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PEER-REVIEWED CONFERENCE REPORT

Roflumilast for Seborrheic Dermatitis

Roflumilast foam is safe and effective for seborrheic dermatitis: >80% of phase 3 study participants achieved clear or almost clear skin at week 8, with improvements in erythema and scaling.

read more on PAGE 6

Topical Gel Plus Finasteride Benefits Androgenetic Alopecia

In a trial including 58 androgenetic alopecia patients, a weekly-applied, growth factor-containing topical gel together with topical minoxidil and oral finasteride significantly improved outcomes.

read more on PAGE 8

Secukinumab As Next Biologic Treatment for HS?

Blocking IL-17A with secukinumab granted >40% of patients with hidradenitis suppurativa a reduction in flares, pain, and abscesses, as shown by the SUNSHINE and SUNRISE trials.

read more on PAGE 17

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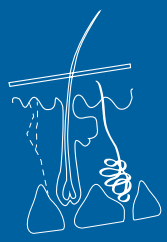

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Contents

Letter from the Editor

Dear colleagues,

The annual meeting of the EADV 2022 congress was again a live and lively event, full of discovery and innovation. After the many web-conferences, the live meeting was well appreciated by thousands of European dermatologists. It was worthwhile to meet live with colleagues and to have continuing medical education with the human touch instead of the click of the mouse.

In psoriasis, systemics (the biologic bimekizumab and the small molecule deucravacitinib) and the new topicals (PDE-4 inhibitors and tapinarof) were the innovations. In atopic dermatitis, the biologics (IL-13 inhibitors and IL-22 inhibitors) and a wide range of Janus kinase inhibitors provide unprecedented introduction of new treatments.

Both in psoriasis and atopic dermatitis, there is a need to develop strategies which we collectively designated as personalised medicine. This implies the development of biomarkers.

At this EADV, the biologics and non-biologic systemics are also developed for different fields in dermatology, where innovations were more seldom: hydradenitis chronica suppurativa, vitiligo, and alopecia areata.

Also sun protection, skin cancer, and pruritus were in the spotlight as common concerns.

The present report aims to give an overview of innovations as presented at EADV 2022.

Best regards,

Peter CM van de Kerkhof

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Biography

Peter C.M. van de Kerkhof is emeritus Professor of Dermatology and immediate past chairman of the Department of Dermatology of Radboud University Nijmegen. He is currently the coordinating Medical Officer of the International Psoriasis Council and chair of the scientific advisory board of the Dutch burn association. He has been working for many years on the pathogenesis and treatment of psoriasis. He has published more than 700 publications in peer-reviewed journals and has given many presentations on invitation at international conferences. He has served as president of the ESDR, EDF, and the International Psoriasis Council, and was board member of various international societies. Current interests are pathogenesis and development of biomarkers for psoriasis; real clinical practice research; and personalised medicine.

Conflict of Interest Statement:
Consultancy services for: Celgene, Almirall, Amgen, Pfizer, Philips, AbbVie, Eli Lilly, Galderma, Novartis, Janssen Biotech, Janssen-Cilag, LEO Pharma, Sandoz, Mitsubishi Tanabe, Bristol Meyer Squibb, UCB, Dermavant.
Speaker services for: Celgene, Almirall, Eli Lilly, Novartis, Jansen-Cilag, LEO Pharma, Sandoz, Bristol Meyer Squibb.

News in Atopic and Seborrheic Dermatitis

Baricitinib possible therapeutic option for children with AD

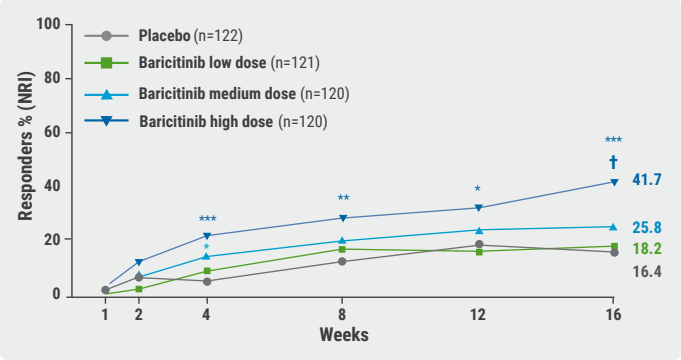
Baricitinib led to clear or almost clear skin in over 40% of participants in the BREEZE-AD-PEDS trial. Children and adolescents with atopic dermatitis (AD) were treated at different dosages of the JAK inhibitor and the high-dose group met the primary endpoint at week 16.

Baricitinib, a JAK inhibitor, has been approved in several countries for the treatment of AD in adult patients and its efficacy has been proven in different studies. "Therefore, it is mandatory to know if this drug is also effective in children and adolescents," stated Dr Antonio Torrelo Fernández (Hospital Infantil Universitario Niño Jesús, Spain) [1]. The phase 3, randomised, placebo-controlled BREEZE-AD-PEDS trial (NCT03952559) randomised 483 patients aged 2 to 18 years to receive baricitinib either at a low, medium, or high dose, or placebo. Dose regimens were adjusted for participants aged <10 years or 10 to 18 years, with daily 0.5 mg/1 mg, 1 mg/2 mg, or 2 mg/4 mg baricitinib. A validated Investigator's Global Assessment (vIGA) score of clear or almost clear skin (0/1) with at least 2 points improvement from baseline marked the primary endpoint at week 16. To be included, patients needed to have moderate-to-severe AD with a history of inadequate response or intolerance of topical treatment plus a disease duration of at least 6 or 12 months, depending on age.

Dr Torrelo Fernández underlined that the 4 study arms were similar in age, gender, race, and geographical region. The mean age was around 12 years and the mean duration of AD was at least 9 years. Participants with vIGA 4 made up between 37.5% and 39.3% of the participants, all other participants had vIGA 3.

In the high-dose baricitinib group, 41.7% reached the primary endpoint at week 16, significantly more than the placebo group (16.4%; P<0.001; see Figure). For the secondary endpoints Eczema Area and Severity Index (EASI)-75 and EASI-90, significant difference was similarly present in the high-dose arm, with 52.6% and 30% responders, respectively (P<0.01). Dr Torrelo Fernández further highlighted that 35.5% of the patients on 2 mg/4 mg of baricitinib had a ≥4-point reduction in the itch numeric rating scale (P<0.05). Dr Torrelo Fernández stated that the vIGA results were consistent in subgroups according to age <10 or ≥10 years and across 3 different weight groups. Of note, there was a very high study adherence with 96.7% of participants completing week 16.

Figure: Percentage responders with vIGA-AD(0/1) with ≥2 points improvement [1]



*, P<0.05; **, P<0.01; ***, P<0.001; †, statistically significant with multiplicity adjustment; NRI, non-responder imputation.

Any treatment-emergent adverse event occurred in 50% of the low-dose and placebo arm, 52.5% in the medium-dose arm, and 50.8% in the high-dose arm. "The severity was low, mild, or moderate in most of the cases and severe adverse events were reported very seldomly," Dr Torrelo Fernández stated. The most common were headache, acne, abdominal pain, and nasopharyngitis. "But you can see again that these adverse events were similarly seen in all 4 groups," Dr Torrelo Fernández stressed.

In summary, baricitinib was assessed as a potential therapeutic option with a favourable benefit-risk profile for children and adolescents between 2 and 18 years, who have moderate-to-severe AD and who are candidates for systemic therapy.

1. Torello Fernández A. Efficacy and safety of baricitinib in a phase 3, randomised, double-blind, placebo-controlled study in paediatric patients with moderate-to-severe atopic dermatitis. D3T01.1E, EADV Congress 2022, Milan, Italy, 7–10 September.

Amlitelimab therapy leads to sustained decrease of IL-22 in AD patients

Amlitelimab treatment significantly decreased serum levels of interleukin (IL)-22, which essentially affects the immune dysregulation in atopic dermatitis (AD), well

after the last application. Hence, this may explain its efficacy in a previously presented randomised, placebo-controlled, phase 2a trial in patients with moderate-to-severe AD.

Amlitelimab is a fully human, non-depleting, non-cytotoxic, anti-OX40 ligand, monoclonal antibody, that inhibits the engagement of OX40 ligand in antigen-presenting cells and blocks both T helper 2 and T helper 1/17/22 cells, which are central to the inflammation and pathological outcomes in AD. Dr Stephan Weidinger (University Hospital Schleswig-Holstein, Germany) and his team evaluated the effects of amlitelimab on IL-22, an important T helper 22 cell-associated disease mediator of AD [1]. Presented was an exploratory serum analysis from patients with moderate-to-severe AD, participating to a double-blind, placebo-controlled, multicentre, phase 2a trial, whose results were presented at a previous meeting [2].

The trial recruited 78 patients, randomised 1:1:1 to intravenous amlitelimab low dose (200 mg/100 mg maintenance every 4 weeks; n=27), high dose (500 mg/250 mg; n=27), or placebo until week 12. Percentage change in Eczema Area and Severity Index (EASI) from baseline to week 16 was the primary efficacy endpoint. In this trial, amlitelimab was well tolerated, with an unremarkable safety profile. The mean percentage change in EASI at week 16 from baseline was -80.12% for low dose amlitelimab (P=0.009) and -69.97% for high dose amlitelimab (P=0.072) versus -49.37% for placebo. Moreover, responders had sustained clinical responses up to week 36.

Serum was collected at baseline, week 4, and week 16, and in the case of responders also at week 24 and week 36. Ultra-sensitive single-molecule immune assay (Simoa) ascertained the IL-22 level.

No difference was detected in the levels of IL-22 between the groups at baseline. Yet, the IL-22 level correlated with disease severity at baseline as measured by EASI (r=0.53; P<0.0001) and Scoring of atopic dermatitis (SCORAD) (r=0.36; P=0.001). Furthermore, a significant reduction in IL-22 levels was observed at week 16 in participants treated with amlitelimab (low-dose P<0.0001; high-dose P=0.001) but not in the placebo group (P=0.381). The amlitelimab-induced decrease in IL-22 levels remained consistent until week 36 in responders, so the strong reduction of IL-22 extended beyond the last application of amlitelimab.

"To conclude, in this phase 2a study, amlitelimab treatment not only induced significant improvements in patients with AD but also significantly reduced serum levels of IL-22, which is an important disease mediator. In good responders, this reduction of IL-22 was maintained up to week 36, so 24 weeks after the last application," Prof. Weidinger concluded. A phase 2b study is now enrolling participants.

1. Weidinger S, et al. Treatment with amlitelimab - a novel non-depleting, non-cytotoxic anti-OX40Ligand monoclonal antibody - reduces IL-22 serum levels in a Phase 2a randomised, placebo-controlled trial in patients with moderate-to-severe atopic dermatitis. Abstract No 743, EADV Congress 2022, Milan, Italy, 7–10 September.
2. Weidinger S, et al. Abstract 203, RAD 2022 Virtual, 9-11 April.

IL-13 inhibition with lebrikizumab shows high maintenance rates in AD

Up to 80.6% of the ADvocate 1 and 2 trial responders on lebrikizumab maintained clear or almost clear skin in the extension phase from weeks 16 to 52. Interestingly, dosing regimens of every 2 (Q2W) and every 4 weeks (Q4W) did not differ greatly in efficacy.

"Lebrikizumab is a specific IL-13 blocker, it does not interfere with IL-4, and we know now that IL-13 is a critical cytokine in AD pathogenesis," Prof. Andrew Blauvelt (Oregon Medical Research Center, OR, USA) announced [1]. The phase 3 ADvocate 1 and 2 trials (NCT04146363, NCT04178967) investigated monotherapy with lebrikizumab versus placebo in patients with moderate-to-severe AD. The study investigated patients who responded in the initial 16 weeks and over the course of 52 weeks. Responders were adolescents (≥12 years) and adults (≥18 years), who reached an Eczema Area and Severity Index (EASI)-75 or an Investigator's Global Assessment (IGA) 0/1, which means clear or almost clear skin at week 16 of the trials.

At week 16, 43.1% and 33.2% of study drug participants achieved an IGA 0/1 and 58.8% and 52.1% an EASI-75 improvement in both trials [1,2]. The responders were then re-randomised to 3 different study arms: continue 250 mg of lebrikizumab Q2W, change to Q4W dosing, or placebo Q2W [1]. At baseline, the average age ranged from 33 to 37.5 years, 45.2% to 65.6% of participants were women, and the mean EASI-75 varied between 2.0 and 2.9.

The results of ADvocate 1 and 2 at week 52 showed 75.8% and 64.6% maintaining IGA 0/1 on the Q2W lebrikizumab regimen in comparison with 74.2% and 80.6% in the Q4W arms. Furthermore, a substantial rate of participants in the

placebo arms continued to have IGA 0/1: 46.5% and 49.8%. "If we look now at EASI-75, we see very similar results, the Q2W dosing is very similar to the Q4W dosing and we still have very high responses in the participants randomised to placebo," Prof. Blauvelt elaborated. The same was true for the maintenance of pruritus improvements.

As for safety results from weeks 0-52 in Advocate 1 and 2, treatment-emergent adverse events were mostly mild (31.1% and 27.5%) and moderate (22.8% and 35.9%). "The highlight here is the 8.3% and 8.1% conjunctivitis in these studies, something we would expect with the mechanism of action, but at levels that I think are quite reasonable," Prof. Blauvelt commented. Collectively, the conjunctivitis cluster was 13.5% and 14.7% through week 52, but according to Prof. Blauvelt, the actual rate went down from week 16 to 52.

"The ADvocate studies showed that specific targeting of IL-13 with lebrikizumab either Q2W or Q4W has high maintenance of efficacy and is reasonably tolerated and safe in adolescents and adults with AD," he concluded.

1. Blauvelt A. Efficacy and safety of lebrikizumab in moderate-to-severe atopic Dermatitis: 52-week results of two randomised, double-blinded, placebo-controlled phase 3 trials (ADvocate1 and ADvocate2). 3D, EADV Congress 2022, Milan, Italy, 7–10. September.
2. Silverberg JI, et al. S026, AAD 2022 Annual Meeting, 25–29 March, Boston, MA, USA.

Does 8 weeks of emollients use prevent AD in high-risk infants?

Newborns subject to a 2-month treatment with emollients had a significantly reduced risk to develop atopic dermatitis (AD) at an age of 6 and 12 months. The adherence of the caregivers to apply the emollient was very high in the intervention group.

Eczema affects up to 20% of the paediatric population and the number of diagnoses continues to rise [1]. Of children with eczema, 60% are predisposed to develop 1 or more atopic comorbidities, such as asthma, allergic rhinitis, or food allergies. Therefore, effective preventive strategies are urgently needed. "When we are born, we experience the most violent environmental change that we will ever experience in our life," Prof. Alan Irvine (Trinity College Dublin, Ireland) stated, referring to the environmental difference pre- and post-birth [2]. Positive results of early studies in 2014 encouraged the Irish researchers to set up the single centre, investigator-blinded STOP AD study (NCT03871998) that tested short-term emollient use for its capacity to prevent AD.

The 321, randomised, high-risk infants with a family history of AD were included from birth to 4 days old. The intervention arm of the study immediately started an 8-week course with a ceramide dominant emollient at a dose of about 7 fingertip units applied twice daily. The control-arm infants received standard skin care. During baseline and control visits at 2, 4, and 8 weeks, skin swabs, measuring of transepidermal water loss (TEWL), natural moisturising factor (NMF), and filaggrin testing were performed. The primary endpoint was the cumulative incidence of AD at 12 months. Secondary endpoints included AD presence at 6 months and the development of NMF and TEWL. Results have been published in *Allergy* [3].

The mean infant age at baseline was just under 2 days and over 80% carried the wildtype filaggrin gene. Adherence in the intervention group was high, with around 90% receiving daily emollient application at weeks 2, 4, and 8. "People were very motivated, they knew what they were trying to prevent disease development," Prof. Irvine commented. The use of emollients in the control group was low.

Reductions in AD risk were significant at 6 and 12 months with an RR of 0.524 (P=0.004) and 0.503 (P=0.002), respectively. Looking at cumulative AD at 12 months, Prof. Irvine highlighted that the biggest difference was noticed in the kids that had AD at 6 and at 12 months, while the intervention had already stopped at 8 weeks. Infants with a loss of function mutation in *FLG* were more prone to AD than the control group. "If we look at the intervention group and stratify by filaggrin mutation status, there is no additional risk of getting AD," Prof. Irvine stressed and continued, "so, what we are seeing clearly here is a treatment-genotype-interaction." The researchers concluded that this significantly reduced AD incidence suggests short-term emollient application as a viable therapeutic model for risk reduction of AD in infancy.

In contrast to this finding, 2 large recent trials found no evidence of a protective effect of emollient use in the first year against AD [4,5]. The authors emphasised that the most notable difference between these randomised-controlled trials and the current one was the timing of the intervention. The treatment in STOP AD began within days of birth during a dynamic period of skin maturation, which might explain the positive effect [3].

1. Kowalska-Oledzka E, et al. J Drug Assess 2019;8:126-8.
2. Irvine AD, et al. Early initiation of short-term emollient use for the prevention of atopic dermatitis in high-risk infants – the STOP AD randomised controlled trial. 09, EADV Congress 2022, Milan, Italy, 7–10 September.
3. Chaoimh CN, et al. Allergy. 23 Aug 2022. Doi: 10.1111/all.15491.
4. Chalmers JR, et al. Lancet. 2020;395:962-972.
5. Skjerven HO, et al. Lancet. 2020;395:951-961.

Roflumilast foam led to high response rates in seborrheic dermatitis

Roflumilast foam could offer a safe and effective treatment for seborrheic dermatitis. Over 80% of phase 3 study participants achieved clear or almost clear skin at week 8, while also experiencing a manifest improvement in manifests of erythema and scaling. At present, there are only limited options of on-label medications for people suffering from this disease.

Seborrheic dermatitis has a prevalence of around 5% worldwide [1,2]. "It's a disease that is very common, yet in my opinion undertreated," Prof. Andrew Blauvelt (Oregon Medical Research Center, OR, USA) stated [1]. Current therapy options include topical steroids and anti-fungals that may have some restrictions regarding side effects or difficulties in use in some body regions, especially the face and hair bearing areas.

Due to positive results in phase 2, a 0.3% foam preparation of the PDE4 inhibitor roflumilast was evaluated in the phase 3 STRATUM study (NCT04973228) on treatment for seborrheic dermatitis. After a 2:1 randomisation, participants received either the active drug foam once daily or a vehicle over 8 weeks. Recruited were 457 participants, among them 7% was between 9–17 years, as the disease already may occur in pubescents. The average age was 42, and there was an equal distribution of men and women.

All participants had an Investigator´s Global Assessment (IGA) ≥3, equalling at least moderate disease and an affected body surface area ≤20%. In practice, over 90% had an IGA of 3 at baseline and on average around 3% of the body surface was affected. Success, in terms of the primary endpoint, meant achieving an IGA of 0/1 corresponding to clear or almost clear skin. The most common body regions involved were scalp in around 90%, face in over 60%, and ears in more or less 50% of the trial population.

Early onset of action

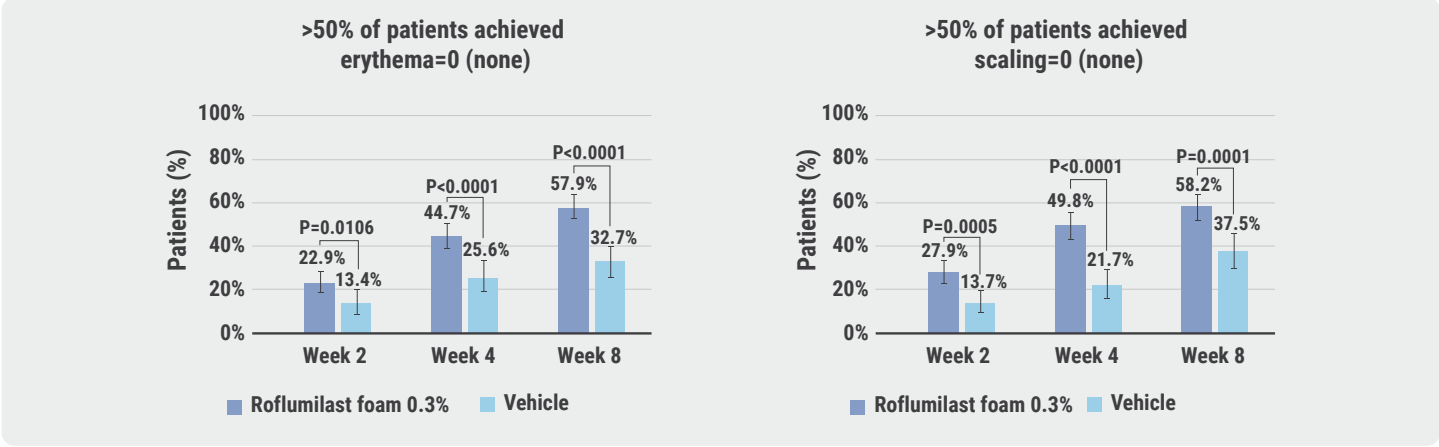
Statistical difference in favour of roflumilast already started at week 2. At week 8, 80.1% of participants attained success with an IGA of 0/1 on roflumilast in comparison with 59.2% on placebo (P<0.0001). Prof. Blauvelt attributed the high placebo rate to the possibility of a beneficial effect through the once daily moisturisation that the vehicle provided. Over half of the participants were completely clear of disease after 8 weeks (50.7%; P<0.0001). Furthermore, 57.9% (P<0.0001) and 58.2% (P<0.0001) achieved scores of 0 for erythema and scaling at week 8 (see Figure) and 63.6% (P=0.0002) experienced a 4-point reduction on the worst-itch numeric rating scale.

The foams with roflumilast and the vehicle were both well tolerated throughout the trial with 97.8% and 94.8% of participants reporting no or only mildly discomforting sensation at week 8. The safety profile did not raise concerns: any treatment-emergent events appeared in 23% on roflumilast versus 21.6% on placebo.

"Many patients responded in this trial, so much so that I called it the "happy trial". Every time I saw patients in this trial, they seemed to be happy," Prof. Blauvelt remarked in view of the results.

1. Blauvelt A. Efficacy and safety of roflumilast foam 0.3% in patients with seborrheic dermatitis in a phase 3 trial. D2T01.3F, EADV Congress 2022, Milan, Italy, 7-10 September.
2. Dessinioti C, et al. Clin Dermatol. 2013;31(4):343-51.

Figure: Efficacy and safety of roflumilast foam 0.3% in seborrheic dermatitis [1]



What Is Hot in Hair Disorders?

Long-term improvement in alopecia areata with ritlecitinib therapy

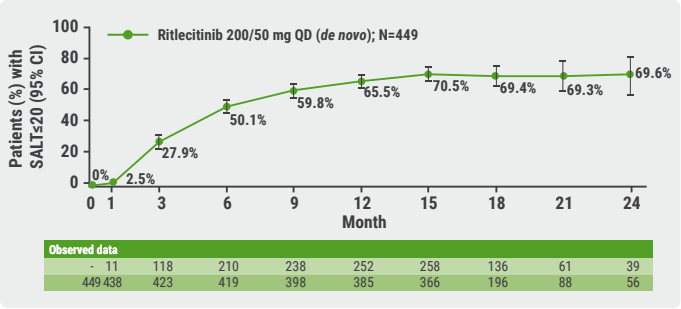
In an interim analysis of the ongoing phase 3 ALLEGRO-LT trial, the investigational JAK3/TEC kinase inhibitor ritlecitinib demonstrated remarkable scalp hair regrowth in both adult and adolescent patients with alopecia areata (AA) over a treatment period of up to 36 months. The safety profile was consistent with the primary ALLEGRO study results and treatment effects were already noted after 3 months.

AA is a T cell-mediated autoimmune disease with an underlying immune-inflammatory pathogenesis characterised by non-scarring hair loss of the scalp, face, and/or body. Ritlecitinib is a selective inhibitor of JAK3 and the TEC kinase that previously showed efficacy in AA in the ALLEGRO phase 2b/3 study (NCT03732807) [1]. At this year´s EADV meeting, Dr Athanasios Tsianakas (Fachklinik Bad Bentheim, Germany) reported interim results from the *de novo* arm of ALLEGRO-LT (NCT04006457), an ongoing phase 3 study investigating the long-term safety and efficacy of ritlecitinib in patients with AA [2].

Included in the ALLEGRO-LT study were either roll-over participants from previous trials or *de novo* participants. *De novo* participants were first treated with 200 mg ritlecitinib, once daily, for 4 weeks (induction dose) followed by the maintenance dose of 50 mg. Key inclusion criteria of *de novo* participants were an age of ≥12 years and a diagnosis of AA with a ≥25% scalp hair loss due to AA. Dr Tsianakas presented the results of the *de novo* arm up to month 36.

The median range of exposure was about 17 months. "All in all, 85% of the included participants were taking the drug for more than 12 months," Prof Tsianakas said. At data cut-off, 21.6% of participants had discontinued, but only 3% due to adverse events. Regarding efficacy, the proportion of participants showing a maximum of 20% hair loss in the Severity Alopecia Tool (SALT) score, a global severity score, was evaluated up to month 24. "We can see that the curve nicely goes upwards until a year and stays steady at about 70%," Prof Tsianakas elucidated (see Figure). The more stringent SALT 10 results level out at about 56% after a year. The high efficacy seen in ALLEGRO-LT is mirrored in the positive participant-reported outcome, the proportion of participants who moderately or greatly improved their Patient Global Impression of Clinical Status (PGI-C) score. Already after 5 months, 57% of participants felt their hair growth had moderately or greatly improved, this percentage went up to about 78% at month 24.

Figure: Response to ritlecitinib therapy based on SALT ≤20 up to month 24 [1]



SALT, Severity of Alopecia Tool; QD, once daily; N, number of patients with observed data; n, number of patients achieving SALT score ≤20.

Among the 447 participants included in the safety analysis, a total of 1,448 adverse events were recorded. From the *de novo* group, 78% developed adverse events but 94.6% of those were mild-to-moderate in severity. The most frequent adverse events were headache, positive SARS-CoV-2 test, and acne. Importantly, no opportunistic infections and no clinically relevant median changes from baseline in haematological parameters were observed.

Taken together, these long-term data are consistent with the primary ALLEGRO study results. In contrast with the 2 other JAK inhibitors developed for AA, baricitinib and deuruxolitinib which both target JAK1 and 2, ritlecitinib is only targeting JAK3. This high selectivity may have advantages regarding the safety profile.

Also effective in alopecia totalis

In a post-hoc analysis of the ALLEGRO study presented as a poster, the efficacy of ritlecitinib at weeks 24 and 48 was assessed across different subgroups based on the presence of alopecia totalis (AT; complete loss of scalp hair) or alopecia universalis (AU; complete loss of scalp, face, and body hair),

subgroups that can be challenging to treat [3]. Of the 718 participants randomised in the ALLEGRO trial, 151 (21%) and 147 (20%) had AT and AU, respectively. Across all ritlecitinib treatment arms, SALT ≤20 response rates were higher in the non-AT/non-AU participants at weeks 24 and 48. However, ritlecitinib was also effective in the AT/AU group with up to 30% of this difficult-to-treat group achieving a SALT ≤20 response at week 48 [4].

1. King B. Efficacy and safety of ritlecitinib (PF-06651600) in patients with alopecia areata and ≥50% scalp hair loss: results from the international ALLEGRO phase 2b/3 randomised, double-blind, placebo-controlled study (NCT03732807). D3T01.1C, EADV Congress 2021 – Virtual, 29 September – 2 October.
2. Tsianakas A. Long-term safety and efficacy of ritlecitinib in adults and adolescents with alopecia areata: interim results from the ALLEGRO-LT phase 3, open-label trial. D3T01.1G, EADV Congress 2022, Milan, Italy, 7-10 September.
3. Kassira S, et al. Int J Dermatol. 2017;56:801-10.
4. Zhang X, et al. Efficacy of ritlecitinib (PF-06651600) in patients with alopecia totalis and alopecia universalis: post hoc analysis of the ALLEGRO phase 2b/3 study. P0486, EADV Congress 2022, Milan, Italy, 7-10 September.

Topical gel plus finasteride beneficial for patients with androgenetic alopecia

In a trial including 58 participants with androgenetic alopecia, a significantly improved effect was present in individuals using a combination of a growth factor-containing topical gel together with topical minoxidil and oral finasteride. Conveniently, the gel only needed to be applied once a week.

Androgenetic alopecia is the most common form of alopecia, which affects primarily men but also 20-50% of patients are women, particularly after menopause. First-line treatments are topical minoxidil and oral finasteride for men, but many patients do not respond sufficiently, and it often takes very long to show effective results. Dr Michela Starace (University of Bologna, Italy) and her team realised the need for adjuvants and newer modalities of treatment to give faster and better outcomes [1]. Therefore, they explored whether non-pharmacological products could increase the effectiveness of treatment for androgenetic alopecia and telogen effluvium.

They formulated a topical treatment including oligopeptides with growth-factor mimicking activity, caffeine, taurine, and a lactoferrin-based iron-chelating complex (GFM-DA gel) and assessed its effectiveness when combined with topical minoxidil and oral finasteride. The gel was administered as add-on treatment once weekly. The 2 combination study arms were compared with 2 control groups that were treated with topical minoxidil or oral finasteride only. All study participants had androgenetic alopecia exceeding grade III, including grades IV and V on the Norwood-Hamilton scale. The primary endpoint was the change in the 7-point Global Photographic Assessment score (GPAS) from baseline to week 12 and 24.

At 12 weeks, the GPAS scores were 1.6 in the minoxidil and 1.1 in the finasteride monotherapy group compared with 1.6 in the group that applied the gel together with minoxidil and 1.8 in the gel-finasteride combination group. Treatment efficacy increased up to week 24: At this time, GPAS scores were 2.2 in the minoxidil only group, 2.4 in the minoxidil plus gel group, 1.9 in the finasteride group, and 2.7 in the group that was treated with both oral finasteride and the gel. The gel was generally well-tolerated.

Dr Starace concluded that adding a once-weekly topical gel containing caffein, growth-factor mimicking agents, taurine, and an iron-chelating complex to androgenetic alopecia drugs produced clinically better results, especially when used together with oral finasteride.

1. Starace M, et al. Efficacy and tolerability of a gel formulation based on mimicking growth factors oligopeptides, taurine and caffeine in adrogenic alopecia subjects treated with topical minoxidil or oral finasteride: A prospective, assessor-blinded, parallel groups study. FC04.09, EADV Congress 2022, Milan, Italy, 7-10 September.

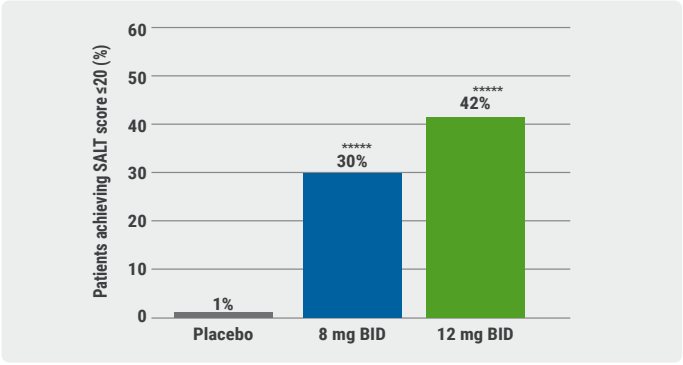
Deuruxolitinib achieves hair regrowth, even in patients with severe alopecia areata

In the phase 3 THRIVE-AA1 trial, the investigative JAK inhibitor deuruxolitinib led to remarkable hair regrowth in patients with severe alopecia areata (AA). Up to 42% of participants achieved the primary efficacy endpoint, e.g. a SALT score ≤20 at week 24, in many cases with a rapid onset of effect. Patients were very satisfied with the treatment results.

Similar to baricitinib, which is already approved for AA in Europe and Japan, deuruxolitinib also targets JAK1 and JAK2. In the multinational, phase 3 THRIVE-AA1 trial (NCT04518995), adult patients with severe AA were included to assess the efficacy and safety of deuruxolitinib with a study duration of up to 32 weeks [1]. Participants were treated with either 8 mg or 12 mg deuruxolitinib twice daily or placebo and had at least 50% scalp hair loss as measured by the Severity of Alopecia Tool (SALT). The primary efficacy endpoint was the percentage of participants achieving a SALT score of ≤20 at week 24. "We also looked at patient satisfaction," Prof. Brett King (Yale University School of Medicine, CT, USA) said. The percentage of responders, defined as "satisfied" or "very satisfied" on the Hair Satisfaction Patient-Reported Outcome (SPRO) scale at week 24 was assessed as a key secondary outcome.

At baseline, participants had a mean SALT score of 88. At week 24, participants treated with both doses of deuruxolitinib achieved the primary endpoint: 42% in the 12 mg dose group and 30% in the 8 mg dose group, compared with 1% in the placebo group achieved a SALT score ≤20 (P<0.0001 vs placebo; see Figure). "In AA, this is truly transformative, we see a very low placebo rate. In severe disease, the chance of spontaneous remission is close to 0," Prof. King said. In the low-dose and high-dose groups, 21% and 35% respectively, achieved an even more stringent SALT score of ≤10 (P<0.0001 vs placebo).

Figure: Proportion of patients achieving SALT score ≤20 at week 24 [1]



SALT, Severity of Alopecia Tool; BID, twice daily; *****, P<0.0001 vs placebo.

Significant changes in SALT score were seen as early as week 4. The agent also led to a significant improvement in eyebrow regrowth. "We wanted to know whether our impression aligns with what patients feel. Indeed, we see a high degree of patient satisfaction with scalp hair," Prof. King said, with 42% responders in the low-dose group and 52% responders in the high-dose group.

Overall, the agent was generally well tolerated and more than 97% of participants will roll over into the open-label, long-term, extension study. According to Prof. King, this data is highly encouraging and supports the potential of deuruxolitinib to regrow hair on the scalp, eyebrows, and eyelashes in patients with AA.

1. King B. Top-line results from THRIVE-AA1: A clinical trial of CTP-543 (Deuruxolitinib), an oral JAK inhibitor, in adult patients with moderate to severe alopecia areata. D3T01.1L, EADV Congress 2022, Milan, Italy, 7–10 September.

Psoriasis and Psoriatic Arthritis: What You Need to Know

Novel oral psoriasis drug maintains efficacy over 2 years

The TYK2 inhibitor deucravacitinib demonstrated stable, long-term efficacy results up to week 112. The outcome measures for the newly FDA-approved drug were very similar to those seen after 1 year.

Deucravacitinib is an allosteric inhibitor of TYK2, which binds to a TYK2 regulatory domain that barely interacts with other JAK enzymes. Compared with JAK1 and JAK3, the selectivity to TYK2 is ≥100-fold and versus JAK2 ≥2,000-fold greater [1,2]. In the POETYK-PSO-1 trial (NCT03624127), participants received either deucravacitinib at a dose of 6 mg once daily (approved dose), placebo from day 1 to week 16, or apremilast as active comparator [3,4]. Thereafter, placebo participants could cross over to the active study drug. At the pivotal primary endpoint (week 16), 58.4% of the participants treated with deucravacitinib achieved Psoriasis Area and Severity Index (PASI)-75 compared with 12.7% of the placebo-treated participants. This rate further rose to 69.3% at week 24 and 65.1% after 1 year. At the same timepoints, the results for the static Physician's Global Assessment (sPGA) of 0/1 were within a similar range: 53.6%, 58.7%, and 52.7%, respectively. Prof. Mark Lebwohl (Icahn School of Medicine at Mount Sinai, NY, USA) presented the latest 112-week extension data on deucravacitinib. Included in the analysis were the longer-term outcomes of all participants who received the active drug from day 1 of the trial, with special focus on the PASI-75 responders at week 16, who entered the open-label extension after week 52 [3].

Of the 332 participants who were initially randomised to deucravacitinib in POETYK-PSO-1, 265 continued in the long-term extension after week 52 and 173 among them had reached PASI-75 before at week 16. Baseline data of these 2 groups varied somewhat with mean values for age of 46 years and 45.2 years, weight 87.0 kg and 84.7 kg, PASI 21.8 and 22.6, and sPGA 3 in 78.5% and 74.6%.

Independent of missing data imputation, the PASI-75 outcomes for the cohort with all participants on continuous deucravacitinib resulted in a rather horizontal graph. Prof. Lebwohl stressed that imputation according to "as observed" or "treatment failure rules" did lead to hardly any change in the results, which he saw as characteristic of a very effective treatment. The outcomes with a modified non-responder imputation (mNRI) went from of 80.2% at week 52 to 82.4% at week 112. The maintenance result for PASI-75 responders at week 16 that started at 90.1% in week 52, attained 91.0% at week 112. sPGA 0/1 was achieved by 66.5% of all extension participants at week 112 and by 73.5% of the 16-week responders.

"So, now, we have a once-daily, oral drug with efficacy similar to biologic agents," Prof. Lebwohl concluded.

1. Burke JR, et al. Sci Transl Med. 2019;11(502):eaaw1736.
2. Wrobleski ST, et al. J Med Chem. 2019;62(20):8973-8995.
3. Lebwohl M. Deucravacitinib long-term efficacy with continuous treatment in plaque psoriasis: 2-year results from the phase 3 POETYK PSO study program. D3T01.1F, EADV Congress 2022, Milan, Italy, 7–10 September.
4. Armstrong AW, et al. J Am Acad Dermatol. 2022;S0190-9622(22)02256-3.

A3 adenosine receptor agonist showed modest efficacy but excellent tolerability

Although reaching statistical significance over placebo, piclidenoson did not surpass apremilast as an active comparator for treating psoriasis. However, a further increase of response after week 16 and a very good safety profile may speak in favour of further research.

Isoforms of adenosine receptors are almost universally present across all cell types, but the A3 isoform is almost exclusively present on inflammatory cells or immunocytes. As a consequence, a target such as piclidenoson, which is a selective activator of the A3 receptor, might provide a selective modulation of the inflammatory signals that are expressed or generated by these immunocytes. The phase 3 COMFORT trial (NCT03168256) explored the small molecule piclidenoson [1]. The agent has demonstrated the ability to inhibit IL-17 and IL-23 expression in keratinocytes [2].

The study randomised 529 patients into 4 different treatment arms with twice-daily medication: piclidenoson 2 mg, piclidenoson 3 mg, placebo, or the active comparator apremilast 30 mg. At week 16 of the 32-week trial, the placebo group was re-randomised to 1 of the 3 active arms. After week 32, an extension up to week 48 was optional.

The study's primary endpoint was met at week 16, as the 3 mg piclidenoson dosing group statistically exceeded the placebo group in the accomplishment of Psoriasis Area and Severity Index (PASI)-75 with 9.7% versus 2.6% (P=0.037). With regard to the trajectory of PASI-75 and Physician's Global Assessment (PGA) response, Dr Kim A. Papp (Probity Medical Research, Canada) pointed out that there appears to be evidence of progressive improvement over time. "While week 16 is the primary endpoint, it is clearly not the endpoint which achieves maximal success and maximal response," Dr Papp underlined.

Any treatment-emergent adverse events incidence of >2% were seen in 14.8% of participants in the piclidenoson group (3 mg), in 27.5% of participants in the apremilast group, and in 25.5% of participants in the placebo group, with the highest incidence in gastrointestinal disorders (0.7%, 6.3%, and 0%).

"Overall, we have superiority of piclidenoson over placebo, we see this interesting progressive improvement in response up to week 32, we see an excellent safety profile, with placebo-like characteristics, and certainly a better tolerability of piclidenoson compared with apremilast," Dr Papp concluded his talk. When asked about a place for new drugs in the light of existing treatments with achievement of PASI-90 and PASI-100, Dr Papp conveyed that there will always be a segment of the population that does not respond and instead of surrendering them, one can continue to look for new therapies. "There are also other opportunities that may avail themselves, because we have not fully explored the capabilities of activating the A3 receptor, so the future is still wide open," Dr Papp stressed.

1. Papp KA. Treatment of plaque psoriasis with piclidenoson: Efficacy and safety results from a phase 3 clinical trial (COMFORT). D3T01.1K, EADV Congress 2022, Milan, Italy, 7–10 September.
2. Cohen S, et a. J Immunol Res. 2018:2310970.

Selective IL-23 inhibitor achieves long-term disease control in many patients with active PsA

Risankizumab demonstrated a maintained efficacy over 100 weeks in the treatment of active psoriatic arthritis (PsA); efficacy increased up to week 40 and

was maintained until the end of the study, independent of previous therapy. Remarkably, up to 44.6% of patients achieved a control of both cutaneous and arthritic disease.

The efficacy and safety of the selective IL-23 blocker risankizumab in PsA was assessed in the phase 3 trial programme KEEPsAKE. "We already know that risankizumab has an important effect on cutaneous manifestations," said Dr Kim Papp (Probity Medical Research, Canada) during the presentation of the 100-week results of the trial programme [1]. The (positive) 24-week results of the double-blind study period were already presented previously [2,3]. At 24 weeks, all patients entered an open-label extension period and placebo patients were switched to risankizumab 150 mg every 12 weeks.

In both the KEEPsAKE 1 (NCT03675308) and KEEPsAKE 2 trials (NCT03671148), 1,407 participants with active PsA who had inadequate response or intolerance to either ≥1 conventional disease-modifying drug in the KEEPsAKE1 trial or to a previous biologic in KEEPsAKE2 were included. The primary endpoint of the double-blind study period was the proportion of participants achieving 20% improvement according to the American College of Rheumatology 20% response (ACR20), a common study endpoint in rheumatology, at week 24.

"These results are beautiful. We can see at week 24 that about 60% achieves an ACR20 response, which is within the expected results for an effective therapy in PsA," Dr Papp explained (P<0.001 vs placebo) [2,3]. In the extension phase, there was a further modest increase until week 40. A similar profile was seen in both KEEPsAKE trials. From week 40 onwards, response was maintained until week 100 (see Figure). "Minimal disease activity is a new buzzword because it shows how well we control both cutaneous and arthritic disease," Dr Papp said. Depending on the statistical analysis used, between 38.2% and 44.6% of participants in the KEEPsAKE 1 and 33.0% and 40.0% in the KEEPsAKE 2 trial achieved this endpoint.

The superiority of risankizumab was also evident for a couple of additional efficacy endpoints, e.g. in different quality-of-life measures and changes in Functional Assessment of Chronic Illness Therapy (FACIT) – Fatigue score. Moreover, the response of the skin was exceptional with more than 70% achieving a Psoriasis Area and Severity Index (PASI)-90 response.

Risankizumab was generally well tolerated with what Dr Papp described as a "quiet safety profile".

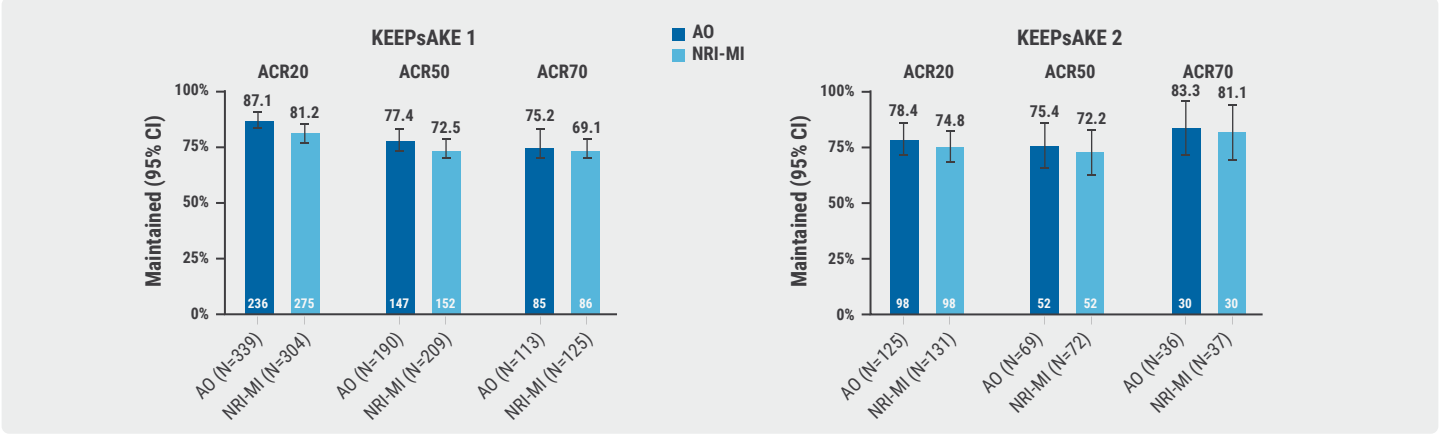
1. Papp K, et al. Efficacy and Safety of Risankizumab for Active Psoriatic Arthritis: 100-Week Results from the KEEPsAKE 1 and KEEPsAKE 2 Trials. D3T01.1D, EADV Congress 2022, Milan, Italy, 7¬¬⊠10 September.
2. Kristensen LE, et al. Ann Rheum Dis. 2021;80:1315–6.
3. Östör A, et al. Ann Rheum Dis. 2021;80:138–9.

AI machine learning algorithm useful in early detection of PsA

A significant lag in diagnosis of psoriatic arthritis (PsA) may result in joint destruction. A machine learning algorithm proofed to be a valuable tool to detect PsA up to 4 years prior to initial diagnosis.

PsA is a good candidate to develop a machine learning algorithm, especially for dermatologists, since it is a prevalent disease, particularly among psoriasis patients, where skin psoriasis usually precedes PsA. Moreover, early diagnosis and treatment can prevent irreversible joint damage and disability. The dermatologist is often the first physician to

Figure: Maintenance of ACR at week 100 in patients originally randomised to risankizumab [1]



AO, as observed; NRI-MI, as observed with missing data imputed as non-responder except those missing due to COVID-19 or geo-political conflict in Ukraine and Russia, which lay on multiple imputation.

suspect PsA. "This is why such an algorithm is important for us," Dr Jonathan Shapiro (Maccabi Healthcare Services, Israel) emphasised [1]. Artificial intelligence (AI)-based decision support tools are urgently needed in this indication, as 10 to 15.5% of psoriasis patients suffer from undiagnosed PsA, and median time to diagnosis is still more than 2 years [2,3]. In addition, rheumatologists are often unavailable.

In a retrospective study, the performance of the machine learning tool PredictAI was evaluated regarding its ability to identify undiagnosed PsA patients 1-4 years prior to the first suspicion of PsA (reference event) [1]. Data was analysed from the 2.5 million members of the Maccabi Healthcare Services Study population. All diagnoses of PsA and psoriasis in the adult population between 2008-2020 were evaluated in the study. As Dr Shapiro explained, the researchers did what is done with all machine learning algorithms: "You take the data you have and divide it in 2 sets: a large set for training the algorithm, and a small set used to train and test your algorithm." Since prevalence of PsA is higher among psoriasis patients compared with the general population, a general population cohort and a psoriasis cohort were formed. The reference event was the first registered diagnosis of PsA by any physician. The algorithm was trained on 4 years of consecutive data preceding the diagnosis.

In the general population cohort, a cut-off point of 99% was chosen compared with a cut-off point of 90% in the psoriasis cohort. In the general population cohort, PredictAI achieved a sensitivity range of 32-42% and a population positive predictive value (PPV) range of 10-8%. In the psoriasis cohort, undiagnosed PsA patients were identified by the algorithm 1 to 4 years before the reference event with a sensitivity range of 38-50% and a PPV range of 30-34%.

Parameters the algorithm found most prominent to help make the prediction whether a patient has or has not undiagnosed PsA were number of psoriasis diagnoses, number of arthralgia diagnoses, and intra-articular injections. Parameters which were not associated with undiagnosed PsA were age and number of eczema diagnoses.

"The closer you move to the time of the reference event (the diagnosis of PsA) the more the performance of the algorithm improves," Dr Shapiro explained. In the psoriasis cohort, PredictAI identified undiagnosed PsA in up to 51% of patients up to 4 years prior to primary care physician´s initial suspicion, potentially reducing time to diagnosis and treatment. Therefore, AI models may play an important future role to improve patient outcomes in this disease.

1. Shapiro J. A machine learning tool for the early identification of undiagnosed psoriatic arthritis patients: is it possible? FC06.02, EADV Congress 2022, Milan, Italy, 7-10 September.
2. Villani AP, et al. J Am Acad Dermatol. 2015;73:242-8.
3. Karmacharya P, et al. J Rheumatol. 2021:48:1410-6.

Novel Developments in Sun Protection

Myths regarding "health benefit" of suntan prevail in majority of population

Despite decades of awareness campaigns, 8 in 10 Europeans still believe tans are attractive, 73% even believes that tans are healthy. This revealed a large survey including data from 17,000 people from 17 countries. Not even at-risk participants can imagine to come home from holidays with "pale skin".

"This research shows just how entrenched the "healthy" suntan myth is, even in those who have already suffered sun damage or developed skin cancer," lead researcher Prof. Thierry Passeron (Université Côte d'Azur, France) commented during the EADV press conference. The survey included 6,000 participants from the United Kingdom, Germany, France, Spain, Italy, and Russia, while the remaining participants were from non-European countries, including North and South America, Africa, Oceania, and Asia [1]. Having a tan is still found attractive in 8 out of 10 Europeans and 73% finds a tan "healthy". Inhabitants from non-European countries were slightly less enthusiastic about suntans than Europeans, with 67% saying a tan was attractive and 59% believing a tan was healthy.

Did prevention campaigns at least result in better-informed, at-risk participants? Not really. According to

a second analysis, awareness of the dangers of the sun was higher in participants with a history of skin cancer, pre-cancerous lesions, photodermatosis, or those taking immunosuppressive or photosensitising drugs. However, even in this at-risk group, 59% said they could not imagine coming back from a holiday without a tan compared with 48% of those without a medical history.

The survey also revealed that only 56% of Europeans know sun protection is useful when the weather is overcast (vs 64% outside of Europe) and 1 in 4 (24%) thought it was safe to go outside without sun protection when they were already tanned (vs 21% outside of Europe). Although 92% of Europeans were aware of the skin ageing risks posed by the sun (86% outside of Europe), 84% admitted they did not protect themselves all year round (79% outside of Europe).

Only 1 out of 10 (10%) Europeans said they routinely or often used all forms of sun protection, such as applying sunscreen, staying in the shade, wearing a hat and protective clothing all year round compared with 14% amongst those outside of Europe. "We must drive awareness of the damage to skin cells caused by exposure to the sun, which can lead to photoaging and skin cancer. This is particularly important in Europe where sun protection appears most inadequate compared with other countries. The public must also understand that they need to protect their skin all year round, even during overcast weather conditions," Prof. Passeron concluded.

1. Passeron T, et al. Sun exposure and associated risks in 17 countries: results from Europe compared to other continents. Abstract No 129, EADV Congress 2022, Milan, Italy, 7–10 September.

Fern extract reverses severe actinic keratosis lesions

The combination of local and oral preparations of polypodium leucotomos extract led to clinical reversal of actinic keratosis (AK) lesions at 12 months in a retrospective Italian trial. Treatment also markedly reduced the occurrence of new lesions.

Previous studies have shown that the extract of the South American fern polypodium leucotomos (PLE) is a powerful antioxidant due to its high content of phenolic compounds [1]. It not only inhibits the generation of reactive oxygen species by ultraviolet light, but also prevents ultraviolet- and reactive oxygen species-induced DNA damage. Therefore, PLE extracts are a common ingredient in sun creams. A study in healthy participants showed that the fern extract is an effective chemophotoprotector against PUVA-induced skin phototoxicity [2]. To investigate if topically and orally PLE is really able to reverse severe actinic damage, a study including 131 patients with severe signs of photoaging and at least 3 AK lesions was performed [3].

Participants were randomised into 3 treatment groups. The first received topical photoprotection with SPF ≥100 together with a topical PLE-preparation alone, the second group was treated in the same way plus the fern extract in an oral form once daily, and the third and control group only used the topical photoprotection. In case new AK lesions were noted, participants were permitted to undergo additional therapy, e.g. imiquimod or cryotherapy. At 12 months, skin changes were evaluated with reflectance confocal microscopy, and clinical changes by 2 different AK-specific scores and the appearance of new AK lesions or the need for specific AK interventions.

Data from 116 participants showed distinct improvements in the AK Field Assessment Scale Area (AK-FAS), especially in the arm also treated with the oral fern preparation: it improved by 26% compared with 4% in participants on topical PLE only, and a worsening by 13% in the control group. "It is interesting that the control group that was given only common advice had increased photodamage and an increased number of new AK lesions," said Dr Stefania Guida (Sapienza University of Rome, Italy) who presented the study results. In contrast, there were no new lesions in both PLE groups. Participants in both intervention groups improved in the Actinic Keratosis Area Score Index (AKASI) score by 7%, whereas there was a deterioration by 6% in the placebo arm (P<0.001).

Reflectance confocal microscopy supported this clinical data: 51% of those receiving the oral and local preparation of PLE and 45% of those receiving the local PLE preparation only had normalisation of the honeycomb pattern compared with 26% in the control group (P=0.04 for both comparisons). Also measured was a difference in the percentage of participants that needed additional therapy due to the occurrence of new lesions, which was necessary in 2% of participants taking both the oral and topical PLE preparation, in 11% of those only taking the topical PLE preparation, and in 38% of controls.

1. Parrado C, et al. Int J Mol Sci 2016;17:pii:E1026.
2. Middelkamp-Hup MA, et al. J Am Acad Dermato 2004;50:41-9.
3. Pellacani G. Topical and topical plus oral immune photoprotection with Polypodium Leucotomos extract in severe actinic damage. A multicenter, randomised, prospective, assessor-blinded, 12-month controlled trial with confocal microscopy evaluation in 132 subjects. FC05.03, EADV Congress 2022, Milan, Italy, 7–10 September.

Vitiligo in 2022

Enhancing re-pigmentation rates with topical ruxolitinib in all body areas

Evaluating phase 3 data of JAK inhibition with ruxolitinib according to different regions of the body demonstrated best results for head and neck with 68.1% of patients reaching >50% repigmentation after 1 year. Of note, also very difficult-to-treat areas like hands and feet responded very well to the treatment.

Within the TRuE-V1 (NCT04052425) and TRuE-V2 (NCT04057573) trials, ruxolitinib cream demonstrated superior efficacy over placebo at week 24, not only in the primary but also all secondary endpoints [1,2]. "We know that the location is very important when it comes to re-pigmentation of vitiligo, and we know that extremities are much more difficult, but also some other areas on the body," Prof. Thierry Passeron (University Côte d'Azur, France) expressed as the underlying reason for an analysis of the data according to efficacy in different body regions [1]. The studies included vitiligo patients ≥12 years of age with ≤10% of depigmented body surface area of which at least 0.5% had to be facial and ≥3% in other body sites. For the new evaluation, endpoints were ≥50% improvement in the Vitiligo Area Scoring Index (VASI50) Score at week 24 in: head and neck, hands, upper/lower extremities, trunk including genitals, feet, as well as total body with exclusion of the face.

In TRuE-V1 and V2, participants were randomised to twice daily 1.5% ruxolitinib cream or placebo until week 24, whereafter all participants continued on the study drug to week 52. At 6 months, the results were in favour of the ruxolitinib cream as compared with placebo, regardless of the body region. Best results for ruxolitinib versus placebo at week 24 were noted in head and neck (45.3% vs 23.8%), followed by the extremities (arms 33.2% vs 8.2%, legs 29.5% vs 12.2%). Prof. Passeron highlighted that even hands and feet, 2 very resistant areas to treat, provided good results. As re-pigmentation treatment in vitiligo takes time, the results of the ruxolitinib groups further improved up to week 52: VASI50 was reached for total body without the facial area in 47.7%, head and neck 68.1%, upper extremities 56.7%, lower extremities 54.5%, trunk 48.4%, hands 38.2%, and feet 29.3%. In comparison, the respective rates for reaching VASI50 in former placebo patients changing to ruxolitinib at week 24 were: 23.3%, 51.0%, 34.9%, 32.3%, 25.4%, 29.2%, and 22.5%. "Not surprisingly, hands and feet that are the most difficult parts to re-pigment, but you can see that even so about one third of the patients reach 50% of re-pigmentation after 1 year of treatment," Prof. Passeron underlined. Interestingly, the increase of patients reaching VASI50 over time did not plateau after 1 year.

"This subanalysis demonstrated that after 6 months and after 1 year, ruxolitinib cream provided not only good results on the face but also on other parts of the body, which is very important for the patients," Prof. Passeron summarised, reminding the audience that it is important to explain to the patients that treatment will go on for a long time.

1. Passeron T. Effect of Ruxolitinib Cream on Achievement of VASI50 by Body Region: Week 52 Pooled Analysis of the TRuE-V Phase 3 Studies. D3T01.1C, EADV Congress 2022, Milan, Italy, 7-10 September.
2. Rosmarin D. Efficacy and safety of ruxolitinib cream monotherapy for the treatment of vitiligo: results from 2 52-week phase 3 studies. S026, AAD 2022 Annual Meeting, Boston, MA, USA, 25–29 March.

Markedly lower skin cancer risk in vitiligo patients

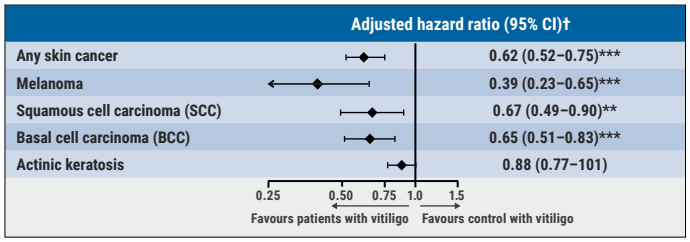
The risk to develop any kind of skin cancer is 38% lower for patients suffering from vitiligo. A significantly lower risk was also found when differentiating according to individual skin cancer type.

Current data on the skin cancer risk in vitiligo patients is not consistent in its results. "There has been a big lack of, particularly European, population-based studies," Dr John Ferguson (St John's Institute of Dermatology, UK) pointed out [1]. To clarify the question, the British investigator team performed a matched retrospective cohort study utilising data from the Optimum Patient Care Research Database (opcrd.co.uk) that contains medical care records from about 10 million UK patients. They matched 60,615 controls to 15,156 patients with vitiligo according to e.g. age, sex, and ethnicity. The participants were registered in the database between 2010 and 2020. A composite of melanoma and non-melanoma skin cancer occurrence was the primary endpoint. Secondary outcomes were individual cancer forms like melanoma, squamous cell carcinoma (SCC), and basal cell carcinoma (BCC).

The characteristics of the study cohort included a median age of 47 and an average follow-up of about 8 years in a study population with 54.5% women. "Around 70% of participants were White, which is slightly lower than the UK population, which kind of makes sense given this condition particularly affects people with darker skin prototypes," Dr Ferguson told.

The results demonstrated a 10-year cumulative skin cancer incidence of 1.3% in vitiligo patients compared with 2% in controls. The adjusted hazard ratio (aHR) of 0.62 (95% CI 0.52-0.75) stood for a 38% reduction in risk for any kind of skin cancer (see Figure).

Figure: Patients with vitiligo carry a lower risk for both melanoma and non-melanoma skin cancer [1]



***, P<0.001; **, P<0.01; *, P<0.05; †, adjusted for age, sex, IMD, ethnicity, BMI, smoking status, alcohol status, history of immunotherapy, phototherapy, and major comorbidities.

Hazard ratios were also significant for the individual cancer types: melanoma aHR 0.39 (P<0.001), SCC aHR 0.67(P<0.01), BCC aHR 0.65 (P<0.001). Concerning actinic keratosis, however, no significant risk-lowering association with vitiligo was discovered.

"Looking into the demographics, this effect is consistent for men and women and different socioeconomic groups," Dr Ferguson informed. In his opinion, the lack of significance for the non-White study population was due to a rather low cancer incidence rate and inadequate power in this subgroup to detect differences.

"We should think of this as being reassuring considering we use phototherapy, we use protopics, we use perhaps other immunosuppressants going forward, which all potentially carries a risk of skin cancer," Dr Ferguson underlined in his summary. But despite the markedly reduced risk of developing skin cancer, he reminded the audience that it is still important to carry on encouraging vitiligo patients to avoid getting burned and to use sun protection appropriately.

1. Ferguson J. Vitiligo is associated with a reduction in the incidence of melanoma and non-melanoma skin cancer: UK population-based cohort study. FC07.06, EADV Congress 2022, Milan, Italy, 7-10 September.

Pruritus Treatment: Novel Agents Entering the Arena

Dupilumab leads to clinically relevant improvements in signs and symptoms of prurigo nodularis

Dupilumab improved in a second trial, not only itch but also skin lesions in patients with prurigo nodularis. Significantly changes were seen as soon as week 24.

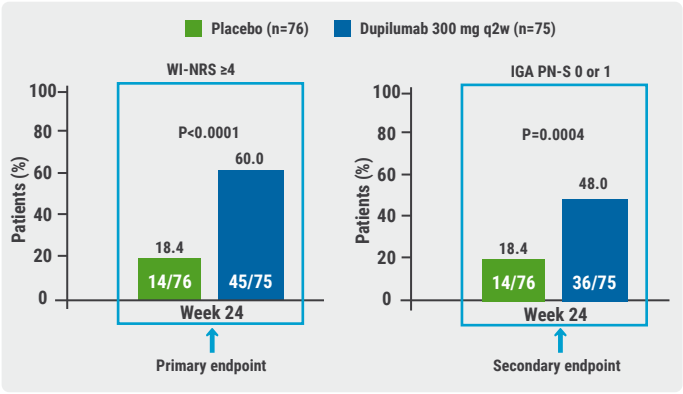
Prurigo nodularis is what Prof. Gil Yosipovitch (University of Miami, FL, USA) called "one of the most challenging conditions that dermatologists deal with." Dupilumab might now present a solution for this difficult-to-treat condition. Following the positive results in a prurigo nodularis phase 2 trial, a second phase 2 trial, LIBERTY-PN PRIME (NCT04183335), was performed to assess the efficacy and safety of dupilumab in prurigo nodularis [1]. The primary study endpoint was the proportion of patients with a ≥4-point improvement (reduction) in their worst itch numerical rating scale (WI-NRS) from baseline to week 24. A clear (0) or almost clear (1–5 prurigo nodularis lesions) outcome in the investigator´s global assessment (IGA) at week 24 was a secondary endpoint.

All enrolled participants suffered from severe itch, a high lesion count, and an impaired quality-of-life. Their prurigo nodularis was inadequately controlled by topical therapy and over two thirds had previously used systemic therapy. "Almost all participants were treated before but a lot of them were treated with antihistamines, which is not helpful,"

Prof. Yosipovitch commented. The study treatment was completed by 59 participants in the placebo group and 74 in the dupilumab group.

At week 24, a statistically significantly higher percentage of participants in the dupilumab group achieved the primary endpoint (60.0% vs 18.4%; P<0.0001; see Figure). Moreover, a significantly higher percentage of participants treated with dupilumab achieved clear or almost clear skin according to the IGA (48.0% vs 18.4%; P=0.0004). "This is a really robust change, considering that these lesions take time to heal," Prof. Yosipovitch commented.

Figure: Proportion of patients with ≥4-point improvement in WI-NRS at week 24 and proportion of patients achieving IGA PN-S 0 or 1 at week 24 [1]



WI-NRS, worst itch numeric rating scale; IGA PN-S 0 or 1, Investigator´s global assessment prurigo nodularis 0 or 1 (equalling clear or almost clear prurigo nodularis lesions).

There was no difference regarding the side effects between dupilumab and placebo. "Clearly, we need treatment for prurigo nodularis and this treatment has shown that it leads to a clinical relevant improvement," Prof. Yosipovitch concluded.

1. Yosipovitch G, et al. Dupilumab significantly improves itch and skin lesions in patients with prurigo nodularis: results from a 2nd phase 3 trial (LIBERTY-PN PRIME). EADV Congress 2022, Milan, Italy, 7–10 September.

Nalbuphine: aspiring to become another treatment for prurigo nodularis?

After demonstrating positive results for all endpoints in the PRISM trial, nalbuphine could be a candidate for an approved treatment for prurigo nodularis. The agent performed significantly better than placebo in reducing itch ≥4 points on the worst itch numeric rating scale (WI-NRS), while also improving quality-of-life and skin lesions.

The latest results of the phase 2b/3 PRISM trial (NCT03497975) were eagerly awaited, as currently approved pharmacologic therapies for prurigo nodularis are still lacking. The trial investigated nalbuphine, a dual κ-opioid receptor agonist/μ-opioid receptor antagonist as treatment for pruritus in prurigo nodularis [1]. Of note, abuse and addiction potential in activation of the κ-opioid receptor was found to be very low to non-existent. Included were 353 patients, randomised to receive either placebo or 162 mg of oral nalbuphine in an extended-release formulation, twice daily, after a 2-week titration.

The participants comprised a multi-ethnic group with a mean age between 56–60 years and a slight predominance for women. In both arms, baseline mean WI-NRS values of 8.6 and 8.7 stood for very severe itch. As for quality-of-life, the participants presented with mean scores of >80 out of 100 points in the Itchy-quality-of-life (ItchyQoL) score. "The majority of the population (60%) had 20–100 nodules which is a lot, 30% had over 100 nodules, and only 10% had up to 20 nodules," Prof. Sonja Ständer (University Medical Centre of Münster, Germany) said.

PRISM met its primary endpoint with significantly more participants responding to nalbuphine with a ≥4-point reduction in their WI-NRS compared with placebo at week 14 (24.7% vs 13.9%; P=0.0157). The significant difference between the 2 responder curves of nalbuphine and placebo began at week 6 (P=0.0027) and continued thereafter. Similarly, the quality-of-life improved significantly from week 6 onwards. The study also looked at the amelioration of pruriginous lesions. "Here we can say that nalbuphine interrupts the itch-scratch cycle and that the lesions can heal," Prof Ständer stated.

Safety results were consistent with nalbuphine's known profile. In line with the nalbuphine versus placebo results, the incidence of ≥1 treatment-emergent adverse event differed between the initial 2-week titration period (66.1% vs 31.3%) and the following fixed-dose therapy (48.2% vs 44.9%). Most common were gastrointestinal disorders, dizziness, and headache. "The safety profile is of course the issue with this drug, but on the other hand we can easily manage them and it's all in the mild and moderate range," Prof. Ständer commented.

All in all, she was very optimistic about nalbuphine as a potential novel treatment in prurigo nodularis.

1. Ständer S. Oral nalbuphine extended-release is effective in severe prurigo nodularis–associated pruritus: results from a phase 2b/3, double-blind, placebo-controlled study. 3K, EADV Congress 2022, Milan, Italy, 7–10 September.

Notalgia paresthetica: may κ-opioid receptor agonists be a long-awaited effective therapy?

Until present, there are no treatment possibilities for notalgia paresthetica, a common sensory neuropathy of the back characterised by chronic pruritus. In a phase 2 trial, difelikefalin led to a rapid decrease in pruritus with first effects seen as early as day 1.

Difelikefalin activates κ-opioid receptors on peripheral sensory neurons and suppresses itch, predominantly by a neuromodulation effect. In an intravenous preparation, it is already approved for the treatment of moderate-to-severe pruritus in adults with chronic kidney disease undergoing haemodialysis. In the phase 2 KOMFORT trial (NCT04706975), the κ-opioid receptor agonist difelikefalin in an oral preparation was evaluated for the treatment of moderate-to-severe pruritus in patients with a confirmed diagnosis of notalgia paresthetica, a common sensory neuropathy of the back characterised by chronic pruritus. After a run-in period, participants were treated with difelikefalin (2 mg, twice daily) or placebo for 8 weeks. The primary study endpoint was the change from baseline in the weekly mean change of daily ≥4-point improvement (reduction) in their worst itch numerical rating scale (WI-NRS) at 8 weeks. The double-blind study phase was followed by an ongoing 4-week active extension. Prof. Mark Lebwohl (Icahn School of Medicine at Mount Sinai, NY, USA) presented the 8-week results [1].

At this time, the change from baseline in WI-NRS score was -4.0 for participants treated with difelikefalin versus -2.4 when treated with placebo (P=0.001). "A significant difference was seen as early as day 1," Prof. Lebwohl commented. Difelikefalin was also superior regarding a couple of secondary study endpoints: 41% of participants treated with difelikefalin achieved a ≥4-point improvement in WI-NRS score at week 8 compared with 18% in the placebo group (P=0.007). In addition, 23% of participants treated with difelikefalin experienced a complete response at week 8 compared with 5% for placebo (P=0.008).

The most commonly reported treatment-emergent adverse events with difelikefalin were dizziness and nausea. All adverse events were mild-to-moderate in severity (see Table). "Dizziness was common on day 1 and 2 but disappeared quickly," Prof. Lebwohl pointed out.

Table: Most commonly reported treatment-emergent adverse events in the KOMFORT trial [1]

TEAEs*	Placebo (n=63)	Difelikefalin 2 mg (n=62)
Nausea	7 (11.1%)	8 (12.9%)
Abdominal pain	8 (12.7%)	7 (11.3%)
Headache	3 (4.8%)	7 (11.3%)
Dizziness	2 (3.2%)	7 (11.3%)
Constipation	4 (6.3%)	6 (9.7%)
Increased urine output	1 (1.6%)	5 (8.1%)

TEAEs, treatment-emergent adverse events.

*Safety analyses were conducted in the safety population, which was defined as all randomised patients who received at least 1 dose of study drug.

The study underscores that difelikefalin has the potential to fill an urgent unmet need and warrants further clinical development in notalgia paresthetica, Prof. Lebwohl concluded.

1. Kim BS, et al. A phase 2 study of oral difelikefalin for moderate-to-severe pruritus in subjects with notalgia paresthetica (KOMFORT). D1T01.3I, EADV Congress 2022, Milan, Italy, 7–10 September.

Pharmacotherapy in Hidradenitis Suppurativa: New Opportunities

High potential for secukinumab as next biologic treatment for HS

Blocking IL-17A with secukinumab led to over 40% of patients achieving Hidradenitis Suppurativa Clinical Response (HiSCR) rates, in addition to a reduction in flares, pain, and abscesses. Together with safety data that was consistent with previous trials, these results make secukinumab a probable candidate for the future treatment of hidradenitis suppurativa (HS).

"HS is an incredibly active field at this moment, which is great for advancing and understanding the biology and

the treatments that we will be able to use," Prof. Alexandra Kimball (Harvard Medical School, MA, USA) expressed [1]. She revealed the results of secukinumab assessed in the SUNSHINE (NCT03713619) and SUNRISE (NCT03713632) trials that recruited over 1,000 patients with HS at 219 sites worldwide. "This is only the second phase 3 programme we have ever seen in HS and the first one since 2016, so it really is a milestone," Prof. Kimball highlighted. The 52-week studies assessed secukinumab after a loading phase administered at dosages of 300 mg every 2 (Q2W) or 4 weeks (Q4W) versus placebo, in adult patients with moderate-to-severe HS. Results of the primary endpoint at week 16, i.e. the proportion of patients achieving HiSCR, were presented.

Although the study was conducted during the COVID-19 pandemic, over 90% of the randomised participants completed week 16. Overall, the mean age was 36.2 years, with a higher proportion of older patients in the Q2W arm of SUNRISE (42.8% between 40 and 65 years). Most participants were women and over 50% weighed 90 kg or more. Hurley stage 2 and 3 proportions differed in SUNSHINE versus SUNRISE with 61.4% and 34.0% versus 56.7% and 40.5%, respectively.

In SUNSHINE, 45% in the Q2W arm achieved HiSCR versus 33.7% on placebo (P=0.0070), while the Q4W arm did not reach the predefined significance threshold. The SUNRISE participants of both treatment groups attained significant HiSCR results with 42.3% (Q2W; P=0.0149) and 46.1% (Q4W; P=0.0022) versus 31.2% on placebo. With regard to reduction of abscesses and nodules, the same treatment groups of the 2 studies demonstrated statistically significant results (see Figure).

One-sided nominal p-values are based on an ANCOVA, the secondary estimand and multiple imputation. Error bars represent SE.

"The top line news here is fabulous: patients are getting better and both studies met their primary endpoint," Prof. Kimball stressed. She furthermore accentuated that not only flaring decreased on the study drug but also pain. In the pooled analysis of pain development within the 2 trials, 38.9% in the Q2W programme achieved a 30% reduction of pain from baseline, significantly more than on placebo (26.9%; P=0.0031). Moreover, a clinically meaningful amelioration of quality-of-life was seen as early as week 2 in an exploratory analysis. As for adverse events, the studies did not reveal unexpected results. "Very reassuring safety data, consistent with what we have seen before and a very clean profile overall," Prof. Kimball stated.

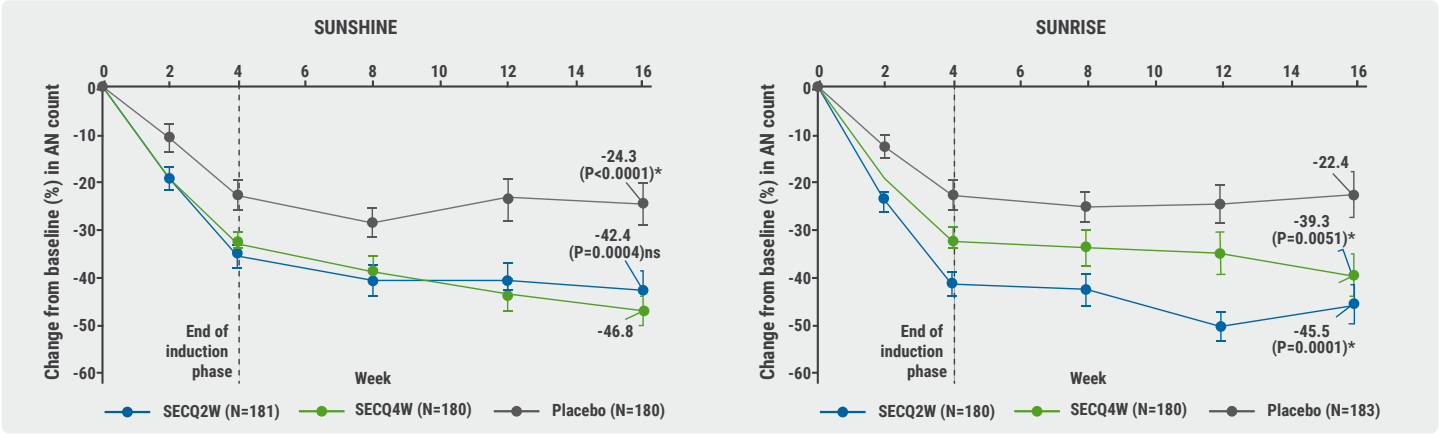
"We expect secukinumab to be a new, safe, and effective addition to our armamentarium in treating HS," she concluded.

1. Kimball A. LBA Secukinumab in moderate to severe hidradenitis suppurativa: Primary endpoint analysis from the SUNSHINE and SUNRISE Phase 3 trials. D3T01.1A, EADV Congress 2022, Milan, Italy, 7–10 September.

Hidradenitis suppurativa: TYK2/JAK1 inhibitor shows promise

Out of 3 parallel tested kinase inhibitors, only brepocitinib met its primary efficacy endpoint of the Hidradenitis Suppurativa Clinical Response (HiSCR) score in a phase 2b study. The TYK2/JAK1 inhibitor also significantly reduced hidradenitis suppurativa (HS) flares.

Figure: Effect of secukinumab on abscess and inflammatory nodule [1]



*, significant compared with placebo; ns, non-significant compared with placebo.
AN, abscess and inflammatory nodule; ANCOVA, analysis of covariance; N, number of patients in group; Q2W, every 2 weeks; Q4W, every 4 weeks; SE, standard error; SEC, secukinumab 300 mg; Wk, week.

"We will look back on this meeting as an important milestone in our understanding of both the treatment and pathophysiology of HS," Prof. Alexandra Kimball (Harvard Medical School, MA, USA) opened her talk on an umbrella study in HS [1]. This study design, novel to dermatology, was used to investigate 3 experimental agents with different modes of action versus placebo in a phase 2b trial (NCT04092452) on patients with moderate-to-severe HS, i.e. Hurley stages 2 and 3. A total of 194 participants were included in the different treatment and placebo groups of this umbrella study. "This design allows you to pool the placebo groups to evaluate against all the different measures at the end," Prof. Kimball explained. The active study drugs included the IRAK4 inhibitor PF-06650833 (400 mg/day), the TYK2 inhibitor PF-06826647 (400 mg/day), and the TYK2/JAK1 inhibitor brepocitinib (45 mg/day). The primary endpoint consisted of the percentage reaching HiSCR at week 16, which stands for a 50% reduction in abscesses and inflammatory nodules compared with baseline.

The mean participant age in the various groups ranged from 37-40 years, BMI from 35.12 to 36.64, and 72.3-87.5% were women. Within the ethnically diverse population, 61.5-72.3% had Hurley stage 2, 20.8-23.4% were previous inadequate responders to anti-TNF, and 10.6-14.6% concomitantly used antibiotics.

The results revealed only significant outcomes for brepocitinib: 51.9% achieved HiSCR versus 33.3% on placebo ($P_{one\text{-}sided}$= 0.0298). The rate of brepocitinib responders differed according to stage with 59.4% responders in Hurley stage 2 and 40% in Hurley stage 3. In addition, brepocitinib significantly reduced the percentage of patients with ≥1 flare compared with placebo (-22.3%, $P_{one\text{-}sided}$= 0.0064). All agents were deemed generally safe and well tolerated, as most observed adverse events were mild or moderate.

"We have been able to test 3 different modalities, this tells us some things about the pathophysiology for HS, which is a very profoundly intense inflammatory process and may require multiple modalities of action to get it under control," Prof. Kimball expressed as part of her conclusion.

1. Kimball A. Efficacy and safety of 3 different kinase inhibitors: brepocitinib (TYK2/JAK1 inhibitor), IL-1 receptor associated kinase 4 (IRAK4) inhibitor, and Tyrosine kinase 2 (TYK2) inhibitor in patients with moderate to severe hidradenitis suppurativa in a Phase 2a umbrella study. 3J, EADV Congress 2022, Milan, Italy, 7–10 September.

Best Of The Posters

Genital psoriasis: high prevalence, often underdiagnosed

According to a cross-sectional survey of patients in the German PsOBest registry, genital psoriasis or psoriasis in other areas of sexual interest is very common. Affected patients often suffer from sexual dysfunction but rarely discuss this problem with their dermatologist.

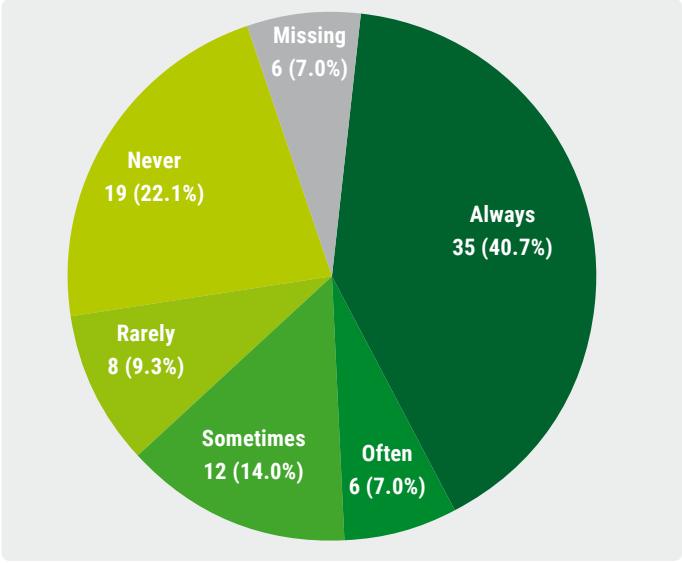
The reported prevalence of genital psoriasis or psoriasis in other areas of sexual interest in individuals already diagnosed with psoriasis varies widely in the literature (17–64%) [1-4]. Dr Toni Klein (University Medical Center Hamburg-Eppendorf, Germany) wished to further explore the prevalence of genital psoriasis and its impact on patients' sexual life [5].

A cross-sectional survey was conducted by sending questionnaires to a random sample of patients registered in the PsOBest registry (NCT01848028) in Germany. Included in the questionnaires were the Genital Psoriasis Symptom Scale (GPSS), which evaluates the severity of 8 genital psoriasis symptoms and the Genital Psoriasis Sexual Impact Scale (GPSIS), which assesses whether patients avoid sexual activity because of genital psoriasis and level of worsening of genital psoriasis symptoms following sexual activity. Moreover, the researchers included questions exploring both generic and psoriasis-specific reasons for sexual impairment (RSI).

From the 2,010 questionnaires that were sent out, the team received 811 responses (40.3%) and analysed 795 (39.6%). Of these, 41.9% were filled in by women, 51.6% by men, and 6.5% did not report their gender. The mean age at onset of psoriasis was 26.6 years and the mean age for the onset of genital psoriasis was 35.0 years, and for psoriasis in other areas of sexual interest 34.1 years.

During the previous 24 months, 1/5 participants experienced genital psoriasis, whilst nearly half experienced psoriasis at any other areas of sexual interest. Genital psoriasis and psoriasis at any ASI had a remarkable impact on sexual function: A majority of participants with genital psoriasis suffered from sexual impairment in the last 30 days and this led to 12.8% of participants avoiding sex altogether, and 40.7% of participants avoiding sex during the last week (see Figure). Despite its high impact, only a quarter of these participants discussed having sexual impairments with their dermatologists.

Figure: Proportion of genital psoriasis patients avoiding sexual activities within the past week [5]



Dr Klein and her team concluded that dermatologists should be aware of the high prevalence of genital psoriasis. Therefore, genital areas shouldn't be neglected when examining patients as psoriasis in this location impairs quality-of-life and often leads to sexual dysfunction.

1. Da Silva N, et al. Eur J Dermatol 2020;30:267-78.
2. Da Silva N, et al. J Eur Acad Dermatol Venereol 2020;34:1010-1018.
3. Da Silva N, et al. PLos Online 2020;15:e0235091.
4. Augustin M, et al. Br J Dermatol 2019;181:358-65.
5. Klein TM, et al. Epidemiological Survey on the Prevalence of Genital Psoriasis and Its Impact on Patients' Sexual Life in Routine Care. P1564, EADV Congress 2022, Milan, Italy, 7–10 September.

High rate of non- or partial responders jeopardises therapeutic success in HS

A real-world study revealed that in daily practice more than half of the patients with hidradenitis suppurativa (HS) show only a partial response when treated with adalimumab. Consequently, partial/non-responders still have a significant burden of disease and it has a higher impact on their quality-of-life.

The TNF-blocker adalimumab was approved for HS following the positive results of the phase 3 PIONEER I (NCT01468207) and II (NCT01468233) trials. But is this biologic also effective in daily practice, where patients differ markedly from those included in clinical trials? To address this issue, Dr Hayley Wallinger (Adelphi Real World, UK) and her team examined the real-world data drawn from the Adelphi HS Disease Specific Programme (adelphirealworld.com), a point-in-time survey of physicians and their consulting HS patients conducted in the USA, France, Germany, Italy, Spain, and the United Kingdom between November 2020 and April 2021 [1].

Physicians provided clinical characteristics, treatment history, and disease stage, whereas patients completed a questionnaire that included details on quality-of-life and work productivity. "We aimed to assess ongoing unmet needs among HS patients receiving biologic therapy," Dr Wallinger explained. The team selected the patients receiving a biologic for at least 16 weeks and had moderate-to-severe disease at the initiation of the treatment. Participants were analysed in 2 groups based on their subjective disease severity: currently mild (responders) versus currently moderate-to-severe (partial/non-responders; PNRES). Out of the 401 participants, 148 were PNRES.

The analysis revealed that a higher proportion of PNRES (62.8%) were in a more severe disease state at the initiation of a biologic than the responders were (38.7%; P<0.0001). The mean number of symptoms currently experienced was significantly higher in PNRES compared with responders (4.6 vs 2.0; P<0.0001), as were the number of body areas affected and the proportion of patients showing flares. Similarly, a higher proportion of PNRES experienced physician-reported general pain/discomfort, restricted/painful limb movements, pain on sitting, inflammation, and drainage. Physicians expressed their dissatisfaction with patients' current HS control in 46.0% of those in the PNRES group compared with 5.9% in the responders's group (P<0.0001). Patients who were considered PNRES reported significantly worse health-related quality-of-life (HRQoL) and Work Productivity and Activity Index (WPAI) due to HS.

This high degree of unmet needs in PNRES observed in this survey suggests the necessity of novel treatments with a better response, which may reduce the burden of moderate-to-severe HS.

1. Wallinger H, et al. Unmet needs among hidradenitis suppurativa patients receiving biologic therapy in the United States of America and Europe by response status: Analysis of a real-world dataset. P0035, EADV Congress 2022, Milan, Italy, 7–10 September.

Decreased overall survival in melanoma patients with low vitamin D

A Spanish study found an independent association of vitamin D deficiency and worse overall survival in patients who were diagnosed with melanoma. This relationship remained when possible confounders like age, gender, season of vitamin measurement, and Breslow index were included in the analysis.

Is there a relationship between vitamin D levels and the prognosis of melanoma patients? This was the question that Dr Inés Gracia-Darder (Son Espases University Hospital, Spain) and her colleagues strove to answer in a retrospective cohort study [1,2]. The 264 investigated patients were treated between 1998 and 2021 for invasive melanoma in the Hospital Clinic in Barcelona and had their 25-hydroxyvitamin D3 levels determined after diagnosis. The study participants were assigned to 1 of 2 groups: those with a vitamin D level <10 ng/mL deemed 'vitamin D deficient' and those with levels ≥10 ng/mL, who were referred to as 'normal/insufficient'. Not only the potential association of overall survival but also the melanoma-specific survival with the plasma levels of vitamin D were analysed.

The baseline characteristics were not significantly different between the study groups. The median age was 57.5 years, 54.2% of participants were women, and the majority had a skin phototype 2 or 3-4. Regarding the melanoma specifics, 63.8% had a superficial spreading subtype, median Breslow index was 1.50 mm, and most tumours were situated on trunk and extremities (45.7% and 34.5%). In more than half of the participants, vitamin D had been measured between October and March.

The results established a reduced overall survival for participants who were vitamin D deficient in the univariate data assessment with an HR of 2.34 (P=0.007). This finding was corroborated in the following multivariate regression that adjusted for possible confounders like age, gender, season of vitamin measurement, and Breslow index (HR 2.45; P=0.007). Interestingly, having a deficiency in vitamin D did not lead to a decreased melanoma-specific survival in both the univariate and the multivariate analysis (P=0.511 and P=0.629). "Previous research has identified that normal levels of vitamin D play a protective role in melanoma survival, and this study aimed to further understand this relationship. Our findings suggest that vitamin D has a significant impact on people with melanoma, showing in particular that vitamin D deficient patients have a lower overall survival, independent of several confounders" Dr Gracia-Darder commented.

Considering these results, more insights are desirable to establish the definite role of vitamin D deficiency in melanoma. The currently active, Belgian, phase 3 ViDMe trial (NCT01748448) that investigates the influence of vitamin D supplementation on malignant melanoma after surgical removal of the primary tumour could shed more light on this matter.

1. Garcia-Darder I, et al. Worse overall survival associated with vitamin D deficiency in melanoma patients. P0762, EADV Congress 2022, Milan, Italy, 7–10 September.
2. Garcia-Darder I, et al. Melanoma Res. 2022;32(5):384-387.