LEAD

Learning for Emerging Allergists and Dermatologists

Canadian Dermatology Today

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Proceedings of the 2024 Symposium on Atopic Dermatitis

Toronto, ON • May 4th, 2024

In this report...

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Abbreviations

AD	ATOPIC DERMATITIS
AE	ADVERSE EVENT
COPD	CHRONIC OBSTRUCTIVE PULMONARY DISEASE
CRSwNP	CHRONIC RHINOSINUSITIS WITH NASAL POLYPOSIS
CSU	CHRONIC SPONTANEOUS URTICARIA
EoE	EOSINOPHILIC ESOPHAGITIS
JAKis	JAK INHIBITORS
LEAD	LEARNING FOR EMERGING ALLERGISTS & DERMATOLOGISTS
MSLs	MEDICAL SCIENCE LIAISONS
NRS	NUMERIC RATING SCALE
PN	PRURIGO NODULARIS
WI-NRS	WORST ITCH NUMERIC RATING SCALE

Welcome and Opening Remarks

Shawn McLaren, Head of Marketing, Dermatology at Sanofi Canada, welcomed everyone to the second-annual LEAD Symposium. He introduced the team from Sanofi Canada, and the LEAD Symposium steering committee and faculty.

Shawn shared an overview of Sanofi, explaining that Sanofi operates in 70 countries. Sanofi Canada was founded in the early 1900s, through a partnership with the University of Toronto, to produce life-saving vaccines. Today, Sanofi Canada invests 20% of its revenues into research and development activities. Sanofi's leading dermatology product, Dupixent, is approved in 58 countries, and has helped over 800,000 patients.

Dr. Prajapati described how the approval of Dupixent (dupilumab) revolutionized the care of AD. There are new two biologic injection medications, and two small molecule tablets on the market for AD, and others are expected to be approved soon. He highlighted that AD is found across all age groups and presents with different clinical phenotypes among different ethnicities. There is also a wide range of severity, from mild and easy-to-treat AD to severe and lifelong AD.

> **"ALTHOUGH COMMON IN CHILDREN, 80% OF CHILDHOOD AD DOES NOT PERSIST BY 8 YEARS OF AGE."**

Frances Vu, Medical Advisor, Dermatology at Sanofi Canada, highlighted that Dupixent is now approved for nine indications in Canada, including chronic rhinosinusitis with nasal polyposis (CRSwNP), asthma, eosinophilic esophagitis (EoE), and prurigo nodularis (PN). Last year, Dupixent was approved for the treatment of atopic dermatitis (AD) in infants aged 6 months and above. This is a testimonial to Dupixent's excellent safety profile and efficacy in AD. Frances explained that type 2 inflammation is the underlying pathology that unites the various indications. In the near future, Sanofi is anticipating Dupixent will be approved for EoE in children 1 year and up, chronic spontaneous urticaria (CSU), bullous pemphigoid, and chronic obstructive pulmonary disease (COPD), among other important indications.

Although common in children, 80% of childhood AD does not persist by 8 years of age. An important question is whether intervening early prevents the atopic march of allergic rhinitis, asthma and other atopic comorbidities. Increasingly, dermatologists are recognizing the importance of asking about comorbidities in the treatment of AD, just as they do with psoriasis.

Meeting Objectives

Dr. Prajapati introduced the meeting's objectives:

- Evaluate the efficacy and safety responses for advanced systemic treatment options for Type 2 inflammatory skin diseases.
- Describe the heterogenous nature of AD and identify strategies to manage special populations with AD with available data, including pediatrics, skin of colour, and indigenous populations.
- Discuss goals of treatment of complex cases and understand practical management considerations for patients with Type 2 inflammatory skin diseases.

Atopic Dermatitis in 2024: Where We Are Today and Where We Are Going

DR. PERRY GREWAL

Dr. Grewal highlighted the current and future treatments for AD. He described the impacts that AD can have on work, sleep, and mental health and noted that three of five patients on systemic immunosuppressants or corticosteroids have inadequately controlled disease.

Available topicals include emollients, moisturizers, corticosteroids, calcineurin inhibitors, and PDE4 inhibitors (including the soon-to-be available roflumilast). Systemic medications include:

- non-biologic medications – phototherapy, corticosteroids, JAK inhibitors (JAKis) cyclosporine, azathioprine, methotrexate, and mycophenolate mofetil
- biologics – tralokinumab and dupilumab

JAKis currently on the market include abrocitinib and upadacitinib. Blocking JAK-1 blocks IL-4 and IL-13 signalling, but JAK1 also blocks other pathways in the receptor cells. This can reduce lymphocyte counts and increase viral infections. Targeting additional pathways could lead to improved outcomes in certain type 2 inflammation-related comorbidities but can also lead to more adverse effects.

Systemic corticosteroids are effective in the short-term for flares, but aren't beneficial in the long term. Methotrexate has moderate efficacy, though the evidence base lacks controlled studies. The adverse events (AEs) associated with methotrexate can be mitigated with proper dosage titration. Cyclosporine can be helpful in complex cases, when biologics are not effective, as short-term rescue therapy, before reinitiating biologic therapy.

Providing an overview of biologic medications, Dr. Grewal clarified that the biologics work in different ways, as tralokinumab blocks the IL-13 cytokine, while dupilumab blocks both IL-13 and IL-4 signalling. One theory is that the IL-4 blockade may

CsA[1,2]	AZA[1,3]	MTX[1,4]	MMF[1,5]	JAKi[6]
Medicinal supervision	Immunization with live organism vaccines not recommended	US boxed warning	Malignant lymphoma and other malignancies, particularly of the skin	Increased risk for developing serious infections
Lymphomas and other malignancies (ie, skin)	Coadministration with ribavirin	Potential for serious toxicity	Increased risk for opportunistic and fatal infections	Lymphoma and other malignancies
Avoid excess unprotected sun exposure	Monitoring of hematologic response	Closely monitor laboratory tests	Neutropenia or pure red cell aplasia	Thrombosis
Infections	Hepatotoxicity	Drug interactions	Avoid live attenuated vaccines	Major adverse cardiovascular events
Renal toxicity	TPMT deficiency or inhibition	Carcinogenesis, mutagenesis, impairment of fertility	GI (eg, tract ulceration, hemorrhage, and perforation)	Laboratory monitoring

Use of systemic immunosuppressive drugs is limited by a number of warnings and precautions.

Chart courtesy of Dr. Perry Grewal

Abbreviations: AD, atopic dermatitis; AZA, azathioprine; CsA, cyclosporine; GI, gastrointestinal; MMF, mycophenolate mofetil; MTX, methotrexate; TPMT, thiopurine S-methyltransferase; JAKi, Janus kinase inhibitors.

1. Sidbury R *et al.* J Am Acad Dermatol. 2014. 2. Teva. Cyclosporine [summary of product characteristics]. 2014. 3. Sandoz. Azathioprine [summary of product characteristics]. 2017. 4. Boehringer Ingelheim. Methotrexate [product information]. 2015. 5. Teva. Mycophenolate mofetil [summary of product characteristics]. 2012. 6. RINVOQ [product monograph]. St-Laurent, Quebec: AbbVie Corporation; 2022.

be important in atopic comorbidities, such as CRSwNP. Dupilumab is now indicated for use in patients 6 months and up.

Dr. Grewal summarized the warnings and monitoring requirements for various systemic immunosuppressive medications **(see tables)**.

Presenting the American Academy of Dermatology 2023 guidelines for the treatment of AD, Dr. Grewal noted the guidelines strongly favor biologics and JAKis for the treatment of AD, and provide conditional recommendations for traditional immunosuppressive medications. The guidelines strongly recommend against systemic corticosteroids in AD treatment. Dr. Grewal said he agrees with not using systemic corticosteroids over the long-term but supports the short-term use of corticosteroids.

The 2023 American Academy of Allergy, Asthma, and Immunology recommendations for the treatment of AD also strongly favored biologics. The recommendations were conditionally in favor of UV phototherapy, JAKis, and cyclosporine for AD. The recommendations were conditionally against methotrexate and corticosteroids. Dr. Grewal said, however, that he is comfortable using methotrexate for AD based on his personal experience, despite the paucity of robust evidence.

Soon-to-be emerging topical therapies include roflumilast; ruxolitinib, a topical JAK1/2 inhibitor that could be available in Q3 of this year for both vitiligo and AD; and delgocitinib, a topical JAK1/2/3 inhibitor that has been mostly studied in chronic hand dermatitis.

Newly emerging systemic therapies include lebrikizumab (an IL-13 inhibitor) and nemolizumab (an IL-31 inhibitor). Amlitelimab (an anti-OX40 ligand therapy) and rocatinlimab (an anti-OX40 monoclonal antibody) are likely to be approved in the next 2 to 3 years and are showing very promising results in phase 3 studies.

Q&A

Dr. Asiniwasis noted the AAD guidelines are expected to change ahead of publication in the *Journal of the American Academy of Dermatology (JAAD)*, with the availability of more up-to-date information, especially regarding topical JAK inhibitors.

	Cyclosporine	Azathioprine	Methotrexate	Mycophenolate mofetil	JAK inhibitors	Tralokinumab and Dupilumab
Baseline only	• Urinalysis • HIV if indicated	• TPMT enzyme levels* • Hepatitis B and C • HIV if indicated	• Hepatitis B and C • HIV if indicated • Pulmonary function tests if indicated	• Renal function • HIV if indicated	• Hepatitis B and C • Tuberculosis • HCG if indicated	• None
Baseline and follow-up monitoring	• Tuberculosis • Renal and liver function • Lipids • Blood pressure • CBC, differential, platelets • Mg^+, K^+, uric acid • HCG if indicated	• Tuberculosis • Renal and liver function • CBC, differential, platelets • HCG if indicated	• Tuberculosis • Renal and liver function • CBC, differential, platelets • HCG if indicated	• Tuberculosis • Liver function • CBC, differential, platelets • HCG if indicated	• Absolute Neutrophil Count (ANC) • Absolute Lymphocyte Count (ALC) • Hemoglobin • Liver function • Lipids	• None

Required laboratory monitoring for systemic treatment.
Chart courtesy of Dr. Perry Grewal
*Dosing may be guided by TPMT enzyme activity
Abbreviations: CBC, complete blood count; HCG, human chorionic gonadotropin.

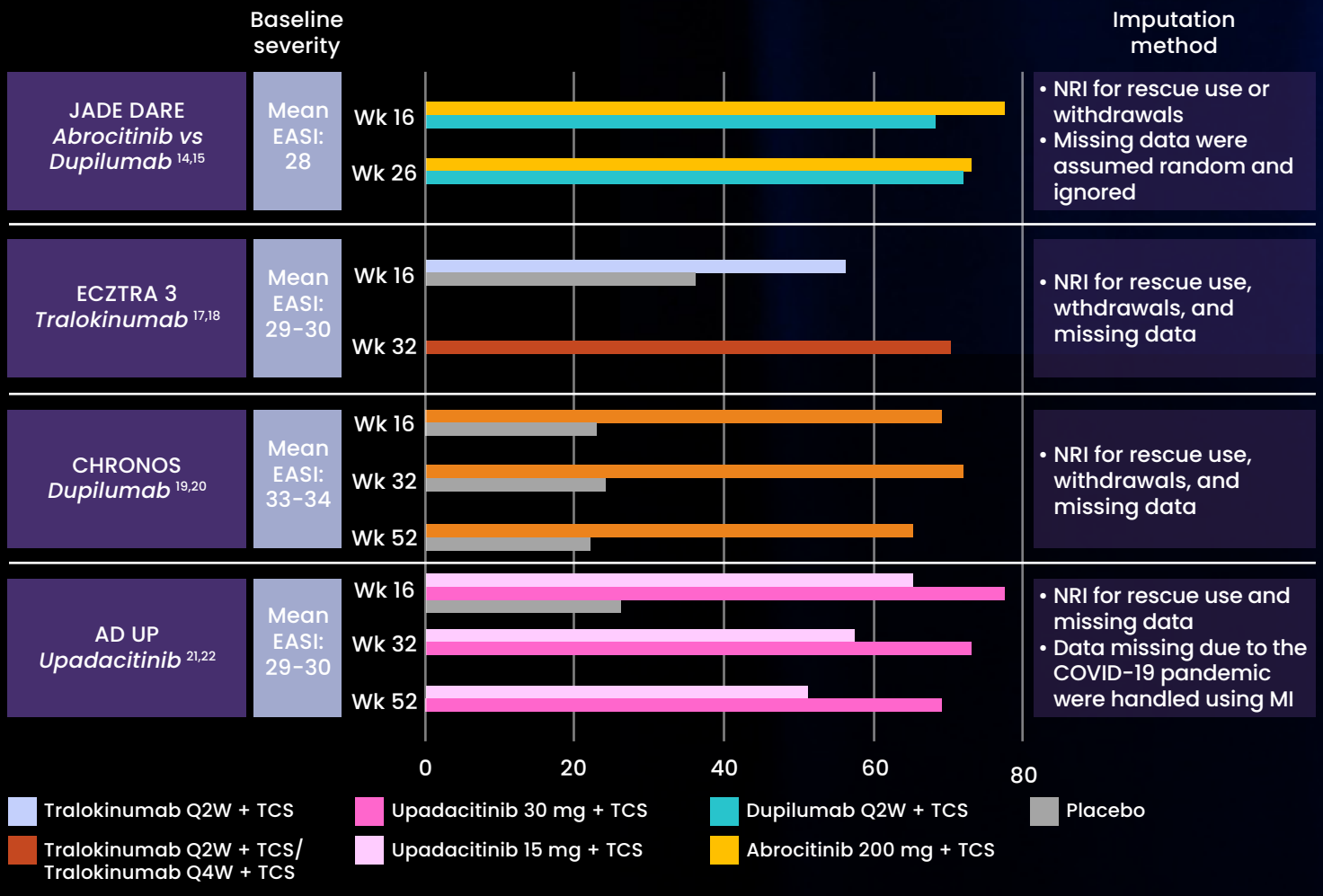
Atopic Dermatitis: Advanced Systemic Treatment Overview

DR. BEZ TOOSI

Dr. Toosi presented an analysis published in the *American Journal of Clinical Dermatology* in 2023, which evaluated the mean EASI scores of patients enrolled in trials for abrocitinib, dupilumab, tralokinumab, and upadacitinib. The mean EASI score in the CHRONOS (dupilumab) trial was 33 to 34, which was higher than trials for the other systemic therapies (28 to 30).

When comparing outcomes across the trials, there is a slight efficacy advantage of JAKis over biologics. However, by week 32 and beyond, the efficacy is comparable. This similar trend emerges when comparing EASI-90 outcomes and the peak pruritus numerical Rating Scale (PP-NRS).

Dr. Toosi presented the data for long-term efficacy of systemic therapies, beginning with dupilumab. The LIBERTY open label extension trial found 89% of patients achieved an EASI-75 response, and this efficacy was sustained over 5 years. Recognizing the frustration that flares pose for patients, Dr. Toosi shared a post-hoc analysis from the CHRONOS trial that showed 84% of adult patients treated with dupilumab were flare-free over 52 weeks of treatment. In the previous year, before dupilumab treatment, the patients enrolled in the study experienced at least one flare. For patients who need to go off treatment, due to travel, hospitalization or another reason, the data shows



EASI-75 Across Systemic Therapies for Adults With Moderate-to-Severe AD
When assessing efficacy of systemic therapies beyond 16 weeks, early between-group differences decrease over time; at the end of the trial, proportions of patients achieving efficacy targets are similar between treatment arms.
Chart courtesy of Dr. Bez Toosi
Abbreviations: EASI, Eczema Area and Severity Index; NRI, non-responder imputation; Q2W, every 2 weeks; Q4W, every 4 weeks; TCS, topical corticosteroid
Adapted from: Silverberg JI, et al. *Am J Clin Dermatol*

that 92% of adult patients with a treatment interruption regained an EASI-75 response. The recapture of response was rapid, within weeks of retreatment.

Reviewing data for tralokinumab, 85% of patients achieved an EASI-75 response at 2 years, based on an interim analysis of ECZTEND data. However, flare rates are higher with tralokinumab, compared to dupilumab; 29% of adult patients treated with tralokinumab experienced a flare after 16 weeks of treatment.

Moving on to JAKis, Dr. Toosi highlighted JADE EXTEND data showing that 85% of adult patients on the 200 mg dose of abrocitinib and 73% of adult patients on the 100 mg dose achieved an EASI-75 response after 5 years. Regarding flares of AD, 39% of patients on the 100 mg dose experienced a flare during the 40-week maintenance period, compared to 17% on the 200 mg dose. Patients who experienced a flare, whether on placebo or abrocitinib, were rescued with 200 mg of abrocitinib and topical corticosteroids. By week 12, 55% of those who experienced a flare initially on the 200 mg dose achieved an EASI 75, compared to 75% and 92% of those on 100 mg and placebo, respectively. Upadacitinib demonstrated similar long-term efficacy results as abrocitinib, though recapture data is not available.

Dr. Toosi highlighted that safety is an especially high priority for AD patients, due to previous experiences with treatment-related AEs. Dupilumab is the only systemic therapy that has safety data of up to 5 years in adults, and also has safety data for children and infants. The most notable safety signal with dupilumab is for conjunctivitis. Dr. Toosi highlighted that the definition of conjunctivitis was broad in the CHRONOS and open-label extension trials for dupilumab, as it included itchy and dry eyes. This broad definition led to conjunctivitis rates of 14% and 20% in the two trials. However, a meta-analysis published in *JAAD* last year analyzed 17 trials and 4,200 patients treated with a biologic for AD and found rates of conjunctivitis of approximately 5%. Dr. Toosi said that in his experience, the conjunctivitis cases are mild and self-limited. He has only had one patient who needed to discontinue dupilumab due to conjunctivitis.

Tralokinumab also has a similarly favorable safety profile, based on 2 years of data. Abrocitinib has an overall acceptable safety profile, though it is associated with is an increased risk of acne, herpes simplex and shingles. Upadacitinib has a similar safety and tolerability profile to abrocitinib.

Q&A

Dr. Megan MacGillivray said many patients want to stop topical treatments when they start dupilumab, despite her encouragement to continue using topical treatments. She asked Dr. Toosi how he approaches this challenge?

Dr. Toosi said he always prescribes topical medications when he initiates a patient on a systemic medication. He encourages them to use the topical medication until they are no longer itchy and their AD is fully clear. Patients respond well to systemics, with sustained efficacy over time, and due to the treatment burden of topical therapy, it is acceptable if patients stop using topicals when they are clear.

Atopic Dermatitis: Special Populations (Pediatrics)

DR. CATHRYN SIBBALD

In Canada, approximately 15% of the pediatric population is affected by AD; 30% of cases are moderate or severe. In 85% to 90% of cases, the onset of AD occurs before age 5. AD affects children in a wide range of ways, including with itch discomfort, sleep disturbance, atopic comorbidities, viral and bacterial skin infections, restricted play, caregiver burden, and the psychological impact of teasing or bullying in relation to the AD. Social embarrassment over AD can also affect confidence and school performance.

Dr. Sibbald presented an analysis of data from the PEDISTAD trial, evaluating height, weight, and body mass index (BMI) in children with AD, compared to age-matched controls. The analysis, presented in a 2024 American Academy of Dermatology poster presentation, suggested that moderate-to-severe AD may hinder growth in children under age 12, possibly due to sleep deprivation, prolonged use of topical or systemic glucocorticoids, and immunosuppressants. This underscores the importance of optimizing AD treatment in the pediatric population.

When diagnosing AD in the pediatric age group, Dr. Sibbald stressed the importance of ruling out immunodeficiency, metabolic disorders, nutritional deficiencies, and other dermatitis (contact or seborrheic). AD is very rare in children below 2 months, necessitating the consideration of possible infections in young infants presenting with an AD-like rash. If the diaper area is involved, the underlying cause is likely to be contact dermatitis or other causes, rather than AD.

For first visits for AD referrals, Dr. Sibbald sends questionnaires to patients asking about their duration of current symptoms (acute, subacute or chronic), prior history of AD (last flare, areas of body affected), current medications for AD, routine skin care (including bathing frequency and products used), possible environmental allergen exposures, and the history of sleep disturbance, behavioral changes, skin infections, allergies, and asthma.

At the first visit, she advises that patients bathe daily in lukewarm water without the use of soap, loofas, baby wipes, or bubble baths. She recommends emollients within 3 minutes of the bath, noting that moisturizing even once per day helps. She recommends against common irritants, such as fragrance and fabric softeners, and advises patients to apply topical medications after bathing, one time per day, to simplify the regimen.

Dr. Sibbald shared a checklist regarding which patients should be prescribed systemic therapy, which was incorporated into the German guidelines for the treatment of pediatric AD. Patients who meet one criterion from each category (severity, burden, and previous treatment) should be initiated on systemic therapy.

Reviewing the treatment landscape for patients between 6 months and 12 years, Dr. Sibbald noted that methotrexate, azathioprine, mycophenolate mofetil, and cyclosporine A are used off label. Systemic corticosteroids, although approved, are generally discouraged due to AEs. Dupilumab is indicated for the treatment of patients aged ≥6 months who have moderate to severe disease and are not adequately controlled by topical therapies or for whom those therapies are not available. Medications being studied for AD in the pediatric population include tralokinumab, lebrikizumab, nemolizumab, upadacitinib, abrocitinib, and baricitinib.

Severity	• PGA 4/5 • EASI 21 • BSA>15% • >10 relapses /yr
Burden	• cDLQI 10+ • Itch 6+ (/10) • Sleep disruption
Local Therapy	• Suboptimal response • No chance of success

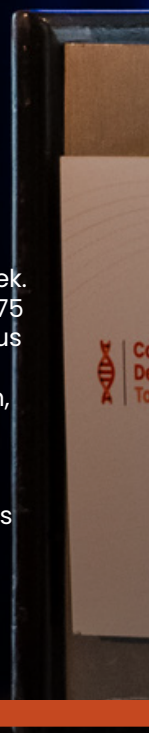
German S3 AD guidelines 2024
Chart courtesy of Dr Cathryn Sibbald

Dr. Sibbald presented data from the phase 3 LIBERTY AD study in children aged 6 months to 5 years with moderate-to-severe AD. In this age group, dupilumab is dosed every 4 weeks. The study evaluated weight-based dupilumab dosages plus topical corticosteroids versus placebo plus topical corticosteroids.

The itch NRS score showed significant improvement for the dupilumab arm, as early as 1 week.

The proportion of patients who achieved an EASI-75 score by week 16 was 53% in the dupilumab arm, versus 11% in the placebo arm. Approximately 28% achieved an IGA score of 0 or 1 by week 16 in the dupilumab arm, versus 4% in the placebo arm.

Dr. Sibbald shared data on safety, showing the risk of herpetic skin infections is generally the same across the placebo and treatment arms, and low rates of conjunctivitis (5% in infants and 6.7% in children; compared to a 4% rate in the placebo group for children). Injection site reactions were slightly higher in the dupilumab. Serious adverse events requiring

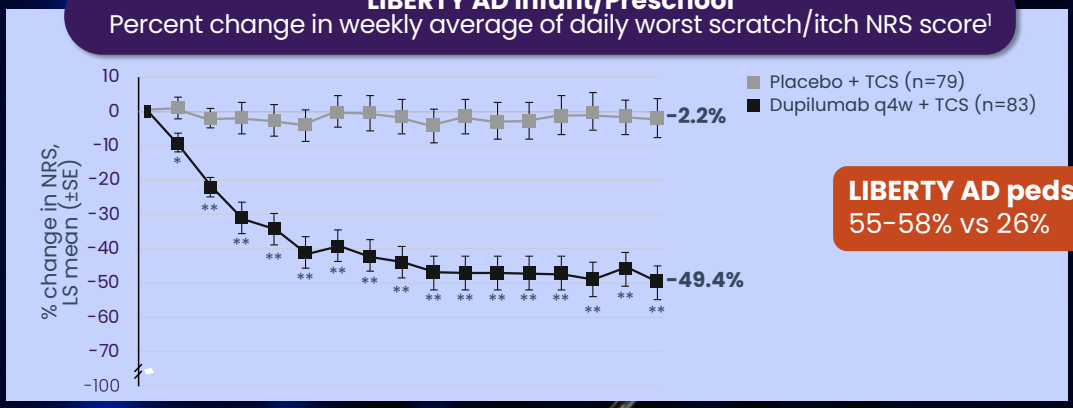


discontinuation and non-herpetic skin infections were higher in the placebo arm. Three years of data in the open-label extension trial also demonstrate reassuring safety data.

Dr. Sibbald shared tips for addressing needle phobia. She admits to patients that the needle may cause a brief pain sensation, similar to a flu vaccine. She doesn't recommend acetaminophen or ibuprofen, as there is no evidence these medications help with injection pain. She finds that ice or Emla cream on the skin helps, as well as keeping the drug at room temperature (out of fridge for 20-30 mins before injection). At Sick Kids, the first dose is administered in the office, so the team can teach the parent the proper technique. They use a parental bear hug (without restraint) and distraction such as a tablet, blowing bubbles, virtual reality, or tactile distraction (vibration).

For inactive vaccines, dupilumab treatment does not need to be interrupted. While 2020 guidelines recommend against live vaccines due to a lack of data, a recent poster presentation of 9 cases of patients who had live vaccines on dupilumab found no adverse effects. This is reassuring data, although from a small cohort.

In adolescents, options include the off-label use of immunosuppressants, as well as dupilumab, tralokinumab, upadacitinib, and abrocitinib. If a child has asthma, rhinitis, or EoE, Dr. Sibbald prefers dupilumab. She has had two teenagers with alopecia areata who have had dramatic hair growth in response to dupilumab, although this can take up to a year to occur. Upadacitinib has rapid efficacy for itch and a rapid off-label benefit for alopecia areata and vitiligo. There is more acne (10-15%) and herpes zoster (1.5%) with upadacitinib, however. JAKis also require lab monitoring, at baseline, one month and then every three months. JAKis also have important drug-drug interactions to consider, including to SSRIs and some antibiotics.



Percent change in weekly average of daily worst scratch/itch NRS score[1]

Chart courtesy of Dr. Cathryn Sibbald

Abbreviations: AD, atopic dermatitis; AE, adverse event; EASI-75, 75% improvement from baseline in Eczema Area and Severity Index; LS, least mean; MI, multiple imputation; NRS, numeric rating scale; q4w, every 4 weeks; SE, Standard error; TCS, topical corticosteroid. Values after first rescue treatment use were set to missing. Patients with missing values at Week 16 due to rescue treatment, withdrawn consent, AE, and lack of efficacy were considered as non-responders. Patients with missing values due to other reasons including COVID-19 were imputed by MI. *p<0.01; **p<0.0001 vs placebo.

1. Paller AS, et al. Presented at ESPD 2022; 20–22 May 2022; Munich, Germany

Q&A

Dr. Asiniwasis asked if a patient requires a live vaccine, do you stop the medication for 4 weeks pre-and post-the vaccine, as recommended by the guidelines?

Dr. Sibbald said she stops dupilumab 4 weeks before a live vaccine but reinitiates dupilumab as early as 2 weeks after the vaccine. Although there is little data, theoretically, dupilumab should not affect the vaccine response.

Dr. Asiniwasis asked if Shingrix has a role in the pediatric realm for patients on dupilumab?

Dr. Sibbald said she doesn't recommend Shingrix in children younger than 18. She said that with JAKis, the focus is on educating patients to contact the clinic immediately if they notice blisters, so that the JAKi can be discontinued and the infection treated.

Dr. Aurelie Sylvain asked when Dr. Sibbald recommends stopping dupilumab, after treatment success for a patient initiated on the biologic before 5 years of age?

Dr. Sibbald said she doesn't usually stop a systemic medication until a patient has been clear for at least a year. She finds this approach builds trust with families, because they understand that the child will not necessarily have to be on life-long treatment. There is also data that you can extend the dosing interval after the 1-year mark, from 2 weeks to 3 weeks for older children, and potentially from 4 weeks to 5 or 6 weeks for younger children. She recommended a gradual process to stop the drug, and a low threshold to return to the previous dosing regimen if the patient has a flare.

Atopic Dermatitis: Special Populations (Skin of Colour and Indigenous Populations)

DR. RACHEL ASINIWASIS

Dr. Asiniwasis highlighted that over 20% of Canadians belong to a visible minority group. Differences in structure, function, and physiology may exist in AD, such as mutations in the epidermal differentiation complex. Beyond this, there are disparities in general health and dermatologic care faced by racial minority groups in North America.

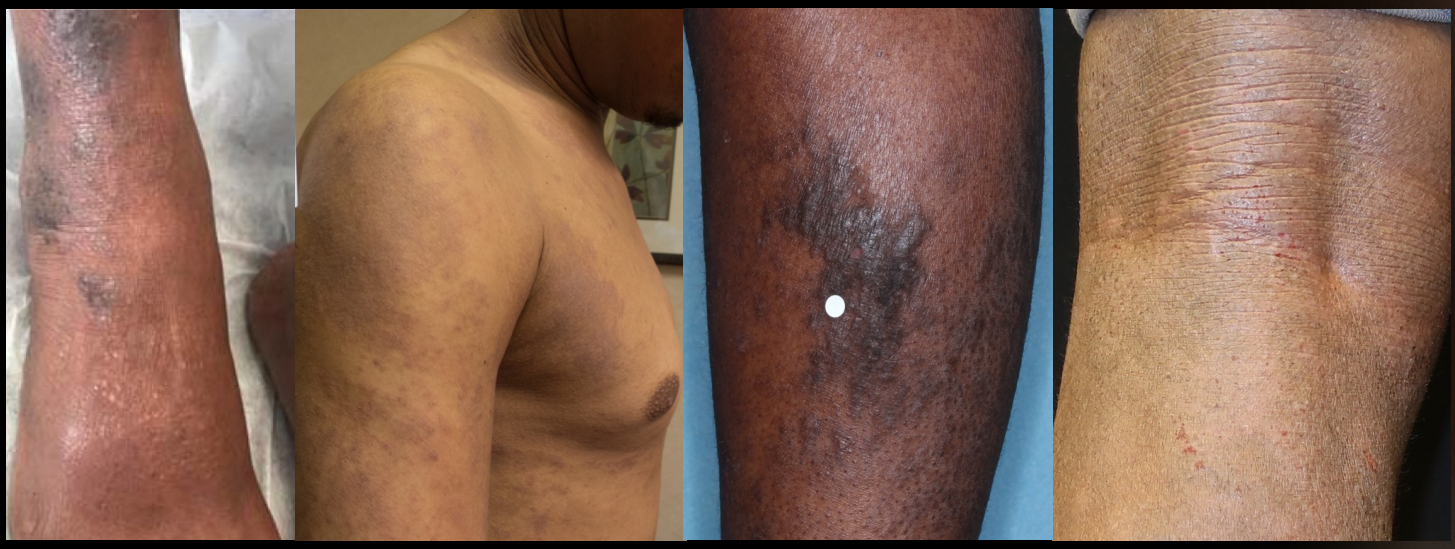
Dr. Asiniwasis noted that common scoring tools that rely on redness ('erythema') underestimate AD severity in darker skin types. In Brown and Black skin, pigmentation changes may be more profound. Dr. Asiniwasis advised looking for violaceous, red-brown, "ashen", brown, or gray hues in Black and Brown skin types. Swelling, itching, and lichenified skin are important indicators for severity.

There are also unique AD morphologies or endophenotypes found in some racial groups/ethnicities. For example, patients of African descent have more perifollicular accentuation and lichenoid papules. Asian groups may have nummular dermatitis. In Dr. Asiniwasis's experience, nummular morphologies and prurigo nodules are common in Indigenous people with AD.

There isn't a lot of data regarding the burden of AD among racial minorities in Canada. In North America, there is a higher AD prevalence in African American, Native Americans, and Asian/Pacific Islander populations, compared to European American populations. African American children face a six times higher risk for severe AD, compared to Caucasian children.

Dr. Asiniwasis underscored that skin of color is underrepresented in dermatology textbooks and in clinical trials. Indigenous people make up about 5% of the world population but represent only 2% of patients enrolled in international AD trials.

Canadian Indigenous peoples are most likely to live rurally and remotely versus the general population, and face disparities in access to health care. Dr. Asiniwasis presented data from the First Nations Regional Health Survey (2008/2010), showing that AD is the top-most commonly



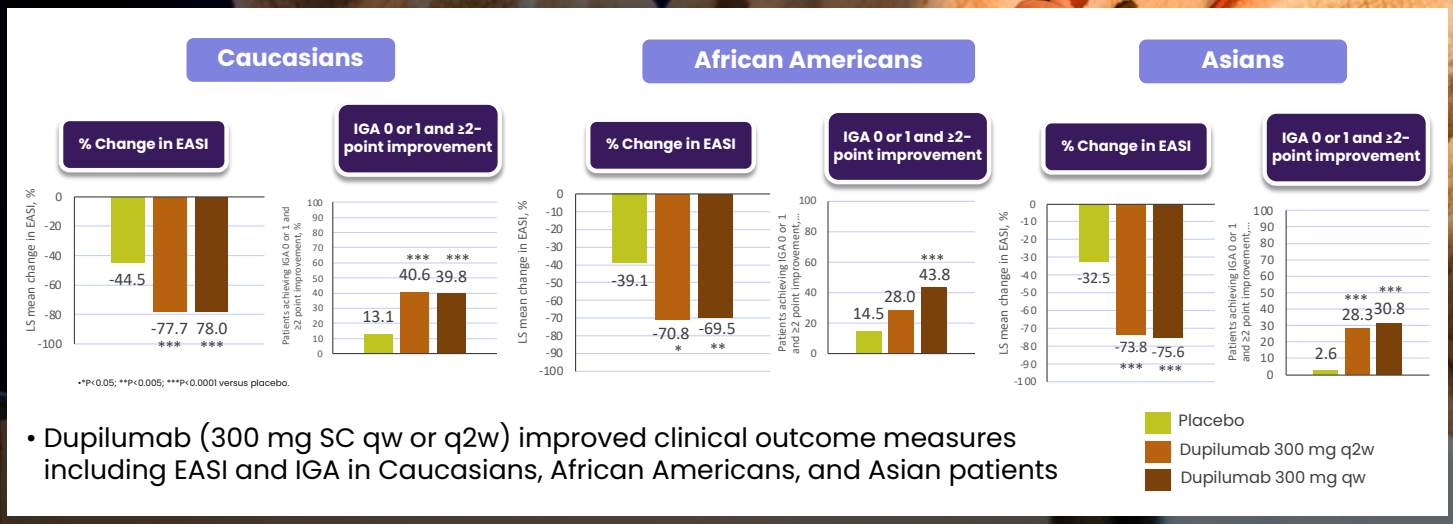
- Lesions are darker and more difficult to distinguish clinically from nonlesional skin
- More likely to have extensor involvement and less frequent flexural involvement
- Treatment-resistant lichenified phenotype
- Lower induction of Th17-related cytokines and upregulation of Th22-related cytokines
- Higher serum IgE

Photos courtesy of Dr. Rachel Asiniwasis
Abbreviations: IgE, immunoglobulin E; Th, T helper.

encountered dermatologic condition, and the third most common condition overall in Indigenous populations in Canada. The survey also found that common barriers for the treatment of chronic conditions for Indigenous people in Canada include a long waiting list, inadequate health care, unavailable services, a lack of transportation and cost. At the same time, AD was the most common chronic condition prompting First Nations youth to seek care. The willingness to overcome significant barriers shows that the condition has a severe quality of life impact on young First Nations people.

Dr. Asiniwasis proposed several solutions, including involving Indigenous communities' involvement in research and knowledge translation and ensuring Indigenous ownership and control of their health data. She highlighted the importance of long-term ongoing research partnerships between Indigenous communities and research initiatives. She introduced pictorial-based guidelines on AD that is accessible to people with a range of reading levels.

Regarding data for targeted biologics in diverse skin tones, Dr. Asiniwasis presented data showing that dupilumab has excellent responses across African American, Caucasian and Asian populations.



- Dupilumab (300 mg SC qw or q2w) improved clinical outcome measures including EASI and IGA in Caucasians, African Americans, and Asian patients

Dupilumab Is Efficacious Across Racial Groups[1]

Chart courtesy of Dr. Rachel Asiniwasis

Abbreviations: DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; IGA, investigator global assessment; LS, least squares; qw, every week; q2w, every 2 weeks; SC, subcutaneous.

1. Alexis AF, et al. J Drugs Dermatol. 2019;18(8):804–813.

Q&A

Dr. Kun Tian said his experience in northern First Nations communities has opened his eyes to the need for far better health care and access. In many cases, patients don't have access to medication they need because of supply chain and storage problems. He underscored the need for dermatologists and allergists to provide continuing education to doctors who practice in the north. Often, by the time he sees patients, they have complications due to advanced skin disease.

Prurigo Nodularis: Systemic Treatment Overview

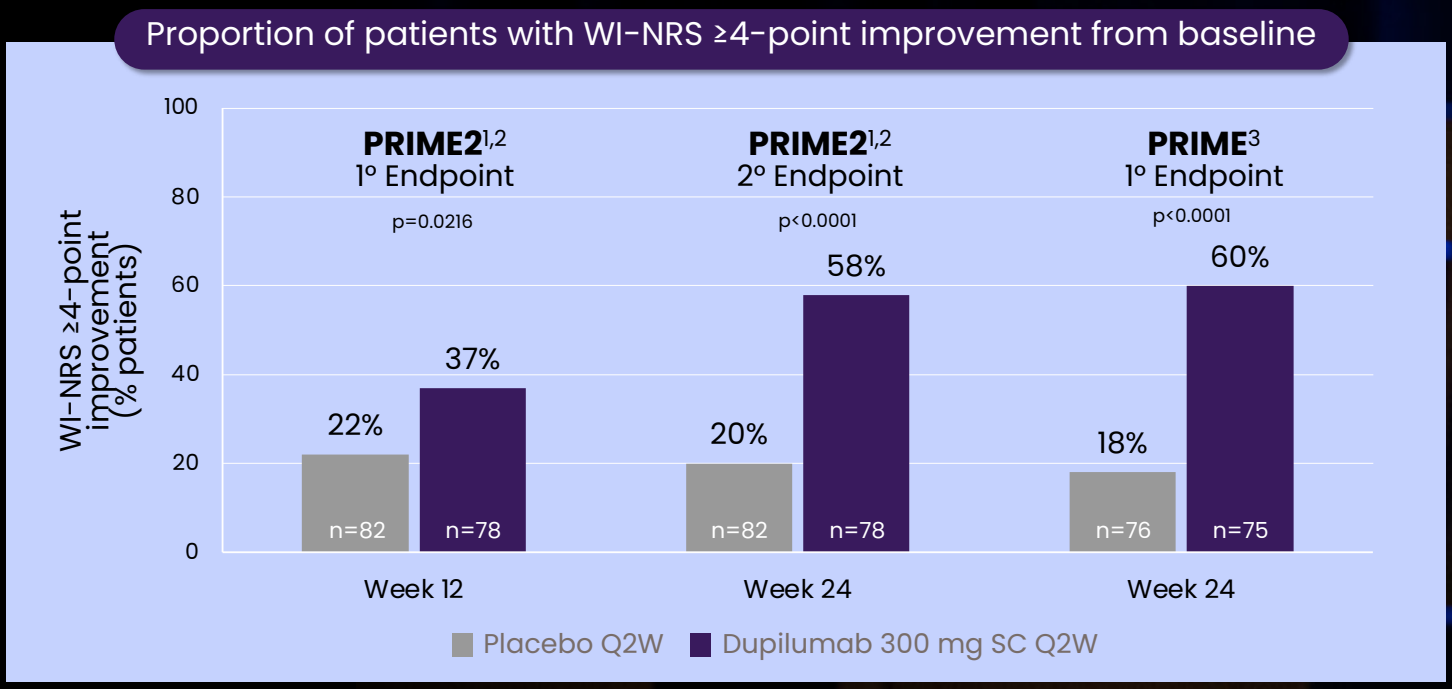
DR. ANNE-MARIE HUNT

Dr. Hunt described the scratch-itch cycle. In most cases, an established underlying etiology causes scratching, which leads to skin-barrier disruption, inflammation and neuronal sensitization. PN presents as itchy, firm, nodular lesions ranging from 3 mm to 2–3 cm. The numbers can vary from a few nodules to hundreds of nodules, which are typically bilaterally distributed on the arms and legs. Excoriations and crusts develop due to ongoing scratching. Dr. Hunt explained that the classic presentation of PN spares areas that are less accessible to scratching, including the mid-back.

Topical options for PN include topical steroids, such as flurandrenolide tape, topical anesthetics, topical calcineurin inhibitors, topical capsaicin, and intralesional corticosteroids. Dr. Hunt remarked that capsaicin is painful when applied and therefore rarely used. Phototherapy is another treatment option. Systemic neuromodulating agents for PN include gabapentin, pregabalin, antidepressants, aprepitant, butorphanol, and thalidomide. Systemic immunomodulating agents include the off-label use of methotrexate, cyclosporine, mycophenolate mofetil, and azathioprine. In Canada, dupilumab is the only immunomodulating agent approved for the treatment of PN.

Dr. Hunt presented the data from PRIME and PRIME2, two randomized, controlled studies that evaluated dupilumab in the treatment of PN. By week 24, 58% to 60% of patients achieved a 4-point or greater improvement in WI-NRS across the two studies (compared to 20% and 18% in the placebo arms). In addition, 45% to 48% achieved an IGA of clear or almost clear by week 24. Reassuringly, rates of conjunctivitis are lower in patients with PN, compared to patients in AD. Skin infections were lower in the dupilumab arms of the studies, due to decreased scratching.

Nemolizumab, not yet approved for PN, has also



Proportion of patients with WI-NRS ≥4-point improvement from baseline

Chart courtesy of Dr. Anne-Marie Hunt

Abbreviations: Q2W, every 2 weeks; SC, subcutaneous; WI-NRS, worst-itch numeric rating scale.

1. Sanofi press release. https://www.sanofi.com/en/media-room/press-releases/2021/2021-10-22-07-00-00-2318876 Accessed June 2022. 2. Yosipovitch G, et al. Presentation at AAD Annual Meeting, 25–29 June 2022. Boston, USA. 3. Sanofi press release. Available at: https://www.sanofi.com/en/media-room/press-releases/2022/2022-01-19-07-00-00-2368986. Accessed June 2022.

demonstrated clinically significant improvement in pruritus and skin lesions in a phase 3 study. Nemolizumab is a monoclonal antibody that blocks a subunit of the IL-31 receptor and is therefore not effective on type 2 inflammation-related comorbidities. The OLYMPIA2 study showed that 38% of patients achieved an IGA of 0 or 1 and at least a 2-point IGA improvement from baseline (compared to 11% in the placebo arm) and 56% saw a worst itch NRS improvement of 4 or greater compared to 21% in the placebo arm. Dr. Hunt explained the OLYMPIA2 endpoints were measured at 16 weeks, and therefore it is difficult to compare between OLYMPIA2 and the dupilumab studies. Peripheral and facial edema were higher in the nemolizumab versus placebo arm (3% versus 2%) of the OLYMPIA2 study. In addition, 5.5% of patients in the nemolizumab arm experienced AD, versus 0% in the placebo arm, as the treatment doesn't target type 2 inflammation. The AD was mostly mild in severity, however, and generally treated with topical therapy without study drug discontinuation.

2023 Canadian Dermatology Today LEAD Symposium on Atopic Dermatitis

Ask the Expert: Panel Discussion

MODERATED BY VIMAL H. PRAJAPATI

Q&A

Eczema patients often require a significant time investment with respect to education and counseling. In the setting of a busy practice, how are you able to effectively meet volume without compromising patient care?

Dr. Asiniwasis recommended handouts and pointed to the Eczema Society as a helpful resource for education. She explained her staff nurse saves her a great deal of time, as the nurse provides the bulk of the education component. She also recommended nurse intakes, with the nurse asking about the patient's medical history, current medications, and allergies, so the physician can review this concisely in advance.

Dr. Sibbald said she reviews her patient list ahead of time. At the beginning of the visit she says, "I see you have been on X and Y medications." This indicates to patients that they aren't required to share their medical history in detail. Focussing on the patient, rather than writing notes, can make the encounter more efficient, as the patient can see that they are being listened to and they don't need to spend as much time advocating for themselves. If a patient brings a long list of previous medications to discuss, she may ask them to email the information so that she can stay on schedule.

Dr. Jack also recommended gathering and reviewing the patient's medical history before the encounter (via nurse interviews or questionnaires). She added it helps when the nurse instructs the patient to disrobe, so that the first step is the visual exam, without delay.

Dr. Jain says that, as an allergist, he saves time by ensuring that the patients who have had skin testing have been counseled on oral challenges before he discusses the skin test result with them. He also ensures that patients with AD receive a handout on managing AD with moisturizing, keeping nails short, etcetera.

Dr. Toosi mentioned that he practices without nurse support. He discusses the options for AD and encourages the patient to take time to consider their preferred treatment. He then books a follow-up phone visit in two to three weeks. AD patients tend to be cautious and want to take time to consider treatment options, so this approach saves time spent in counselling.

Dr. Grewal reiterated that it's invaluable to have nurses who can take a medical history, do the paperwork for biologic access, and provide education. With this approach, patients feel they have received comprehensive care, even when they only spent a few minutes with the physician.

Dr. Ringuet added that visuals help patients understand treatment options quickly. The office has an iPad with easy-to-understand graphs comparing the efficacy of various options over the short and long-term, as well as the rates of adverse events.

Dr. Hunt uses a three-page questionnaire that includes questions about the patient's quality of life, past medical history, possible contraindications for systemic treatments, and their insurance coverage. She reads through this questionnaire before each consult so that she is aware in advance of what the optimal treatment will be for the patient.

Dr. Prajapati said his clinic uses a three-page intake form as well. The first consult is virtual, with the nurse. The nurse spends 15 to 45 minutes on the phone with the patient to go through the questionnaire. In the nurse consult, the patient is asked about their motivation for treatment. "If you know they're not interested in systemic therapy, you shouldn't waste your time."

Dr. Prajapati also recommended platforms like OceanMD which integrate into the electronic medical record and send questionnaires to patients in advance, and input the information into the EMR. Dr. Prajapati also suggested having patients fill out a questionnaire in the waiting room can also save time for clinicians who do not have nurse support. Dr. Prajapati said, like Dr. Sibbald, he doesn't look at the computer when interviewing patients. He focuses on two key questions: how much the condition bothers the patient and whether the patient prefers topical, systemic medication, or whether they don't have a preference so long as the treatment is effective.

Dr. Jack added that letting the patient know they don't have to make a decision on their treatment plan on the day of their visit improves efficiency because "it allows you to move on with your day, and patients love the idea of seeing you again."

Dr. Amiirah Aujnarain, a pediatric allergist, shared that she created YouTube videos about AD, food allergies and other common conditions. Her clinic shares these videos with patients ahead of the consult. The videos answer most of the questions that patients have, so this is another option for improving efficiency.

What is the best way to get involved in research or clinical trials?

Dr. Ringuet said there are many ways to engage in research. He recommended starting as a sub-investigator, with a principal investigator at a center that is already experienced in clinical trials. It is more challenging to initiate a research trial on your own; if this is something one wants to pursue, Dr. Ringuet recommended reaching out to pharmaceutical industry representatives about phase 4 trials (such as registry-based trials). Once an investigator has phase 4 research experience, it is easier to gain credibility and lead phase 2 or phase 3 trials. However, phase 2 and 3 trials impose a significant organizational burden, and a research coordinator is required. Various organizations can help with contract negotiation and ethics approval.

Dr. Grewal also recommended starting as a sub-investigator, to learn standard operating procedures, ethics requirements, and protocol development. It's expensive to set up the infrastructure (equipment, staff, and training) for clinical trials, and it often takes several years to build up to the principal investigator level.

Dr. Jain recommended working with a principal investigator who has experience with Health Canada audits and sponsor audits. He added principal investigators face a significant burden in organizing sub-investigators to provide coverage when the principal investigator is not available.

How do you find grants and how do you estimate your budget for clinical trials?

Dr. Jack suggested academic organizations, including the Canadian Institutes of Health Research. She also recommended

the Canadian Dermatology Association and other Societies. Foundations set up by industry, like the LEO Foundation, offer another alternative. Canadian dermatologists can also apply to the National Institutes of Health and organizations like the Patient-Centered Outcomes Research Institute (PCORI). For those new to research, Dr. Jack recommended industry-funded investigator-initiated grants. For budgeting, Dr. Jack advised factoring time spent investing in the grant-writing process into costs.

Dr. Sibbald recommended the smaller scale Pediatric Dermatology Research Alliance (PeDRA) grants, which are accessible to new-to-practice dermatologists. The grant application process is much less burdensome, compared to others. Skin Canada also provides small-budget grants. Dr. Sibbald recommended accounting for all ancillary costs as well, which can run as high as an additional $5,000.

What are some strategies to stay engaged with industry?

Dr. Jain recommended letting industry medical representatives know that you're interested in being involved in medical activities. Although training discourages industry involvement, Dr. Jain recommended engaging with industry, pointing out industry is driving innovation. In addition, medical science liaisons (MSLs) can help with sharing research. He recommended starting with involvement in educational activities at a regional level and moving from there to the national level.

Dr. Asiniwasis said MSLs often provide helpful summaries of relevant papers. The MSLs can help dermatologists keep up to date and help with statistical analysis questions.

Dr. Prajapati added that MSLs are often willing to share slide decks presented at conferences, and may be willing to let a physician use some of that information in their own presentations.

Dr. Toosi said conferences are a great opportunity to connect with industry representatives.

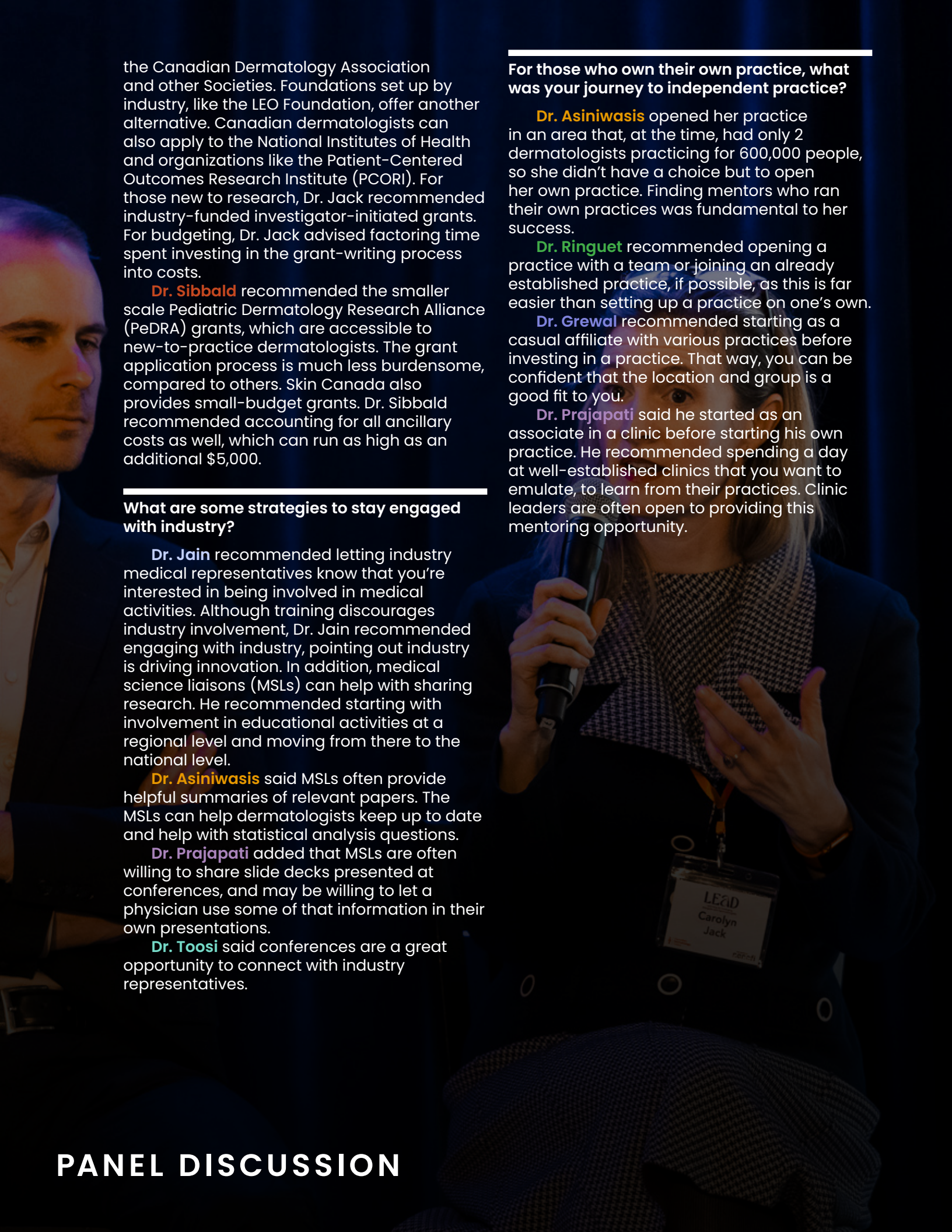
For those who own their own practice, what was your journey to independent practice?

Dr. Asiniwasis opened her practice in an area that, at the time, had only 2 dermatologists practicing for 600,000 people, so she didn't have a choice but to open her own practice. Finding mentors who ran their own practices was fundamental to her success.

Dr. Ringuet recommended opening a practice with a team or joining an already established practice, if possible, as this is far easier than setting up a practice on one's own.

Dr. Grewal recommended starting as a casual affiliate with various practices before investing in a practice. That way, you can be confident that the location and group is a good fit to you.

Dr. Prajapati said he started as an associate in a clinic before starting his own practice. He recommended spending a day at well-established clinics that you want to emulate, to learn from their practices. Clinic leaders are often open to providing this mentoring opportunity.



PANEL DISCUSSION

Conclusion

Dr. Prajapati thanked Catalytic Health for their incredible effort in putting together the LEAD Symposium. He expressed deep gratitude to Sanofi Canada for supporting dermatologists' and allergists' continuing education and recognizing the unmet need for an educational program for new-to-practice dermatologists and allergists. Rohit Khanna, President of Catalytic Health, thanked Dr. Prajapati for conceiving of the LEAD Symposium, and the work he put into ensuring a diverse, highly informative program. He also thanked the steering committee and faculty for their willingness to share their expertise and engage in important knowledge transfer for dermatologists and allergists. The symposium was adjourned.

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Canadian Dermatology Today is published four times yearly in English and French and is circulated to over 1,000 dermatologists across Canada. It features peer-edited articles that present robust clinical perspectives and practical insights on the management of dermatologic disease and performance of aesthetic procedures.

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