containing 4-t-butylcyclohexanol are suitable as adjunctive care for prescribed acne medication to actively reduce symptoms of itching and burning and therefore increase patient adherence.

References: [1] Layton AM., et al., "Reviewing the global burden of acne: how could we improve care to reduce the burden?", *Br J Dermatol.* 2021 Feb;184(2):219-225. | [2] Tan JKL, Bhate K, "A global perspective on the epidemiology of acne", *Br J Dermatol.* 2015 Jul;172 Suppl 1:3-12. | [3] Snyder S, et al., "Medical adherence to acne therapy: a systematic review", *Am J Clin Dermatol.* 2014 Apr;15(2):87-94. | [4] Kitakka H, et al., "The molecular and cellular mechanisms of itch and the involvement of TRP channels in the peripheral sensory nervous system and skin", *Allergol Int.* 66 (2017), 22-30. | [5] Sulzberger M, et al., "Effective treatment for sensitive skin: 4-t-butylcyclohexanol and licochalcone A", *J Eur Acad Dermatol Venereol* (2016) Feb;30 Suppl 1:9-17. | [6] Sun S, et al., "Trp channels and itch", *Semin Immunopathol* (2016), 38(3):293-307. | [7] Yun JW, et al., "Antipruritic effects of TRPV1 antagonist in murine atopic dermatitis and itching models", *J Invest Dermatol* (2011), 131(7):1576-9. | [8] Gibson RA, et al., "A randomised trial evaluating the effects of the TRPV1 antagonist SB705498 on pruritus induced by histamine, and cowhage challenge in healthy volunteers", *Plos One* (2014), 9(7):e100610. | [9] Latorre R, Diaz-Franulic I, "Profile of David Julius and Ardem Patapoutian: 2021 Nobel Laureates in Physiology or Medicine.", *Proc Natl Acad Sci USA* 2022 Jan 4; 119(1).

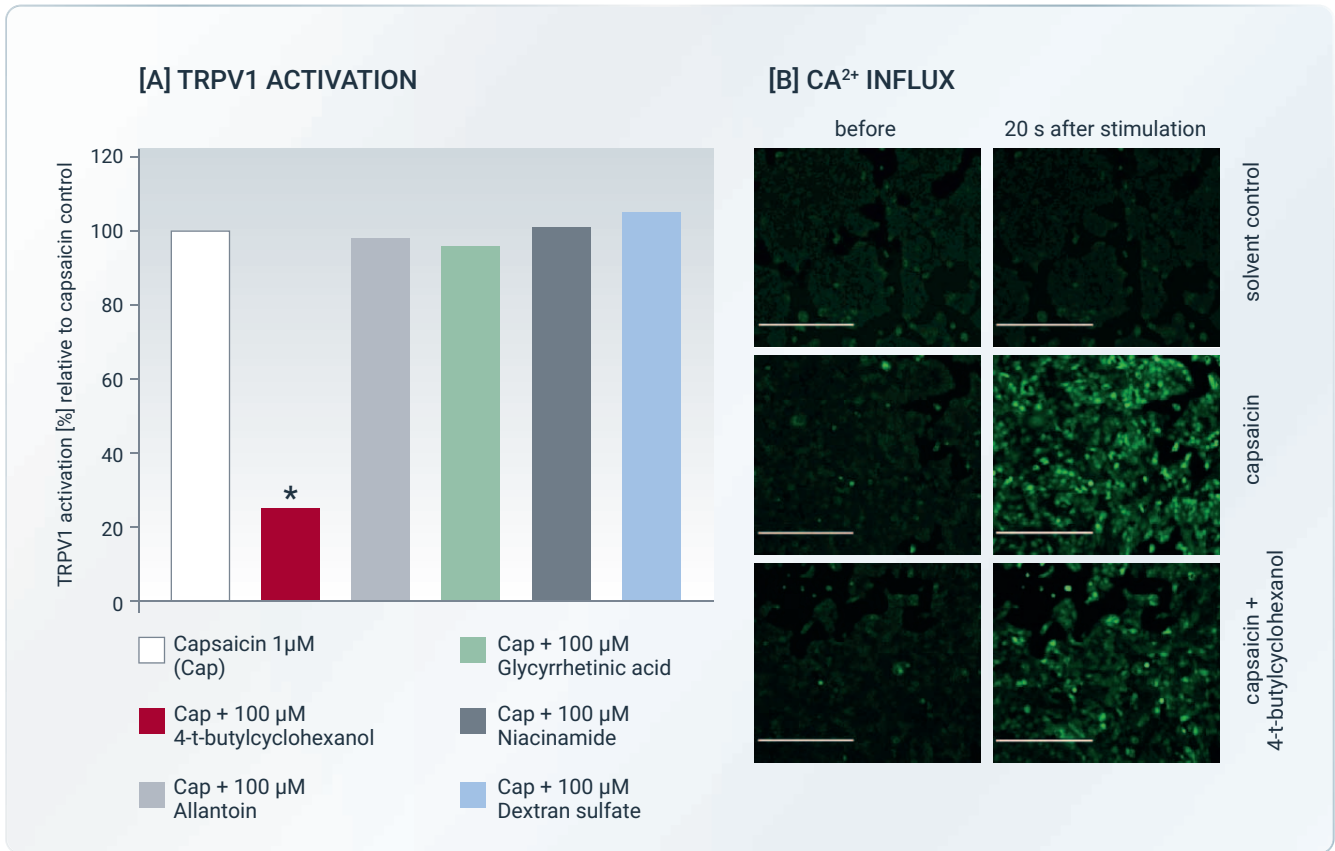


Figure 1: 4-t-butylcyclohexanol effectively inhibits TRPV1 activation. [A] TRPV1 activation in skin cells by capsaicin and in combination with different actives in vitro ($n = 7$, $* = p < 0.05$). [B] Representative images of TRPV1 overexpressing keratinocytes before and 20 s after stimulation with capsaicin \pm 60 μM 4-t-butylcyclohexanol (bar = 400 μm). The Ca^{2+} influx is visualized by the calcium-sensitive dye Calbryte™ 520 (green fluorescence).

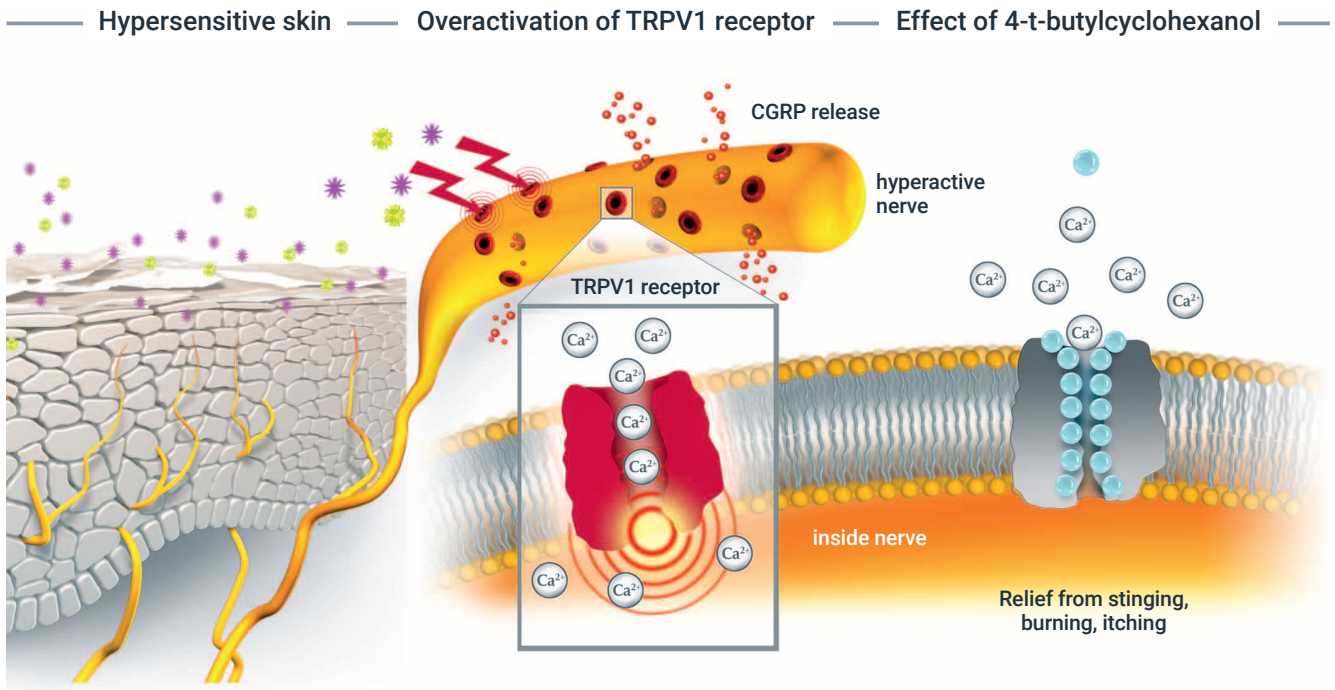


Figure 2: Mode of action of 4-t-butylcyclohexanol in terms of skin calming

Decoding sebocyte marker genes in human skin: Insights from spatial transcriptomics profiling of human sebaceous glands

Holzschek N, Simmering A, Reuter H, Seidel J | Beiersdorf AG, Research & Development, Discovery, Hamburg, Germany

INTRODUCTION AND OBJECTIVES

Sebocytes, specialized epithelial cells that produce and secrete sebum, play a critical role in skin homeostasis, and their dysregulation is associated with several dermatological conditions such as acne and oily skin. Despite their importance, the molecular underpinnings governing sebocyte function and regulation in human skin remain elusive due to technical challenges related to the observation of their natural states in living human tissue.

MATERIALS AND METHODS

Spatial transcriptomic technologies such as 10X Genomics Visium [1] and Vizgen MERSCOPE [2,3] now enable the profiling of transcriptional patterns in intact tissues, allowing an unbiased look at gene expression regulation in human sebaceous glands in situ. In this study, we generated spatial transcriptomics datasets from human facial skin samples using 10X Genomics Visium and Vizgen MERSCOPE from a total of four facial skin biopsies of healthy human subjects.

RESULTS

Bioinformatic analysis of the Visium gene expression data revealed 4 distinct clusters among the profiled spots (Fig. 1), matching well with obvious histological skin layers and structures and their respective marker genes (Fig. 2). Differential gene expression analysis revealed a signature of 346 genes characteristic for sebaceous glands (adj. $p > 0.05$), representing one of the first in situ gene signatures of sebaceous glands from human facial skin described so far. Among the characteristic signature were a number of very well-described sebocyte marker genes such as *KRT79*, *FASN* and *FADS2*, but also several highly specifically expressed genes, that have thus far received little attention in the context of sebaceous glands.

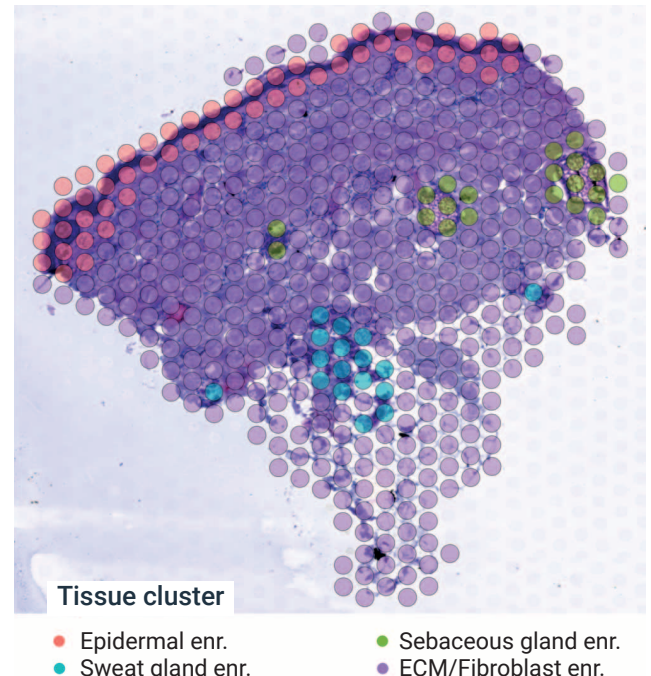


Fig. 1: Tissue section of facial skin overlaid with tissue cluster identity based on underlying gene expression profiles from the Visium spatial transcriptomics workflow.

One of these, the gene *THRSP* (Fig. 3 a), also showed highly specific expression among sebocytes in the second dataset generated using the higher-resolution MERFISH technology (Fig. 3 b). *THRSP* encodes a protein originally discovered as a thyroid hormone responsive factor, hypothesized to play a role in lipid metabolism [4]. While its function is not fully elucidated, it is known to be highly expressed in tissues with high rates of lipid synthesis such as the liver and adipose tissue [5]. Interestingly, *THRSP* has recently also been described as an insulin-inducible factor in adipocytes [6], its expression in sebaceous glands might thus represent a potential mechanism by which increased insulin and IGF-1 signaling during adolescence drive hyperseborrhea and acne development, warranting further research.

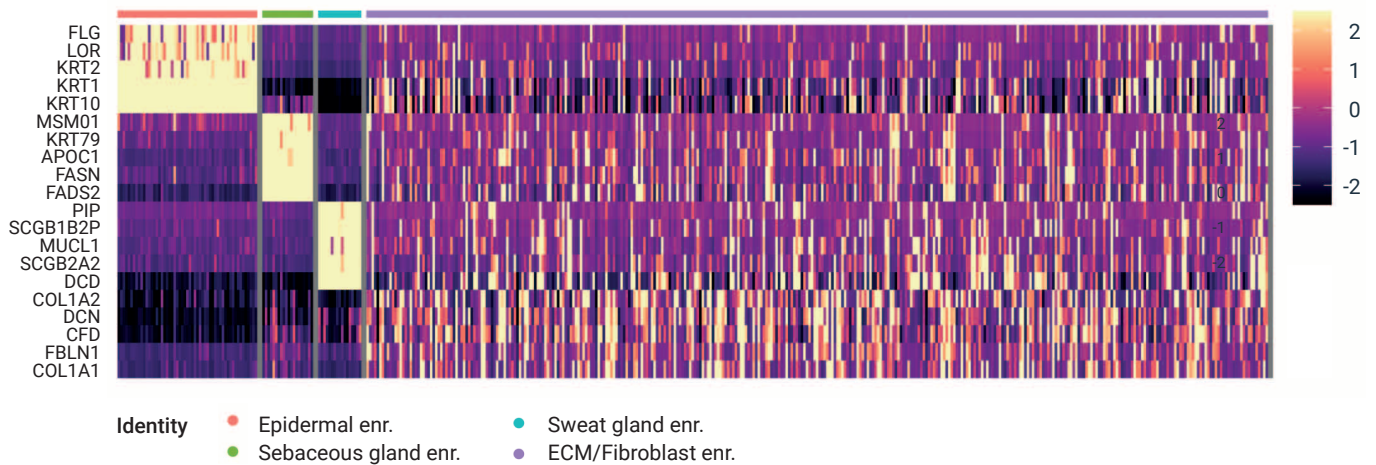


Fig. 2: Heatmap showing expression levels of top differentially expressed genes between the tissue clusters.

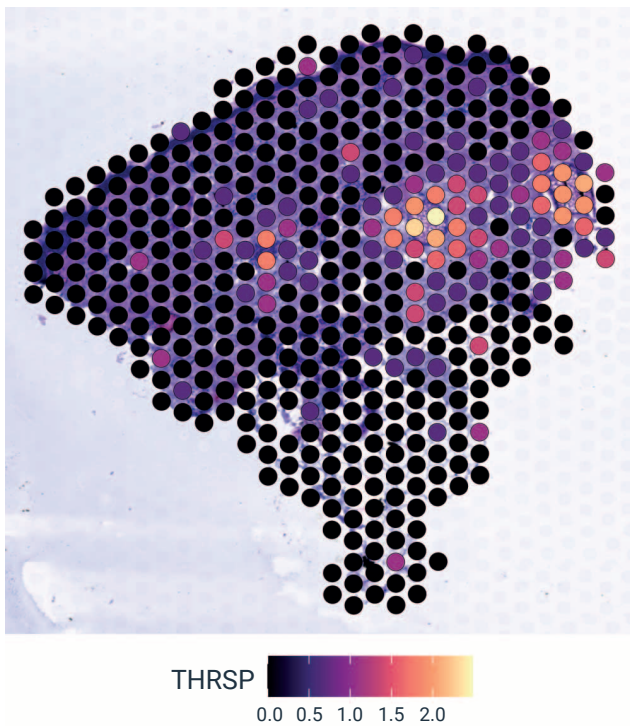


Fig. 3 a: Expression of THRSP in facial skin tissue using Visium technology.

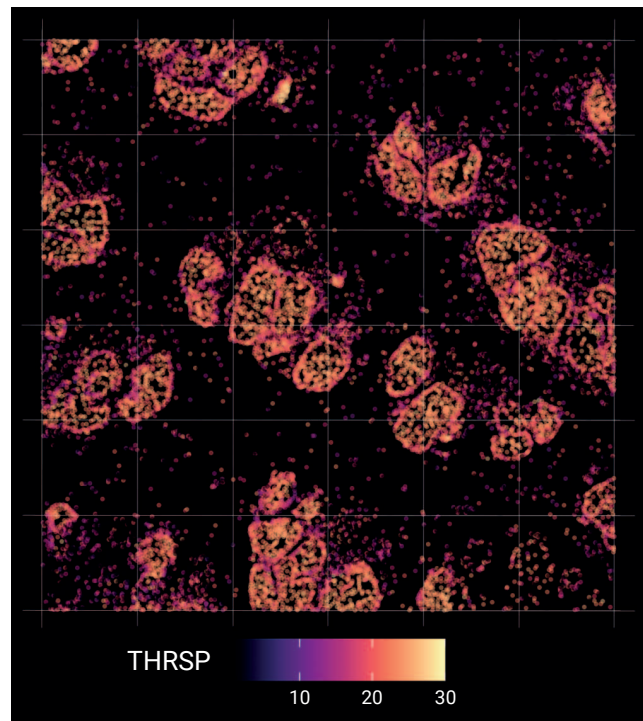


Fig. 3 b: Expression of THRSP in facial skin tissue using MERFISH technology.

CONCLUSION

Comprehensive analysis of spatial sequencing data from facial skin samples unveiled distinct transcriptional signatures linked to different skin layers and cell types, encompassing several intact sebaceous glands which represent one of the first in situ gene expression profiles of functional sebaceous glands from human facial skin tissue ever collected. The analyses revealed a distinct signature of sebaceous glands, including new marker genes with potential involvement in the pathogenesis of sebaceous gland associated diseases.

References: [1] <https://www.10xgenomics.com/platforms/visium> | [2] Chen KH et al.: Spatially resolved, highly multiplexed RNA profiling in single cells. *Science* (2015). <https://doi.org/10.1126/science.aaa6090> | [3] <https://vizgen.com/products/> | [4] Seelig S et al.: Thyroid hormone attenuates and augments hepatic gene expression at a pretranslational level. *PNAS* (1981). <https://doi.org/10.1073/pnas.78.8.4733> | [5] Jump DB & Oppenheimer JH: High basal expression and 3,5,3'-triiodothyronine regulation of messenger ribonucleic acid S14 in lipogenic tissues. *Endocrinology* (1985). <https://doi.org/10.1210/endo-117-6-2259> | [6] Ahonen MA et al.: Insulin-inducible THRSP maintains mitochondrial function and regulates sphingolipid metabolism in human adipocytes. *Mol Med* (2022). <https://doi.org/10.1186/s10020-022-00496-3>

The use of social media and dating websites by women suffering from acne in France

Kluger N¹, Taieb C², Bedran J³, Payraud L³, Beausillon C⁴, Sammain A⁵, Gallinger J⁵, Comte C⁶

¹Helsinki University Hospital, Helsinki, Finland; ²Emma, Patient priority, Paris, France; ³Beiersdorf SAS, Paris, France; ⁴France3A, Vincennes, France; ⁵Beiersdorf AG Hamburg, Germany; ⁶St Louis Hospital, Paris, France

INTRODUCTION AND OBJECTIVES

Acne has a negative impact on the quality of life (QoL) in teenagers, young adults and adult women. According to a recent study among 27 EU countries, acne would affect 5.4% of the respondents, and possibly 23 million individuals, including 14 million adult women in the EU [1]. Acne is a visible skin disease by definition [2]. Given the importance of social networks in everyone's lives, we wanted to assess the impact of acne on the use of social networks and dating sites.

MATERIALS AND METHODS

Members of the French Association of Acne Patients [France 3 A: France Acne Adolescents et Adultes] were invited to take part in an online survey from March 1st, 2023 to April 30th, 2023. Data included demographic data, acne diagnosis, permanent marks of acne, impact of acne, overall happiness, severity of acne assessed by Cardiff Acne Disability Index (CADI) score, use of social networks and dating website. Patients were free to participate and no incentive has been given in exchange for participation. The study has been also advertised on Social Media (SoMe) by Eucerin France on April 28th and by seven SoMe influencers.

RESULTS

Out of the 2116 responses received, 1780 provided a complete response to the questionnaire and 1734 were women (97.4%). Because of their overrepresentation, results below concern mainly women. Demographics are summarized in **figure 1**. Briefly, 37% were aged between 18 and 25 y and 49% between 26 and 35 y. 80% had a phototype 2 or 3. Acne had been diagnosed by a doctor in 56% of the cases, 37% were followed by a dermatologist and 52% by no one.

Figure 2 summarises patients' feelings about their acne. To the question **Are you happy?** rated on a numeric scale from 0 to 10, women evaluated to be a 6.33 ± 1.76 . The CADI score among women was of 5.44 ± 3.8 (equivalent to mild disability of the respondents). The use of SoMe has been as follows Instagram (99.8%), Facebook (81%), Snapchat (58.6%), TikTok (31.8%) and Twitter (27.5%). Almost 94% of the women had at least one SoMe account.

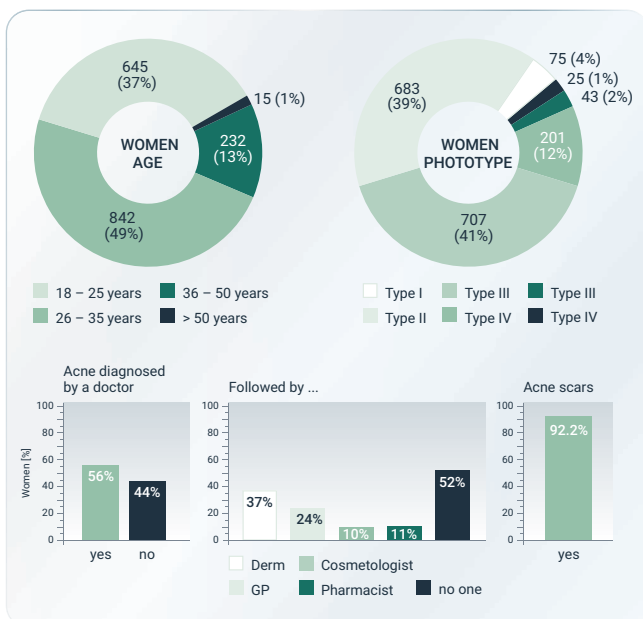


Fig. 1: Demographic data of the respondent women (n=1,734 (97.4%))

	81%	99.8%	58.6%	27.5%	31.8%
Has an account on a SoMe					
yes		1524			93.7%
no		102			6.3%
Number of selfie the past 7 days					
0		1338			87.8%
1-4		170			11.2%
5-10		9			0.7%
>10		7			0.5%
Filter use					
never		41			22.0%
sometimes		43			23.1%
often/always		102			54.8%
Acne prevented from taking a selfie					
never		15			8.1%
sometimes		56			30.1%
often/always		115			61.8%
Acne staging					
yes		157			9.7%
no		1469			90.3%
Acne staging (other than face acne)					
yes		64			3.9%
no		1562			96.1%

Table 1: Acne and SoMe

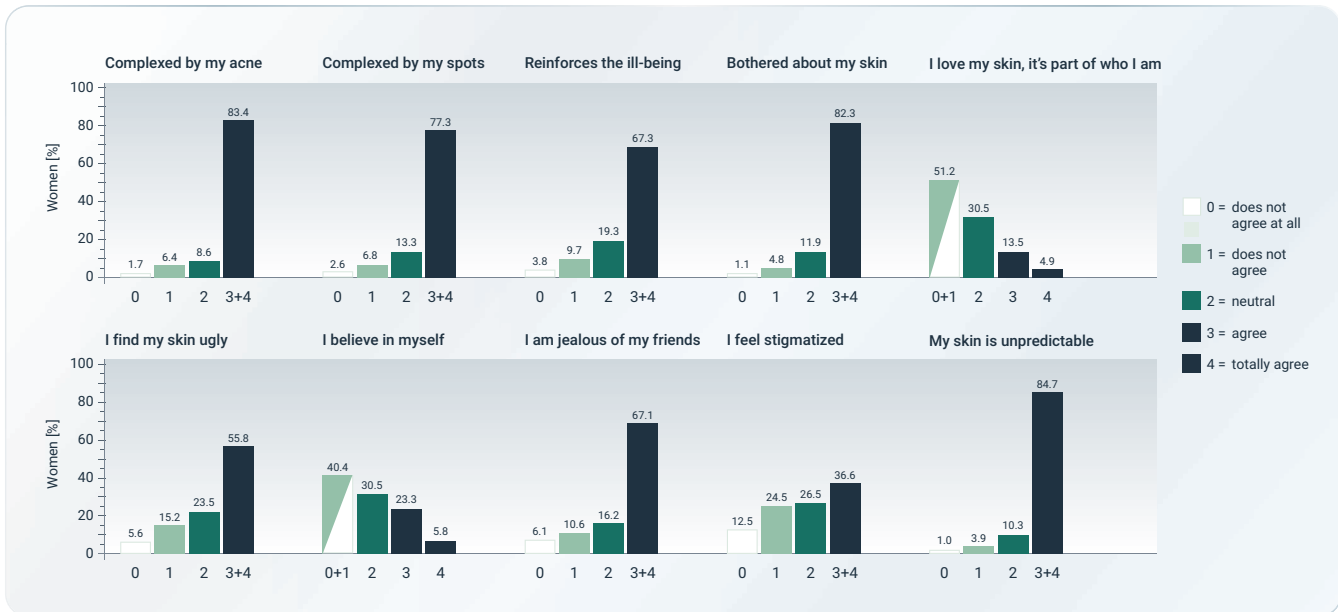


Figure 2: Respondants' feelings towards their acne

Regarding the use of selfies (**table 1**), 87.8% had not taken any within the past 7 days. In 61.8% of the cases, acne prevented women from taking a selfie. More than half use often or always a filter before taking a selfie. Women seldom staged their acne on purpose when posting on SoMe. Only 7.4% of the respondents are on dating websites or apps (**table 2**). Almost 91% agree that acne had an impact on the profile picture, over a third (35.8%) think that acne has an impact on likes/matching and almost 70% an impact on meeting the date in real life. Among those that are not on a dating website, 50% agree that acne had an impact on their subscriptions to the dating websites, out of which 45% confirm it was due to the severity of the acne. However, we found no link between CADi score and being on SoMe or on dating websites.

CONCLUSION

The impact of acne on self- image is well-known. We show here that, in the light of the social media era, the need for recognition by the others through selfies, stories, likes, acne has clearly an impact on young women. The impact is highlighted by the way that women with acne show themselves on SoMe. As they are self-aware of their image, a large majority avoid taking any selfie, or tend to modify their images through filters. Although women are less present on the dating websites than men, women with acne have an increased pressure, both when it comes to present themselves on the dating website but also when it comes to meeting their date in real life. These findings highlight the need to raise awareness and to provide an appropriate support for adult women with acne, to promote a greater self-acceptance and an improved quality of life.

Has a profile on a dating website		
yes	120	7.4%
no	1506	92.6%
Acne has an impact on the profile picture?		
Does not agree at all	5	4.2%
Does not agree	1	0.8%
Neutral	5	4.2%
Agree + Totally agree	109	90.8%
Acne has an impact on matching/likes?		
Does not agree at all	13	10.8%
Does not agree	15	12.5%
Neutral	49	40.8%
Agree + Totally agree	43	35.8%
Acne has an impact on a meeting IRL		
Does not agree at all	4	3.3%
Does not agree	11	9.2%
Neutral	23	19.2%
Agree + Totally agree	82	68.3%
If not on any dating websites: Acne ...		
... has an impact on the decision-making		
Does not agree at all	348	23.1%
Does not agree	140	9.3%
Neutral	269	17.9%
Agree + Totally agree	747	49.7%
... severity has an impact on the decision-making		
Does not agree at all	369	24.5%
Does not agree	172	11.3%
Neutral	283	18.8%
Agree + Totally agree	680	45.2%

Table 2: Impact of acne on dating website

References: [1] Richard MA, Paul C, Nijsten T, Gisondi P, Salavastru C, Taieb C, Trakatelli M, Puig L, Stratigos A; EADV burden of skin diseases project team. Prevalence of most common skin diseases in Europe: a population-based study. *J Eur Acad Dermatol Venereol.* 2022 Jul;36(7):1088-1096 | [2] Cribrier B, Aroman MS, Merhand S, Aubert R, Audouze A, Legrand C, Carre M, Raynal H, Baissac C, Taieb C, Richard MA. Prevalence of visible skin diseases: An international study of 13,138 people. *J Eur Acad Dermatol Venereol.* 2023 Feb;37(2):e180-e182

Assessing tolerance, efficacy, and quality of life improvements of a skincare regimen in a multicenter study in Germany, France, Spain, Middle East, Africa and Latin America

Real-world-evidence on acne-prone skin with post-acne marks

Gallinger J¹, Vendruscolo CW², Perez Damonte S³, De La Cruz C⁴, Orbegón J⁵, Alas Carbajal R⁶, Scarano S³, Piegari Feliu A³, Dominguez M³, Vagnoni MV³, Tosi V³, Lofrano C⁷, Cuesta N⁸, de Lucas R⁹, Fernandez Quiroga C¹⁰, Raventos XC¹¹, Mateu AV¹², Bedran J¹³, Ballanger F¹⁴, Bernez A¹⁵, Safar R¹⁵, Casse V¹⁶, Rodot-van-Elslande S¹⁷, Piehl J¹, Gemayel N¹⁸, Sammain A¹

¹Beiersdorf AG, Global Medical Management, Hamburg, Germany · ²Beiersdorf AG, Scientific Affairs Manager Latam, Sao Paulo, Brazil ·

³Claim, Safety And Efficacy Clinical Trials, Buenos Aires, Argentina · ⁴Dermacross Dermatology Clinic, Dermatology, Santiago, Chile ·

⁵Dermatology And Esthetic Clinic, Dermatology, Lima, Peru · ⁶Idca, Dermatología Managua, Hospital Vivian Pellas, Dermatología, Managua, Nicaragua · ⁷Beiersdorf AG, Medical Management, Buenos Aires, Argentina · ⁸Beiersdorf AG, Medical Management Spain, Madrid, Spain ·

⁹Hospital Universitario La Paz, Madrid, Spain · ¹⁰Hospital sant Joan d'Espí Moises Broggi, Barcelona, Spain · ¹¹Hospital de Mollet, Barcelona, Spain ·

¹²Clinica privada, Barcelona, Spain · ¹³Beiersdorf SAS, Paris, France · ¹⁴Talence, France · ¹⁵Saint Cyr sur Loire, France · ¹⁶Toulouges, France ·

¹⁷Nice, France · ¹⁸Beiersdorf Middle East FZCO, Dubai Media City, UAE

INTRODUCTION AND OBJECTIVES

Acne is a highly prevalent skin condition that affects people globally and is a primary contributor to post-inflammatory hyperpigmentation (PIH) and erythema (PIE). These Acne sequelae, also known as "post-acne marks" can negatively impact the quality of life (QoL) and result in significant psychological distress. While options for treating PIH are limited, Thiazolyl Resorcinol (Thiamidol) has recently emerged as a highly effective inhibitor of human tyrosinase that can significantly reduce PIH.

The aim of this research was to investigate the effectiveness of a skincare regimen in reducing blemishes, post-acne marks, and enhancing the quality of life (QoL). The skincare regimen included 1) a cleanser, 2) a hydrogel formulation containing Thiamidol, Salicylic acid, and anti-inflammatory Licochalcone A, and 3) a daycare with UV-filters.

MATERIALS AND METHODS

A 12-week, uncontrolled, multicenter study was conducted. Patients with mild to moderate acne, PIH and PIE, and impaired QoL (Cardiff Acne Disability Index [CADI] score ≥ 3) applied the formulation twice daily and the daycare in the morning. The investigators assessed Acne, PIH and PIE on a 5-point IGA-scale (Investigators Global Assessment), counted lesions and rated the process of discoloration using a new PIH-scale based on the extended Fitzpatrick skin types at baseline, and after 4, 8 and 12 weeks. Patients assessed the efficacy and tolerability of the product and the improvement of CADI and additional QoL questions as well as an overall happiness score.

RESULTS

658 patients from 15 countries (mean age 25.5 y, 80% women, 20% men, Fitzpatrick skin types: FST I 3.7%, FST II 28.8%, FST III 42.8%, FST IV 21.1%, FST V 2.9%, FST VI 0.8%) finished the study; examples shown in fig 1. 59% of the patients did not receive any medical therapy, 41% were stable on maintenance treatment for at least 1 month.

Clinical grading confirmed a significant reduction of IGA for Acne, PIH, PIE (fig. 2) and lesion count (fig. 3). Skin evenness, measured with the newly developed tool "PIH-Scale" (fig. 4) significantly improved. Subject-

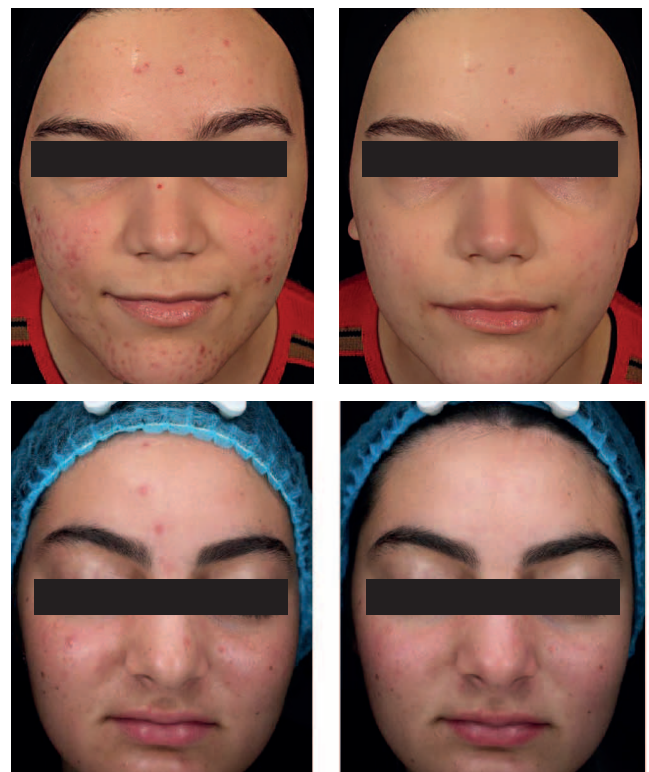


Fig 1: Pictures of exemplary patients at baseline and after 12 weeks of regular use of cleanser, hydrogel formulation and daycare.

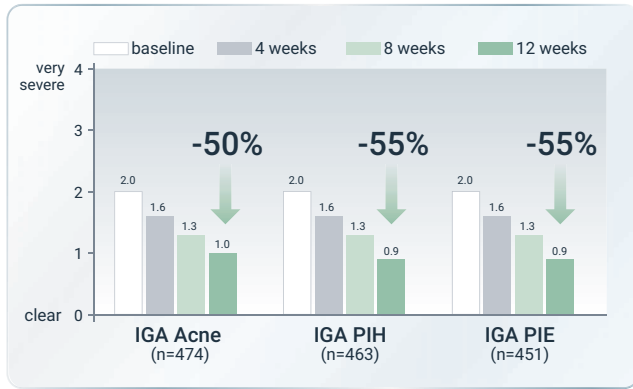


Fig 2: Investigators global assessment (IGA) of Acne, PIH and PIE conducted by dermatologists on a 5-point scale. IGA Acne, PIH and PIE continuously reduced significantly during the course of the study.

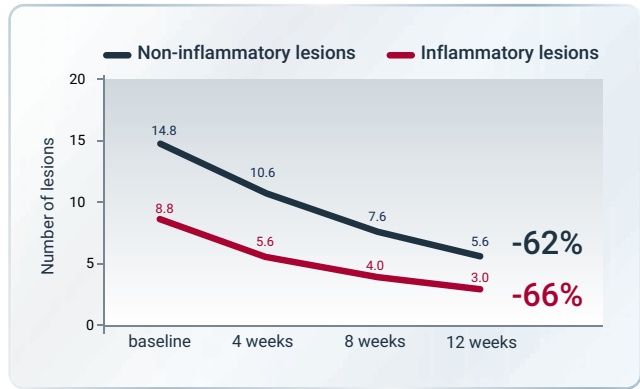


Fig 3: Lesion count conducted by dermatologists. Inflammatory lesions (IL) and non-inflammatory lesions (NIL) reduced significantly during the course of the study.

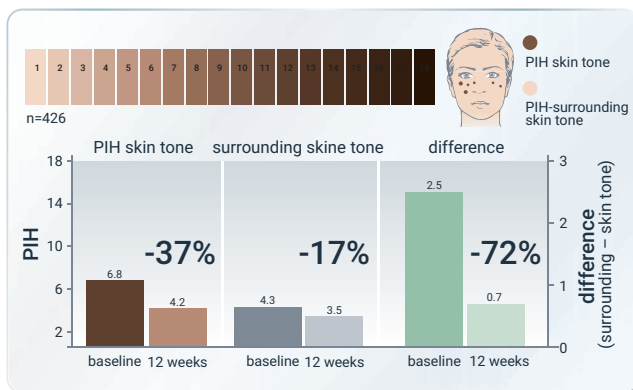


Fig 4: Process of discoloration measured using a new PIH-scale based on the extended Fitzpatrick skin types (18 nuances). The discoloration of one pronounced post-acne mark (acne-related PIH) was assessed at each time point compared to the skin tone surrounding the mark. The discoloration of the post acne mark was significantly reduced, while the surrounding skin reduced color intensity on a much lesser extent, resulting in a strong increase of skin evenness (+72%).

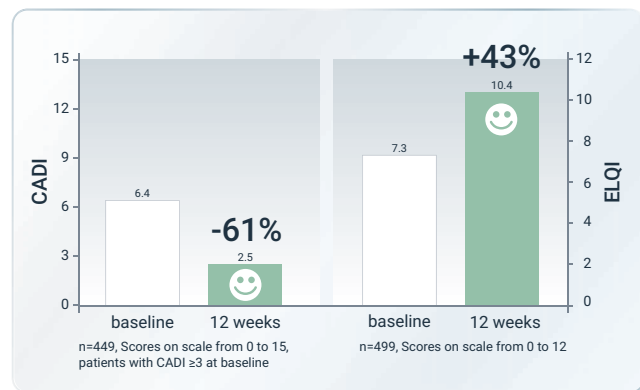


Fig 5: [A] CADI (Cardiff Acne Disability Index) and [B] ELQI (Eucerin Life Quality Index) as measurement of improvement of Quality of Life in Acne patients. CADI scores significantly decreased, and ELQI scores significantly increased during the study, proving strong increase of Quality of Life.

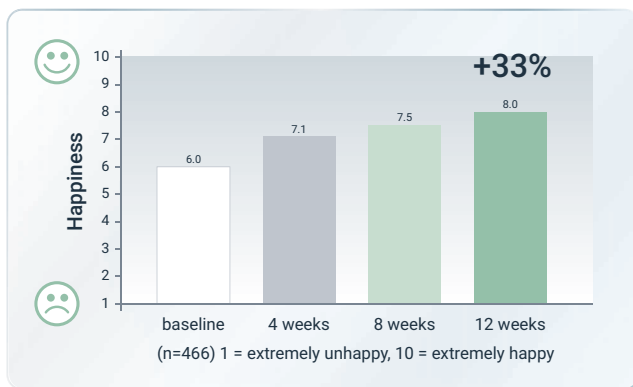


Fig 6: The overall happiness of the subjects was assessed using 10-step scale. Happiness continuously increased significantly during the course of the study.

tive evaluation confirmed the efficacy against post-acne marks and blemishes (e.g.: 84.7% confirmed: "Improved my skin like nothing before"; n=405). The CADI Score (fig. 5A), the ELQI score (fig. 5B) as well as overall happiness (fig. 6) improved significantly during the study: 71% of patients were more happy after 12 weeks compared to beginning of the study with an average increase of 33% of overall happiness. 99% of dermatologists would recommend the products to their patients following the study (n=574).

DISCUSSION

The results show that the Thiamidol, Salicylic Acid and Licochalocone A containing skincare regimen significantly reduces both blemishes and post-acne marks, providing physical and emotional relief, ultimately improving patients' quality of life and overall happiness in real-life conditions.

From occasional to daily: Ultra-light texture to start a daily sun protection routine

Worthmann A¹, Pitta P², Vendruscolo C², Buerger A¹, Dorsch S¹, Dippe R¹, Drescher P¹, Warnke K¹
¹Beiersdorf AG, Hamburg, Germany, ²Beiersdorf AG, Sao Paulo, Brazil

INTRODUCTION AND OBJECTIVES

Consistent sun protection is crucial for preventing skin damage from UV radiation, blue light, and environmental pollutants. However, adherence to sun protection routines is often hindered by heavy, greasy textures. A product offering high protection from UV and Blue Light with a lightweight, moisturizing formula could significantly improve user adherence and satisfaction.

In this study we determine an everyday sun protection product that provides extensive protection with an ultra-light texture, featuring Licochalcone A and a moisture complex. The product offers UVB/UVA protection and blue light defense, anti-oxidant efficacy, increased moisture, and a pleasant sensory experience.

MATERIALS AND METHODS

Sensory study: A two-week product-in-use test was conducted with 162 volunteers (18-40 years old). Moisture levels were measured on 35 female volunteers' inner forearms using a corneometer 2 hours after a single application.

Anti-oxidative measurement: An ex vivo method evaluated antioxidant efficacy using skin fragments from elective plastic surgery of a 35-year-old male participant. Skin fragments were treated with the investigational product (2mg/cm²) for four days and exposed to daily UV (10J/cm²), infrared IR (360J/cm²), and visible light VIS (100J/cm²) radiation. Culture medium was replaced daily, and irradiation occurred for three consecutive days. Oxidative species were detected using DCFH-DA fluorogenic dye.

A similar protocol was followed using cigarette smoke to simulate pollution, with fragments exposed to two cigarettes' total burning. Negative control was DMEM High Glucose.

RESULTS

The product demonstrated excellent galenic properties with 0% residue, stickiness, and greasiness. 89% of participants confirmed immediate moisture provision, and 100% found the product easy to spread. Reapplication was favored by 90% of users.

The product presented a very high UVA and UVB protection and exhibited significant antioxidative and anti-pollution action, reducing oxidative species formation by 27% under UV, IR, and visible light exposure (fig.1), and by 29% when exposed to cigarette smoke (fig.2). Moisture levels increased by 25% (fig.3).

CONCLUSION

The introduced sun protection product represents a promising option for improving adherence to daily sun protection routines, owing to its ultra-light galenic properties and high protection levels. By addressing common barriers such as texture and user experience, this innovative formula encourages consistent use, promoting healthier skin and better protection against environmental stressors.

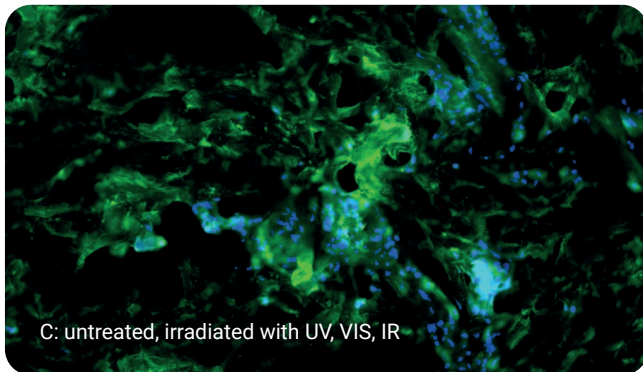
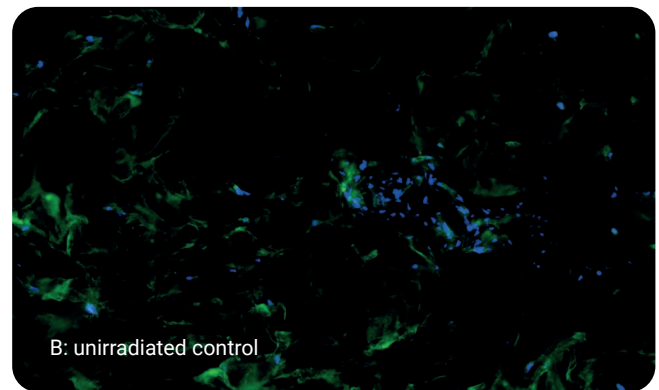
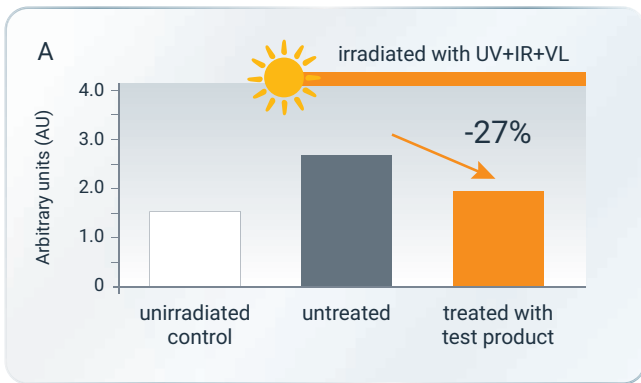


Figure 1: Oxidative species formation after UV, VIS and IR irradiation. A: Semi-Quantification of the formation of Oxidative Species. B, C, D: Semi-quantification by imaging the fluorescence emitted by labeling the oxidative species with DCFH-DA. B: unirradiated control; C: UV, VIS, IR; D: UV, VIS, IR + product. All images were obtained at 20x magnification.



Figure 2: Semi-Quantification of Oxidative Species formation after cigarette smoke exposure. DCFH-DA staining.

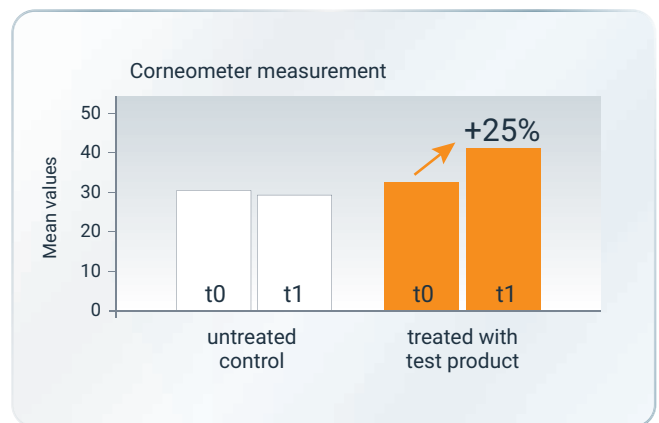


Figure 3: Corneometry measurement: blind, results vs untreated 2h after single application on the inner forearm on 35 female volunteers (18-65 years).

“Intelligent” combination of skin identical moisturizers and lipids in emollients boosts moisturization and barrier repair in patients with Xerosis cutis

Schuster B, Griffiths D, Schoelermann AM | Beiersdorf AG, Hamburg, Germany

INTRODUCTION AND OBJECTIVES

Xerosis cutis is characterized by decreased stratum corneum (SC) hydration and impaired skin barrier function. According to modern corneotherapy, preparations with skin identical moisturizers and lipids can restore the impaired intracellular lipid bilayer and substitute the lack of natural moisturizing factors (NMFs) observed in Xerosis. Urea, a potent natural NMF, is considered gold standard in the treatment of Xerosis cutis.

In the following we summarize findings of three studies (*in vivo* and *ex vivo*) to explore if the application of “intelligently” formulated, biomimetic emollients have advantages compared to standard moisturizers in terms of moisturization, depth of moisturization and skin’s own repair processes.

MATERIALS AND METHODS

“Intelligently” formulated, biomimetic emollients containing 10% urea plus further skin identical NMFs as well as ceramides were tested in three studies:

1. Double-blind, vehicle-controlled clinical study (n=44, very dry skin). Application of biomimetic emollient and two vehicles (vehicle and vehicle “plus” with added urea and lactate) twice daily to inner forearms for 2 weeks. Skin hydration levels were measured using Corneometer CM 825, transepidermal water loss (TEWL) was measured using Tewameter 300.
2. Randomized, controlled study (n=26, normal skin). Application of the biomimetic emollient and two vehicles (vehicle and vehicle “plus” with 10% urea added) twice daily to inner forearms for 2 weeks. Deep SC hydration was measured using KOSIM IR, a method which combines near infrared spectroscopy and confocal microscopy for selective, depth resolved determination of water in different areas (Fig. 1). This enables the depth resolved determination of water content *in vivo*.
3. Double-blind, vehicle-controlled clinical study (n=22, very dry skin). Application of the biomimetic emollient and vehicle twice daily to inner forearms for 2 weeks. Suction blister samples were obtained for gene expression analysis using RT-PCR.

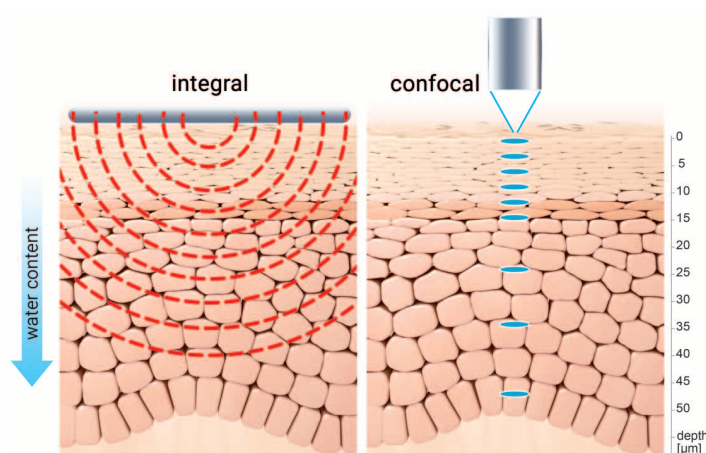


Figure 1: KOSIM IR combines near infrared spectroscopy and cofocal microscopy for depth resolved determination of water content

RESULTS

1. Corneometry showed a significant improvement in skin hydration in all groups after 2 weeks compared to baseline, with the biomimetic emollient showing superior efficacy compared to vehicle and vehicle plus ($p < 0.05$, Fig. 2). Furthermore, TEWL was significantly reduced after 2 weeks of treatment with biomimetic emollient and vehicle plus ($p < 0.05$), but not with vehicle alone.

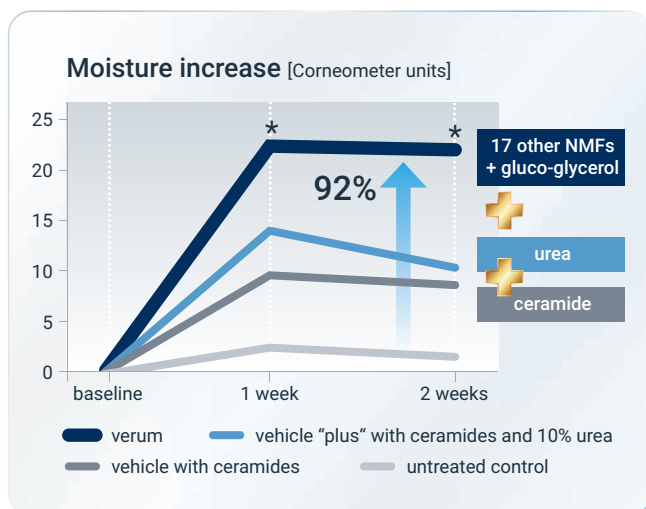


Figure 2: Improvement of moisture content after application of emollients with and without ceramides, urea, further NMFs and gluco-glycerol. *significant improvement compared to control and vehicle.

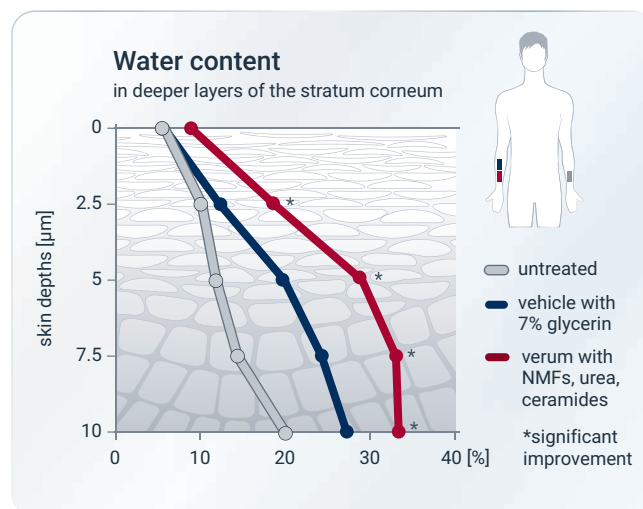


Figure 3: Water content in deeper layers of the stratum corneum, measured by KOSIM IR. *significant improvement

CONCLUSION

2. KOSIM IR showed a significantly higher water content in the SC up to a depth of 10 µm in treated compared to untreated skin ($p < 0.05$). Water content was significantly higher in areas treated with the biomimetic emollient and vehicle plus compared to vehicle ($p < 0.05$), with the highest water content observed for areas treated with the biomimetic emollient (Fig. 3).

3. Relative gene expression data of suction blister roofs showed a significant upregulation of markers of barrier function (FLG, FLG2, IVL, TGM1, Krt10, KLK7, CASP14, CDSN, OCLN, CLDN1, KLK5, LOR), skin hydration (AQP3, AQP9, ELOVL4) and skin lipid metabolism (SMPD1, FADS1, HMGCR) compared to vehicle (all $p < 0.05$, Fig. 4).

The results show that the efficacy of moisturizers containing urea can be further enhanced when combined with further skin identical NMFs and lipids. More precisely, this combination showed superior moisturization of the skin *in vivo*, also in deeper layers of the SC. Furthermore, the analysis of gene expression data suggests that treating the skin with intelligently formulated emollients could support skin's own barrier repair processes, going beyond passive skin hydration and barrier stabilization.

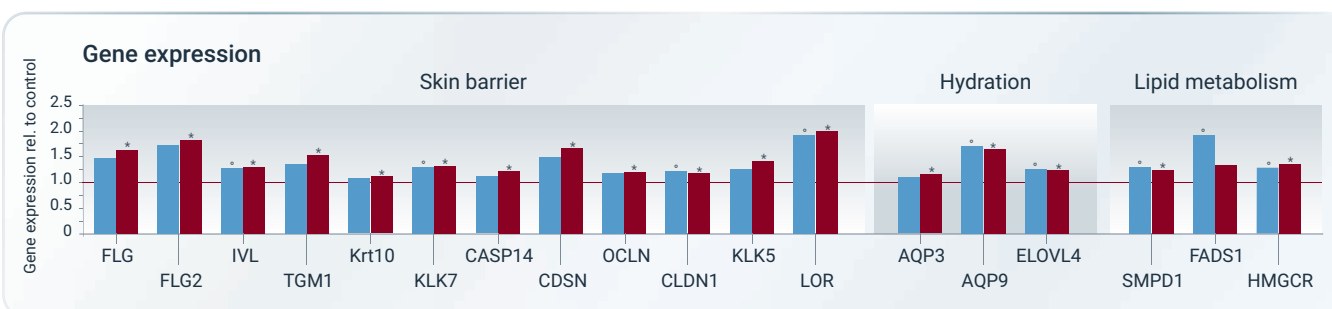


Figure 4: Relative Gene expression data of suction blister samples obtained from 22 female volunteers. Level of significance $*p < 0.05$ (Wilcoxon signed-rank test). ■ verum relative to untreated control, ■ verum relative to vehicle. Verum significantly different to untreated (*) and vehicle (*)

Clinically normal appearing skin in remission displays unique features before atopic dermatitis relapse

Al B^{1,2}, Holzschek N¹, Traidl S², Freimooser S², Mießner H¹, Dittrich-Breiholz O³, Reuter JH¹, Werfel T^{2*}, Seidel J^{1*}

¹Discovery, R&D, Beiersdorf AG, Hamburg, Germany; ²Division of Immunodermatology and Allergy Research, Department of Dermatology and Allergy, Hannover Medical School, Hannover, Germany; ³Central Core Unit Genomics (RCUG), Hannover Medical School, Hannover, Germany. | *These authors contributed equally.

INTRODUCTION AND OBJECTIVES

Atopic dermatitis (AD) is a recurring skin disease marked by lesions at specific body sites. The active lesional state has been well-researched in the past and is characterized by an immune response driven by the TH2/22 axis. However, little is known about the immune state in skin between lesions and what factors trigger new relapses in AD.

We therefore aimed at understanding the pathophysiology of AD relapses and specifically at assessing the role of the immune system before new lesional outbreaks.

STUDY DESIGN

We collected 5 mm skin biopsies and blood samples from healthy (H; n=6), from lesional (L; n=4) and from ex-lesional (ExL; n=24; only 22 included in analysis) patients. To avoid measuring strong therapeutic effects, ExL patients were biopsied 1–2 weeks after cessation of topical treatment or 3–6 weeks after cessation of UV therapy and their relapse at the biopsied and other sites was documented in a daily diary for the following 2 months (fig. 1).

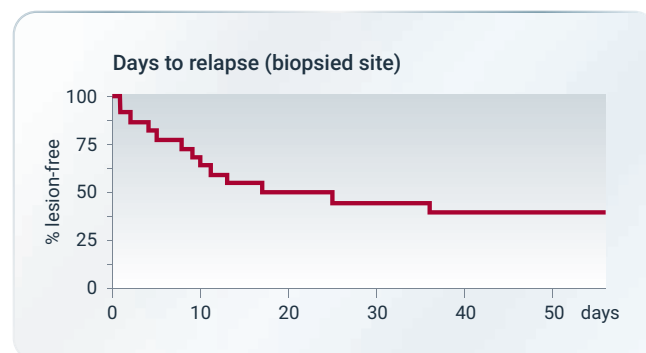
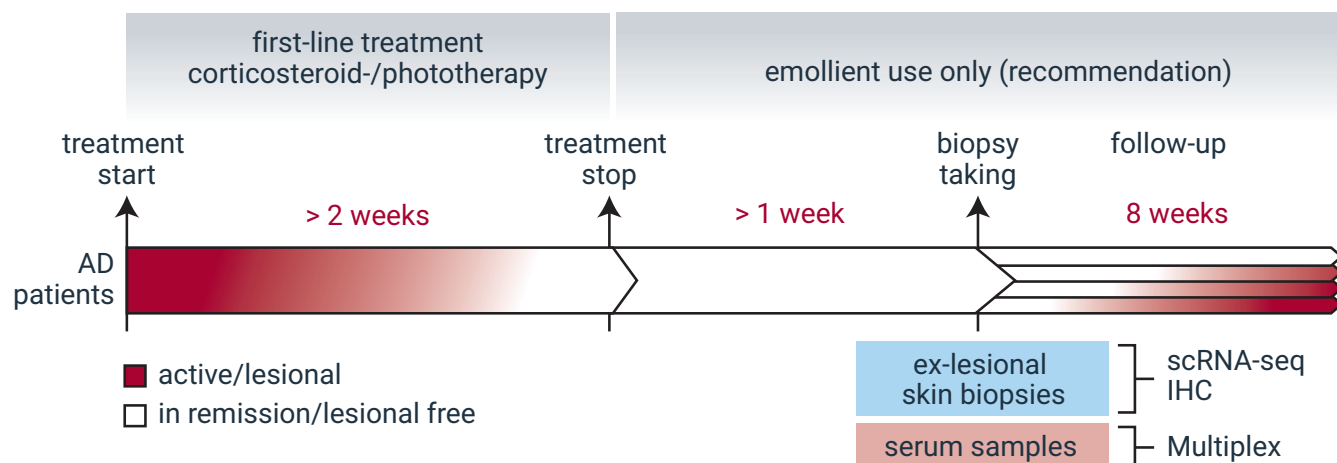


Fig. 2: Days to relapse (biopsied site)

Of these patients, 13 experienced relapses at the biopsied site and 9 did not within the observed time frame (fig. 2). We refer to the relapsing patients or the pre-relapse state as R and the non-relapsing as NR in the following.

One half of the skin biopsies was used for single cell sequencing (scRNA-seq) using the Chromium Controller (10X Genomics) and the NovaSeq 6000 Sequencing System (Illumina) and data were processed using the Cell Ranger pipeline and analyzed in R using Seurat v4. The other biopsy half was used for immunohistochemistry stainings. Blood samples were analyzed using the Bio-Plex Pro™ Human Chemokine Panel, 40-Plex (Bio-Rad).

Fig. 1: Study design



RESULTS

The local lymphoid response before relapses:

CD3+ T cell levels were significantly elevated in R using immunohistochemistry (fig. 3). In the scRNA-seq data, the lymphoid cluster contained 7 subcluster, with the T helper cell cluster Tef1 constituting 48.53% of all lymphoid cells (fig. 4). The TH2 cytokine IL-13 was significantly upregulated in R using scRNA-seq (fig. 5).

Skin that relapsed within the next days was characterized by T cell infiltration and increased IL-13 production.

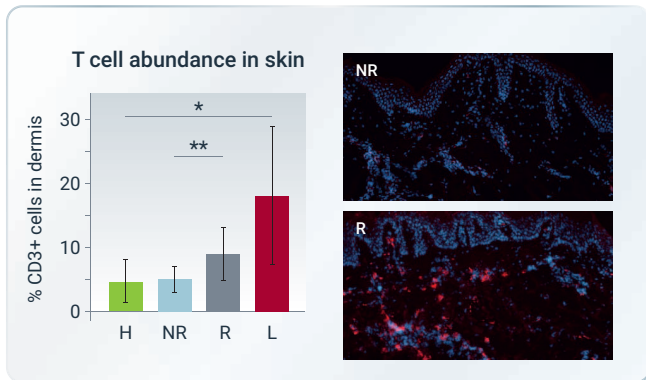


Fig. 3: T cell abundance in skin

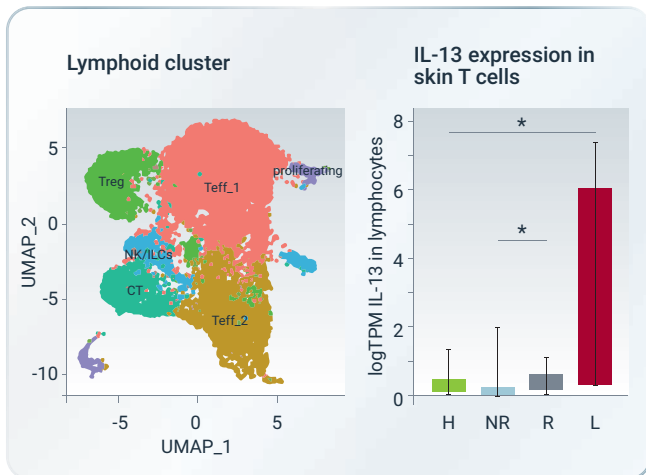


Fig. 4: Lymphoid cluster (left); Fig. 5: IL-13 expression in skin T cells (right)

Antigen presenting cells in the pre-relapse state:

Neither CD68+ macrophages nor CD11+ dendritic cells (DCs) were significantly upregulated in R using immunohistochemistry (fig. 6). In the scRNA-seq data, the antigen presenting cell (APC) cluster comprised 7 different cell clusters, with Mac_1 and moDCs constituting most cells (fig. 7). Phagocytosis marker (MRC1, CD163, MARCO, LAMP1) and immune cell attracting enzymes (CCL18, CCL13, CCL14, CCL2) were significantly upregulated in R compared to NR using scRNA-seq (fig. 8, 9).

Skin macrophages in the pre-relapse state showed higher expression of phagocytosis and immune cell attraction genes.

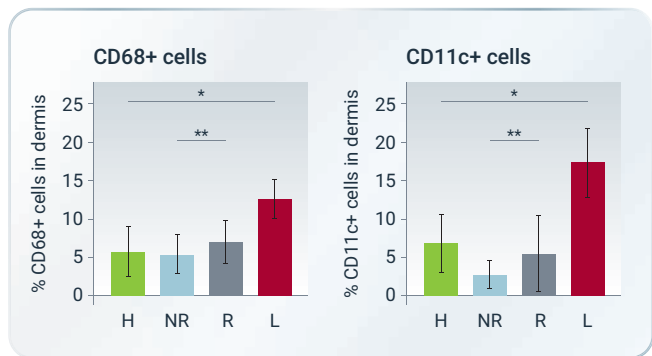


Fig. 6: Macrophage and DC abundance in skin

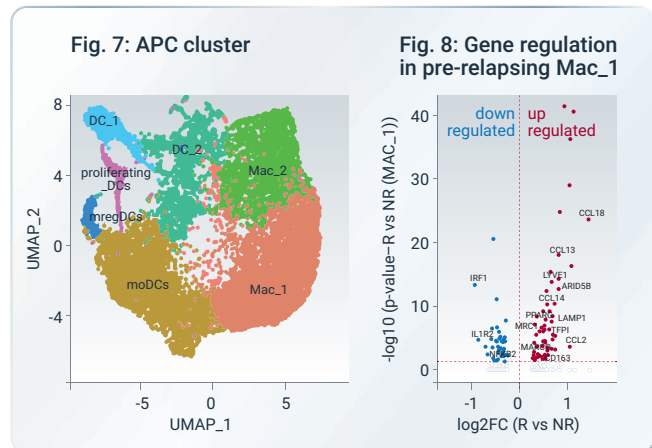


Fig. 7: APC cluster (left); Fig. 8: Gene regulation in pre-relapsing Mac_1 (right)

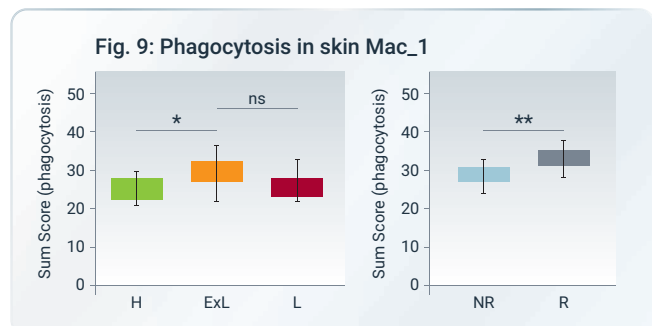


Fig. 9: Phagocytosis in skin Mac_1

The role of the systemic immune signal in AD relapses:

18 out of 22 patients experienced relapses at any body site one week after biopsy taking (fig. 10). Out of 40 tested proteins the TH2 associated cytokines IL-4 and CCL27 showed the most pronounced differences between patients in blood sera that relapsed in the first week after sample taking compared to those who relapsed later (fig. 11, 12).

An increased systemic TH2 response preceded new AD relapses.

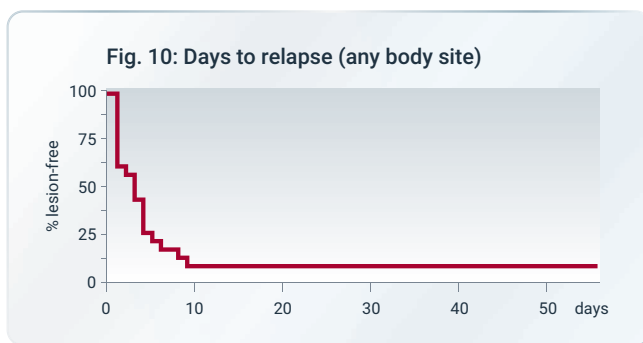


Fig. 10: Days to relapse (any body site)

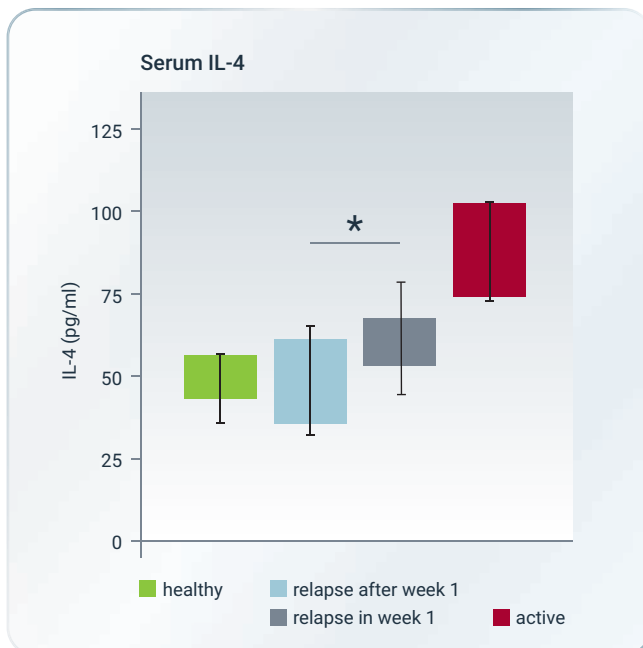


Fig. 11: Serum IL-4



Fig. 12: Serum CCL27

CONCLUSION

Our first findings indicated that skin before new AD relapses is already characterized by an infiltration of T cells. Additionally, a weakly upregulated type 2 immune response was detected both locally in the skin and systemically in the blood before new relapses occurred. Interestingly, we also found that pre-relapsing skin displays relapse-specific features such as elevated macrophage phagocytosis.



Eucerin[®] SKIN RESEARCH

FOR MORE THAN 100 YEARS Eucerin[®] HAS BEEN PIONEERING
MEDICAL SKIN SCIENCE AND INNOVATION.

Skin is much more than our body's protective shield – it is alive; it reflects and affects how we feel inside. When our skin is healthy and radiant we feel comfortable and at one with ourselves.

That is why we at Eucerin[®] dedicate all our passion and expertise to your demanding and sensitive skin. We develop clinically proven dermo-cosmetic solutions to protect, repair and sustain the health and beauty of your skin, giving you the feeling of confidence and well-being.

For more than 100 years we have been pioneering medical skin science and innovation. Today, Eucerin[®] is trusted and recommended by dermatologists and pharmacists all over the world.

Eucerin[®] LIFE-CHANGING POWER OF DERMATOLOGICAL SKINCARE