

## ABOUT THE AUTHOR

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Dr. Annie Langley completed her residency training in dermatology at the University of Ottawa and is a board-certified dermatologist in both Canada and the United States. She completed her medical training and an MSc in Epidemiology at Queen's University and undergraduate studies in Cell Biology at McGill University. She has a combined hospital/community practice in medical dermatology in Ottawa. Her clinical interests are broad and include cutaneous drug reactions, atopic dermatitis, psoriasis and hidradenitis suppurativa.

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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,<sup>1</sup> as well as the impact of biologic therapy in atopic dermatitis and the risk of growth suppression.<sup>2</sup>

#### ***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.<sup>1</sup> 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,<sup>3</sup> which has been revised by Errichetti and Zabotti, 2023<sup>4</sup> in **Figure 1**.

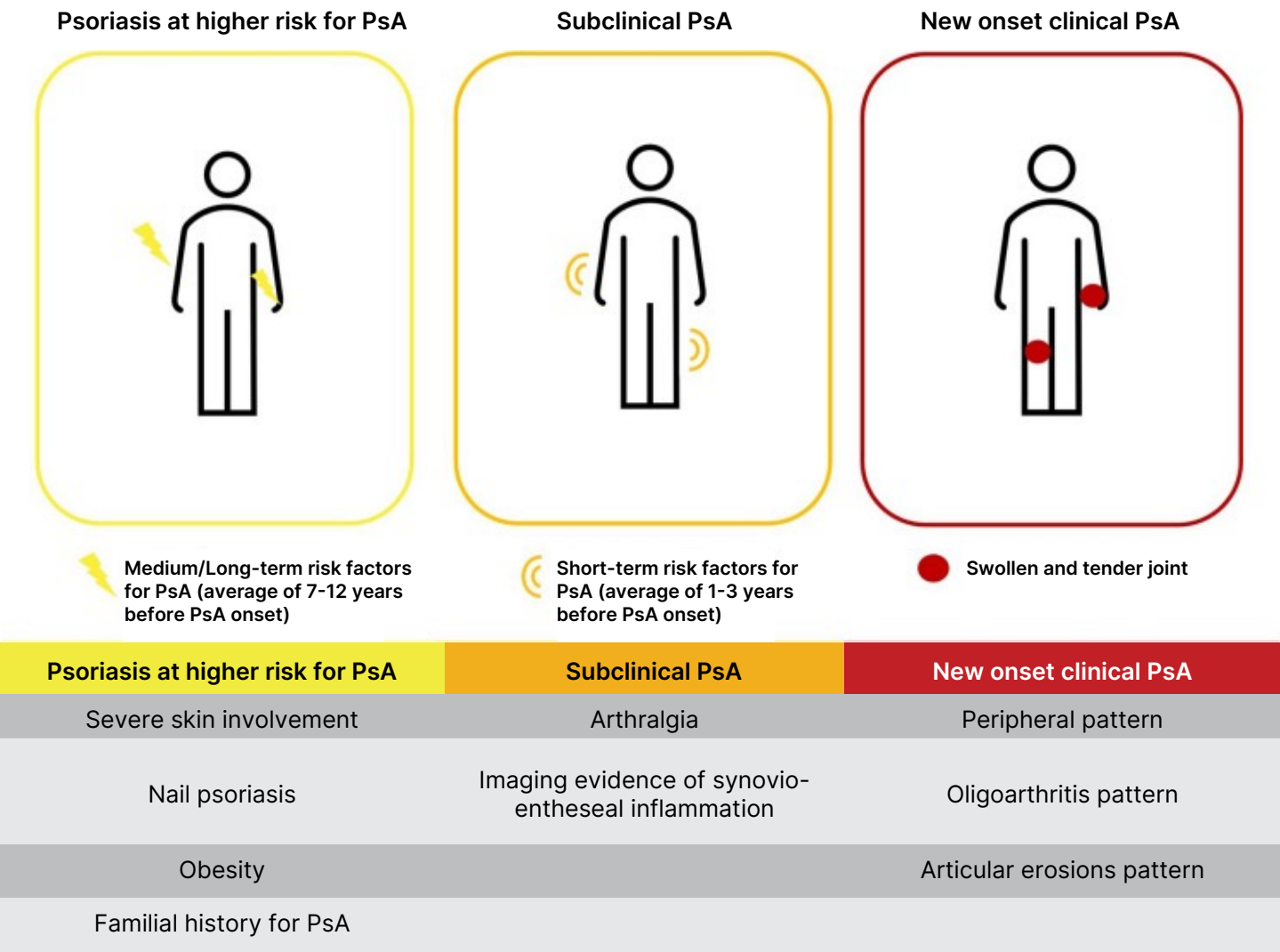
Given this temporal progression and the shared inflammatory mediators in the pathophysiology of psoriasis and psoriatic arthritis, it is biologically plausible that early use of biologic agents in this timeframe may delay or prevent the progression to psoriatic arthritis.

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

of psoriatic arthritis among psoriasis patients on biologics,<sup>5-8</sup> some studies show an increased risk.<sup>9</sup> 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.<sup>9</sup> 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.<sup>9</sup> 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.<sup>2</sup>

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.



**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<sup>4</sup>

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## **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.<sup>10</sup> 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.<sup>2</sup> 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.<sup>2</sup>

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.<sup>11</sup>

Dr. Hunger provided a review of several new and emerging biologics and small molecules for treating HS, including sonelokimab, lutikizumab, remibrutinib and upadacitinib.<sup>12</sup> 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,<sup>13</sup> 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).<sup>14</sup> 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.<sup>15</sup> 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.<sup>16</sup> 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.<sup>17</sup>

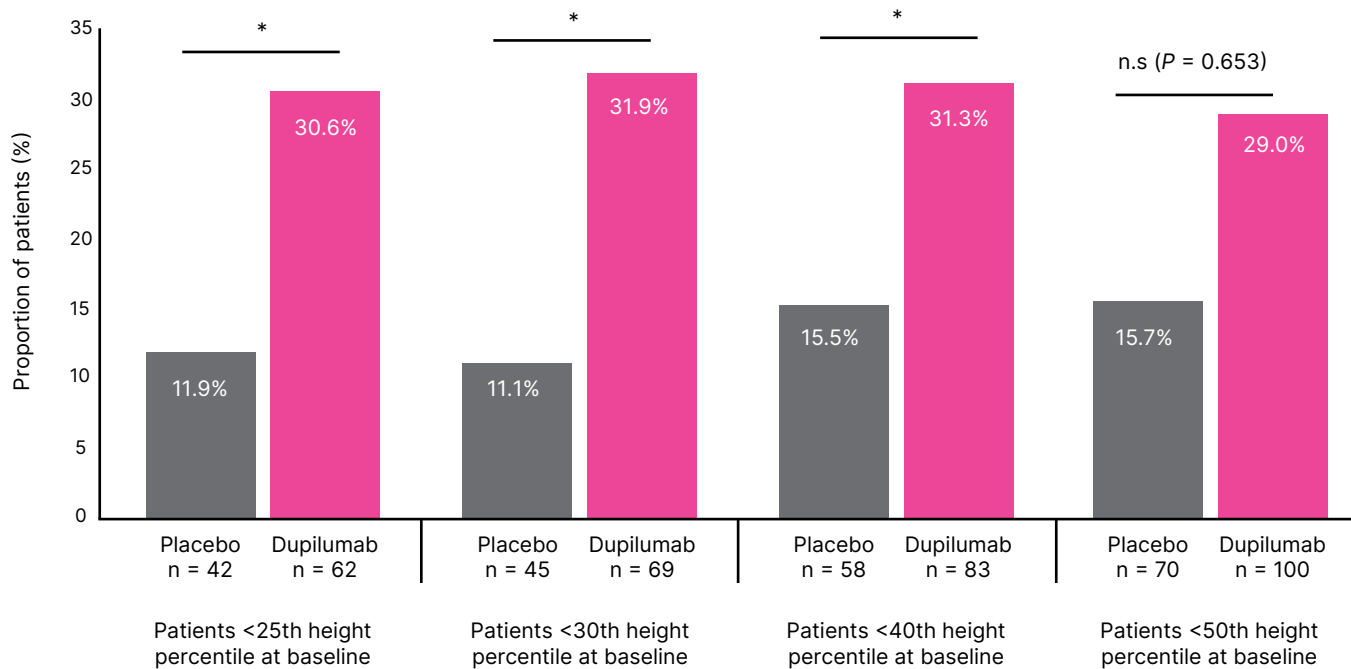
### **Supportive agents for weight loss**

Several sessions examined new supportive therapies for HS, including novel agents to assist in symptom improvement through weight loss. Hughes et al.<sup>18</sup> 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,<sup>12</sup> the use of oral roflumilast was reviewed in a single-centre prospective study.<sup>19</sup> 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 $\geq 5$ -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 achieving 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<sup>2</sup>

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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

## References

- Armstrong A. Does psoriasis treatment prevent the development of psoriatic arthritis? In: Proceedings of the 33rd EADV 2024 Congress, 2024 Sept 24-28. Amsterdam, Netherlands
- Irvine, A. Growth analysis in children aged 6 to 11 years with severe atopic dermatitis and impact of 16 weeks of dupilumab treatment on height. In: Proceedings of the 33rd EADV 2024 Congress, 2024 Sept 24-28. Amsterdam, Netherlands
- De Marco G, Zabotti A, Baraliakos X, Iagnocco A, Aletaha D, Gisondi P, et al. Characterisation of prodromal and very early psoriatic arthritis: a systematic literature review informing a EULAR taskforce. RMD Open. 2023;9(2):e003143. doi: 10.1136/rmdopen-2023-003143.
- Errichetti E, Zabotti A. Biologics in prevention of psoriasis to psoriatic arthritis transition: the need of prospective analyses and stratification according to time-related risk factors. Dermatol Ther (Heidelb). 2024;14(1):1-3. doi: 10.1007/s13555-023-01072-1.
- Watad A, Zabotti A, Patt YS, Gendelman O, Dotan A, Ben-Shabat N, et al. From psoriasis to psoriatic arthritis: decoding the impact of treatment modalities on the prevention of psoriatic arthritis. Rheumatol Ther. 2024;11(4):963-976. doi: 10.1007/s40744-024-00680-3.
- Acosta Felquer ML, LoGiudice L, Galimberti ML, Rosa J, Mazzuocollo L, Soriano ER. Treating the skin with biologics in patients with psoriasis decreases the incidence of psoriatic arthritis. Ann Rheum Dis. 2022;81(1):74-79. doi: 10.1136/annrheumdis-2021-220865.
- Gisondi P, Bellinato F, Targher G, Idolazzi L, Girolomoni G. Biological disease-modifying antirheumatic drugs may mitigate the risk of psoriatic arthritis in patients with chronic plaque psoriasis. Ann Rheum Dis. 2022;81(1):68-73. doi: 10.1136/annrheumdis-2021-219961.

8. Singla S, Putman M, Liew J, Gordon K. Association between biological immunotherapy for psoriasis and time to incident inflammatory arthritis: a retrospective cohort study. *Lancet Rheumatol*. 2023;5(4):e200-e207. doi: 10.1016/S2665-9913(23)00034-6.
9. Meer E, Merola JF, Fitzsimmons R, Love TJ, Wang S, Shin D, et al. Does biologic therapy impact the development of PsA among patients with psoriasis? *Ann Rheum Dis*. 2022;81(1):80-86. doi: 10.1136/annrheumdis-2021-220761.
10. Paller A, Geng B, Irvine A, Adams B, Ardeleanu M, Zhang A, et al. Growth analysis in children aged less than 12 years with moderate-to-severe atopic dermatitis. *Journal of the American Academy of Dermatology*. 2024;91(3), AB1. doi:10.1016/j.jaad.2024.07.015.
11. Papp K, Bachara FG, Porter ML, Forman S, Sofen H, Szepletowski J, et al. Efficacy and safety of izokibep, a novel IL-17A inhibitor, in moderate-to-severe hidradenitis suppurativa: Week 12 results from a randomized, double-blind, placebo-controlled, multicenter, phase 3 study. In: *Proceedings of the 33rd EADV 2024 Congress*, 2024 Sept 24-28. Amsterdam, Netherlands.
12. Hunger R. Focus on hidradenitis suppurativa- new and emerging treatments. In: *Proceedings of the 33rd EADV 2024 Congress*, 2024 Sept 24-28. Amsterdam, Netherlands
13. Kimball A, Ackerman L, Lima H, et al. A phase 2 multicenter randomized, double-blind, placebo-controlled study to evaluate the safety and efficacy of lutikizumab in adult patients with moderate-to-severe hidradenitis suppurativa who have failed anti-TNF therapy. In: *American Academy of Dermatology Annual Meeting*. 2024 Mar 8-12. San Diego, CA.
14. MoonLake Immunotherapeutics. MoonLake Immunotherapeutics achieves landmark milestone with positive Phase 2 results for Nanobody® sonelokimab in hidradenitis suppurativa. 2023 June 25 [cited 2024 Nov 15]. Available from: <https://ir.moonlaketx.com/news-releases/news-release-details/moonlake-immunotherapeutics-achieves-landmark-milestone-positive>
15. Kimball AM, Kirby B, Bechara GF, et al. Efficacy and safety of the IL-17A- and IL-17F-inhibiting Nanobody® sonelokimab in patients with moderate-to-severe hidradenitis suppurativa (HS): Week 24 results from the Phase 2 MIRA trial. In: *American Academy of Dermatology Annual Meeting*, 2024 Mar 8-12. San Diego, CA.
16. Kimball AB, Prens EP, Bechara FG, et al. Efficacy and safety of the oral Bruton's tyrosine kinase inhibitor, remibrutinib, in patients with moderate-to-severe hidradenitis suppurativa in a randomized, phase 2, double-blind, placebo-controlled platform study. In: *American Academy of Dermatology Annual Meeting*, 2024 Mar 8-12. San Diego, CA.
17. Kozera E, Flora A, Frew JW. Real-world safety and clinical response of Janus kinase inhibitor upadacitinib in the treatment of hidradenitis suppurativa: a retrospective cohort study. *J Am Acad Dermatol*. 2022;87(6):1440-1442. doi:10.1016/j.jaad.2022.07.047.
18. Hughes R et al. Semaglutide for weight loss in obese patient as an adjunctive treatment for hidradenitis suppurativa: its impact on disease control and quality of life. *Proceedings of the 33rd EADV 2024 Congress*. 2024 Sept 24-28. Amsterdam, Netherlands.
19. Nielsen, VW, Holgersen NK, Ring HC, Thyssen JP, Gyldenløve M, Thomsen SF, et al. Effectiveness and safety of oral roflumilast in patients with hidradenitis suppurativa: a prospective single-center study. *Journal of the American Academy of Dermatology*. 2024;91(3), AB192. doi:10.1016/j.jaad.2024.07.765.