Systemic Treatment for Psoriasis: What Is on the Horizon?
Many treatments are already available for psoriasis, with even more in the pipeline. A withdrawal analysis showed impressive response maintenance by a novel oral TYK2 inhibitor.

All Patients with GPP Benefitted from IL-36 Inhibitor Therapy
Subgroup analyses of the phase 2 Effisayil 1 trial showed that the IL-36 receptor antibody spesolimab was effective in all patients with generalised pustular psoriasis (GPP), independent of baseline characteristics.

New Treatments for HS: IL-17 Inhibitors Next in Practice?
Therapy options for patients with hidradenitis suppurativa (HS) still fall short. The next agents that approach approval will likely be IL-17 inhibitors, according to a scoping review.
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Dear colleagues,

The SPIN 2022 Congress was held between 06–08 July 2022 in Paris, France. The congress was dedicated to inflammatory skin diseases and provided a comprehensive overview of the state-of-the-art and insights into its clinical course and innovative pathogenesis-based treatments.

The revolutionary development of small molecules and biologics in the treatment of atopic dermatitis has changed clinical practice. Furthermore, new findings on the clinical relevance of biomarkers may help move towards personalised medicine in the future: Carriers of a filaggrin gene variant proved to have a high risk for bacterial infections.

The innovations in the management of psoriasis are a continuous evolution of more effective and safe treatments targeted at pathogenesis-relevant aspects with little collateral damage concerning side effects. Insights into the relevance of clear skin for long-term sustainable control of disease and comorbidities have changed clinical practice. Furthermore, research on biomarkers provides future opportunities for personalised care, such as drug levels and HLA-Cw6 status.

The management of patients with vitiligo, hidradenitis suppurativa, and alopecia areata was limited to a few treatments with poor outcomes until recently. Now, it is clear that the innovations in therapeutic possibilities of inflammatory skin diseases also provide a new future perspective for patients suffering from these conditions.

Best regards,
Prof. Peter CM van de Kerkhof
Therapies for atopic dermatitis: still moving forward

The armamentarium of topical and systemic treatments for atopic dermatitis (AD) is constantly growing. In the future, this will not only allow for higher therapeutic goals in the cutaneous domain but may also broaden the choice of targets in features like comorbidities.

"Over the last couple of years, we have seen new treatments, and there are still new ones coming – is this really the revolution for AD?" Prof. Christian Vestergaard (Aarhus University Hospital, Denmark) asked, laying the land for his talk [1].

The incidence of AD has risen by 2–3 times over the last 3 decades, making it the most prevalent skin disease. Although the proportion of children with AD (15–20%) is higher than the percentage of adults (2–10%), numerically, adults are more common as patients. At the beginning of AD, genetic and environmental factors impair the skin barrier. As part of the type-2 inflammation cascade, the skin generates upstream molecules such as TARC, TSLP, IL-25, and IL-33 that induce various cytokines, e.g. IL-4, IL-5, IL-31. "These will increase the itch and thereby the vicious circle," Prof. Vestergaard stressed. Subsequent scratching further impairs the skin barrier and entails a downregulation of structural proteins. "This leads to a lower differentiation of keratinocytes and lipids, which, in turn, induces inflammation and is in itself also induced by inflammation," he further explained the pathophysiology of AD. Thus, various cytokines are potential targets for therapies. Furthermore, there are currently ongoing clinical trials exploring drugs aiming at Janus kinases (JAK), phosphodiesterase (PDE)4, as well as the H4-receptor that is found in a variety of cells, including lymphocytes and keratinocytes.

In the SOLO 1 and 2 trials (NCT02277743 and NCT02277769), up to 51% of participants on dupilumab reached an Eczema Area and Severity Index (EASI)75 score as a key secondary outcome [2]. "We saw it within 1–2 months, and I dare say that this revolutionised the way that we started to treat AD," Prof. Vestergaard commented. Also, the IL-13 inhibitor tralokinumab demonstrated significant superiority over placebo in EASI75 responses and Investigator’s Global Assessment (IGA) 0/1 [3]. Nemolizumab, an IL-31 inhibitor, showed itch reduction and improved sleep quality [4]. As examples of small molecule agents with proven efficacy, Prof. Vestergaard mentioned baricitinib, abrocitinib, and upadacitinib [1]. In the BREEZE trial program, baricitinib significantly improved EASI75 responses, which were further increased when adding topical steroids in BREEZE-AD7 (NCT03733301). 48% on 4 mg versus 23% on placebo (P<0.01) [5]. Abrocitinib was tested against placebo and in comparison with dupilumab (NCT03720470), also outperforming the latter in terms of EASI75 (abrocitinib 200 mg 70% vs dupilumab 300 mg 58%) and EASI90 (abrocitinib 200 mg 46% vs dupilumab 300 mg 35%) responses [6]. Moreover, very convincing results were observed for upadacitinib. In the Measure Up 1 trial (NCT03569293), EASI75 and EASI90 were achieved by 80% and 66% on 30 mg of the study drug, compared with 16% and 8% on placebo, respectively [7]. "Now we are talking about EASI90 among the AD patients, so the next step will be to talk about EASI100. I don’t know when that will happen, but if we look at the development of psoriasis, I think we should be there in a couple of years," Prof. Vestergaard added. Progress has also been made in topical treatments for AD, e.g. with the JAK1 inhibitor delgocitinib and the PDE4 inhibitor crisaborol, both demonstrating significant efficacy in the treatment of AD.

The concept of treatable traits in AD

Looking at the so-called treatable traits of AD besides the skin domain, comorbidities, psychological and occupational domains should also be considered. "One thing is an EASI90, but we also need to look at whether the patients are sleeping well, whether the depression disappeared, or whether they are going to work again," Prof. Vestergaard stressed. Data about important patient’s goals for their AD treatment identified "being itch-free", "getting better skin quickly", and "healing of all skin defects" as the top 3 and, according to Prof. Vestergaard, these areas are currently already covered.
“But we also have to look at regaining control of the skin disease, maybe inducing remission, having confidence in the therapy, being free of pain, and having no fear that the disease will become worse,” Prof. Vestergaard mentioned as an outlook.

5. Reich K et al. JAMA Dermatol. 2020;156:1333-143

Children with AD: high risk of bacterial infections in carriers of a filaggrin gene variant

Superinfections are the most common complications in atopic dermatitis (AD). When lesions become excoriated, they act as a gateway for the entry of infectious agents. Furthermore, a disruption of the normal skin microbiome contributes to infections.

As Prof. Alina Suru (Carol Davila University of Medicine and Pharmacy, Romania) pointed out, patients with AD have an increased risk of infection due to defects in the skin and further cutaneous innate and adaptive immune abnormalities with type-2 inflammation. *Staphylococcus aureus* colonisation and cutaneous dysbiosis are additional factors that leave AD patients prone to infections [1]. AD-associated skin infections can progress to systemic complications such as sepsis, endocarditis, and septic arthritis. Whereas infectious complications must be treated with antibiotics, it is controversial whether to use antibiotics simply in exacerbations of AD [2]. Up to 90% of patients with AD are colonised by *S. aureus*, but it is difficult to distinguish between colonisation and infection. When commensal bacteria of the skin decrease, the virulence of *S. aureus* is enhanced, as commensal bacteria modulate the immune system to minimise inflammation and outcompete pathogens like *S. aureus* [2,3].

A loss-of-function variant in the filaggrin gene is associated with early-onset AD. “Patients with this gene variant have a 7 times higher risk of having 4 or more episodes of skin infections requiring antibiotics than those without the variant,” Prof. Suru explained.

AD flares can mask bacterial infections

Bacterial infections in paediatric AD can manifest as impetigo, cellulitis, erysipelas, and skin abscesses. In *S. aureus* infections, honey-coloured crusts and pustules are evident, whereas β-haemolytic streptococcus present as well-defined, bright red erythema, thick-walled pustules, and heavy crusting [2,3]. “Things are complicated by the fact that features of flared AD such as increased erythema can mask or resemble signs of infections,” Prof. Suru said.

Bacterial infections can be managed by topical or systemic treatment, such as fusidic acid or mupirocin in localised infections, and systemic antibiotics, such as cephalxin, if the lesions are spread out over the body. If the infection is invasive, intravenous antibiotics are indicated, and in the case of methicillin-resistant *Staphylococcus aureus* (MRSA), antibiotics to which the organism is sensitive should be used [4].

Prof. Suru concluded that the best way to prevent skin infections in AD patients is to eliminate predisposing factors by improving skin barrier defects and by sufficient anti-inflammatory maintenance medication (see Figure).

**Figure:** The risk of skin infections can best be minimised by skin barrier improvement and anti-inflammatory therapy [1]

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Men on biologics report fewer adverse events than women

Results from Dutch pharmacovigilance data on biologic treatment showed a significant difference in the frequency of adverse drug reactions (ADR) in men and women. Interestingly, this did not lead to a discrepancy in patient-reported disease burden among the 2 groups.

“In general, we know that women experience more ADRs, and these more often lead to hospitalisation than in men,” Ms Jette van Lint (Pharmacovigilance Centre Lareb, the Netherlands) stated [1]. Around 5% of unplanned hospital admissions are caused by ADRs [2]. Factors contributing to this difference in ADR reporting by men and women may include hormones, pharmacokinetics and pharmacodynamics, besides behavioural variance and social roles [1,3].
"We aimed to investigate differences in nature, frequency, and burden of patient-reported ADRs of biologics," Ms van Lint explained. The prospective cohort study analysed monitoring data on patients treated with biologics for an immune-mediated inflammatory disease from 9 Dutch hospitals. The most common treatment indications were rheumatic diseases (73%), such as rheumatoid arthritis and psoriatic arthritis. Adalimumab and etanercept accounted for 67% of biologic drugs. Thus, the final study cohort consisted of 748 consecutive patients with a rheumatic disease on adalimumab or etanercept. Among these participants, 59% were women. The mean age of included women and men was 56.6 and 58.2 years, respectively, and 48% of all participants reported at least 1 ADR. As a result, Ms van Lint revealed that a significantly higher proportion of women (55%) reported an ADR compared with 38% of men (P<0.001). The 882 ADRs that were reported were classified into 264 different types, of which 71 were reported by men and women equally. At first, a significant difference in ADR distribution was identified. Ms van Lint further explained that included women reported a higher frequency and a wider variety of injection site reactions, and they more often reported haematoma and cystitis. Yet, after the correction for multiple testing, this statistical significance was no longer present. In terms of ADR burden, a trend towards a higher impact on the male population was observed, but the difference was not statistically significant. Nevertheless, some ADRs stood out, such as pneumonia, which was reported as highly burdensome by both sexes.

"We cannot confirm a causal relationship between the ADR and the biologics. On the one hand, this is a limitation because we cannot be sure that the reported complaints are actually caused by the biologic. Still, on the other hand, this provides insights into the way patients experienced the ADR," Ms van Lint discussed. "I think, in conclusion, it is very important for clinicians to be aware of these differences," she highlighted.

No adverse pregnancy outcomes in patients exposed to baricitinib

Atopic dermatitis and alopecia areata may present in women of childbearing age. Therefore, data on unintentional exposure during pregnancy is important. According to an analysis of a pharmacovigilance system, pregnancies with reported exposure to the JAK inhibitor baricitinib showed similar clinical outcomes compared with pregnancies in the general population.

All JAK inhibitors are contraindicated during pregnancy, and women of childbearing age should use effective contraception. But many pregnancies are not recognised in time to avoid drug exposure. Therefore, an analysis of phase 3 randomised-controlled trials (RCTs) and post-marketing sources, including the use of baricitinib in rheumatoid arthritis, alopecia areata, and atopic dermatitis during pregnancy, was performed to shed some light on a possible deleterious effect [1]. All pregnancy events identified in RCTs and post-marketing sources, including spontaneous reports to the global Lilly pharmacovigilance system through 13 August 2021, were included.

Clinical outcomes of pregnancy included live births, spontaneous abortions, elective terminations, and pregnancies with pending outcomes at the time of cut-off data and patients lost to follow-up. Overall, 91 pregnancies could be identified, 77 with maternal exposure to baricitinib and 14 with paternal exposure. Of the pregnancies with maternal exposure to baricitinib, 8.1% in the post-marketing data and 22% in the RCT ended in spontaneous abortion. This falls in the range of the estimated 10–20% of clinically recognised pregnancies in the general population that end in miscarriage or spontaneous abortion [2,3]. Most spontaneous abortions (83%) occurred during the first trimester (2 out of 3 in the post-marketing population and 8 out of 9 in the RCTs). Only 2 congenital malformations were reported in the analysis, both in the post-marketing sample: 1 anencephaly, resulting in spontaneous abortion, and 1 hip dysplasia ending in a live birth.

The authors concluded that the clinical outcomes of pregnancies with reported exposure to baricitinib seem comparable to those observed in the general population in Europe and the US. However, due to the low number of cases, especially regarding paternal exposure, and scarce information, risk assessment is challenging. Therefore, pregnancy outcomes in patients treated with baricitinib will be monitored through ongoing surveillance. In addition, prescribers should follow guidance on contraception during the use of baricitinib in women of childbearing age.


**Conceptual framework of adverse drug reactions may improve treatment of patients with IMIDs**

A conceptual framework may offer practical solutions when dealing with adverse drug reactions (ADRs) in immune-mediated inflammatory diseases (IMIDs). Researchers identified 6 main themes, which influence the timecourse of ADRs.

Many patients with IMIDs suffer from ADRs during chronic drug treatment. Usually, only ADRs that occur with drug use are reported. However, the Dutch pharmacist and researcher Ms Jette van Lint (Pharmacovigilance Centre Lareb, the Netherlands) proposed that the patient-reported medical information on the common patterns in the course and timeframe of ADRs, which are often overlooked, may provide valuable further insights for finding practical solutions when dealing with ADRs in patients with IMIDs [1].

Ms van Lint and her team used qualitative data from the Dutch Biologic Monitor (DBM) to assess the patient’s descriptions of the course of ADRs they experienced. Of consecutive patients using biologics mainly for IMIDs, 53% (n=730) reported 2,035 ADRs and elaborated on the course of those reactions in an open-ended text field in a web-based questionnaire, which they completed bi-monthly. Two pharmacovigilance assessors analysed these answers, ultimately visualising the findings on an Ishikawa diagram. “We developed a conceptual framework with 4 themes including descriptive items and 2 other themes including the factors which influence the course of ADRs,” stated Ms van Lint (see Figure). The descriptive themes were the moment or period of ADR occurrence, its frequency, duration, and the time associated with the administration moment. The identified influencing factors were categorised either under the theme of triggering factors for ADR occurrence or aggravation or improving factors.

The conceptual framework of the patient-reported descriptions of the course of ADRs of biologics provides information on a broader level and supplements the currently available information on the nature and frequency of ADRs. It will support the healthcare professionals dealing with ADRs to find practical solutions and may thereby optimise the medical treatment of patients with IMIDs.


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Figure: Conceptual framework of descriptions of the course of adverse drug reactions reported by patients using a biologic for immune-mediated inflammatory diseases [1]
Psoriasis: The Beat Goes On

Systemic treatment for psoriasis: what is on the horizon?
Many treatment possibilities are already available for psoriasis, but there is even more to come. A promising novel oral therapy is in the pipeline with TYK2 inhibition, which showed impressive response maintenance in a withdrawal analysis.

As Prof. Diamant Thaci (University of Lübeck, Germany) pointed out, previously, researchers focused more on pathogenesis, whereas in the future, the phenotype of the patients is expected to play an important role [1].

It is crucial to recognise generalised pustular psoriasis (GPP), a rare type of psoriasis. Frequently it presents with flares of widespread sterile pustules on a background of red and tender skin. IL-36 plays a key role in the pathogenesis of the disease. Published phase 2 data of spesolimab, an anti-IL-36 receptor antibody, showed that more than half of the participants achieved complete clearance of pustules with a single dose of the drug within a week [2]. Imsidolimab is another anti-IL-36 receptor monoclonal antibody that led to rapid and sustained improvement in GPP signs and symptoms, in a phase 2 trial presented at the previous European Academy of Dermatology and Venereology (EADV) congress [3]. In Prof. Thaci’s view, the efficacy of the anti-IL-36 agents will be not an issue but safety. “This will be crucial for establishing these agents as a treatment option,” he said.

A novel treatment option for plaque psoriasis is the dual blockade of IL-17A and IL-17F by bimekizumab, which is supposed to be more efficient than the blockade of IL-17A only. Indeed, in the phase 3b trial BE RADIANT, treatment with bimekizumab resulted in greater skin clearance (PASI100 response) than treatment with secukinumab over 16 and 48 weeks [4]. “We will see in registries whether similar data is found in the daily practice,” Prof. Thaci said. An unexpected result of the trial program with bimekizumab was that PASI100 achieved at 16 weeks could be maintained over 2 years. “Finally, this agent also has a scratch: patients treated with bimekizumab get more candidiasis. How important this is in daily practice will be shown in the future,” Prof. Thaci explained.

Another novel treatment option is sonelokimab, an anti-IL-17A/F nanobody. This agent blocks the homodimers of IL-17A and IL-17F and the heterodimer IL-17A/F. In a phase 2 dose-finding trial, this agent showed an excellent treatment response, with rates for PASI90 and PASI100 ranging from 79.2% to 90.4% and 40.4% to 56.9%, respectively [5].

Effective oral therapy on the horizon
“In atopic dermatitis, we have a JAKmania, but in psoriasis, we have a TYKmania,” Prof. Thaci said. Deucravacitinib is an oral TYK2 inhibitor that selectively inhibits TYK2 via an allosteric mechanism by uniquely binding to the regulatory domain rather than to the active domain where JAK1/2/3 inhibitors bind. This unique binding provides high functional selectivity for TYK2, which might have advantages regarding tolerability [6]. “Deucravacitinib is more effective than apremilast, which is not a high hurdle. But what is interesting is that if you stop treatment, patients maintain PASI75 for 6 months (see Figure). This has never happened before with an oral drug: this is a new quality. There is a place for oral therapy in psoriasis,” Prof. Thaci said [7]. In addition, there will be a couple of novel topical preparations. “If you were expecting nothing on the horizon for psoriasis, I must tell you that there is,” Prof. Thaci concluded.

Figure: Maintenance of PASI75 response through week 52 following deucravacitinib withdrawal [7]

Topical therapy in psoriasis: an important partner in combination therapy

The therapeutic efficacy of a systemic agent can not only be enhanced by dose escalation but also by combination with topical treatment. Choosing the right vehicle is especially important in scalp psoriasis.

In many patients, psoriasis shows a relapsing course with remissions and exacerbations and is sometimes refractory to treatment. In case of systemic treatment, escalating dosage, shortening injection intervals, or switching therapy is not the only way to enhance therapeutic efficacy. As Prof. Peter van de Kerkhof (Radboud University Medical Centre, the Netherlands) pointed out in his lecture, adding topical therapy to systemic agents might be a smart way to improve efficacy without safety concerns [1]. Today, combination therapies have shown improved efficacy compared with monotherapy with systemic agents [2]. Until today, topical corticosteroids play a key role in the treatment of psoriasis, especially for localised disease, due to their anti-inflammatory, antiproliferative, immunosuppressive, and vasoconstrictive effects.

Topical corticosteroid therapy in combination with etanercept has shown improved efficacy without any increased safety concerns. Another recommended topical combination is calcipotriol plus betamethasone dipropionate. Together with adalimumab, this combination showed superior efficacy compared with adalimumab monotherapy at 4 weeks. Moreover, patients treated with conventional disease-modifying drugs may benefit from the addition of topical agents. By adding calcipotriol to methotrexate, a lower cumulative dose of the latter could be observed, and there was an increased time to relapse after its discontinuation. Another study showed that the clinical response was enhanced by adding calcipotriol plus betamethasone dipropionate ointment to low-dose cyclosporin. Topical calcipotriol treatment has also been shown to improve the efficacy of acitretin.

Taken together, topical corticosteroids in psoriasis are still strong options in the management of the disease. Of note, the optimal vehicle choice is often the one the patient is most likely to use [2]. For example, the scalp can successfully be treated with solutions, foam, or spray, whereas creams are preferred for glabrous skin. In every case, patient preference should be considered when selecting the most appropriate vehicle.

GPP flares: pronounced undertreatment is common

According to a US retrospective analysis of healthcare records from 2015 to 2020, a quarter of patients with general pustular psoriasis (GPP) flares receive no treatment at all. Despite severe and potentially life-threatening symptoms, many patients were only treated with pain medication and topical steroids.

Due to the rareness and unpredictability of GPP flares, only minimal research documenting the characteristics of these events has been performed. “Therefore, our study aimed to characterise flare episodes in GPP patients and respective treatments,” said Dr Wendell Valdecantos (Boehringer Ingelheim Pharmaceuticals, CT, USA), who presented the study [1].

This retrospective descriptive study included adult patients with GPP (ICD-10 code L40.1) identified in US electronic health record (EHR) data between 1 July 2015 and 30 June 2020. Only patients with at least 12 months of healthcare activity documented in the EHR after the GPP diagnosis and with notes available were included. An algorithm identified flare episodes based on diagnosis coding, setting of care, type of provider, GPP disease terms, and flare terms found in the EHR. Flare episodes were defined as consecutive days that a flare was documented in the records and were characterised by the frequency of occurrence per patient, the setting of care where they were identified, the type of specialist managing the episode, associated symptoms, and the treatments before, during, and after the episode.

Of the 48.6 million patients with EHR notes available, 1,535 patients with GPP were identified. Of these, 271 patients had at least 1 flare episode documented in their records and accounted for 513 flare episodes during the study period. More than 80% were Caucasian. Most flares occurred in the outpatient setting (57%), followed by inpatient and emergency room settings. Most flares occurred 1 month after an initial GPP diagnosis. As Dr Valdecantos pointed out, “87% of patients had flares identified on the same day they got the diagnosis.” Various treatments were used: most commonly, both during the episode (in 35% of cases) and up to 30 days prior to an episode (in 22% of cases), were topical steroids, followed by opioids and other oral agents. “Of note, 21% of patients were using opioids for flare episodes, and 25% were not receiving any treatment during the episode and up to 30 days after,” Dr Valdecantos commented.

References:
Despite the limitation of a retrospective study, this data shows a significant unmet need for the treatment of GPP flares, as evidenced by patients seeking treatment in inpatient and especially emergency room settings and the lack of advanced therapies beyond topical steroids. "Lastly, treatment with opioids was common during flare episodes, indicating the need for pain management," Dr Valdecantos concluded.


All patients with GPP benefit from IL-36 inhibitor therapy

The IL-36 receptor antibody spesolimab showed to be effective in all patients with generalised pustular psoriasis (GPP), independent of age, sex, race, BMI, IL-36RN mutation status, and different physician global assessment scores. This was the result of a subgroup analysis of the phase 2 trial Effisayil 1.

In the 12-week randomised, placebo-controlled, phase 2 Effisayil 1 trial (NCT037832792), a single intravenous dose of the anti-IL-36 receptor antibody spesolimab led to a higher incidence of skin clearance compared with placebo: 54% of patients in the spesolimab group versus 6% in the placebo group achieved complete clearance of pustules, corresponding to a general pustular psoriasis global assessment (GPPGA) pustulation subscore of 0 (primary endpoint) [1]. The key secondary endpoints were a GPPGA total score of 0 or 1 (clear or almost clear skin).

At the SPIN meeting, a subgroup analysis of this trial assessed the treatment effects of spesolimab on the primary and key secondary endpoints in pre-specified patient groups according to age, sex, race, BMI, and different physician global assessment scores for pustular psoriasis [2].

Efficacy of spesolimab was consistent across all pre-specified subgroups for the duration of the study. Subgroup treatment effect estimates were generally comparable to those of the overall trial population. Interestingly, spesolimab efficacy was independent of IL-36RN mutation status; the proportion of IL3-6RN-negative patients achieving the primary endpoint was 9/21 patients (42.9%) with spesolimab and 0/11 patients with placebo; for IL-36RN-positive patients, 7/8 (87.5%) with spesolimab and 1/6 (16.7%) with placebo achieved the primary endpoint (interaction P=0.982).

The authors concluded that the efficacy of spesolimab was consistent across all pre-specified subgroups and was generally comparable with the overall trial population.


IL-17A/F inhibitor bimekizumab shows higher response and maintenance rates compared with secukinumab

An analysis of the long-term efficacy of bimekizumab versus secukinumab found greater proportions of response and maintenance for the IL17A/F inhibitor. In the phase 3b BE RADIANT trial, 88.0% of bimekizumab and 79.1% of secukinumab responders reaching a Psoriasis Area and Severity Index (PASI) ≤2 at week 16 upheld response to week 48.

Data obtained from psoriatic patients has revealed that not only the achievement of clear or almost clear skin is very important, but also the durability of the therapy effect [1,2]. With this in mind, a post-hoc analysis of the phase 3b, head-to-head BE RADIANT trial (NCT03536884) was performed, which evaluated participants achieving a PASI ≤2 or 0 on bimekizumab or secukinumab at week 16 in their ability to maintain the response continuously through week 48 [3].

After randomisation, 743 trial participants received either 320 mg of bimekizumab 4- or 8-weekly or 300 mg of secukinumab every week until week 4 and every 4 weeks thereafter. Overall, baseline characteristics were evenly distributed except for the severity of psoriasis, noted as a higher percentage of Investigator’s Global Assessment (IGA) scale 4 in the bimekizumab arm (35.1%) versus the secukinumab group (27.6%).

Study results at week 16 revealed an achievement of PASI 0 in 61.7% in the bimekizumab arm and 48.9% in the secukinumab arm, whereas PASI ≤2 was found in 85.3% and 76.5%, respectively. Comparing the maintenance rates, 63.7% of participants on bimekizumab and 54.3% of those on secukinumab were able to retain PASI 0. A continuance of PASI ≤2 response from week 16 to 48 was detected in 88% of the bimekizumab and 79.1% of the secukinumab group. Of note, 93% (bimekizumab) and 87.4% (secukinumab) of study participants who started with a PASI 0 at week 16 held up a PASI ≤2 through to week 48.
So, in conclusion, the higher percentages of bimekizumab-treated participants reaching PASI 0 or ≤2 at week 16 versus those in the secukinumab arm were perpetuated into higher rates of continuous maintenance of response with ongoing treatment up to 48 weeks.


Greater PASI reductions lead to less impairment in social and sexual life

Both therapies with guselkumab and adalimumab improved social relationships and sexual health in patients with psoriasis compared with placebo at week 12. At week 24, guselkumab was superior to adalimumab regarding the improvement of social relationships and sexual health.

Data on the association of social relationships and sexual health with different psoriasis treatments is scarce. Therefore, an analysis of phase 3, randomised, double-blind VOYAGE 1 and 2 trials (NCT02207231 and NCT02207244) assessed the influence of therapy with guselkumab or adalimumab on social relationships and sexual difficulties in patients with psoriasis [1]. Impairment in these domains was assessed with questions 8 and 9 of the Dermatology Life Quality Index (DLQI) (being question 8 the following: "Over the last week, how much has your skin created problems with your partner or any of your close friends or relatives", and question 9: "Over the last week, how much has your skin caused any sexual difficulties"). Impaired social relationships and sexual difficulties were defined by a response of "a lot" or "very much".

At baseline, patients with higher Psoriasis Area and Severity Index (PASI) tended to have also greater difficulties in these domains, which was especially true for women. After treatment with guselkumab and adalimumab, the proportion of participating men and women having difficulties in their social or sexual life declined. Greater improvements were seen in patients with a better PASI response.

At baseline, 31.2% to 34.9% of men and 38.9% to 44.1% of women had difficulties in social relationships. At week 12, a significant improvement could be seen with active treatments compared with placebo in both sexes. Both social and sexual impairments further improved continuously through week 24. At this time, in both sexes, treatment with guselkumab resulted in a significantly lower proportion of patients with impaired social relationships or sexual difficulties versus placebo, but also versus adalimumab. At week 24, only 3.8% of women treated with guselkumab versus 14.1% with adalimumab still had impairment in their social life (P<0.001). The percentage of patients with sexual impairment was similar (2.1% of women treated with guselkumab compared with 11.0% of those treated with adalimumab; P<0.001).

The authors concluded that in both men and women with psoriasis, guselkumab treatment resulted in lower proportions of patients with impaired social relationships or sexual difficulties compared with placebo at week 16 and adalimumab at week 24.


Paediatric psoriasis: ixekizumab beneficial in difficult-to-treat areas

High clearance rates in challenging body areas of children were observed on long-term ixekizumab treatment for psoriasis. After 108 weeks, scalp psoriasis, for example, was cleared in 76.2% and genital psoriasis in 87.5% of patients.

Psoriasis involving certain difficult-to-treat areas of the body can account for a more substantial impact on quality-of-life than might be expected from just looking at the surface area involved [1]. Thus, an international group with primary investigator Dr Marieke Seyger (Radboud University Medical Centre, the Netherlands) focussed on the long-term efficacy of ixekizumab in children and adolescents with moderate-to-severe psoriasis, especially in these areas [2]. They presented data from the phase 3 IXORA-PEDS trial (NCT03073200) and its open-label extension until week 108.

Of the 171 participants randomised in the placebo-controlled study phase, 83.7% concluded the extension phase after more than 2 years. The mean age at baseline was between 13 and 14 years, and the diagnosis of psoriasis had been established at a mean of 4.7 years before. The overall efficacy results showed Psoriasis Area and Severity Index (PASI)75, 90, and 100 responses of 91.7%, 79.0%, and 55.1%, respectively [1]. A considerable proportion of participants in the placebo and the ixekizumab arms presented with affections in challenging
areas at baseline: nails (Nail Psoriasis Severity Index Score (NAPSI) >0: 21.4% and 29.6%, respectively), scalp (Psoriasis Scalp Severity Index score (PSSI) >0: 89.3% and 88.7%), and palmoplantar (Palmoplantar Psoriasis Area and Severity Index (PPASI) >0: 16.1% and 14.8%) [2]. The detailed analysis of these sites found clearance of psoriasis in a substantial percentage of participants at week 108: 68.1% achieved NAPSI=0, 76.2% PSSI=0, 90% PPASI 100, and 87.5% had no psoriasis on the genitals. Furthermore, a significant reduction in itch from baseline (P<0.001) was observed.

The investigators further emphasised that these challenging body areas significantly impact patients’ quality-of-life.

Psoriasis patients see great benefit in achieving complete skin clearance

From patients’ point of view, reaching Psoriasis Area and Severity Index (PASI) responses of 90/100 is often linked to an emerging feeling of large benefit through treatment. The likelihood of a 0/1 score in the Dermatology Life Quality Index (DLQI) is heightened by factors such as biologic therapy and higher age.

How important are high levels of skin clearance for patients with psoriasis and their quality-of-life? To answer this question, Prof. Matthias Augustin (University Medical Centre Hamburg, Germany) and his group performed a retrospective cohort study based on data from the PsoBest registry [1]. The study analysed PASI, DLQI, and Patient Benefit Index (PBI) 1 year after starting systemic treatment for psoriasis. Over 3,800 adults with moderate-to-severe disease who continued until visit 4 at 12 months were evaluated. As for previous treatments, 45.2% never had systemic therapy, and 14.9% already had been on biologics, the latter representing 41.3% of systemic treatments.

The clinical outcomes revealed that about one-third of patients presented with PASI 100 or 90/100 after 1 year. This coincided with a DLQI of 0/1, which stands for “no impact on quality-of-life” in 47.2% of cases. However, around 10% of patients still had a DLQI >10.

Assessing therapy achievements from the patients’ point of view, PBI values of ≥3.5 were observed in 24.2% of cases, indicating the highest treatment benefit. Again, a high level of skin clearance showed a positive effect on this outcome: PASI100 and 90/100 were associated with 49% and 36.1% of PBI ≥3.5, respectively, while this score was only achieved by 10.4% of those with PASI <75 (see Figure).

Several baseline factors have an impact on the likelihood of an unimpaired quality-of-life (DLQI 0/1). The odds were increased by treatment with biologics (P<0.001), higher age (P=0.002), and longer-standing disease (P=0.004). The chances of DLQI 0/1 were lower in the case of >2 comorbidities (P=0.004), female sex (P=0.001), and raised BMI (P=0.002).

In his summary, Prof. Augustin highlighted 3 aspects of the results: only a minority of psoriasis patients achieved complete skin clearance after 12 months of systemic treatment; those with better skin clearance reached a DLQI 0/1 or a PBI ≥3.5 at higher proportions; and a completely cleared skin is of key importance for the patients.

The Future Is Bright for Vitiligo

Predilection sites for skin signs of vitiligo disease activity determined

The distribution of disease activity signs shows a discrepancy between segmental and non-segmental vitiligo. The new study also detected hotspots for the presence of different activity signs, such as the Koebner phenomenon and hypochromic areas.

As the course of depigmentation in vitiligo is difficult to foresee, the possibility of determining skin signs of activity may be helpful for disease management [1]. A study by Dr Liesbeth Delbaere and colleagues (Ghent University Hospital, Belgium) aimed to establish the prevalence of confetti-like depigmentation, the Koebner phenomenon, and hypochromic areas/borders [2]. An association to clinical activity was found for these signs that are included in the Vitiligo Signs of Activity Score (VSAS) [3].

The study included 503 vitiligo patients, of whom 446 had non-segmental and 57 had segmental disease [2]. At least 1 activity sign for vitiligo was found in 51% of patients with non-segmental disease, yet only in 9% of patients with the segmental form. Furthermore, in non-segmental vitiligo, all 3 activity signs were observed in around one-third to one-fourth of patients, while in segmental vitiligo, the Koebner response did not occur, and confetti-like depigmentation was rare.

Looking at 15 different body areas in those with non-segmental vitiligo, confetti-like depigmentation was present in around 40% on dorsal arms, feet, and ankles. The highest prevalence of the Koebner phenomenon was seen in around 30% on the back of hands and anterior legs. Hypochromic borders occurred most frequently on anterior arms and legs.

Based on the evaluation of 65 body locations, joints on posterior elbows/hands and anterior knees were similarly recognised as hotspots for confetti-like depigmentation and Koebner response (see Figure). In confetti-like depigmentation, the front ankle joint and, in the Koebner phenomenon, the front elbow and shoulders were also included. Hotspots for hypochromic areas were different and less concise: whole back, posterior legs, elbows, and axilla. The investigators expressed that knowing where the hotspots are will help to improve and simplify clinical detection of signs.

Vitiligo-childhood onset commonly under 10 years

In a Tunisian single-centre study, over half of the children with vitiligo were 1–8 years old at diagnosis. Due to the lack of a standard, administered therapies varied with a preference for topical corticosteroids (TCS) in monotherapy or combination treatment.

To gather insight into childhood-onset vitiligo, a single-centre study on clinical profile and therapeutic management was conducted in Tunisia. The study included 205 young patients observed from 2006 to 2021 [1]. It comprised a little more girls than boys, with a mean age of 10.2. On average, 14 months passed before the diagnosis, and 55% of the children had an early onset at the age of 1–8 years at first lesion manifestation. Common vitiligo constituted the great majority of clinical varieties (93.2%). Segmental, guttate, and linear vitiligo only presented in a few cases. Face (44%), lower (36.5%), and upper limbs (25.4%) were involved most often. Over half of the children presented with generalised vitiligo (54.1%), while 45.8% suffered from localised disease. In 14% of cases, other family members also had a diagnosis of vitiligo.

As no standard therapy for children with vitiligo is available, treatments showed great variety. More than one-third was...
treated with TCS (36%), 17% with a combination of TCS and antioxidants, and 11% received TCS plus tacrolimus. Among other treatments used were: TCS plus calcipotriol (8%), tacrolimus monotherapy (7%), and 308-nm excimer lamp (5%). Overall, these therapies were beneficial in about three-quarters of the cases, with 8% achieving complete remission, 21% stable disease, and 48% developing re-pigmentation. In contrast, 23% experienced an extension of their lesions during the treatment.

In summary, the authors stated that local treatments, in particular TCS alone or combined with other agents, are the most privileged in childhood vitiligo as they are well tolerated and associated with good response.


Where Are We Now in Hidradenitis Suppurativa

New treatments for HS: IL-17 inhibitors next in practice?
More therapy options are still lacking to manage most patients with hidradenitis suppurativa (HS) effectively. The next agents that approach approval will likely be IL-17 inhibitors.

"We have some kind of explosion of new studies in HS: around 140 studies are registered in clinical trials, and approximately half of them concern phase 1, 2, or 3," Dr Axel Villani (University of Lyon, France) said in his opening remarks on pipeline treatments [1]. Many of the different agents tested in HS can already be found in trials on psoriasis. "HS and psoriasis share some similarities in terms of molecular signature and inflammation, but they are not exactly the same," Dr Villani pointed out.

Among the manifold possible treatment targets influencing the immune response in HS are IL-1, IL-17, IL-23, IL-36, and B-cells. Research on IL-1 includes 2 small studies on MABp1 (NCT02643654) and anakinra (NCT01558375), and a phase 2 trial on bremekimab (NCT03512275), in which the IL-1α inhibitor demonstrated significant efficacy with about 60% achieving Hidradenitis Suppurativa Clinical Response 50 (HiSCR50), both in participants who were anti-TNF naïve (P=0.02) or who had anti-TNF failure (P=0.04) [2–4]. In terms of IL-23 and IL-36, there is 1 active (NCT04876391) and 1 completed (NCT04762277) spesolimab study, but results have not been published yet. Moreover, the PDE4 inhibitor apremilast has been evaluated as a therapeutic agent in HS. Interesting results came from an investigation that followed responders (n=8) from a small study over 2 years and found prolonged responses at 1 and 2 years [5]. B-cells and plasma cells are still controversial potential treatment targets in HS. "There is a lot of recruitment of plasma cells and B-cells in the skin at least at the acute phase of the disease, but the main concern is that we don’t know if they are protectors or pathogenic cells," Dr Villani explained. Recently, Bruton’s and spleen tyrosine kinases have been proposed as possible subjects of further research [6].

IL-17 inhibitors may be the next available agents
To date, IL-17 inhibitors are the most advanced new therapies under development for HS. Published data on brodalumab, bimekizumab, and secukinumab is available [7]. An open-label study on brodalumab (NCT04249713) included 10 participants who all reached HiSCR50, and 80% also showed a category change in International Hidradenitis Suppurativa Severity Score System (IHS4) [8]. No adverse events of grade 1 or 3 were reported. Available bimekizumab results come from phase 2 trials [7]. One study (NCT03248531) encompassed a placebo and a bimekizumab arm plus an adalimumab group as active control [9]. At week 12, the results for HiSCR50, 75, and 90 were 24%, 11%, and 0% for placebo, 60%, 39%, and 17% for adalimumab, as compared with 57%, 50%, and 35% in the
bimekizumab arm, respectively. Efficacy of bimekizumab was also seen in IHS4 score ameliorations. No new safety signals were found compared with the profile known from studies in other indications [7]. Based upon these promising results, the phase 3 BE HEARD I study (NCT04242446) was initiated and is currently active. "When it comes to secukinumab, we are expecting to see the results perhaps at the upcoming EADV congress. Up to now, the data we have comes from a poster that clearly showed achievement of Physician Global Assessment (PGA) response and lower inflammatory lesions at week 16 compared with placebo," Prof. Thrasyvoulos Tzellos (Nordland Hospital Trust, Norway) explained, as he presented the IL-17 data in a complementing talk. The phase 2 results are already available (NCT02421172). Furthermore, the phase 3 SUNRISE trial is underway (NCT03713632). "Most probably, we are talking about 2 drugs that will come to the market soon, hopefully," Prof. Tzellos predicted.

**IHS4 better suited as an outcome measure in HS trials?**

The International Hidradenitis Suppurativa Severity Score System (IHS4) includes and accentuates draining tunnels. Compared with the currently most often used Hidradenitis Suppurativa Clinical Response (HiSCR) score, IHS4 shows advantages in illustrating study outcomes.

Unlike in psoriasis and atopic dermatitis, the inflammatory element of hidradenitis suppurativa (HS) advances [1]. "We have a disease that progresses from an inflammatory component to a scarring component if the inflammatory part is not treated well and early enough," Prof. Thrasyvoulos Tzellos (Nordland Hospital Trust, Norway) stated. Up to now, adalimumab is the only approved biological treatment, thus, there is still a high unmet need. Still, there is somewhat unimpressive data on drug survival rates of adalimumab in HS (56.3% at 1 year and 30.5% at 2 years), with ineffectiveness being the main reason for discontinuation [2]. Currently, the common treatment goal is a 50% reduction in the HiSCR score [1]. "Do we need higher threshold outcomes in order to depict higher inflammatory effects?" Prof. Tzellos asked. As phase 2 data from bimekizumab (NCT03248531) showed that the use of higher HiSCR thresholds was able to demonstrate drug efficiency and simultaneously reduce the rate of placebo response (see Figure), his answer was ‘yes’ [1,3].

Prof. Tzellos continued that using HiSCR involves an inherent problem, as it only measures a reduction in the total count of abscesses and nodules but disregards draining tunnels. This may lead to study results in which participants who reach HSCR100 still have actively draining tunnels. A validated score that captures all the components is the IHS4 score [4]. It includes draining tunnels and assigns different weights to the different types of lesions: nodules are multiplied by 1, abscesses by 2, and draining tunnels by 4. A post-hoc analysis of individual patient data from the PIONEER 1 and 2 trials (NCT02906930 and NCT01468233) that used the IHS4 score led to decreased placebo response rates between 4.5% and 12% [1,5]. “Actually, it reduced it to the rates we are familiar with in psoriasis and atopic dermatitis,” Prof. Tzellos commented. Further analysis of PIONEER 1 and 2 data by the Hidradenitis Suppurativa Foundation identified and externally validated IHS4-55 as an important dichotomous outcome [1]. “IHS4-55 will replace HiSCR because it has the same abilities when it comes to discriminating treatment groups, but it does not have the same drawbacks HiSCR has, as it includes dynamically draining tunnels in a validated manner,” Prof. Tzellos summarised.

Figure: Is there a potential to aim for more ambitious HiSCR thresholds? [3]
New Treatment Options in Alopecia Areata

Alopecia areata: light at the end of the tunnel

Alopecia areata (AA) has lacked effective treatment options for decades, and there is an unmet medical need for a reliable therapy in moderate-to-severe cases. With the approval of the first JAK inhibitor pending, there is a treatment for severe cases, "enfin".

AA is a chronic relapsing inflammatory disorder characterised by a non-scarring hair loss on the scalp and/or body. "Being able to do something for these patients has been life-altering for them," said Prof. Maryanne Senna (Harvard Medical School, MA, USA) [1]. Hair loss has important implications regarding self-image, attractiveness, desirability, youthfulness, and self-esteem. "There is an insufficient acceptance that hair loss is an important medical problem," she said.

With a global prevalence of 2%, AA affects both sexes and has an initial onset typically before age 30. Around 10–20% of the patients will develop alopecia totalis. "In the US, until June 2022, no approved treatments for AA were available. Prior to this, we did not really have options for these patients," Prof. Senna said.

2014-2022: An eight-year success story of JAK inhibitors

A breakthrough in therapy was a publication in 2014, where in a patient with plaque psoriasis, the oral JAK inhibitor tofacitinib reversed alopecia universalis [2]. "This set the wheels in motion," Prof. Senna explained. But why are JAK inhibitors so successful? According to a simplified overview of AA pathogenesis, cytotoxic T cells penetrate the proximal anagen hair bulb and initiate an autoimmune attack in response to a still unrecognised antigen. Both CD8-positive and NKG2D-positive T-cells are the major effectors in AA pathogenesis. Cytokines involved in AA pathogenesis, including IFN-y and IL-15, activate signalling via the JAK-STAT pathway. Modulating the signalling at the point of JAKs decreases the inflammatory response. The recent FDA approval was the consequence of the positive results of the oral selective JAK1/2 inhibitor baricitinib in 2 phase 3 trials, BRAVE-AA1 (NCT03570749) and BRAVE-AA2 (NCT03899259) [3]. In these trials, participants had a Severity of Alopecia Tool (SALT) ≥50, and 44% had alopecia totalis at baseline. All 1,200 participants were randomised to once-daily placebo, 2 mg or 4 mg of baricitinib. At week 36, the primary endpoint, a SALT ≤20, was achieved overall by 38.8% (baricitinib 4 mg), 22.8% (baricitinib 2 mg), and 6.2% (placebo) participants in BRAVE-AA1 and 35.9%, 19.4%, and 3.3%, respectively, in BRAVE-AA2. "A subgroup analysis revealed that those with very severe AA showed higher efficacy rates. It provides confidence that even in our most severe patients, we can have a response," Prof. Senna commented. The most common adverse events were acne, increased creatine kinase, and elevations of LDL and HDL cholesterol. Notably, there was only 1 cardiovascular event, a case of myocardial infarction in a 44-year-old with multiple risk factors.

As Prof. Brett King (Yale University School of Medicine, CT, USA) emphasised in his virtual lecture on JAK inhibitors in AA, baricitinib also leads to a regrowth of eyebrow and eyelash hair [4]. "In severe AA, JAK inhibitors should be our first-line treatment option, and we have far more data than with all the other agents," he said. Intralesional steroid injection is the mainstay of therapy for adults with limited disease (e.g. ≤20% scalp hair loss), but for severe AA, systemic therapy is warranted (see Figure).

Unfortunately, therapy with topical JAK preparations proved ineffective for the treatment of AA [5,6].

Figure: Alopecia areata treatment algorithm [4]

Limited AA
• Intralesional CS
• Topical CS ± topical minoxidil 5%
• Topical immunotherapy
• Oral minoxidil

Moderate AA
• Topical CS ± topical minoxidil 5%
• Oral minoxidil
• Pulsed CS
• JAK inhibitors
• Other systemic immunosuppressive drugs

Severe AA
First-line:
• JAK inhibitors
• ± oral minoxidil
• ± intralesional CS
Second-line:
• Other systemic immunosuppressive drugs
• ± oral minoxidil
• ± intralesional CS

Dupilumab: another star on the horizon

The story does not end with the JAK inhibitors. "An atopic background might also play a role in some of our patients,"
Prof. Senna continued. A phase 2 trial published last year showed the efficacy of the IL-4/13 inhibitor dupilumab [7]. In this trial, 60 adult participants with SALT ≥50 were included and randomised to dupilumab or placebo. Among them, 38% had a history of atopic dermatitis (AD), 11% had active AD, 45% had a family history of AD, and 30% had total IgE levels ≥200 IU/mL. Interestingly, the effect of dupilumab differed according to the baseline IgE levels of the patients: 22.5% of those with IgE <200 reduced their scalp hair loss by 50% compared with 46.2% of those with baseline IgE ≥200. “Baseline IgE may aid in dupilumab treatment selection for AA patients,” Prof. Senna commented.

Regrowth within 12 months in most cases of AA
According to textbooks, in 50% of patients, hair will regrow spontaneously within 6 months. In 70% of cases, recovery will occur within 12 months. “But what we notice is that the 30% of patients who have persistent AA over 12 months come back to us,” Prof. Sinclair said, signalling an unmet need. According to an Australian expert consensus statement, patients with a solitary stable patch of AA <12 months have only a 13% risk of developing chronic AA. However, 30.6% of patients with chronic AA will progress to alopecia totalis if not on treatment [3]. As Prof. Sinclair pointed out, the question is whether therapy can alter the risk of progression in chronic AA. This seems to be the case with systemic corticosteroids. “Systemic steroids are the treatment most commonly used, but 50% will relapse if the dose is reduced or stopped,” Prof. Sinclair concluded.

Best of the Posters

Psoriasis treatment: no elevation of MACE and VTE on deucravacitinib
In a special analysis of safety data from phase 3 trials on deucravacitinib, increased frequency of major cardiovascular events (MACE) or venous thromboembolism (VTE) was not found compared with apremilast therapy. Even though many participants had an elevated cardiovascular (CV) risk at baseline, event rates were low and constant over longer drug exposure.

Alopecia areata pathogenesis: known genetic background, unknown environmental triggers
Alopecia areata (AA) is a polygenic and multifactorial autoimmune disease that results in non-scarring hair loss. Both local and systemic environmental factors can trigger the disease.

As Prof. Rodney Sinclair (University of Melbourne, Australia) pointed out, AA is a multifactorial disease with a known genetic background and unknown environmental triggers [1]. Both innate and acquired immunity are involved in the pathogenesis of AA. In a genome-wide association study, 139 single nucleotide polymorphisms could be identified that are significantly associated with AA [2]. Unknown environmental triggers can be divided into local and systemic factors. Local factors are a loss of hair follicle immune privilege causing inflammatory cells to swarm and attack the hair bulb in what is known as the “swarm of bees”. Both intrafollicular CD8 cells and multiple cytokines and chemokines are involved in this process. Systemic factors that might trigger AA are increased serum IFN-γ and serum autoantibodies.

As the diagnosis of psoriasis has been linked to an increased risk of MACE and thromboembolic events, knowledge about a potential further increase of risk through anti-inflammatory medication is important [1,2]. In this context, Prof. Mark Lebwohl (Icahn School of Medicine at Mount Sinai, NY, USA) and colleagues investigated exposure-adjusted incidence rates of MACE and VTE in the treatment of psoriasis with the TYK2 inhibitor deucravacitinib [1]. The analysis was performed on data from the phase 3 POETYK PSO-1 and
Comorbid anxiety and depression may benefit from psoriasis treatment with certolizumab

Treatment of psoriasis with certolizumab could also have a positive impact on depression or anxiety. This is suggested by the results of a pooled analysis of the phase 3 CIMPASI-1 and -2 trials, in which almost half of the depressive and nearly one-third of the anxiety patients achieved a substantial reduction in their disease scores.

A diagnosis of depression and anxiety is more likely in patients with psoriasis than in the general population, and an association between the depression risk and the disease severity has also been identified [1,2]. But does the treatment of psoriasis with certolizumab pegol also affect comorbid anxiety or depression? Pooled data from 3-year phase 3 CIMPASI-1 and -2 trials (NCT02326298 and NCT02326272) was used to assess the resolving rate of these conditions through the Hospital Anxiety and Depression Scale (HADS) [3]. HADS allocates higher values to more severe symptoms, and scores of 11–21 stand for moderate-to-severe disease, while values ≤7 represent no anxiety/depression.

CIMPASI-1 and -2 included a double-blind treatment and maintenance phase from weeks 0–16 and 16–48, followed by an open-label extension through week 144 and a safety follow-up to week 152. The 361 participants with psoriasis receiving certolizumab pegol every second week, received a dosage of 200 mg or 400 mg. The mean baseline age was 45.3 years, and 36.8% were women. The mean baseline Dermatology Life Quality Index (DLQI) was 14.0, the mean HADS-Anxiety was 6.2 with 13.3% ≥11, and the mean HADS-Depression was 4.9 with 9.7% ≥11.

In general, about 31.3% of the participants with anxiety and 47.1% of those with depression achieved HADS scores ≤7. The analysis also revealed a mean reduction of the HADS-Anxiety score of 3.4 after 16 weeks of certolizumab pegol, which further lowered to -4.1 at week 144. The decrease in the HADS-Depression score was also carried on from -5.0 (week 16) to -5.1 (week 144). Of note, a difference of 1.7 is considered minimal clinically important.

The lead author Prof. April Armstrong (Keck School of Medicine of USC, CA, USA) and her colleagues pointed out that, although the number of enrolled participants with anxiety and depression was limited, certolizumab was associated with durable improvements in anxiety and depression for psoriasis patients over 3 years.

Dose tapering in psoriasis is associated with a low relapse rate

Among investigated psoriasis patients receiving biologics, 88% remained in sustained clinical response after 8 months of dose tapering. The low relapse rate, together with remarkable cost savings, supports this approach as an effective strategy for treating psoriasis.

Biologic therapy results in long-term low disease activity or even clinical remission in patients with moderate-to-severe psoriasis; the downside is the high costs. Dr Juan Raul Castro Ayarza (Medicarte, Colombia) and his team performed a cohort study to investigate whether optimisation of treatment by a progressive dose reduction or increase of the administration interval can still prevent relapses in these patients [1].

Patients presenting with psoriasis to a specialised, multicentre health institution in Colombia who were above 18 years of age and treated with biologic therapy with a sustained response for at least 12 months were included. They were treated with different biological agents, including anti-TNFs, ustekinumab, secukinumab, ixekizumab, guselkumab, and risankizumab. Optimisation strategy was achieved either by dose reduction or interval administration increase. Of the 467 patients, 12.2% (n=57) met the optimisation strategy criteria. The majority were men (65%) with a median age of 57 years and a duration of psoriasis of 15 years. They were receiving treatment for 4 years, and the dose tapering was done over 8 months. In 85.8% of patients, the tapering strategy was performed by an increase in the application interval and the remaining 14.2% by dose reduction. Among the patients undergoing the optimisation strategy, 16.4% (n=14/85) received ustekinumab, 14% (n=20/142) adalimumab, 12.6% (n=9/71) secukinumab, 12.3% (n=8/65) ixekizumab, 10% (n=3/30) etanercept, and 7.5% (n=3/40) guselkumab. Psoriasis Area and Severity Index (PASI) >10 was defined as a relapse, and Kaplan-Meier estimates were used to calculate the relapse rate by biologic therapy.

Overall, only 12% (7 out of 57) of patients relapsed, and the incidence rate was 2.2 person-months (95% CI 0.97–4.4). No significant differences in relapse rates according to the type of medication were detected. As such, 88% of patients in the tapering strategy remained in sustained clinical response after 8 months.