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Pathways to Optimizing Clinical Outcomes and Quality of Life in Atopic Dermatitis Care

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ABOUT THE AUTHORS

Jensen Yeung, MD, FRCPC

Dr. Jensen Yeung obtained a Bachelor of Science (Honours) and his Doctor of Medicine from McMaster University in 2001. The same year, he began his dermatology residency training at the University of Toronto. During his residency training, he spent six months in Australia, New York, and Boston, gaining clinical experience and acquiring the newest knowledge in melanoma and dermoscopy from leading experts. In 2005, he was selected by the residency program as the co-chief resident for the year. Having obtained his board certification from the Royal College of Physicians and Surgeons of Canada in 2006, Dr. Yeung joined the Faculty of Dermatology at the University of Toronto, where he ran teaching clinics at both Women's College Hospital and the Sunnybrook Health Sciences Centre. In 2007, he was promoted to medical director for the Ricky Kanee Schachter (RKS) Dermatology Program at Women's College Hospital, where he ran a melanoma, psoriasis, and General Dermatology clinic. In 2013, he switched from RKS to PERC. He took on the new role as the Medical Director of the Phototherapy Education and Research Centre (PERC), where he runs a weekly psoriasis and phototherapy clinic. In 2014, he and Dr. Dana Jerome started a monthly combined psoriasis and psoriatic arthritis clinic at PERC. From 2011 to 2020, he worked at Dr. Kim Papp's research facility in Waterloo and participated in nearly 200 phase 1 to 4 clinical trials. Dr. Yeung has also supervised and mentored many research students and residents, which has led to more than 250 peer-reviewed publications. He is an associate editor at the American Journal of Clinical Dermatology, Journal of Cutaneous Medicine and Surgery (JCMS), and Canadian Dermatology Today. In addition, he is a Medical Board Member at the National Psoriasis Foundation (NPF) and a councilor at the International Psoriasis Council (IPC). He is an associate professor at the department of Medicine at the University of Toronto. He has received several teaching awards, including the Best Resident Teacher award in 2005, the 2008 Women's College Hospital Department of Medicine Postgraduate Teaching Award, the 2009 University of Toronto Dermatology Postgraduate Program Staff Teaching Award, and the 2022-2023 University of Toronto Department of Medicine Excellence in Postgraduate Teaching Award.

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Dr. Ringuet is a board certified dermatologist who practices in Quebec City at the Centre de Recherche Dermatologique du Québec Métropolitain (CRDQ) and in Montreal at the McGill University Health Center (MUHC). He obtained a bachelor degree in biology before his medical training (MD) and his dermatology residency at Laval University in Quebec City. During his medical training, he also completed a master in experimental medicine (MSc.) in the field of skin bioengineering at the Centre de Recherche en Organogénèse Expérimentale de l'Université Laval (LOEX). After his post graduate studies and since 2020, Dr. Ringuet is practicing with his team at the Centre de Recherche Dermatologique du Québec Métropolitain (CRDQ) as a principal investigator and medical director. His team is dedicated in allowing Quebec's patients to access top quality and innovative clinical research focused on inflammatory dermatological diseases. Dr. Ringuet research interests are mainly psoriasis and its variants, atopic dermatitis, vitiligo and alopecia areata. As of today, he led as a principal investigator more then 50 clinical trials of phase 2, 3 and 4 in those indications leading to varied peer reviewed publications, talks and lectures. He also practices in Montreal at the MUHC as an assistant clinical professor since 2025 contributing to the continuous medical education and training of medical students and dermatology residents. His commitment to his peers is also reflected in his role at the Canadian Dermatology Association (CDA) where he took on the role of Treasurer Elect and Treasurer of the Finance and Audit Committee in 2024-2025 and is also a member of the Education Committee from 2024 to present. In addition, he is involved as a reviewer for various journals including the Canadian Medical Association as well as the Journal of Cutaneous Medicine and Surgery (JCMS) for which he stands as an associate editor. Based on his clinical work, commitment to patient care and advancement of the specialty, Dr. Ringuet received the recognition of Dermatologist of the Year 2024 by the Canadian Skin Patient Alliance (CSPA).

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Pathways to Optimizing Clinical Outcomes and Quality of Life in Atopic Dermatitis Care

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Many systemic atopic dermatitis (AD) therapies improve the skin before alleviating pruritus. As a result, dermatologists primarily rely on objective skin-focused measures to assess efficacy. Canadian Dermatology Today, spoke with Dr. Jensen Yeung and Dr. Julien Ringuet about the importance of integrating patient-reported outcomes into routine assessment, particularly given the emergence of novel therapies that provide rapid antipruritic benefit.

How well do clinical scores, such as the Investigator's Global Assessment (IGA) score and the Eczema Area and Severity Index (EASI) reflect the burden of AD for patients?

Dr. Jensen Yeung: The EASI and IGA score are physician-rated instruments that capture visible cutaneous signs. They do not measure the multidimensional burden of disease on patients.

For example, it is well documented that anxiety and mood disorders are more prevalent in patients with AD. However, time constraints often limit dermatologists from routinely assessing the psychosocial consequences of AD.

In addition, AD often causes significant itch that affects sleep and self-confidence. It can also affect patients' participation in school, sports, hobbies, and work. Furthermore, AD greatly impacts caregivers, who spend a great deal of time providing care and support, and they may be affected by the patient's sleep disruption. EASI and IGA do not capture these burdens of disease.

Dr. Julien Ringuet: Many studies have demonstrated that patients rank itch and sleep disturbance as the two most impactful AD symptoms in relation with their quality of life **(Figure 1)**. While these domains are not captured in measures like IGA or EASI, they are reflected in the Dermatology Life Quality Index (DLQI) as well as in some mixed tools like SCOring Atopic Dermatitis (SCORAD). The peak pruritic numeric rating score (PP-NRS) is another easy and accessible validated tool to assess the itch component of AD in clinic.

Itch and sleep disturbance can have far-reaching underestimated impacts. In children, they can impair their capacity to focus at school. For adults, these symptoms can impact their work performance. We have all encountered patients with moderate-severe AD who, after initiating effective therapy, report doing better at school or at work. Therefore, real-world data consistently demonstrates that treatment efficacy in AD extends beyond cutaneous outcomes, with additional benefits for sleep, anxiety, and self-image and potentially life trajectory.

You've made a clear case for why patient-reported outcomes should be integrated into clinical practice, but doing so can be challenging. How do you assess quality-of-life outcomes in your practices?

JR: Incorporating either PP-NRS (24h retrospective question) or the mean weekly pruritis NRS is pretty straightforward, as these require only a single patient-reported score. In my practice, the results of this score can influence my clinical decision-making. For example, if a patient says that itch is their main problem, and their itch has been relieved, I am less inclined to change

their therapy if they have minor signs of residual disease on the skin.

The DLQI takes more time, but it is nonetheless feasible to incorporate in clinical practice, as patients can fill out the questionnaire prior to the visit, in the waiting room or with a member of the clinical team.

How might emerging treatments, such as nemolizumab, shift our expectations around symptom control and patient quality-of-life in AD?

JY: As for novel systemic agents, there are currently three biologics and two systemic JAK inhibitors approved for the treatment of AD in Canada. These therapies have allowed us, in recent years, to target a more ambitious treatment goal such as EASI 90. In contrast, there are 12 biologics and 2 novel oral agents approved for the treatment of psoriasis. Having more treatment options is certainly more than welcomed in AD. In its phase 3 trials, nemolizumab has demonstrated significant itch reduction within two days of treatment which is one of its major strengths.

JR: When we assess the systemic medications currently available for the treatment of AD, the speed of onset for symptoms relief can be quite long with biologics. JAK inhibitors have a more rapid onset of action but come with higher counseling burden as well as safety concerns to discuss with patients (risk-benefit profile). Especially for biologics, pruritus is usually only ameliorated after the skin signs improves. By contrast, nemolizumab provides rapid antipruritic benefit prior to significant skin clearance **(Figure 2)**. Once nemolizumab becomes available, the shared decision-making approach for treatment decision should include discussions on whether patients prefer rapid relief of itch or earlier resolution of visible lesions and the burden associated with both.

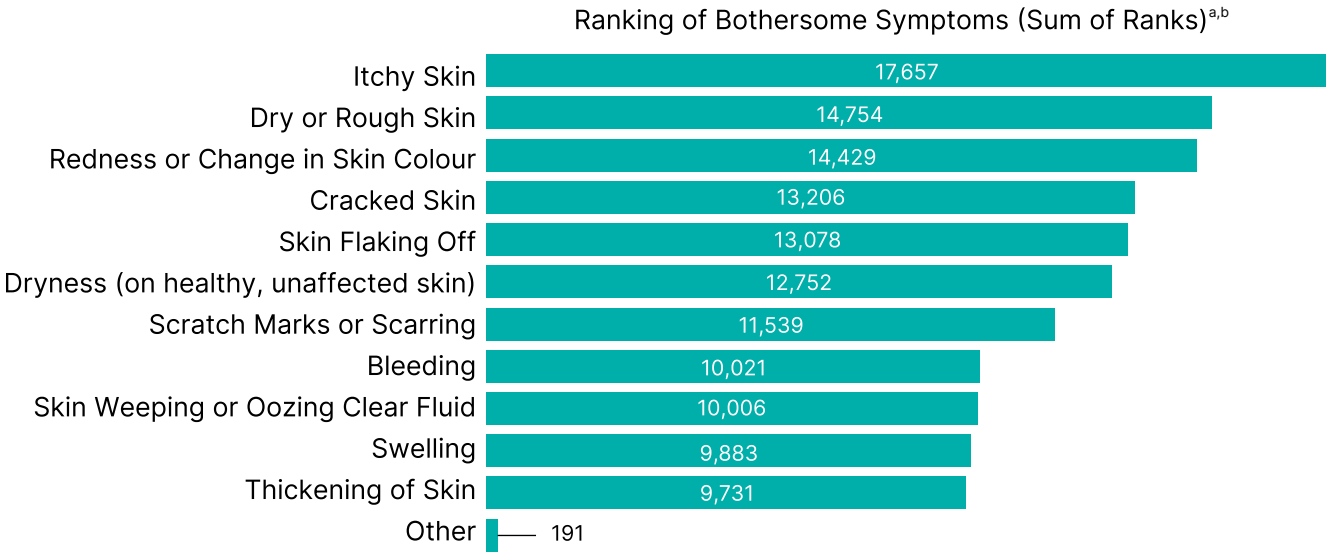

Figure 1. Itchy skin is also the most bothersome symptom of atopic dermatitis. Participants were asked: Please rank your symptoms in order from 1 to least, where 1 is the most bothersome and the last of the symptoms is the least bothersome. A Survey Q317: Please rank your symptoms in order from 1 to LEAST where 1 is the most bothersome and the last of the symptoms is the least bothersome. B Explanation of the sum of ranks calculation: Assume that 4 symptoms are ranked. The number of times a symptom is ranked first is multiplied by 4; the number of times a symptom is ranked second is multiplied by 3; the number of times a symptom is ranked third is multiplied by 2; and the number of times a symptom is ranked fourth is multiplied by 1. Number of respondents who rank symptom first (e.g., 24 · 4 = 96); number of respondents who rank symptom second (e.g., 35 · 3 = 105); number of respondents who rank symptom third (e.g., 46 · 2 = 92); number of respondents who rank symptom fourth (29 × 1 = 29). Calculate the sum of ranks by adding all the subtotals (e.g., sum of ranks for symptom: 96 + 105 + 92 + 29 = 322); *adapted from Silverberg et al., 2023*

For patients with moderate-to-severe AD, what clinical and patient-reported outcomes do you target, and how do you define success over time?

JY: In 2023, a group of Canadian dermatologists published treat-to-target criteria for AD, which integrate patient-reported outcomes and physician-rated measures.[1] These targets vary depending on treatment duration. For example, the targets are more stringent after 1 year versus 4 months of treatment.

It is absolutely essential to incorporate patient's own assessment of their response to determine whether treatment modification should be implemented. Some patients would prefer agents that are perceived to be safer but are slower acting. For others, rapid improvement is important.

JR: In addition to the **treat-to-target paper**, the Aiming High in Eczema/Atopic Dermatitis (AHEAD) **recommendations** are useful, as they include optimal and moderate targets. This can help prescriber and patients set their preference and realistic expectations.

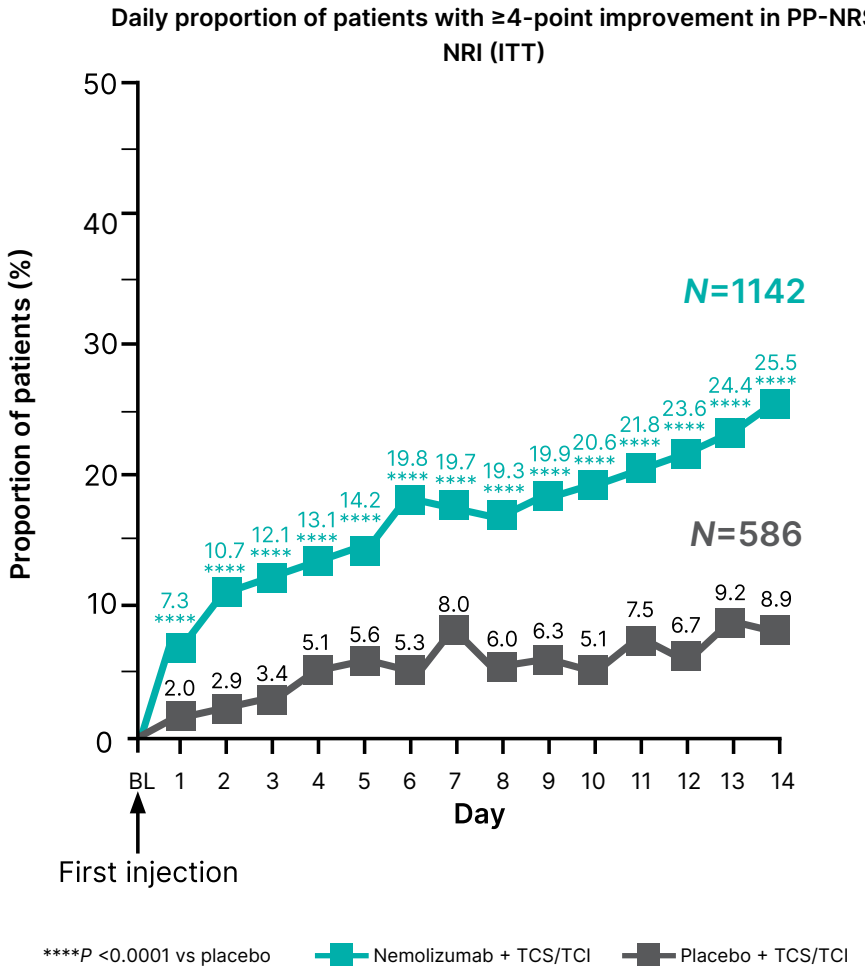

Figure 2. Post-hoc pooled analysis of daily proportion of patients with ≥4-point improvement in PP-NRS in ARCADIA 1&2.; used under Open Access license (https://creativecommons.org/licenses/by-nc/4.0/); *adapted from Ständer et al., J Eur Acad Dermatol Venereol. 2025 Dec 16. doi: 10.1111/jdv.70250.*

Abbreviations: BL: baseline; **ITT:** intent-to-treat; **N:** total number of patients; **NRI:** non-responder imputation; **PP-NRS:** peak pruritus numerical rating scale; **TCI:** topical calcineurin inhibitors; **TCS:** topical corticosteroids. Percentage (%) are based on the number of patients in each treatment group (N).

How do the mechanisms of action of IL-4/13 antagonists, IL-31 antagonists, and JAK inhibitors explain some of the efficacy and safety differences between systemic AD therapies?

JR: Biologics targeting IL-4 and IL-13 effectively reduce type 2 inflammation in the skin. In contrast, JAK inhibitors exert broader effects by blocking multiple cytokine signaling pathways across various tissues. Initially, IL-31 receptor antagonists were thought to primarily alleviate pruritus, as IL-31 receptors are present on sensory nerves and IL-31 has been a known potent pruritogen. However, emerging evidence demonstrates that IL-31 also activates inflammatory cells, promoting secretion of IL-4 and IL-13, and thereby amplifying type 2 inflammation. Therefore, inhibition of IL-31 not only directly reduces neuronal activity associated with itch but also indirectly improves inflammatory responses in the skin **(Figure 3)**.

How would you describe nemolizumab's impact on skin lesions over time, based on data from the ARCADIA 1 and 2 clinical trials and the long-term extension trial?

JY: In ARCADIA 1 and 2, 42-44% of patients achieved EASI 75 after 16 weeks of nemolizumab. And at the start of the long-term extension trial, 38% of these patients were EASI 75 responders. In those who completed 104 weeks of the long-term extension trial, 88% of those patients achieved the EASI 75 endpoint, and around 60% of patients achieved an IGA of 0 or 1. This shows that that efficacy continued to improve over time, and the response was well-sustained.

JR: With the dupilumab trials, there were very few treatment options, so continuation rates were high by necessity. In the nemolizumab LTE trial, 56% of patients had completed 104 weeks at the latest interim analysis cut off shown below. The fact that a very high proportion of these patients in the nemolizumab LTE remained on therapy despite other available treatments suggests strong satisfaction with efficacy and tolerability **(Figure 4)**.

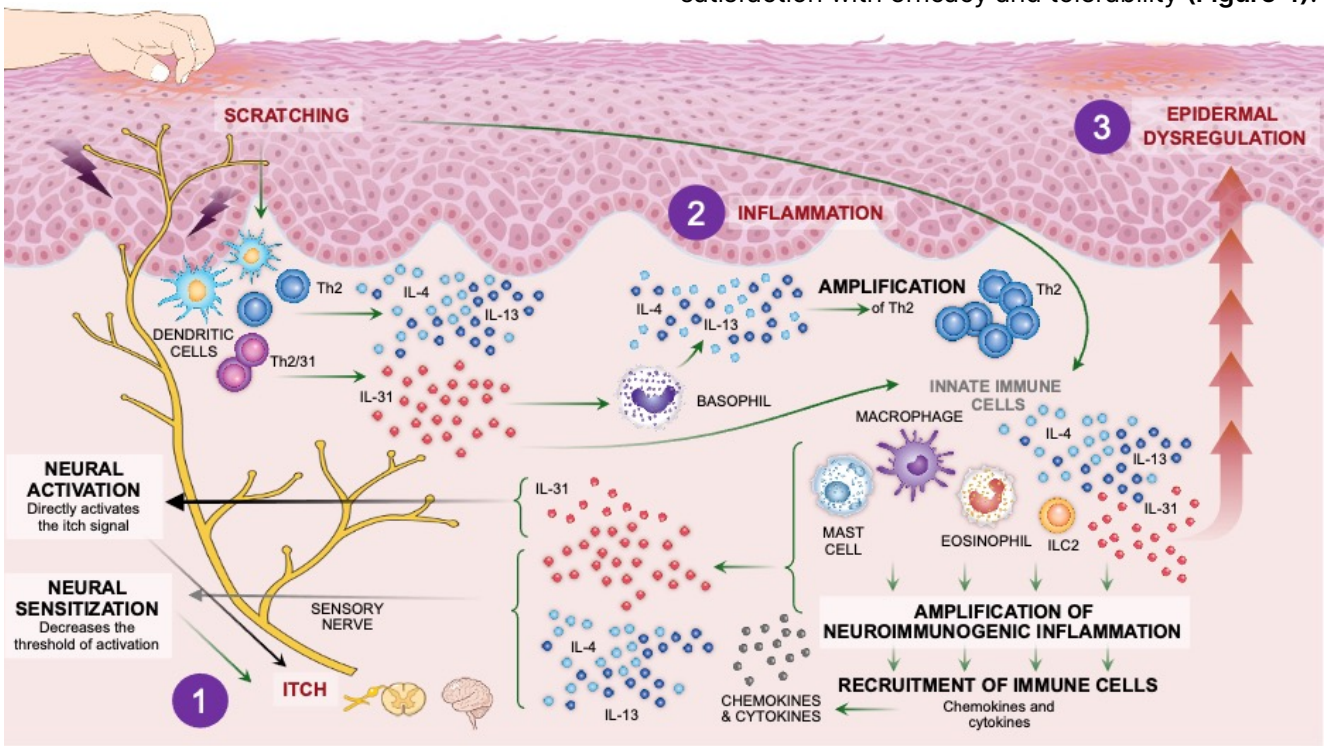

Figure 3. Itch mechanism in atopic dermatitis; *adapted from 1. Steinhoff M et al. J Allergy Clin Immunol 2022;149:1875-98; 2. Herbert DR et al. Int J Mol Sci 2019;8:20:2276; 3. Nemmer JM et al. Front Med (Lausanne) 2021;8:639097; 4. Cornelissen C et al. J Allergy Clin Immunol 2012;129:426-33, 433.e1-8; 5. Bilsborough J et al. J Allergy Clin Immunol 2006;117:418-25; 6. Nobbe S et al. Acta Derm Venereol 2012;92:24-8*

When a patient is considering treatment options, how would you explain the difference in the response for itch and skin lesions with nemolizumab, compared to other therapeutic options?

JR: It's important to set expectations for patients. On the positive side, we can tell patients that nemolizumab has a high probability of rapidly relieving their itch as well as their sleep as a direct positive consequence. On the other hand, I would counsel patients that the lesions may take longer to improve, compared to some other treatments. Although a significant proportion of patients respond quickly to nemolizumab, it can take up to 12 or 24 weeks for patients to notice improvement in inflammation.

JY: I believe that it is essential to ask patients which aspect of AD bothers them the most. In my experience, most patients would prioritize rapid itch reduction over early improvement of visible lesions in the management of AD.

The ARCADIA 1 & 2 trials demonstrated remarkable pruritus improvement on day 2. How might nemolizumab's speed and robustness of itch response impact treatment satisfaction and persistence on therapy?

JY: As Julien mentioned earlier, many studies have shown that patients rank itch and sleep disturbance as the most bothersome AD symptoms. If patients experience early reduction of itch, it will provide confidence to them that they are responding well to the treatment and that they will most likely stay on the treatment, even if they may not have noticed visible improvement in their lesions.

JR: A post-hoc analysis of ARCADIA patients who participated in the long-term extension showed that approximately 52% of partial- and non-responders at week 16 achieved EASI 75 after an additional 20 weeks of treatment. This is encouraging. This data means that as long as a patient's itch is controlled, we can expect continued improvement on the skin signs when they continue therapy for up to 6-8 months **(Figure 5)**.

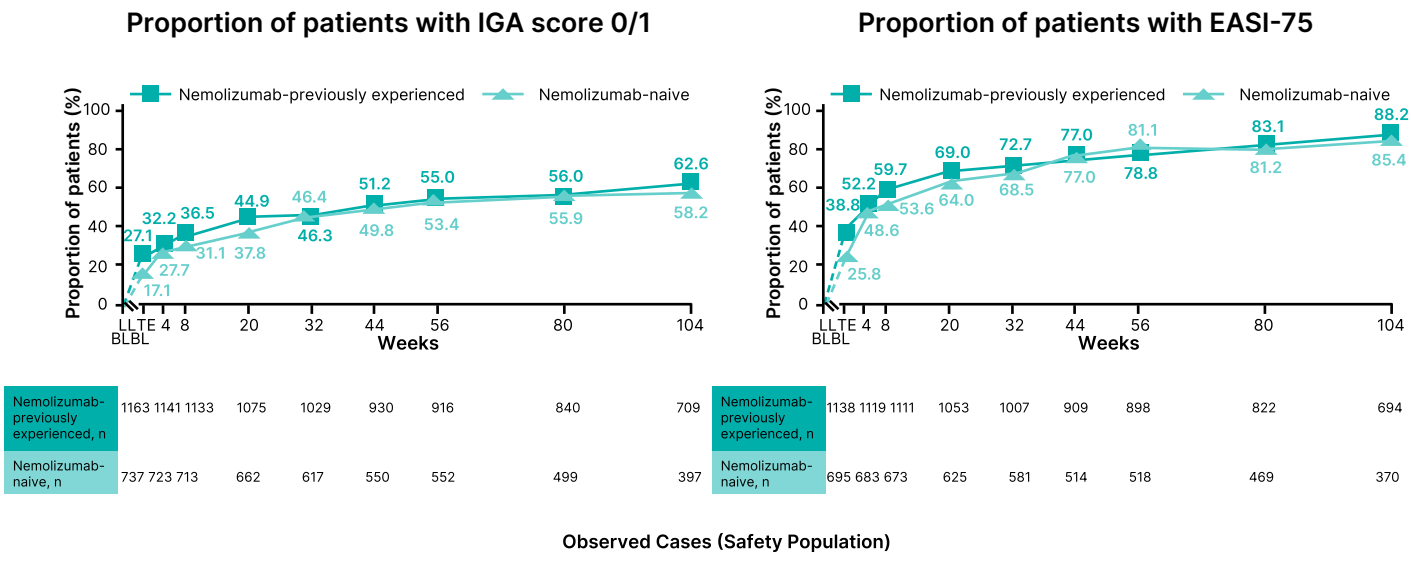

Figure 4. Improved and sustained IGA 0/1 and EASI-75 responses in evaluable patients with moderate-to-severe AD through 104 weeks; *adapted from Silverberg et al., 2025 (e-poster)*

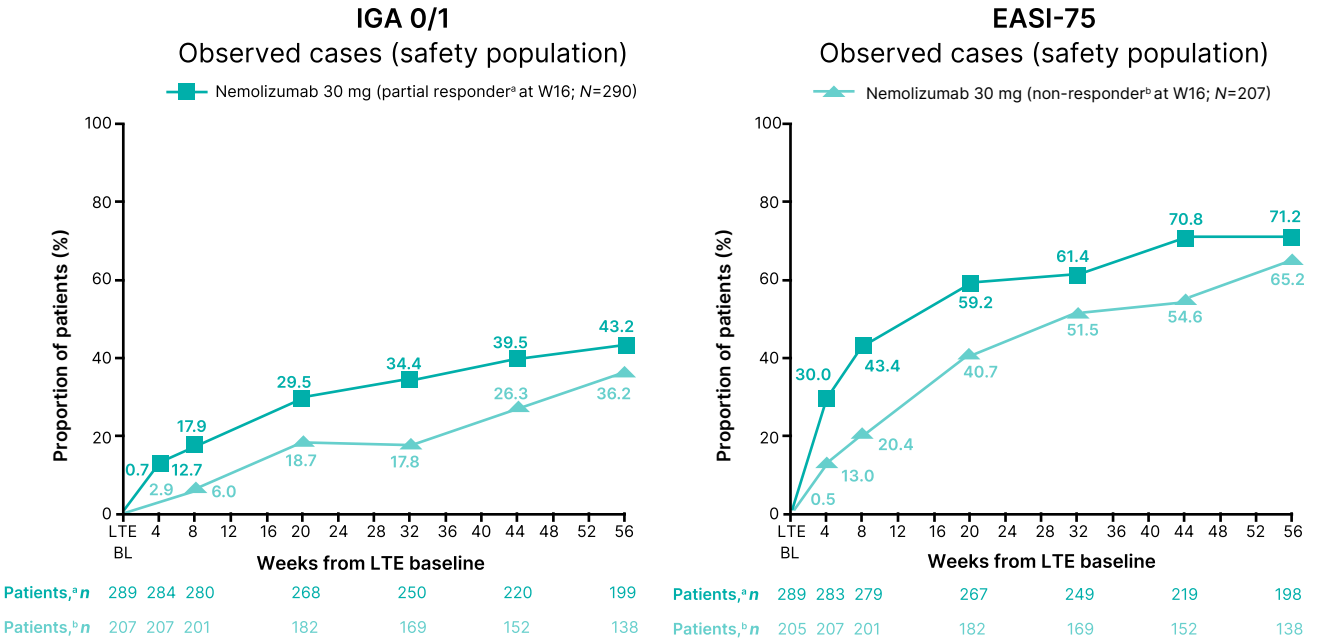

Figure 5. ARCADIA 1&2 (post hoc analysis): IGA 0/1 and EASI-75; *adapted from e-poster presented at Annual Meeting of American Academy of Dermatology (AAD), March 07-11, 2025, Orlando, Florida.*

Abbreviations: BL: baseline; **EASI:** Eczema Area and Severity Index; **EASI-50/75:** ≥50/75% improvement in Eczema Area and Severity Index from initial baseline; **IGA:** Investigator's Global Assessment; **LTE:** long-term extension; **N:** number of patients in the treatment group; **n:** number of patients with available data; **W:** week.

a Partial response defined as ≥50% but <75% improvement in EASI or IGA 2/3, with ≥1-point improvement.
b Non-response defined as not achieving EASI-50 and having IGA 3/4, with no improvement.

What are other practical considerations that could impact treatment satisfaction for systemic AD treatments?

JR: Dosing frequency is important. With nemolizumab, the initial dosing schedule of every 4 weeks (with potential for every 8-week dosing in clinical responders at week 16) might be more attractive to patients, given that the presently available biologics need to be administered every 2 weeks in the first months of treatment.

From a safety perspective, the available nemolizumab data suggests that we don't need to be concerned about ocular surface disease (conjunctivitis, keratitis, etc.), which is associated with IL-4 and IL-13 inhibitors. Overall, the safety data for nemolizumab is reassuring, with no signal for serious adverse events.

JY: Some patients prefer an oral agent while others prefer an injection, so the route of delivery is a personal preference.

Adverse events are understandably another important consideration for patients. In addition to ocular surface diseases, IL 4/13 inhibitors have been linked to instances of facial erythema. Both of these side effects can be bothersome for patients. JAK inhibitors increase the risk of infection and require lab monitoring which could be a deterrent to some patients. Finally, the Patient Support Program (PSP) is an extremely important component of advanced systemic treatments in AD as well.

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Reference

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