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Highlights from the 33rd Congress of the European Academy of Dermatology and Venereology (EADV)

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Introduction

The 33rd congress of the European Academy of Dermatology and Venereology (EADV) was held in Amsterdam, the Netherlands from Sept 24–28, 2024. With over 17,000 participants, this meeting had the highest attendance of any EADV congress to date. The meeting featured over 160 symposia and 20 subspecialty sessions and provided updates and data on new and emerging therapies for a number of skin conditions. This article will highlight interesting findings in atopic dermatitis, psoriasis, and hidradenitis suppurativa (HS).

Reducing the risk of disease comorbidities in psoriasis and atopic dermatitis through biologic therapies

An interesting theme discussed in several late-breaking sessions was the possibility for biologic therapies in atopic dermatitis and psoriasis to reduce the risk of disease comorbidities. Below, I will review presentations by Drs. Armstrong and Irvine, who presented data examining the association of biologic therapy in psoriasis and the risk of subsequent development of psoriatic arthritis,[1] as well as the impact of biologic therapy in atopic dermatitis and the risk of growth suppression.[2]

Biologics for psoriasis and the risk of future psoriatic arthritis

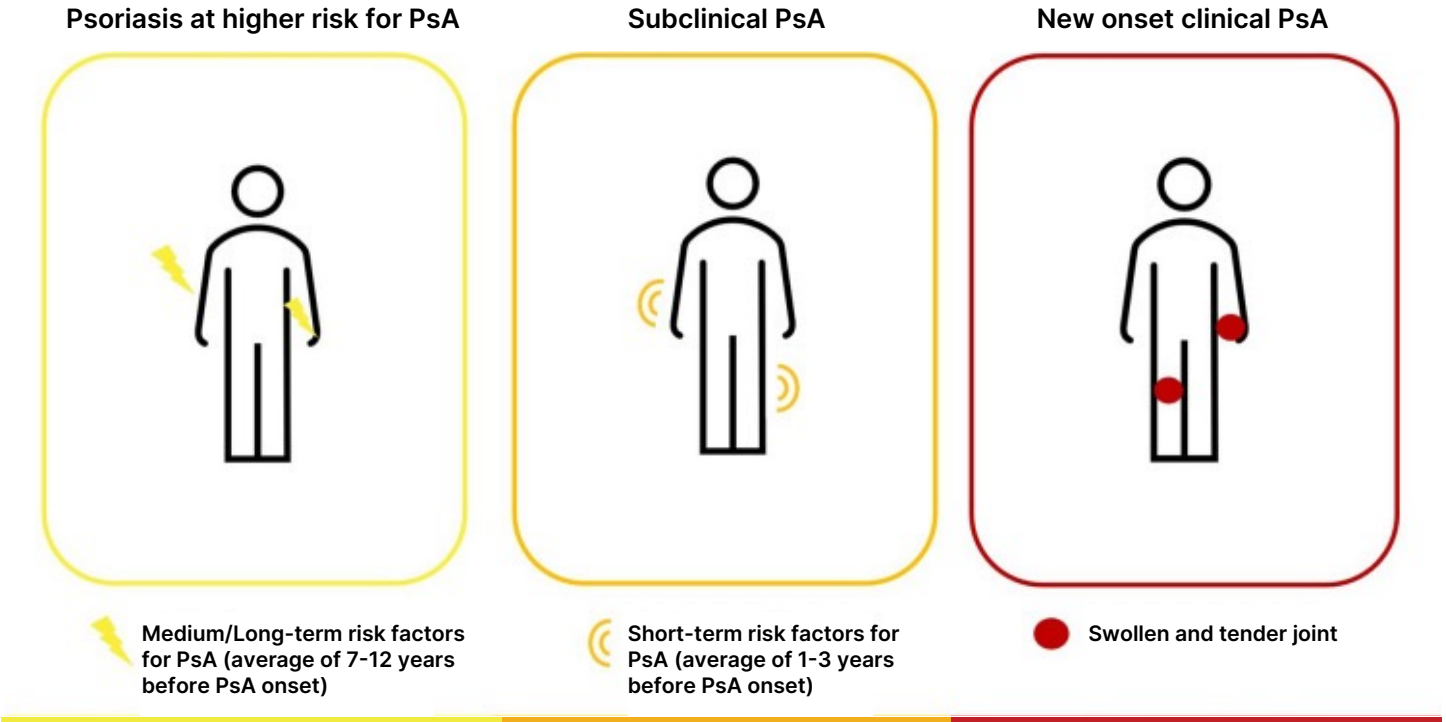
Observational studies suggest that approximately one-third of patients with psoriasis develop psoriatic arthritis, with joint changes usually occurring following psoriasis development.[1] This temporal progression from skin to joint involvement was initially described in the nomenclature put forth by the European Alliance of Associations for Rheumatology (EULAR) task force,[3] which has been revised by Errichetti and Zabotti, 2023[4] in **Figure 1**.

Given this temporal progression and the shared inflammatory mediators in the pathophysiology of psoriasis and psoriatic arthritis, it is biologically plausible that early use of biologic agents in this timeframe may delay or prevent the progression to psoriatic arthritis.

However, the literature to date on this topic is unclear. While many studies show a reduction

of psoriatic arthritis among psoriasis patients on biologics,[5-8] some studies show an increased risk.[9] In her presentation, Dr. Armstrong discussed how significant biases may be impacting these later findings, namely, 1) protopathic bias and 2) survival time bias. For instance, if you consider a typical severe psoriasis patient in your practice who reports joint issues, it is conceivable that you might be more likely to prescribe a biologic agent that also addresses psoriatic arthritis, which could create the impression that the biologic is increasing the risk of psoriatic arthritis. This is referred to as protopathic bias, which is a type of confounding by indication. This bias is likely also at play when comparing different biologic classes. Retrospective studies show that interleukin (IL)-23 agents have the lowest risk of progression to psoriatic arthritis.[9] However, a more likely explanation is that this medication class was chosen for these patients due to a perceived lower risk of psoriatic arthritis. Lastly, survival time bias may explain why psoriatic arthritis occurs earlier among psoriasis patients on biologics.[9] Usually, we prescribe biologics to more severe patients who have "survived" longer with their psoriasis, and are further along on the temporal progression from skin to joint involvement compared to those receiving other treatments.[2]

Overall, while the evidence to date is inconclusive, it is biologically plausible that biologics for psoriasis might reduce the risk of progression to psoriatic arthritis. Ideally, prospective controlled studies are required to further elucidate this potential association.



Psoriasis at higher risk for PsA	Subclinical PsA	New onset clinical PsA
Severe skin involvement	Arthralgia	Peripheral pattern
Nail psoriasis	Imaging evidence of synovio-entheseal inflammation	Oligoarthritis pattern
Obesity		Articular erosions pattern
Familial history for PsA		

Figure 1. Biologics for psoriasis and the risk of future psoriatic arthritis.
Legend: The transition from psoriasis to clinical psoriatic arthritis (PsA) occurs through two stages: (1) "psoriasis at higher risk for PsA," including patients with a medium-long-term risk (average of 7–12 years) of developing PsA (i.e., those with severe skin involvement, nail psoriasis, obesity, and/or familial history for PsA); (2) "subclinical PsA," including patients with a short-term risk (average of 1–3 years) of developing PsA (i.e., those with arthralgia and/or imaging evidence of synovio-entheseal inflammation). Such phases precede "clinical PsA," which may present with three main patterns, including "peripheral," "oligoarthritis," and "articular erosions"
Source: Errichetti and Zabotti, 2023[4]

Biologics for atopic dermatitis and the risk of growth suppression

It is well known that patients with severe atopic dermatitis are predisposed to growth suppression.[10] Potential mechanisms for this include chronic inflammation, stress, sleep disruption, and the effects of systemic/systemically absorbed topical corticosteroids. Dr. Irvine from Ireland presented a post hoc analysis from the Liberty-AD PEDS phase 3 trial looking at the role of dupilumab on the growth of children with severe atopic dermatitis.[2] Children aged 6 to 11 years with severe atopic dermatitis were randomized 1:1 to receive either placebo or dupilumab 300 mg subcutaneously every 4 weeks (both groups were also allowed mild-to-moderate topical corticosteroids). Height was measured at baseline and after 16 weeks of treatment. While growth is expected over this timeframe in children of this age group, the proportion of patients showing at least a five percentile increase in height was consistently and statistically significantly higher in the dupilumab group vs the placebo group. This was observed across all baseline height percentiles (ranging from <25th height percentile to <50th height percentile). Notably, the difference in the proportion of patients reaching this five percentile height increase was quite striking, with some groups reaching over a 25% difference in just a 16-week period.[2]

Overall, this rigorous and controlled data provides compelling evidence that early treatment with dupilumab for severe AD in childhood can have a quick and meaningful impact on improving growth, which may offer lifelong benefits for these patients **(Figure 2)**.

Treatment update for hidradenitis suppurativa

Biologics & small molecules

A number of new biologics and small molecules for HS were reviewed including IL-17, IL-1, tyrosine kinase, and Janus kinase (JAK) inhibitors.

Izokibep is a novel IL-17A inhibitor small molecule therapy designed to overcome limitations of traditional monoclonal antibodies. Izokibep is approximately one-tenth the size of monoclonal antibodies, which enables it to reach higher drug concentrations typically only achievable with intravenous administration. Dr. Papp presented data from a phase 3 trial demonstrating an improvement in the HS Clinical Response of 75% (HiSCR75) of 33% (compared to 21% in the placebo arm) after just 12 weeks of treatment.[11]

Dr. Hunger provided a review of several new and emerging biologics and small molecules for treating HS, including sonelokimab, lutikizumab, remibrutinib and upadacitinib.[12] Sonelokimab is an IL-17A and IL-17F inhibiting nanobody composed of three domains, two with high affinity for IL-17A and IL-17F, and a third that binds to human albumin, allowing for higher drug concentrations to be reached at sites of inflammatory edema. In a phase 2 trial with 24 weeks of follow-up,[13] HiSCR75 was achieved in 56.9% of patients (placebo data for 24 weeks was not reported, but 12-week data previously published shows HiSCR75 29% change compared to placebo).[14] Lutikizumab, the first IL-1 inhibitor studied for HS, is a dual-variable domain IL-1 alpha/IL-1 beta antagonist. In phase 2 studies, lutikizumab reached HiSCR75 in 45.9% of patients compared to 17.5% in the placebo group.[15] Remibrutinib, the first agent studied for HS that specifically targets B-cells, is an oral Bruton's tyrosine kinase inhibitor that prevents B-cell conversion to plasma cells. In Phase 2 studies, HiSCR75 was achieved in 42.4% of patients compared to 18.4% in the placebo group.[16] Lastly, data from a retrospective cohort study on upadacitinib was reviewed, showing a HiSCR75 response rate of over 90% after 12 weeks of therapy. Prospective, controlled trials are required to verify this impressive response.[17]

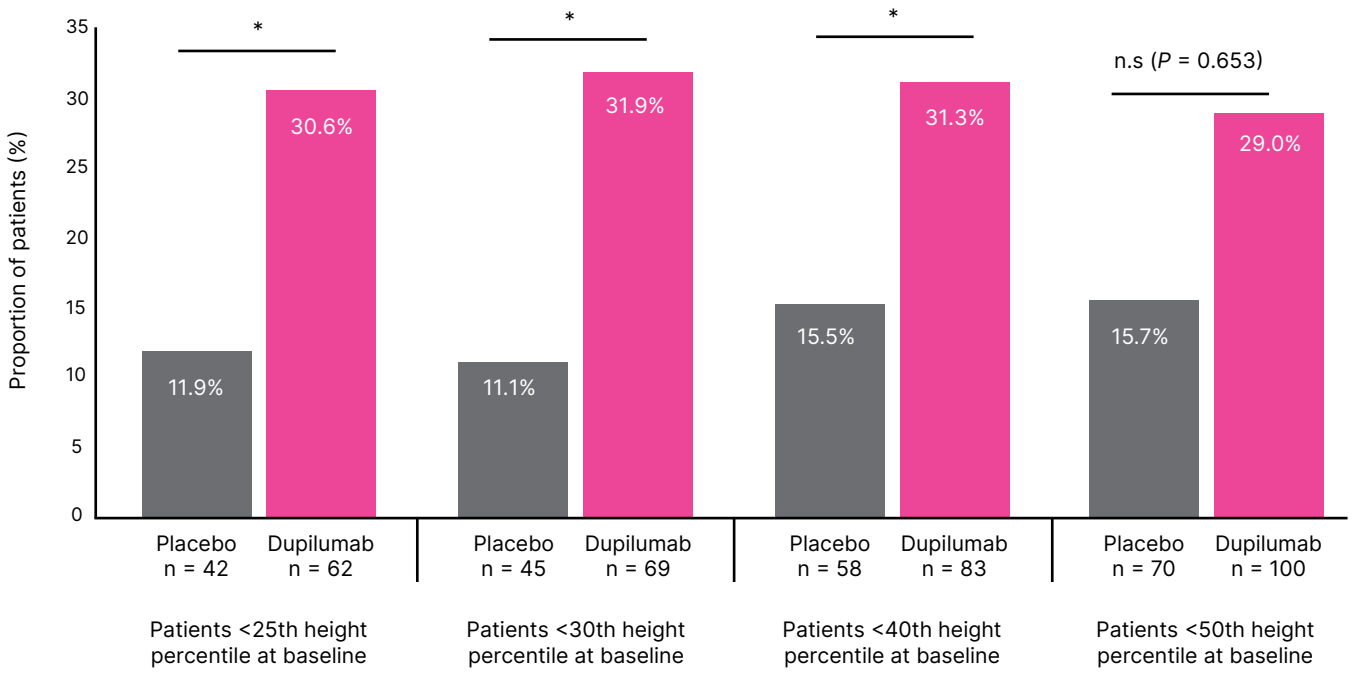
Supportive agents for weight loss

Several sessions examined new supportive therapies for HS, including novel agents to assist in symptom improvement through weight loss. Hughes et al.[18] presented the first published data for the use of semaglutide in HS during a poster presentation. In this retrospective, non-controlled study, thirty HS patients of all severities on various conventional HS therapies were concomitantly treated with semaglutide for weight loss over a mean period of 8.2 months. The mean weight loss was 6.1 kg, with one-third of patients losing at least 10 kg. Patient-reported HS flares decreased from a mean of once every 8.5 weeks to once every 12 weeks, and one-third of patients experienced at least a four point reduction in the Dermatology Life Quality Index (DLQI). Of note, the mean dose of semaglutide used in this study (0.8 mg weekly) is far below the 2.4 mg weekly licenced dose for weight loss (the authors stated supply issues).

In the session by Dr. Hunger described above,[12] the use of oral roflumilast was reviewed in a single-centre prospective study.[19] While weight loss was not the intent of this treatment, it is a common side effect of roflumilast and likely contributed to the improvement in HS scores. The weight loss observed was quite striking and far greater than the semaglutide study described above over a shorter follow-up period (median <4 months). Sixteen patients with HS with insufficient response to topical therapy and oral antibiotics were treated with oral roflumilast at a dose of 500 mcg once daily. They achieved a median weight loss of 9 kg and a corresponding median DLQI

Results

Proportion of patients 6 to 11 years with **lower stature** at baseline, showing a **≥5-percentile improvement in height** following 16 Weeks **treatment with dupilumab**



*P < 0.05 vs placebo BL, baseline; DUPI, dupilumab; PBO; placebo

Figure 2. Dupilumab vs placebo and growth
Legend: Liberty-AD PEDS phase 3 trial of dupilumab 300mg subcutaneous every 4 weeks vs placebo among patients aged 6-11 years with severe atopic dermatitis with lower stature at baseline. Over 16 weeks of observation, the percentage of patients acheiving at least a 5 percentile increase in growth was consistently and statistically significantly higher in the dupilumab group. This was observed across all baseline height percentiles.
Source: Irvine 2024[2]
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improvement of 12 points. While these studies with different populations and study designs are not directly comparable, the data suggest that both semaglutide and oral roflumilast may be considered as weight loss agents in HS, with greater potential weight loss with roflumilast.

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Financial Disclosures

Honoraria: Abbvie, Arcutis, Bausch, Biojamp, Boehringer Ingelheim, Ceravae, Galderma, Jansen, Kenvue, Leo, L'oreal, Lilly, Novartis, Pfizer, Sanofi, SUN-pharma, UCB, Vichy

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