Medicom International Conference Series in Dermatology

2019 AAD Annual Meeting

American Academy of Dermatology

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PEER-REVIEWED CONFERENCE REPORT

Late Breakers
IL-1α is a novel promising therapeutic target in atopic dermatitis; a dual IL-17A/F blocker showed unprecedented efficacy in psoriasis; and a Bruton's tyrosine kinase inhibitor seems to be active in pemphigus.

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JAK Inhibitors: a New Frontier
More than 50 cytokines use the JAK/STAT signaling pathway. The novel JAK inhibitors have already shown activity in dermatologic indications like alopecia areata and atopic eczema.

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Hair Loss: No Reason for Therapeutic Nihilism
Hair loss is extremely distressing, particularly for women. Combination therapy is most successful; and recent trials demonstrate efficacy of platelet-rich plasma injections.

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MEDICOM MEDICAL PUBLISHERS

Editor Prof. Peter van de Kerkhof, Radboud University Medical Center, the Netherlands

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Letter from the Editor

Prof. Peter van de Kerkhof

Dear Reader,

The 2019 AAD Annual Meeting was a meeting filled with broad innovations covering the entire field of dermatology. In this report, you will find several highlights.

Innovation in dermatology is no longer limited to a few areas. For example, innovations in psoriasis have expanded to atopic dermatitis, hidradenitis suppurativa, urticaria, and vitiligo. Important innovations are biologics with different targets but also small molecules, including Janus kinase inhibitors. In particular, several IL-17 and IL-23 blockers have opened new perspectives for long-term control of psoriasis. Anti-IL-4 and IL-13 are the new options for the treatment of atopic dermatitis.

Also covered in this conference report are new leads in hair loss, vitiligo, and non-melanoma skin cancers. The classical treatments and low-level laser light therapy for alopecia androgenetica, as well as the value of dermatoscopy in hair diseases were highlighted. Janus kinase inhibitors for vitiligo offer new options in this frequent disease, which often is so difficult to treat. For the treatment of acne, there was a focus on hormone therapy and a new narrow-spectrum tetracycline: sarecycline.

The AAD 2019 was a large educational event where new innovations were presented and classical treatments were positioned in the perspective of personalised treatment.

Best Regards,
Peter CM van de Kerkhof
Radboud University Nijmegen Medical Centre, the Netherlands

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 practise research; and personalised medicine.

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Dermatology in the future: **Access to the right drug will be a global challenge**

Interview with AAD president
Prof. George J. Hruza
conducted by Dr Susanne Kammerer

President of the American Academy of Dermatology, Adjunct Professor at St Louis University, and Director of the Laser & Dermatologic Surgery Center in St Louis, USA.

Prof. Hruza, what are your highlights of this AAD meeting?

This is a though question. About 18,000-20,000 people came to the meeting, including 9,500 medical professionals and a huge international presence. Talks are all about the new stuff, like the biologic drugs enabling us to treat inflammatory diseases such as psoriasis and atopic dermatitis better than ever before. There are also exiting new developments in skin cancer treatment, as drugs for advanced squamous cell carcinoma of the skin have come out for the first time. There are also new technologies. I just saw an ad for a device that induces rapid whole-body muscle contractions, so people could get tight muscles without even going to the gym. In the procedural area, I learned about an investigational drug for cellulite that breaks up the collagen bands after being injected into the bands so that dimpling is reduced. And there are of course advocacy matters, especially in the US where we have big issues with cost of medications.

How can you insure access to the right drugs?

It's not easy. We have these revolutionary medicines to treat psoriasis or atopic dermatitis. Yet, the costs can be quite prohibitive. The insurers oblige us to follow the so-called "step therapy", but it really is "fail first therapy". We have to put patients through all the older medications and their inherent potential side effects, just to prove that they fail and the patients have to go on suffering until then. I think this is just not the right way to go. We also have to deal with pre-authorisations. In the US, we have hundreds of medications that must be approved by the insurers, even generic ones, before treatment. This is totally ridiculous and a waste of time, staff, and resources, as in 90+% of cases they finally approve it. We are fighting these restrictions in all the states and at the federal level.

With all the online possibilities, do you think it is still worth to attend an AAD meeting?

If you want to learn about, for example, some specific drug, this is to some extent possible online. However, there are important other aspects. One is the possibility of a live connection to an expert speaker whom one can ask questions in real time. It is so much more effective than online watching; even if online questions are possible. The actual exchange is important; be it during the session or afterwards as the speakers often stick around for questions. The other part is the interaction with other dermatologists on a personal level: it is so important and valuable. I think most people feel the same, as our meeting gets bigger and better every year.

What is your most important goal as president of the AAD?

My mission is to help my fellow dermatologists to maintain and, if necessary, recapture their "joy of dermatology". I have been doing my work for over 30 years and I still love it every day: interacting with the patient, keep on learning, trying new things. However, in the US, we are having a lot of regulatory and electronic health record hassles resulting in the fastest rate of burnout among medical specialists. For me, the Academy's role is to be a bit of a cheerleader that also tries to reduce some of these burdens such as providing templates for automated prior authorisation or helping with electronic health record issues.

What is the major future challenge in dermatology?

In the US, very few dermatologists are now going into private practice; they are mostly employed by hospitals, universities, private equity-backed groups, and even insurance companies. So, there is a loss of independence. Those dermatologists may be thinking that their employer will take care of all the regulatory burden and advocate for them, which is not true but could reduce their bond to the Academy.

In the long term, our big challenges with augmented intelligence have just started. Dermatology is a visual field and computers can be used to analyse images. A software programme has already shown that it could determine if something is benign or malignant; in some cases even better than a dermatologist. But while many of our members see this as a threat, I think we need to embrace it as a tool that we integrate into our work. It is never going to replace our experience, our judgement, and most importantly the connection to the patient. I think that patients want, even crave, the human connection, and we have to make sure they have access to it. At the moment, however, we do not have enough dermatologists in the US. The average wait time to see a dermatologist is 77 days.

Late-Breakers

Secukinumab maintains improvements in psoriasis through 5 years of treatment

At the 2019 AAD meeting, 5-year follow-up data from the extension cohort of the phase 3 core trials ERASURE/FIXTURE was presented that showed that the IL-17A blocker secukinumab maintains long-term high levels of efficacy [1, 2].

Patients from the ERASURE/FIXTURE trials who gained a 75% response in the Psoriasis Area and Severity Index (PASI) were randomised in 2:1 ratio at week 52 to either the same dose of secukinumab (300 mg/150 mg, continuous-treatment) or placebo (treatment-withdrawal) every 4 weeks, until week 156 or relapse, defined as a >50% reduction in maximal PASI from core study baseline. Patients experiencing relapse with placebo received secukinumab. At week 156, all patients received open-label secukinumab treatment with those on 300 mg continuing 300 mg and those on 150 mg opting to receive 150 mg or 300 mg.

PASI responses were sustained with secukinumab until week 260 (PASI 75/90/100: 85.1%/67.2%/37.8%). "Over 60% of patients were clear or almost clear according to the global assessment of the investigators up to 5 years," said Prof. Richard Langley (Dalhousie University, Canada) during the presentation. In patients treated with 300 mg secukinumab, the mean PASI score was 2.2 at week 260. In addition, secukinumab had a favourable safety profile with no increase in adverse events over time. Long-term treatment with secukinumab revealed no new safety signals. In addition, the treatment had a long-term favourable effect on quality of life.

1. Langley RG, et al. N Engl J Med 2014;371:326-38.
2. Langley RG. Abstract 10052, AAD Annual Meeting, 1-5 March 2019, Washington DC, USA.

Bermekimab - a future treatment for atopic dermatitis?

Atopic dermatitis (AD) involves barrier defects of the epidermis as well as skin inflammation and is often characterised by a debilitating itch. The role of interleukin-1 alpha (IL-1α) is not yet completely understood. "It is not clear what role IL-1α plays in skin, but it is already an important player in oncology," said Prof. Eric Simpson (Oregon Health & Science University, USA) during his presentation [1].

The new anti-IL-1α antibody bermekimab binds to all forms of IL-1α and neutralises it without targeting IL-1ß. A total of 38 patients with moderate-to-severe AD who did not show adequate response to topical corticosteroids were included in the trial. After a washout phase, they received weekly subcutaneous injections of 200 mg or 400 mg of bermekimab. The treatment period lasted 4 (200 mg) or 7 (400 mg) weeks with follow-up until week 9. Primary endpoint was drug safety and tolerability. Secondary endpoints included multiple disease severity measurements.

The higher dose showed to be more effective: mean clinical improvement assessed by different AD scores including EASI (Eczema Area and Severity Index), SCORAD (Severity Scoring of Atopic Dermatitis), GISS (Global Individual Signs Score), and IGA (Investigator Global Assessment) was 51% in the 400 mg cohort compared with 17% in the 200 mg group. Significant improvements were seen in all single scores. In addition, quality of life, assessed by the DLQI (Dermatology Life Quality Index), improved by 70%. At week 7, 25% of patients treated with 400 mg had a ≥2-point amelioration in IGA reaching nearly clear or clear skin (IGA 0/1). At this time, 82% of patients achieved an improvement of the EASI score by 50%, and 71% of patients had a 75% improvement in the EASI score.

Rapid itch reduction

In addition, bermekimab showed a remarkable antipruritic effect: 75% of patients treated with the higher dose reached a ≥4-point reduction on a numerical rating scale (NRS) for worst itch, and average itch scores at weeks 7 were also lower compared with baseline. "Targeting IL-1α with this drug in adults with moderate-to-severe AD really showed a nice early signal for improved signs and symptoms. The rapid reduction in itch and pain may be caused by the role of IL-1α in nerve potentiation," suggested Prof. Simpson. Drug related toxicities were not apparent, but injection site reactions occurred in 3 patients. Based on the results, bermekimab will be further investigated in phase 3 studies as a novel treatment for AD.

1. Simpson E. Abstract 11191, AAD Annual Meeting, 1-5 March 2019, Washington DC, USA.

JAK1/2 inhibitor effective in alopecia areata

The Janus kinase (JAK) inhibitor CTP-543 showed promising results in patients with moderate-to-severe alopecia areata (AA) according to interim results from a phase 2a study [1]. CTP-543 inhibits both JAK1 and JAK and is a modified version of the JAK inhibitor ruxolitinib, currently approved for the treatment of myelofibrosis and polycythaemia. In total, 104 adults with AA having at least a ≥50% hair loss were randomised to receive 4 or 8 mg CTP-543 twice daily or placebo for 24 weeks. Primary efficacy endpoint was a 50% relative reduction in Severity of Alopecia Tool (SALT) score from baseline to 24 weeks. Significantly more patients in the 8 mg group reached this endpoint compared with placebo (47.0% vs 8.6%; P<0.001). "Curves split after 16 weeks with the 8 mg dose, but we still see a steep increase of response until week 24," explained James Cassella (Concert Pharmaceuticals, USA). An analysis according to subtype of AA showed a similar overall scalp regrowth response rate between patchy AA and alopecia universalis and alopecia totalis.

The JAK inhibitor was generally well tolerated with headache, cough, upper respiratory tract infections, acne, and nausea being the most common adverse events. No serious adverse events were reported. Due to these positive interim results, the company will begin an open-label trial to test whether the JAK inhibitor in a dose of 16 mg once daily is as effective as the 8 mg twice-daily dose.

1. Cassella J. Abstract 11291, AAD Annual Meeting, 1-5 March 2019, Washington DC, USA.

Novel anti-IgE drug enables durable urticaria control

In a previous phase 2b study (NCT02477332), the anti-IgE drug ligelizumab achieved greater control of symptoms compared with omalizumab and placebo in patients with chronic spontaneous urticaria (CSU) inadequately controlled with standard of care including H1-antihistamines for up to week 20 (last treatment at week 16). The results of an open-label 1-year extension study were presented, and more than 50% of CSU patients treated with ligelizumab had complete symptom control [1].

As much as 70.6% (226/320) of patients entered the extension study, with 88.9% (201/226) completing 1 year of treatment. Efficacy of therapy was assessed on the 7-day urticaria activity score (UAS7). During the first 12 weeks of the extension study, 52.2% of patients treated with ligelizumab attained a complete symptom control (UAS=0). "Complete responses were sustained and over half of the patients achieved UAS=0 at the end of week 52," said Dr Diane Baker (Baker Allergy, Asthma, and Dermatology Clinic, USA). Throughout the 1-year treatment period, 75.8% of patients cumulatively experienced complete symptom control at least once by the end of the extension study.

1. Baker D. Abstract 11224, AAD Annual Meeting, 1-5 March 2019, Washington DC, USA.

Dual IL-17A and IL-17F blocker leads to unprecedented response rates in psoriasis

Data from a randomised extenstion study showed that patients with moderate-to-severe plaque psoriasis attained durable complete and near-complete responses for more than a year with a dual inhibitor of IL-17 [1]. Both IL-17A and IL-17F are expressed in psoriasis lesional skin and have the ability to synergise with other cytokines to amplify inflammation. This is the pathogenetic rationale to block IL-17F in addition to IL-17A. Bimekizumab is an antibody that neutralises the biologic function of both.

In the original 12-week BE ABLE 1 study previously presented, therapy with bimekizumab led to rapid, substantial clinical improvements in patients with moderate-to-severe plaque psoriasis [2]. More than 70% of patients treated with 160, 320, or 480 mg bimekizumab reached an improvement of the PASI by 90% (PASI90 response) in this trial. At this year´s AAD meeting, results were presented of the phase 2b extension study BE ABLE 2 after 60 weeks of follow-up [6]. In this extension, almost all patients who initially had PASI90/100 with bimekizumab maintained the responses during 60 weeks of follow-up. Similarly, patients who switched from placebo to bimekizumab and attained PASI90/100 responses maintained the status long-term. Across all doses evaluated in the study, 80-100% of responding patients remained in response at 60 weeks. "We have not seen responses like this," said Dr Andrew Blauvelt (Oregon Medical Research Center, USA). "In addition, we have a consistent safety profile, as would be expected with an IL-17 blocker. These results really support the view that IL-17A and IL-17F blockade is useful in psoriasis."

The most frequent treatment-emergent adverse events were oral candidiasis and nasopharyngitis (13% each). All cases of oral candidiasis were localised, superficial infections of mild or moderate intensity that resolved with standard treatment. No serious treatment-emergent adverse events occurred in more than one patient. These results validate dual

neutralisation of IL-17A and IL-17F as a new therapeutic approach, which might result in slightly improved efficacy compared with IL-17A blockade alone.

1. Blauvelt A. Abstract 11180, AAD Annual Meeting, 1-5 March 2019, Washington DC, USA.
2. Papp K, et al. J Am Acad Dermatol 2018; 79:279-86.

Thicker AK lesions benefit from laser pretreatment with high channel density

Photodynamic therapy (PDT) is an approved treatment of actinic keratosis (AK). A study showed that ablative fractional laser pretreatment can enhance its efficacy: a high laser channel density should be chosen in patients with hyperkeratotic lesions [1].

AK is an intraepidermal proliferation of dysplastic keratinocytes that develops in response to chronic exposure to UV radiation. There are numerous treatment methods. One of the most effective is PDT, which involves the use of a topical photosensitising agent such as methyl aminolevulinate (MAL) before exposure to an activating light source to generate reactive oxygen species that lead to cell death. However, stratum corneum is a major barrier for drug permeation, thus decreasing transdermal MAL uptake. Therefore, different pretreatment options have been assessed to enhance PDT efficacy, including microdermabrasion, microneedling, and ablative fractional laser pretreatment. The latter has been shown in a previous study to be effective in enhancing the penetration and accumulation of photosensitisers [2].

In the present study, Dr Yeo-Rye Cho (Dong-A University Busan, Korea) and her colleagues assessed whether there are differences dependent on the chosen laser channel density of the microscopic ablation zones. Korean patients (n=47) with 312 AK lesions were enrolled in the study and treated with 5.5% ablative fractional laser (AFL)-PDT, 11% AFL-PDT, or 22% AFL-PDT and received 1 session of PDT after AFL therapy. Treatment efficacy was determined based on the regression of lesions over time; and accumulated levels of bioconversion to protoporphyrin IX (PpIX), side effects, and cosmetic outcomes were assessed.

Higher channel density associated with higher response rates

No difference was observed in the protoporphyrin IX accumulation between the different groups. "Obviously, the lowest channel density was sufficient to achieve maximum drug penetration," said Dr Cho. However, a significant difference between the complete response rate at 3 months, and in particular at 12 months were noted. After a year, 60.9% of the patient in the 5.5% group compared with 74.0% in the 11% group, and 81.1% in the 22% group showed a complete response (P=0.003). Most benefits were noticed in patients with Olsen grade III lesions, a score for AK that grades severity/thickness of individual AK lesions. After 12 months, 38.2% in the 5.5% group compared with 57.1% in the 11% group and 68.8% in the 22.0% group showed a complete response (P=0.043). "Patients with thick lesions seem to benefit most from the 22% density as the debulking effect is more pronounced," said Dr Cho. There were no differences with regard to side effects; rates of erythema were similar in all 3 groups. In addition, the cosmetic effect was comparable. There were no differences with regard to side effects; rates of erythema were similar in all three groups. In addition, the cosmetic effect was comparable.

"As AK with severe hyperkeratosis showed a better long-term complete response rate with lesser recurrences, we recommend AFL with higher laser channel density when AFL-PDT is used to treat AK with severe hyperkeratosis," concluded Dr Cho.

1. Cho Y-R. Abstract 11263, AAD Annual Meeting, 1-5 March 2019, Washington DC, USA.
2. Ko DY, et al. J Eur Acad Dermatol Venereol 2014;28:1529-39.

New standardised cantharidin product against molluscum contagiosum efficacious in two phase 3 trials

The two trials CAMP-1 and CAMP-2 demonstrated a high efficacy of VP-102, a topical therapy containing a solution of 0.7% cantharidin in a novel, single-use applicator to treat and eradicate molluscum contagiosum (MC) [1].

MC is a common and highly contagious skin disease. Since it is self-limited in healthy individuals, treatment is not always necessary. Nonetheless, issues such as lesion visibility, underlying atopic disease, and the desire to prevent transmission may prompt therapy. "Sometimes the infection persists for over 2 years, so there is a medical need for an approved treatment for this disease," said Prof. Lawrence Eichenfield (University of California, San Diego School of Medicine and Rady´s Children´s Hospital, USA).

Current treatment consists of cryosurgery curettage followed by cantharidin treatment. P102 is a novel standardised cantharidin product with a special applicator that allows precise dosing of MC lesions. It contains a visualisation agent to identify which lesions have been treated. The active ingredient cantharidin is a naturally occurring vesicant that

causes degeneration of the desmosomal plaque through protease activation. Another advantage of this novel product is its long-term stability at room temperature.

Prof. Eichenfield presented two randomised, double-blind, multicentre, placebo-controlled trials that evaluated the efficacy of VP-102 compared with placebo in subjects with MC. In total, the trials enrolled 528 subjects age 2 and older with MC at 31 centres in the United States. Subjects were treated once every 21 days with topical solution of 0.7% cantharidin for up to 4 applications. Complete clearance of molluscum lesions was evaluated by assessment of the number of lesions at study visits over 12 weeks.

After this time, 46% of subjects treated with VP-102 in the CAMP-1, and 54% percent of participants treated in the CAMP-2 trial achieved complete clearance of all treatable molluscum lesions vs 18% and 13% of subjects in the placebo groups (P<0.0001 in both studies). By day 84, VP-102 treated subjects had a 69% and 83% mean reduction in the number of molluscum lesions, a pre-specified endpoint, in CAMP-1 and CAMP-2 respectively, compared with a 20% increase and a 19% reduction for patients on the vehicle cream.

VP-102 was well tolerated in both trials; most adverse events were in the mild category in both studies. "An approved therapy that can minimise molluscum infection would be certainly very helpful for our patients and their parents," concluded Prof. Eichenfield.

1. Eichenfield LF. Abstract 11251, AAD Annual Meeting, 1-5 March 2019, Washington DC, USA.

Increased cancer risk for patients with keloids

A nationwide Taiwanese cohort study identified an augmented cancer risk in subjects with keloids when compared with those with normal wound healing [1].

Keloids are the result of abnormal wound healing that may happen after damage to the dermis due to trauma or injury. They are characterised by benign, fibrous proliferations that extend beyond the initial wound margins. The rationale for investigating a possible association between keloids and the risk for cancer was based on the knowledge that cancerous cell growth often starts in a sclerotic microenvironment. One focus of the investigation was placed on the occurrence of skin cancer. Data from almost 780,000 persons with an about equal distribution of males and females was analysed. In total, 17,401 adults with keloids were matched according to gender and age with 69,604 controls without keloids. Statistical identification of the relative risk for cancer was established using a Cox proportional hazards model. Both groups were comparable with regard to baseline characteristics.

In sum, 893 cases of cancer were newly diagnosed within the keloid group during the study years 1998-2010. This resulted in a 50% augmented overall cancer risk for the keloid-bearing study population. The overall relative risk for skin cancer turned out to be 1.73 in patients with a keloid. This risk was even higher for the males who had more than a 2-fold risk for skin cancer (relative risk 2.16). Women with keloids had an elevated risk for pancreatic cancer. Even after adjusting for known risk factors like liver cirrhosis, diabetes mellitus, and chronic pancreatitis, women with keloids still had a more than double the risk (relative risk 2.19). The authors suggest regular skin screenings in men and women with keloids, as well as ultrasound diagnostics for females as a preventive measure.

1. Hong KCH. Abstract 11228, AAD Annual Meeting, 1-5 March 2019, Washington DC, USA.

Bruton's tyrosine kinase inhibitor highly effective in pemphigus vulgaris

An oral inhibitor of Bruton's tyrosine kinase (BTK) together with very low-dose prednisone induces control of disease activity in patients with pemphigus at 12 weeks. This was the shown in the phase 2 Believe-PV proof of concept study [1]. The current standard of care is high-dose corticosteroids with prednisone-equivalent doses of ≥1 mg/kg with high toxicity and/or rituximab plus moderate-to-high initial doses of corticosteroids (≥0.5-1mg/kg).

"Despite the recent FDA approval of rituximab for moderate-to-severe pemphigus, there remains an unmet need for a quick-acting, steroid-sparing, anti-inflammatory treatment for this rare disease," said Prof. Dedee Murrell (University of New South Wales, Australia). BTK inhibition interrupts multiple signalling pathways in immune cells, but not in T cells. In this way, B cell function can be impaired without reducing B cells directly. The agent proved also to be effective in naturally occurring pemphigus in dogs, even without corticosteroids.
The presented study included 27 patients with mild-to-severe pemphigus with an average duration of 6 years. Of these, 18 patients had relapsing disease and the remainder had newly diagnosed pemphigus. A majority (16 patients)

had severe disease, as assessed by the standardised Pemphigus Disease Activity Index (PDAI) corresponding to a score of ≥15. Only 1 patient was negative for anti-desmoglein antibodies.

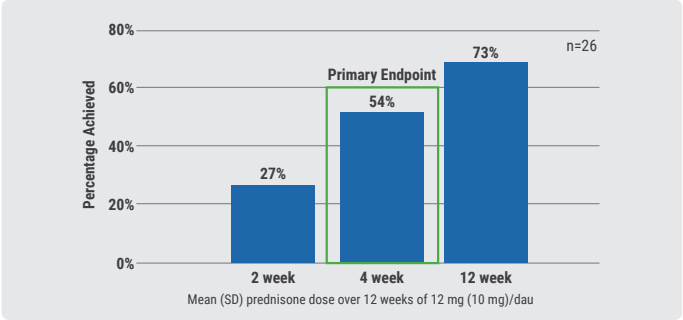
The mean corticosteroids dose at baseline was 14 mg/day, although that ranged from no steroids to 30 mg/day. The study consisted of a 12-week treatment phase and a 12-week follow-up phase. The primary endpoint was control of disease activity at day 29 as evidenced by no new lesions while on ≤0.5 mg/kg/day of corticosteroids. Secondary endpoints were complete remission, minimisation of prednisone usage, change in anti-desmoglein autoantibody levels, and clinical assessments including the PDAI and the Autoimmune Bullous Skin Disorder Intensity Score.

By the end of week 4, 54% of patients had achieved the primary endpoint, and 73% of patients reached the primary endpoint by the end of week 12 (see Figure). During this period, the mean prednisone dose was 12 mg/day. In addition, therapy was associated with up to a 65% median reduction in autoantibody levels at week 12. The agent demonstrated a favourable tolerability and risk/benefit profile.

"Obviously, the agent has the potential to eliminate or at least significantly reduce the need of corticosteroids in pemphigus patients that have very few treatment options," concluded Prof. Murrell. The clinical efficacy demonstrated in the Believe-PV trial in combination with a favourable safety profile supports the further development of the molecule. Currently the company is recruiting patients for a phase 3 trial.

1. Murrell D. Abstract 10086, AAD Annual Meeting, 1-5 March 2019, Washington DC, USA.

Figure: The Bruton's tyrosine kinase inhibitor achieves control of disease activity in patients with pemphigus within a treatment period of 4 weeks [1]



SD, standard deviation. Primary endpoint: CDA within 4 weeks on low dose corticosteroids (low dose equals less than 0.5 mg/kg/day). mITT used to report CDA rates, excluding 1 patient who dropped out due to treatment-emergent adverse events. Figure kindly provided by Dr Murrell.

Serlopitant reduces pruritus associated with psoriasis

Although many physicians associate pruritus primarily with atopic dermatitis, it is also very common in psoriasis where the majority of patients (60-90%) suffer from itch [1].

"Patients consider pruritus one of the most important and troublesome symptoms of psoriasis, affecting their daily activities and emotional wellbeing," said Dr David Pariser (Pariser Dermatology Specialists Virginia, USA) during his presentation of the trial. At present, treatments for psoriasis do not consistently alleviate associated pruritus. Serlopitant is an oral, once daily neurokinin-1 receptor antagonist that demonstrated significant reduction in pruritus in phase 2 studies in patients with chronic pruritus and prurigo nodularis [2]. In the present trial, the agent was assessed in patients with psoriasis and worst itch according to an NRS (WI-NRS) at baseline (score ≥ 7) [3]. Primary endpoint was the WI-NRS 4-point responder rate at week 8, and the secondary endpoint was the WI-NRS 4-point responder rate at week 4.

At week 8, 33.3% of patients treated with serlopitant had a response compared with 21.1% in the placebo arm (P=0.028). The corresponding rates at week 4 were 20.8% for serlopitant vs 11.5% for placebo (P=0.039). Treatment was also well tolerated with no serious adverse events reported for serlopitant and TEAEs occurred with similar frequency in both groups. "As therapy with serlopitant resulted in a clinically meaningful improvement of pruritus associated with psoriasis, we plan a phase 3 study of serlopitant for this indication," concluded Dr Pariser.

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2 Yosipovitch G, et al. J Am Acad Dermatol 2018;78:882-91.
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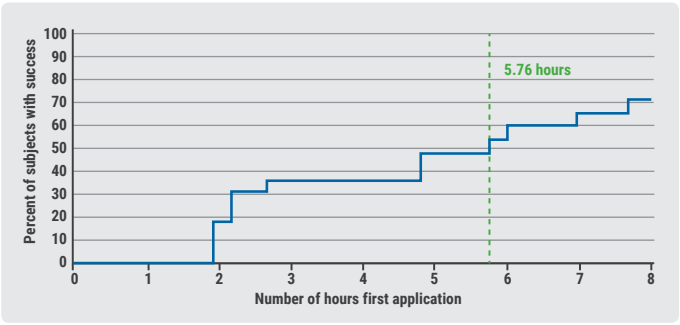
Atopic Dermatitis: **Many New Therapies in the Pipeline**

New and emerging atopic dermatitis therapies

The therapeutic landscape of atopic dermatitis changed tremendously in the previous decade. Novel insights into the pathogenesis enabled researchers to find important targets for therapy. With regard to topical therapy, novel hyperselective phosphodiesterase-4 blockers show promising results.

Increased cyclic adenosine monophosphate (cAMP) phosphodiesterase (PDE) activity in peripheral blood leukocytes is associated with the immune and inflammatory hyperreactivity that characterises atopic dermatitis (AD). PDE inhibitors exert an anti-inflammatory action by increasing the intracellular cAMP concentration, inhibiting the production of inflammatory cytokines (interferon-gamma, TNF-alpha, IL-4, IL-12, IL-17a, and IL-23) and other inflammatory mediators. "Difamilast is a novel hyperselective PDE-4B Blocker that looks really promising," said Prof. David Cohen (New York University School of Medicine, USA) [1]. In animal models, PDE-4B turned out to be a key regulatory and therapeutic target to reduce inflammation [2]. In a poster presented during the AAD meeting, a 1% ointment containing difamilast demonstrated rapid itch relief with a median time to pruritus improvement of only 5.76 hours (see Figure), which was sustained at 29 days in patients with moderate-to-severe AD [3]. In addition, there was both a marked improvement in EASI score and sleep disturbance in patients treated twice daily with the ointment [3]. Another novel anti-inflammatory inhibitor of PDE-4 is crisaborole ointment (2%). Phase 3 studies in children and adults with mild-to-moderate AD have shown that crisaborole leads to clear or almost clear skin in about a third of patients [4,5]. "As in all studies with topical agents, there was also a sizeable effect of the vehicle, because AD patients have a benefit of the regular use of emollients," said Prof. Cohen.

Figure: Median time to improvement of pruritus after treatment with difamilast. Success defined as Verbal Rating Scale (VRS) of 0 (No Itch) or 1 (Low) with ≥1-Point Reduction from Baseline [3]



Note: Subjects who achieved a success more than 8 hours after first treatment are not displayed in figure. ITT population; subject responses. Kaplan-Meier plot.

IL-4/IL-13 blockade offers long term durable responses

The IL-4/IL-13 blocker dupilumab is at present approved for adult AD patients with moderate-to-severe disease. "I tend to warn my patients of conjunctivitis, which is the most frequent adverse event that is seen in 10-15% of patients. However, this side effect is easily manageable," said Prof. Cohen. The responses seen with dupilumab are also durable, as demonstrated in the LIBERTY AD CHRONOS trial [6]. In this trial, dupilumab added to standard topical corticosteroid treatment for 1 year improved AD signs and symptoms, with acceptable safety.

There are also promising study results with dupilumab in adolescents, with a third obtaining almost clear skin [7]. In adolescents with severe disease, a high medical need exists for an effective treatment. "Hopefully, this study will lead to the approval of dupilumab in adolescents," said Prof. Cohen.

Selective IL-13 blockers in the pipeline

Tralokinumab is an interesting new agent that blocks IL-13 only. In a phase 2 study, therapy with tralokinumab in combination with topical steroids led to significant reductions in S. aureus colonisation compared with topical steroids with placebo [8]. "This is an interesting study, because now we have documented that if you get greater control of the disease, you also induce a change in the microbiome," said Prof. Cohen. This effect might potentially lead to fewer skin infections and AD flares, in addition to improving disease severity scores.

JAK inhibitors are also an interesting addition to the AD armamentarium. Baricitinib is already approved for the therapy of rheumatoid arthritis, and a phase 2 study showed

that this JAK inhibitor is also efficacious in AD [9]. The agent showed rapid improvements in EASI, itch, sleep disturbance, and quality of life, with significant improvements seen as early as week 1. A big advantage of the JAK inhibitors is that they can be administered orally. In rheumatology, there have been recent concerns about potential thromboembolic risks with the two JAK inhibitors, baricitinib and tofacitinib [10]. "Right now, the adverse event profile looks good, but we will see how things develop. Thromboembolic events will be the caveat of these drugs," concluded Prof. Cohen.

Another novel topical option is tapinarof cream. This agent demonstrated efficacy for patients with either psoriasis or AD. Its anti-inflammatory properties are mediated through activation of the aryl hydrocarbon receptor in multiple cell types. In addition, tapinarof impacts barrier gene expression in primary human keratinocytes. "In a dose-finding study it was tested in various doses and there is certainly some efficacy here," said Prof. Cohen. All newer therapies offer the opportunity for a more targeted approach with fewer potential adverse events.

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Food triggers eczema – an imperturbable belief of patients

Dr Peter Lio (Northwestern University Chicago, USA) discussed possible food triggers in eczema patients [1]. The role of food allergies is not only an important issue for patients but also for clinicians. Patients are often convinced that food is the main driver of their AD, or parents believe it is a trigger in their children with AD. Studies have shown that there is indeed an increased risk of true food allergy in patients with AD, which is positively correlated to an increasing severity of the disease. Severely affected infants have a nearly 6 times elevated relative risk for an IgE-mediated food allergy [2]. Roughly one third of children with AD have IgE-mediated food allergy [3]. "Many patients believe that food allergy is what is driving their eczema, and that is the part we do not really think bears out in clinical trials," said Dr Lio. According to his experience, patients perceive adverse reactions to food at a rate 10 times as high as their true prevalence. A trial that Dr Lio stated to be his "favourite study" assessed the relationship between food allergy and AD, both before and after treatment in an established AD population [3]. During an open trial of topical tacrolimus, a decrease in parental food allergy concern during good control of their child's eczema was observed: 95% of parents felt at the beginning of the trail that food allergy exacerbated their child´s AD. Tacrolimus treatment durations were 3 to 45 months. In this time, parental concern of food allergy decreased significantly ($P<0.001$). Additionally, estimated food reactions decreased by approximately 80% during 1- and 6-month periods.

Effective therapy – less parental concern

An effective topical therapy was able to significantly reduce the level of concern about food reactions. The authors concluded that successful, stable therapy of AD reduces perceived food reactions and appeases parental fears about food allergy. "Studies have shown that there is a powerful placebo effect in many conditions with dietary change," said Dr Lio. This might explain the persuasion of many parents that their children´s eczema are triggered by certain food. On the other hand, there is no doubt that eating healthy is a good thing that may have a positive skin effect due to an influence on the microbiome.

Another trial assessed the association of food allergy and AD exacerbations [4]. Analysed were children who had been referred between 2001 and 2011 for one or more suspected food allergies, and who underwent double-blind, placebo-controlled food challenges (DBPCFCs) as part of regular care. A total of 1,186 DBPCFCs were studied. In this trial, sensitisation occurred significantly more often in children with previous AD. However, children with no other symptoms than AD and worsening AD reacted no more often than the placebo group. The authors therefore concluded that children with exacerbation of AD in the absence of other allergic symptoms are unlikely to be food allergic. "We wish foods were the cause for eczema! It would be easier! But we are not that lucky," concluded Dr Lio.

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Psoriasis and Biologics: **The Beat Goes On**

With an increasing number of biologics to treat moderate-to-severe psoriasis, selection of the right drug becomes a real challenge for every dermatologist. Therapy should be guided by comorbidities but also by individual patient preferences. Novel drugs are not only more effective but also safer than conventional immunosuppressive drugs.

At present, there are numerous treatment possibilities for psoriasis. But how does one choose the right agent? Selection of therapy has to take comorbidities into account. "The first question, I ask my patients is, do you have joint pain?" said Prof. Mark Lebwohl (Mount Sinai School of Medicine, USA) [1]. All tumour necrosis factor alpha (TNF-α) blockers are also effective in psoriatic arthritis (PsA). Other treatment possibilities are ustekinumab, apremilast, and the IL-17 blockers secukinumab, ixekizumab, and brodalumab.

Higher risk of non-melanoma skin cancer with TNF-alpha blockers

The correlation between treatment and cancer was assessed in an analysis that included 49 clinical trials, involving up to 13,977 patients on the TNF-α blocker etanercept [2]. When non-melanoma skin cancer (NMSC) and *in situ* malignancies of the bladder were excluded, there was no elevated risk for malignancies in patients with psoriasis or PsA treated with etanercept. Risk of lymphoma was elevated in patients with rheumatoid arthritis (RA) treated with etanercept; in psoriasis patients there was a 2-fold increased risk, but this failed to meet statistical significance. The only markedly elevated risk was found with regard to squamous cell carcinoma: Psoriasis patients with low sun exposure had a 2-fold elevated risk whereas those with high sun exposure had nearly a 5 times elevated risk [2]. In a trial including patients with RA, TNF-α blockers caused 1 additional malignancy in 6-12 months [3]. "However, this is a different population from dermatology and the studies have methodical flaws," said Prof. Lebwohl. Nonetheless, there seems to be an increase in NMSC, melanoma, and lymphoma but not in most solid tumours. Lung cancer is only elevated in patients with chronic obstructive pulmonary disease.

IL-17 and IL-23 blockers do not elevate cancer risk

The risk of cancer seen with TNF-α blockers cannot be extrapolated to other biologics. On the contrary, blocking IL-17 could even be protective as IL-17-mediated inflammation promotes tumour growth and progression in the skin, which has been demonstrated in a well-established inflammation-associated tumour mouse model [4]. Up to now, therapy with IL-17 blockers has not been associated with an increase of malignancies. The same holds true for IL-23 blockers such as guselkumab or tildrakizumab.

The positive data on newer biologics is in stark contrast to the cancer risk of conventional immunosuppressive drugs. Incidence of NMSC increases in organ transplant patients with duration of immunosuppression therapy [5,6]. A 5-year cohort study assessing the risk of malignancies in 1,252 psoriasis patients treated with cyclosporin showed a 6-fold elevated risk for skin cancer, but no risk elevation for non-skin cancer [7]. In RA patients, therapy with methotrexate was associated with a 50% increased malignancy risk and a 3-fold increased risk of both melanoma and lung cancer [8]. On the other hand, acitretin and retinoids seems to be protective [9]. "If I have a patient with a history of squamous cell carcinoma, I give acitretin. But, unfortunately, this agent has only a modest anti-psoriatic activity," said Prof. Lebwohl. Table 1 shows the influence of different anti-psoriatic drugs on common comorbidities.

Table 1: Selection of biologics according to comorbidities [1]

Drug	PsA	Obesity	Cardiac	CA
Etanercept	+	+	+	-
Adalimumab	+	+	+	-
Infliximab	+	+	+	-
Certolizumab	+	+	+	-
Ustekinumab	+	+	+	+/-
Secukinumab	+	+	?	+/-
Ixekizumab	+	+	?	+/-
Brodalumab	+	+	?	+/-
Guselkumab	?	+	?	+/-
Tildrakizumab	?	+	?	+/-
Risankizumab	?	+	?	+/-
Mirikizumab	?	+	?	+/-
Apremilast	+	+	?	+/-
Methotrexate	+	x	+	-
Cyclosporine	+/-	+	?/-	x
Acitretin	+/-	+	?/-	+

CA, carcinoma; PsA, psoriatic arthritis.

Therapy should not only be guided by comorbidities, but also by patient´s preferences. "Patients who cannot easily self-inject every 1-2 weeks need either a pill or medication that requires infrequent injections," recommended Prof. Lebwohl in his lecture on "psoriasis pearls"[10]. IL-23 antibodies like guselkumab, tildrakizumab, or risankizumab have to be administered every 8 to 12 weeks only. Despite these long intervals, over 80% of patients in the VOYAGE 1 trial achieved a PASI90 response through week 156 with guselkumab.

Since October 2017, teens (>12 years) with moderate-to-severe psoriasis can be treated with the IL-12/23 blocker ustekinumab. This approval was based on a phase 3 study that showed that in at least two thirds of patients aged 12 to 17 who were treated with ustekinumab had clear skin or minimal disease at week 12 [11]. The safety profile was similar to that seen in studies of adults with plaque psoriasis.

IL-17 blocker: safe when accidentally overdosed

Up to now, there have been more than 100 cases of mostly unintentional overdoses of secukinumab. Fortunately, there are no reports of unusual adverse events. "In most cases we do not see any adverse events," said Prof. Lebwohl. In the event of an overdose, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment can be instituted immediately. Two cases of intentional overdoses have been published [12]. Both patients were treated with 450 mg secukinumab (instead of 300 mg) to gain a complete response, and the dose was well tolerated.

IL-17A also plays an important role in immunological protection against infections, especially against fungal infection. According to published clinical trials of IL-17 inhibitors, *Candida* infections were reported in 4.0% of patients treated with brodalumab, 2.1% with secukinumab, and 3.3% with ixekizumab vs 0.3%, 2.3%, and 0.8% of those who received placebo or active comparators [13]. According to Prof. Lebwohl, patients treated with these agents should be monitored for *Candida* infections. Most of them are mild to moderate in severity. His "pearl" for management is oral fluconazole in a single dose of 150 mg.

IL-17 and IL-23 blockers: no risk of tuberculosis reactivation

Another "psoriasis pearl" that Prof. Lebwohl shared with his audience is that there is no risk of tuberculosis (TB) reactivation when treating psoriasis patients with IL-17 or IL-23 blockers. This was shown in an analysis of 25 patients with a past history of either pulmonary TB, latent tuberculosis infection (LTBI), or a positive TB test [14]. Despite their TB status, they were treated with secukinumab for 363 days due to a negative test result at screening. None of the patients received TB treatment during the trial, and there was no TB reactivation during or after the trial. One patient who was negative at baseline was diagnosed with LTBI following retest according to local guidelines (Argentina) on day 141 while on therapy with secukinumab. He was treated with isoniazid 300 mg daily and completed the study without dose interruption of secukinumab.

Ixekizumab, another IL-17 blocker, also has been shown to be safe in patients with TB as no TB reactivations were found in 11 clinical trials [15]. As Prof. Lebwohl pointed out, there is also reassuring data with regard to the IL-23 blocker guselkumab. In the VOYAGE trials, 130 patients tested positive for LTBI at baseline and were randomised to placebo, guselkumab, or adalimumab. All of them received concomitant anti-TB treatments and there was no TB reactivation during the trial.

In contrast to the cytokine blockers, all TNF-α inhibitors are associated with an increased risk of reactivation of TB in patients with LTBI, because TNF-α is a key cytokine that protects host-defence against *Mycobacterium tuberculosis*. TB is frequently extrapulmonary in patients on TNF-α inhibitors. Therefore, testing patients for TB is mandatory before initiating treatment. TB reactivation has also been seen after therapy with conventional immunosuppressants such as methotrexate, even in low doses.

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JAK Inhibitors: **A New Frontier in Dermatology**

JAK inhibitors: a new therapeutic tool for dermatologists

JAK inhibitors are a versatile novel drug class that will play a role in different dermatological indications because they block numerous cytokines that play a key role in the pathogenesis of different dermatologic conditions.

"The therapeutic tools of a dermatologist moved from less targeted therapies such as corticosteroids to more target therapies such as TNF-α blockers or cytokine blockers," explained Prof. Brett King (Yale School of Medicine, USA) [1]. The Janus kinase (JAK) family is composed of 4 members: JAK 1,2,3, and tyrosine kinase 2 (TYK2). They play a key role in growth, development, and differentiation [2]. More than 50 cytokines use the JAK-signal transducer and activator of transcription (STAT) pathway. JAK-STAT pathways are involved in signal transduction of many cytokines such as interferon-gamma (IFNγ), IFN-α, IL-2, IL-4, IL-7, IL-9, IL-15, and IL-21, IL-5, IL-6, IL-12, IL-13, and IL-23 [3].

JAK-inhibitors are currently registered for the treatment of RA, myeloproliferative diseases, and polycythaemia vera. Tofacitinib, ruxolitinib, and baricitinib are the most frequently used JAK inhibitors, and it has been shown that venous thrombosis is a signal for JAK inhibitors. "From experiences in RA, we know that especially in combination with non-steroidal anti-inflammatory drugs there is also a risk of gastrointestinal perforation – but this might look different, if these agents are used in dermatologic conditions," concluded Prof. King.

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JAK inhibitors: a pathogenesis-directed therapy for alopecia areata

Preliminary data has shown that JAK inhibitors could represent a promising novel way to treat alopecia areata (AA), a non-scarring alopecia, which affects about 1-2% of the population.

Most commonly it presents as round patches of alopecia. "AA is not cosmetic; it is something we have to treat because it is frequently emotionally devastating," said Prof. Brittany Craiglow (Yale University School of Medicine, USA) [1]. A review including 11 trials with data from 1,986 patients with AA demonstrated that patients have a really low health-related quality of life (HRQoL), which is similar to patients with atopic dermatitis or psoriasis [2]. Before medical therapy is started, HRQoL and psychosocial functioning should be evaluated in every patient.

Up to now, there were no reliably, effective treatments, especially for advanced disease. Topical, intralesional, and systemic corticosteroids were the mainstay of treatment. Research using human clinical samples and a mouse model demonstrated that cytotoxic T lymphocytes mediate AA in part through JAK signalling. IL-15 and IFNγ are key cytokines in the development of AA. As JAK inhibitors block these cytokines, they prevented disease development in a mouse model [3]. The story of the JAK inhibitors broke after a psoriasis patient with concomitant AA was treated with the JAK inhibitor tofacitinib and experienced a complete regrowth of hair [4]. After this experience, the first open-label trial with the JAK inhibitor tofacitinib was performed. In this trial, 32% of patients experienced 50% or greater improvement in the SALT score [5]. Another 32% of patients showed hair growth of 5-50%, and 36% did not respond to treatment. Drug cessation resulted in disease relapse in 8.5 weeks. In this trial, ophiasis AA subtypes were more responsive than alopecia totalis and alopecia universalis subtypes. In another open-label trial with the JAK inhibitor ruxolitinib, which is administered orally, 9 out of 12 patients demonstrated response, with average hair regrowth of 92% [6]. In both trials, there were no serious adverse events.

"Today we know that a long duration (≥10 years) of complete hair loss is a negative predictor for response to treatment," said Prof. Craiglow. Scalp, eyebrows, and eyelashes show all a similar response, but response of one of these sites does not predict response of another. JAK inhibitors were generally well tolerated, although some patients developed acne or weight gain during therapy.

Topical treatments for limited disease

"When patients stop therapy, they lose their hair again," said Prof. Craiglow. Another study has shown that adolescents have a good response to tofacitinib [7]. "Of course, we would love to have topical treatments, but studies are not out yet, and we only have a couple of case reports with mixed results," said Prof. Craiglow. In a pilot study with 10 patients, a 2% tofacitinib ointment led to a mean improvement by 35%. One patient experienced a substantial and two patients partial hair regrowth [8]. There might be some benefit of a vehicle that enhances delivery, e.g. a liposomal base or solution.

According to Prof. Graiglow, topical therapy will be primarily for patients with small hairless areas. "If you want to treat your patient with JAK inhibitors, the potential for adverse events including malignancy and serious infections must be discussed with the patient and their family," recommended Prof. Craiglow. "Most of the patients need treatment indefinitely, but some can taper dose. Next year, hopefully we will have some approved therapies, as there are many clinical trials underway," concluded Prof. Craiglow.

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Can JAK inhibitors close the current therapeutic gap in AD?

Immune dysfunction and epidermal barrier dysfunction are two key factors in the atopic dermatitis (AD) pathogenesis. "In my belief, the most promising approach is not improving the barrier function, but primarily using anti-inflammatory agents," said Prof. Eric Simpson (Oregon Health & Science University, USA) [1]. At present, there are two important therapeutic gaps: "We need a more efficacious topical therapy than non-steroidals without significant burning or safety concern, and we would love to have pills in moderate-to-severe disease," said Prof. Simpson. JAK inhibitors have the potential to fill these gaps. At present, there are two phase 2 trials with JAK inhibitors in AD.

A Japanese phase 2 study was performed with the topical JAK inhibitor delgocitinib in adult patients with moderate-to-severe AD [2]. In this trial, the JAK inhibitor ointment, applied twice daily, led to a significant dose dependent change in the EASI (each dose $P<0.01$ compared with vehicle). In the highest concentration (3%), EASI was reduced by -72.9% after 4 weeks. In addition, there was a significant reduction of itch, noticed as early as day 1 nighttime. The agent was well tolerated with only 1 case of burning.

Another phase 2 trial was performed with the JAK1/2 inhibitor ruxolitinib in 307 adult patients with moderate-to-severe AD [3]. Twice daily treatment with a cream containing 1.5% ruxolitinib led to 71.6% improvement in the EASI at 4 weeks compared to a 15.5% improvement in baseline EASI score in a vehicle control group. In addition, rapid and sustained reductions in pruritus, assessed in an NRS, were observed with changes as early as within a day from the initiation of therapy. Taken together, topical JAK inhibitors show equal potency to topical steroids with possibly less burning.

Phase 2 trials with oral JAK inhibitors like baricitinib, abrocitinib, and upadacitinib showed rapid itch reduction and reduced inflammation by 1-4 weeks due to targeting several key cytokines in AD. Oral JAKs are now in phase 3 trials. "The dosing of the JAKs will be most critical: low doses show less efficacy but are very safe; high doses might have a better efficacy than dupilumab but come with off-target effects on platelets, blood counts, or the risk of infection," concluded Prof. Simpson.

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Hair Loss:
No Reason for Therapeutic Nihilism

Today, many therapeutic options are available for hair loss. With regard to therapy, combinations seem to work best. Platelet-rich plasma (PRP) has shown to be efficacious in a number of patients with almost no downtime.

"My first approach to the hair loss patient is to determine the type or the aetiology of hair loss," recommended Dr Glynis Ablon (Ablon Skin Institute, USA) [1]. A medical history is of key importance as the intake of several medications can cause or enhance hair loss. In particular, antidepressants, blood pressure medications, anticoagulants, and gout medications often lead to hair loss, which is typically seen after a lag time of 2-3 months. Before treatment is started, causes of hair loss have to be identified.

Androgenetic alopecia (AGA) is the most common type of hair loss, affecting 50% of males over the age of 40 and 75% of females over 65 [2]. It is often accompanied by diffuse telogen effluvium [1]. "Especially for women, hair loss is psychologically distressing. They feel it is unnatural for their hair to thin," said Dr Melissa Piliang (Cleveland Clinic, USA) [3]. Despite the high prevalence of hair loss in elderly women, they feel they "are the only one". Trials have shown that women with hair loss had a pattern of less adaptive function and a negative body image [4,5]. As much as 55% of patients even displayed symptoms of depression (i.e. anxiety in women, aggressiveness or hostility in men) [5]. Treatment of hair loss produced an improvement in 89% of women and 76% of men [5]. Therefore, every hair loss patient is in need of an empathetic approach. This has also been shown in a twin study: factors associated with increased frontal hair loss and thinning of hair included higher severity of stress [6]. In addition, illness, weight loss, and nutritional deficiencies (i.e. iron, vitamin D, and zinc) are common triggers.

Trichoscopy: an important diagnostic tool

Trichoscopy should be utilised to diagnose early AGA in men and women. Typical results in AGA show hair shaft diameter diversity. In AGA, hair follicles get progressively smaller with each anagen, and are finally replaced by fibrous tracts. In the trichoscopy, there is a >20% variability together with a dermoscopic sign of miniaturisation (see Figure).

"If you use a normal dermatoscope, just take a picture with your phone through the dermatoscope and then enlarge the image on the screen to recognise the hair diameter diversity," recommended Prof. Antonella Tosti (University of Miami, USA) [7]. With this picture, the disease can be easily explained to patients. Regrowing hair has a reduced thickness in AGA but a normal thickness in telogen effluvium, which can be easily recognised in the trichoscopy. In addition, an absence of variability is typical in telogen effluvium. As trichoscopy results are so obvious, scalp biopsy is rarely required to diagnose AGA. Diffuse, rapid onset of hair loss is uncommon in AGA and should always raise suspicion for a systemic illness including a nutritional deficiency, thyroid disease or malignancy, or an autoimmune aetiology, e.g. a diffuse type of alopecia areata. Nail changes are often seen in alopecia areata. In this case, a biopsy is key to the right diagnosis. Trichoscopy is also useful for follow-up during therapy.

Lab work mandatory

Lab work should be done in every hair loss patient: most important is the free/total testosterone, DHEA-S, prolactin,

Figure: A typical sign of AGA is the miniaturisation of the hair follicles [7]

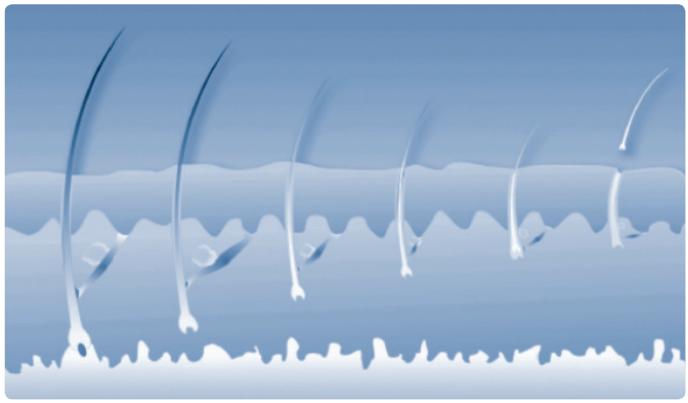

Figure kindly provided by and adapted from Prof. Tosti.

thyroid function test, and ferritin. However, one has to bear in mind that many patients take high-dose biotin that can interfere with laboratory results. Therefore, clinicians should be prepared to critically evaluate laboratory results and correlate their findings with the clinical picture. With regard to therapy, all treatment options should be discussed with the patient. As Dr Jeff Donovan (Donovan hair clinic, Canada) pointed out in his lecture, the main treatment for male and female pattern hair loss are minoxidil, anti-androgens, low level laser therapy, and PRP [8]. In the current guideline, finasteride, dutasteride, and minoxidil are recommended for male and minoxidil for female patients [9].

In total, 30% of all patients get cosmetically significant improvements with minoxidil solution or foam. Patients with shorter duration of hair loss and smaller area of thinning, and larger numbers of non-vellus miniaturised hairs respond better to this treatment. The efficacy of topical minoxidil can be enhanced by several methods, all of them are off-label uses. Minoxidil can be applied by dermarolling or by combining it with tretinoin. The latter is known to increase the percutaneous absorption of minoxidil and therefore to enhance the response of AGA to minoxidil. This combination enables a once-daily application of minoxidil, instead of the twice-daily recommended application. In a trial, the once-daily application of 5% minoxidil together with 0.01% tretinoin proved to be equally effective as the twice-daily application [10]. "Basically, all methods of getting more minoxidil to the follicle are useful," Dr Donovan explained.

Combinations work best

"I would always start with concomitant supplements, as there are interesting products out there, e.g. those that contain anti-inflammatory agents like biocurcumin or anti-oxidants like tocotrienols," recommended Dr Ablon [1]. Other treatment possibilities are low level light lasers or topical finasteride application with or without microneedling. "I think, combinations work best in hair loss," said Dr Ablon.

The energy used in Low Level Laser Light Therapy (LLLT) is from the red or near-infrared spectrum (<500 mW, no heat). The exact mechanism of action of LLLT in hair growth is not known; however, several mechanisms have been proposed. It has a biostimulatory effect and influences mitochondrial oxidative metabolism by stimulation of transcription factors (nerve growth factor, neurotropin receptor, and nuclear factor kappa B) [11]. In addition, it decreases inflammation. Another hypothesis is that it acts on epidermal stem cells, and shifts follicles back into the growth cycle. LLLT prolongs duration of anagen phase, increases rates of proliferation in active anagen hair follicles, and prevents premature catagen development [11]. Research data shows that it is effective in both men and women [2].

Platelet-rich plasma therapy: always worth a try

A general body of evidence has recently emerged demonstrating a positive response from treatments with PRP injections [12-15]. When platelets are activated, 7 or more growth factors are released. Platelets contain additional proteins, cytokines, and bioactive factors. PRP leads to enhanced healing, proliferation, differentiation, and angiogenesis of dermal papillae and stem cells. "PRP acts like a fertiliser on hair growth," said Dr Ablon, although not all patients respond to the procedure. The plasma is directly injected into the patient's hair follicles in a process that takes no more than 10 minutes. The procedure is not painful, so no anaesthetic cream is required. After the initial treatment, injections are repeated once a month for the next 3 months, and then once every 3 months for androgenetic alopecia or once every 3 to 6 months for other forms of alopecia seem to have high success and satisfaction rates. Unfortunately, not everyone is a candidate for PRP therapy. Certain hair loss patients, including those with hereditary hair thinning or baldness, show a good response. PRP may be used in conjunction with other treatments to give patients best possible results.

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Vitiligo: The Beginning of a New Era

Vitiligo in children

Half of all vitiligo patients have an onset before the age of 20, and children comprise 25% of all vitiligo patients. "If this disorder begins in childhood, it is often associated with profound emotional trauma. Affected children often have longstanding social adjustment issues," said Prof. Pearl Grimes (Vitiligo & Pigmentation Institute of Southern California, USA) [1].

Most bothersome sites are the face and legs. If the disease starts early, it has a greater severity. Vitiligo is seen more frequent in children with atopic dermatitis [2]. Ezzedine et al. (2014) identify 2 clinical subtypes of vitiligo: those with early onset disease (<12 years) are characterised by a family history of vitiligo, a family history of premature greying, and halo nevi; those with late onset disease (>12 years) often have acrofacial localisation [3]. Research has shown that cosmetic camouflage leads to a significant improvement in quality of life in children with vitiligo [4].

Compared with adults, comorbidity with regard to autoimmune disease is lower in children, but multiple studies have documented an increased frequency of thyroid disorders [5-7]. "I strongly recommend that you get a thyroid panel if this is the only lab you do," said Prof. Grimes. In children, there is a higher incidence of segmental vitiligo (see Figure). "Treatment goal is to stabilise and improve quality of life. Fortunately, excellent therapeutic outcomes are often achieved in children," said Prof. Grimes. To treat vitiligo successfully, a multi-modality approach is warranted: It is important to decrease the oxidative stress and the aberrant immune response, and to stimulate melanocyte regrowth and proliferation. Oral corticosteroids (prednisone 5-10 mg daily) are necessary to stabilise vitiligo. Narrowband UVB phototherapy is an effective method to stimulate repigmentation: in a retrospective study, a repigmentation rate of >75% was achieved in 45.4% of cases [8]. In general, children show enhanced repigmentation compared with adult patients. In addition, "vitamin D is a powerful antioxidant and is often deficient in patients with vitiligo, especially when they get older. Therefore, we should also always check vitamin D levels in our patients," recommended Prof. Grimes.

Figure: Distribution of the clinical types of vitiligo differs between children and adults [1]

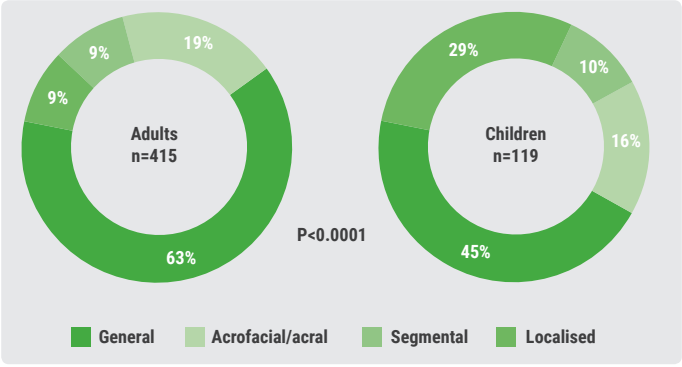

Figure kindly provided by Dr Grimes.

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Surgical treatment for selected vitiligo cases

Dr Iltefat Hamzavi (Henry Ford Hospital, USA) pointed out that surgical management is a safe and effective treatment modality for selected patients with vitiligo [1]. Surgery is often recommended for patients resistant to other therapies, and different techniques exist. Cultured melanocyte transplantation consists of the separation of epidermal cells obtained from a donor site and spreading these cells on the depigmented and dermabraded recipient area. This method allows for treatment of large, irregular areas. A repigmentation rate of 75-84% can be expected. Unfortunately, increased time for culture, special training, personnel, and equipment is needed. The same holds true for melanocyte keratinocyte transplant procedure. With this method, 84% repigmentation is possible. Another surgical technique is punch grafting, which is readily available, and does not require additional equipment or training. "Unfortunately, the cosmetic effect is poor, we often see a cobblestone-like effect, and typically adjuvant UV treatment is necessary," said Dr Hamzavi.

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JAK-inhibitors: an emerging treatment option for vitiligo

Therapeutic options have historically been limited. JAK inhibitors are a novel therapeutic possibility, which have shown to be remarkably effective and are currently being tested in clinical trials. Research in vitiligo has made significant progress in the past 10 years. "Our improved understanding of its pathogenesis is leading to encouraging new treatments," said Prof. John Harris (University of Massachusetts, USA) [1]. The most promising strategies at this time focus on targeted immunotherapy.

Vitiligo is an autoimmune disease of the skin mediated by CD8+ T cells that kill melanocytes. In addition, expression of IFN-γ is increased in the lesional skin. Neutralisation of IFN-γ prevents CD8(+) T cell accumulation and, as a result, depigmentation, suggesting a therapeutic potential for this approach [2]. In addition, the chemokine CXCL10 plays a critical role in both the progression and maintenance of vitiligo [3]. JAK inhibitors are effective in vitiligo, presumably via inhibition of IFN-γ signalling in the skin [4]. A 20-week, open-label, proof-of-concept trial of twice-daily topical treatment with the JAK inhibitor ruxolitinib cream (1.5%) provided significant repigmentation in facial vitiligo and may offer a valuable new treatment option [5]. Another vitiligo patient was successfully treated with the oral PAN-JAK inhibitor tofacitinib [6]. Three clinical trials with JAK inhibitors in vitiligo are currently ongoing.

Tissue resident memory T cells: the culprits for high relapse rates

"Unfortunately, with JAK inhibitors we have the problem we see in all vitiligo treatments: if you stop therapy, it relapses exactly in the same spots due to an autoimmune memory," said Prof. Harris. The risk of relapse after successful repigmentation in vitiligo is estimated to be 40% within the first year. Tissue-resident memory T cells are probably responsible for the high relapse rate. "A study showed that if you block IL-15 in mice, you can block relapse [7]. This might be the cornerstone of durable treatment results. Studies in humans will follow," said Prof. Harris.

Another active and promising area of research is to design pharmacological compounds that can specifically activate melanocyte precursors in the hair follicle in order to obtain faster, better, and more durable repigmentation, and to find agents that are able to normalise melanocyte stress. Afamelanotide, an analogue of α-melanocyte-stimulating hormone, which can induce tanning of the skin, is potentially useful in dark skinned individuals [8]. This was shown in a clinical trial where the efficacy and safety of combination therapy with this agent together with narrowband-UVB phototherapy was compared with phototherapy alone. All study participants had Fitzpatrick skin phototypes III to IV and a confirmed diagnosis of non-segmental vitiligo that involved 15% to 50% of total body surface area. Response in the combination therapy group was superior to that in the narrowband-UVB monotherapy group at day 56 ($P<0.05$). For the face and upper extremities, a significantly higher percentage of patients in the combination therapy group achieved repigmentation, and at earlier times. In the combination therapy group, repigmentation was 48.6% at day 168 vs 33.3% in the phototherapy group. "However, the response was more noticeable in patients with Fitzpatrick skin phototypes IV to VI and there is only a moderate improvement compared to phototherapy alone," said Prof. Harris.

Maintenance therapy with tacrolimus

To prevent relapse in vitiligo, a maintenance therapy should be applied. "Topical steroids could be effective, but data is still lacking," said Thierry Passeron (Hospital of Nice, France) [9]. Efficacy of topical 0.1% tacrolimus twice weekly was assessed in a randomised, double blind, placebo-controlled study in 16 patients [10]. In this trial, 48.4% of lesions in the placebo group showed depigmentation, compared with 26.8% in the tacrolimus group ($P=0.059$). The authors concluded that maintenance therapy with tacrolimus ointment is effective in preventing the depigmentation of vitiligo patches that have previously been successfully repigmented.

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What's New and Hot in Acne

Oral antibiotics for acne treatment

Dermatologists prescribe more oral antibiotics than physicians of other specialities [1]. The main indication is acne vulgaris. The novel narrow-spectrum antibiotic sarecycline is a valuable new treatment for moderate-to-severe acne. Oral antibiotics are indicated in patients with inadequate response to topical treatments and acne involving multiple body areas [2]. Divergent opinions concerning dosing, duration of treatment, and follow-up period still exist, according to Dr Neal Bhatia (Therapeutics Clinical research, USA) [1].

Tetracyclines – mainstay of oral antibiotics for acne

Consensus statements include that antibiotics for acne should be combined with topical therapies (i.e. benzoyl peroxide or retinoid), and tetracyclines are recommended as first-line drug. Treatments and therapy duration should be limited with regard to the induction of resistance. Other agents like erythromycin and azithromycin should be restricted to cases were tetracyclines cannot be used [3]. Tetracyclines represent 75% of antibiotics prescribed in dermatology. Low-dose doxycycline treatment (40 mg) has been shown to be superior to placebo as well as high-dose therapy (100 mg).

In comparison with minocycline, doxycycline entails more gastrointestinal problems especially in its hyclate formulation. Furthermore, it has a higher potential to induce photosensitivity and vaginal candidiasis. Doxycycline should be taken with a large glass of water and food to reduce side effects. Other methods to improve tolerability are staying upright for a few hours after intake, correct application of sunblock, and adding probiotics to the diet. Advantages of minocycline are related to the multiple anti-inflammatory effects, higher reduction in P. acnes, and a higher follicular concentration due to its lipophilia. Minocycline can induce epidermal pigmentation such as blue-black colouring near scars or blue-grey hyperpigmentation of normal skin on arms and legs. In multiple trials, these phenomena appeared only after ≥8 months of treatment and a cumulative dose of ≥70 g of minocycline.

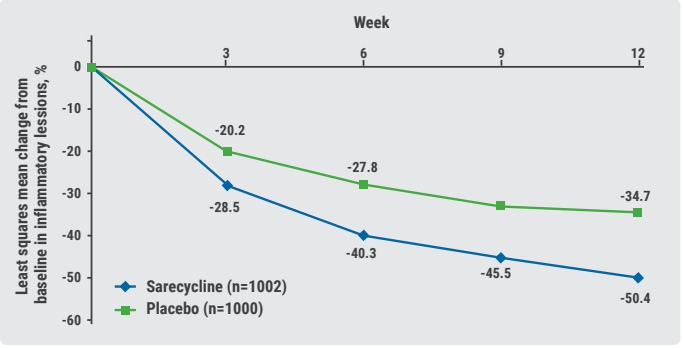
Sarecycline – a new kid on the block

The novel narrow-spectrum tetracycline-class antibiotic sarecycline has been FDA-approved for moderate-to-severe acne in patients ≥9 years of age in October 2018. Sarecycline is taken once daily in a weight-based dosage independent of food intake. It is not only anti-inflammatory but also blocks protein biosynthesis. Two identically designed pivotal phase 3 trials included approximately 2,000 patients aged 9-45 years with moderate-to-severe facial acne defined as an IGA ≥3, 20-50 inflammatory lesions, ≤100 noninflammatory lesions, and ≤2 nodules [4]. Sarecycline 1.5 mg/kg/day was investigated against placebo over 12 weeks.

Results of the pooled intention-to-treat population showed significant superiority of sarecycline starting at week 3 and a mean change in percent of inflammatory lesions of 34.7% and -50.4% for placebo and sarecycline, respectively (see Figure). In addition, non-inflammatory lesions were notably reduced. The most common adverse event was nausea, occurring in 3.2% of sarecycline and 1.7% of placebo patients. Phototoxic effects and vaginal yeast infections in females occurred in less than 1% of patients.

In general, antibiotic treatment should be limited to 3 to 4 months. The decision of when to end systemic antibiotics is particularly influenced by disease severity, resistance potential, and response. The latter should be evaluated after the first 6-8 weeks.

Figure: Sarecycline leads to a significant reduction of inflammatory lesions [4]



Pooled ITT population; P<0.001.

New data on isotretinoin use

A Cochrane review published in 2018 assessed the efficacy of oral isotretinoin for acne in 31 published studies [5]. "However, all included studies had a limited design," said Prof. Diane Thiboutot (Penn State Clinical and Translational Science Institute, USA) in her lecture on isotretinoin considerations [6]. Therefore, the authors are unsure if isotretinoin improves acne severity compared with standard oral antibiotic and topical treatments when assessing the change in total inflammatory lesion count, but it may slightly improve physician-assessed acne severity [6].

Another study published last year showed that isotretinoin changes the microbiome in acne [7]. During treatment, "healthy" bacteria such as ribotype 3 showed an upward trend compared with ribotype 6 bacteria that are associated with acne. Propionibacterium species globally decreased during treatment. However, 38% of patients had still high Propionibacterium and a low proportion of ribotype 3 after treatment. "This result shows that assessment of microbiome could possibly serve to identify the 10-20% of patients who need isotretinoin retreatment," concluded Prof. Thiboutot.

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Should we use more hormonal therapy?

"At the moment, hormonal therapy in acne is considered an 'alternative treatment'," said Dr Julie Claire Harper (Dermatology & Skin Care Center, USA) [1]. However, both oral contraceptives and spironolactone have been shown to be effective in acne. The oral contraceptives norgestimate, norethindrone acetate, and drospirenone have been FDA approval for women ≥15 years of age who desire contraception and are unresponsive to topical anti-acne medications. Unfortunately, all combined oral contraceptives (COCs) increase the risk of venous thromboembolism and breast cancer [2,3].

A Japanese study showed, that spironolactone is also effective in acne [4]. In total, 64 females completed the 20-week study. All of the patients exhibited clinical improvement, which was considered excellent in 53% and good in 47% of patients [4]. Due to the development of gynecomastia in 3 males, treatment was discontinued in all male subjects. The aldosterone antagonist spironolactone has no FDA approval for the treatment of acne. Side effects are dose-related. Routine potassium monitoring is unnecessary for healthy women taking spironolactone for acne as one study showed a risk of hyperkalaemia of 0.72% in this population [5]. "To be on the safe side, you should check potassium levels in older women or in those with renal or cardiac disease," recommended Dr Harper.

Data from a Danish drug registry has shown that there is no evidence of increased risk of breast, uterus, or ovarian cancer with spironolactone use [6]. For acne, dosages between 25 and 200 mg spironolactone should be used. "I prefer a maximum dose of 100 mg because higher doses cause higher rates of side effects," said Dr Harper. The concomitant use of oral contraceptive lessens menstrual irregularities, the most frequent side effect during spironolactone intake. In addition, pregnancy is prevented, which is mandatory as spironolactone can lead to feminisation of male foetuses.

With both COCs and spironolactone, it can take 3 months to see a meaningful response. "However, I think we should get to hormonal therapy faster, also to spare antibiotics," concluded Dr Harper.

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Pearls of the Posters

Numerous interesting e-posters attracted the attention of the attendees: guselkumab shows good clinical response rates long term in patients with and without psoriatic arthritis, and tralokinumab seems to be an interesting novel option for atopic dermatitis. Another study shows that bone mineral density should be monitored in pemphigus patients.

Plaque psoriasis – Efficacy of guselkumab

Guselkumab is a fully human monoclonal antibody that acts as a blocker of IL-23. The ongoing pivotal phase 3 trials VOYAGE 1 and 2 have demonstrated significant efficacy of guselkumab for the treatment of moderate-to-severe plaque psoriasis in comparison with an active comparator and placebo. The current investigation analysed pooled data from VOYAGE 1 and 2 with regard to long-term efficacy in patients with or without psoriatic arthritis (PsA) [1].

In VOYAGE 1, over 800 patients were treated with either (1) 100 mg guselkumab at week 0, 4, and 12, and then every 8 weeks, (2) placebo at week 0, 4, and 12, followed by guselkumab at week 16 and 20, and every 8 weeks thereafter; or (3) adalimumab until week 47. From week 52 onwards, all patients received 100 mg guselkumab open-label until week 156. The study design for the nearly 1,000 patients in VOYAGE 2 was similar, but the open-label guselkumab phase in weeks 76-156 was preceded by a randomised withdrawal.
For the current analysis, data from VOYAGE1 and VOYAGE 2 was pooled for patients from groups 1 and 2. Data was analysed based on the self-reported psoriatic arthritis status at baseline. Together, 83.1% and 82.6% of the patients on the IL-23 blocker reached clear or almost clear skin according to the assessment of the global investigator (IGA 0/1) at week 100 and week 156, respectively. In addition, there was no difference in the response rate based on the presence of PsA: at week 100, patients with PsA at baseline showed a response rate of 85.4% compared with 82.7% without PsA. Psoriasis Area and Severity Index (PASI) 90 rates at week 100 and 156 were 81.4% and 78.6% in patients with baseline PsA compared with 80.1% and 79.7% without baseline PsA. According to the authors, this novel analysis shows that treatment with guselkumab is highly effective independent of the PsA status at baseline over 3 years. The drug was also well tolerated.

1. Kimball AB et al. ePoster No. 10064, AAD Annual Meeting, 1-5 March 2019, Washington DC, USA.

Pemphigus patients prone to osteoporosis

Patients suffering from pemphigus or bullous pemphigoid often have various comorbidities [1]. They also are at risk for a lower bone mineral density through factors such as long-term steroid medication, inflammation, and low vitamin D.
Dr Raj Chovatiya (Northwestern University Feinberg School of Medicine, USA) and his colleagues investigated whether there is an association between the risk for osteoporosis or pathologic fractures and pemphigus or bullous pemphigoid patients, and also looked for fracture predictors. The authors analysed data from over 198 million people of all ages that received treatment in emergency rooms all over the USA from 2006-2012. Among these adults and children were 4,502 cases of pemphigus and 8,863 of bullous pemphigoid.

After adjusting for risk factors such as sex, age, income, previous long-term steroids, and insurance, there was still a significantly elevated risk of osteoporosis and pathologic fractures in pemphigus patients. The researchers found a 2.54-fold elevated relative risk for osteoporosis, a 2.2-fold elevated relative risk for osteopenia, a 2.04-fold elevated risk for general pathologic fractures, and a 1.46-fold elevated risk for pathologic femur or verbal fractures. The odds ratio for osteomalacia was very high, at 29.7. In patients with bullous pemphigoid, the odds for pathologic fractures and osteoporosis were also elevated (1.52 and 1.55).
The risks for osteoporosis and pathologic fractures were further increased by a history of long-term steroid use. In addition, female sex and increasing number of chronic diseases were identified as significant predictors for any fracture. Pemphigus or bullous pemphigoid patients with fractures had increased hospital admission rates. The total costs of care were significantly higher when a fracture occurred in these patients. Due to these results, the study authors concluded that there might be a possible benefit of fracture prevention and osteoporosis screening for patients suffering from these diseases.

1. Chovatiya R et al. ePoster No. 8514, AAD Annual Meeting, 1-5 March 2019, Washington DC, USA.

Tralokinumab improves eczema and reduces *staphylococcus aureus* colonisation in AD

The fully human, monoclonal, IL-13 blocker tralokinumab showed to be highly effective in patients with moderate-to-severe atopic dermatitis (AD) [1]. Dysregulation of

cell-mediated immune response plays a key role in the pathogenesis of AD. As a result, IL-13 and other type 2 cytokines are overexpressed.

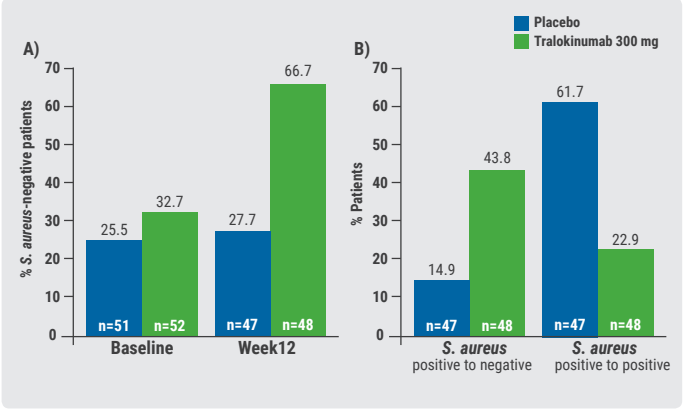
The presented phase 2b trial included 204 adult patients with moderate-to-severe AD. For 12 weeks, 3 randomised groups of study subjects were treated with either 45 mg, 150 mg, or 300 mg of tralokinumab every second week, with a fourth group receiving a placebo. All patients were on a background treatment with topical corticosteroids (WHO class 3). These steroids were applied ≥1 time daily during 2 weeks before receiving tralokinumab, and, if necessary, throughout the rest of the trial. Efficacy was assessed by the percentage of subjects reaching an Investigator's Global Assessment (IGA) score of 0 or 1, corresponding to clear or almost clear skin with a ≥2-point decrease from baseline and changes in Eczema Area Severity Index (EASI) (co-primary endpoints).

Influence on microbiome and biomarkers

To gain further insight, data was also collected on the intensity of colonisation with *Staphylococcus aureus*, which can trigger disease flares. Several potential AD-associated biomarkers, such as immunoglobulin E (IgE), periostin, chemokine ligand 17 (CCL17), and dipeptidyl peptidase-4 (DPP-4) were also measured. The application of the highest tested dosage of tralokinumab (300 mg) resulted in a significant reduction of -4.9 in EASI at week 12 (P=0.01). Compared with placebo, nearly 18% more patients reached the IGA response (26.7% vs 11.8%).

Abundance of *Staphylococcus* colonisation and serum levels of CCL17 both correlated with disease severity (EASI) at baseline. A negative status for *S. aureus* in lesional skin at week 12 was seen in 66.7% of tralokinumab patients, compared with 27.7 % of patients who received placebo (see figure). Patients treated with tralokinumab showed decreased levels of periostin (-31.3% vs +1.9%), CCL17 (-40.0% vs +37.4%), and IgE (-22.3% vs +1.6%) compared with placebo, while DDP-4 was slightly increased (+7.3% vs +3.9%). Upper respiratory infections were the most common treatment-emergent adverse events in both groups. They occurred in 3.9% of patients in the pooled tralokinumab dose groups compared with 3.9% of placebo patients. Headaches appeared in both 2% of pooled tralokinumab and placebo groups.

Figure: Proportion of patients with A) *S. aureus*-negative lesional skin at baseline and at week 12, and B) shift from S. aureus-positive at baseline to *S. aureus*-negative at week 12 and *S. aureus*-positive both at baseline and week 12 in lesional skin [1]



In conclusion, tralokinumab not only induced clinical improvement but also decreased *S. aureus* and several serum biomarkers. Greatest improvements with tralokinumab therapy were achieved in patients with high DPP-4, low periostin, and a positive status for S. aureus at baseline.

1. Guttman-Yassky E et al. ePoster No. 8690, AAD Annual Meeting, 1-5 March 2019, Washington DC, USA.

Intralesional 5-fluorouracil induced high clearance rates in cutaneous squamous cell carcinoma

Treatment of cutaneous squamous cell carcinoma (cSCC) primarily consists of surgical removal. The intralesional application of 5-fluorouracil might be a non-surgical alternative for select cases of cSCC, although currently no trial data exists.

Dr Emma Guttman-Yassky (Mount Sinai School of Medicine, USA) presented data from a reported retrospective single-centre analysis of 37 adults, which included a total of 195 cSCC tumours. The authors evaluated the efficacy of 5-fluorouracil in cSCC, including other patient and tumour characteristics, such as lesion, sex, and immunosuppression status [1].

Patients had a mean age of 70.5 years. The overall clearance rate was 87.2% (response in 170 tumours). Lesions of the extremities had a better percentage of clearance (arms 91%, legs 92%) than tumours on the face and neck (59%). Odds of treatment failure were higher in bigger tumours. Immunosuppressed patients had lower clearance rates (76%) compared with immunocompetent individuals (91%). According to the authors, the efficacy of this treatment should be assessed in a larger, prospective trial.

1. Hamad J et al. ePoster No. 8558, AAD Annual Meeting, 1-5 March 2019, Washington DC, USA.