A SPECIAL SUPPLEMENT OF CANADIAN DERMATOLOGY TODAY

USING IL-17s FOR THE TREATMENT OF PSORIASIS IN 2024: A ROUNDTABLE DISCUSSION

Susan Poelman, MD, Anatoli Freiman, MD

ABOUT THE PANELIST

Susan Poelman, MD

Dr. Poelman is a Clinical Associate Professor at the University of Calgary and is co-director of Beacon Dermatology. She completed her master's degree and medical school at the University of Calgary and residency at McGill University and the University of British Columbia. She has been in practice in dermatology for over 14 years. She currently serves as president of the Canadian HS Foundation and is actively involved in clinical research trials. She has been an invited speaker at national and international meetings and has served on the board of directors for the Canadian Dermatology Association, Women's Dermatologic Society and the Alberta Society of Dermatology.

Anatoli Freiman, MD

Dr. Anatoli Freiman is a Toronto dermatologist specializing in medical, surgical and cosmetic dermatology. He completed medical school training at McGill University and dermatology residency at McGill University and the University of Toronto. Dr. Freiman is an author and medical educator with many publications in dermatology and is a frequent lecturer at medical conferences. He is the chair of the Canadian Dermatology Association Sun Protection Program and is an expert on many editorial and advisory boards. Dr. Freiman is the Medical Director of the Toronto Dermatology Centre, a comprehensive dermatology clinic in Toronto.

USING IL-17S FOR THE TREATMENT OF PSORIASIS IN 2024:
A ROUNDTABLE DISCUSSION

The anti-IL-17 class is not only highly effective in treating psoriasis, but also other comorbidities associated with type 2 inflammation. Data presented by Dr. Kim Papp at the European Academy of Dermatology and Venerology in 2022 shows that brodalumab (Siliq), in particular, can effectively treat psoriasis even among patients for whom other IL-23- and IL-17-targeting biologics don't work or have lost effectiveness over time. However, Brodalumab's black box warning can be a prescribing barrier, especially among new-to-practice physicians. In this roundtable discussion, Dr Anatoli Freiman and Dr Susan Poelman, who both have wide clinical and research expertise in biologic therapies for psoriasis, share how they weigh clinical and real-world data of IL-17 cytokine inhibitors (secukinumab, ixekizumab, & bimekizumab) and IL-17 receptor antagonists (brodalumab) when treating psoriasis.

I'd like to start with a broad question. What patient and clinical factors do you consider when deciding to initiate an IL-17 medication?

Dr. Susan Poelman (S.P.): IL-17 medications work rapidly, and they're very effective in treating psoriasis. There is some exciting, new data showing that IL-17 medications work well for psoriatic arthritis. For this reason, IL-17 medications are rapidly becoming the standard of care in psoriatic arthritis. This class is also beneficial in the treatment of other comorbidities, such as hidradenitis suppurativa. The only patients for whom I wouldn't prescribe IL-17 medications are patients with a history of inflammatory bowel disease.

Dr. Anatoli Freiman (A.F.): For a large segment of moderate-to-severe psoriasis patients, IL-17 medications offer an impressive combination of efficacy, rapid speed of onset, and safety. Our centre participated in studies of anti-IL-17 medications, especially brodalumab, which has increased my comfort with prescribing these medications. Anti-IL-17 medications can also provide effective treatment of psoriatic arthritis, and this is recognized among our rheumatology colleagues. We know that about 25% to 30% of patients with psoriasis may develop psoriatic arthritis, but it is often underdiagnosed. Clinicians need to be aware that psoriatic arthritis can develop later in the course of the psoriatic disease.

Some dermatologists initiate patients with psoriasis on IL-23 inhibitors simply because they feel they're safer. Do you have safety concerns with IL-17 medications?

AF: Anti-IL-17 medications are generally very safe. There is the black box warning with brodalumab, and this simply requires a conversation, to put it into perspective for the patient **(see Box 1)**.

> ***Suicidal ideation and behavior, including completed suicides, have occurred in patients treated with SILIQ. A causal association between treatment with SILIQ and increased risk of suicidal ideation and behaviour has not been established.***

Box 1: *SILIQ Product Monograph, March 6, 2018; available at chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://pdf.hres.ca/dpd_pm/00044076.PDF*

SP: I don't have any major safety concerns with the IL-17 inhibitor class. Bimekizumab, in particular, is associated with a higher incidence of oral candidiasis. This isn't difficult for the dermatologist to manage, but it can add time to the counselling conversation, and it requires the prescriber to treat this side effect if it occurs.

How do you set treatment goals for your patients when you prescribe IL-17medications?

SP: I tell them they can expect their skin will become clear or almost clear. I am quite confident that I can achieve that with the currently available options.

Dermatol Ther (Heidelb) (2022) 12:1777-1792

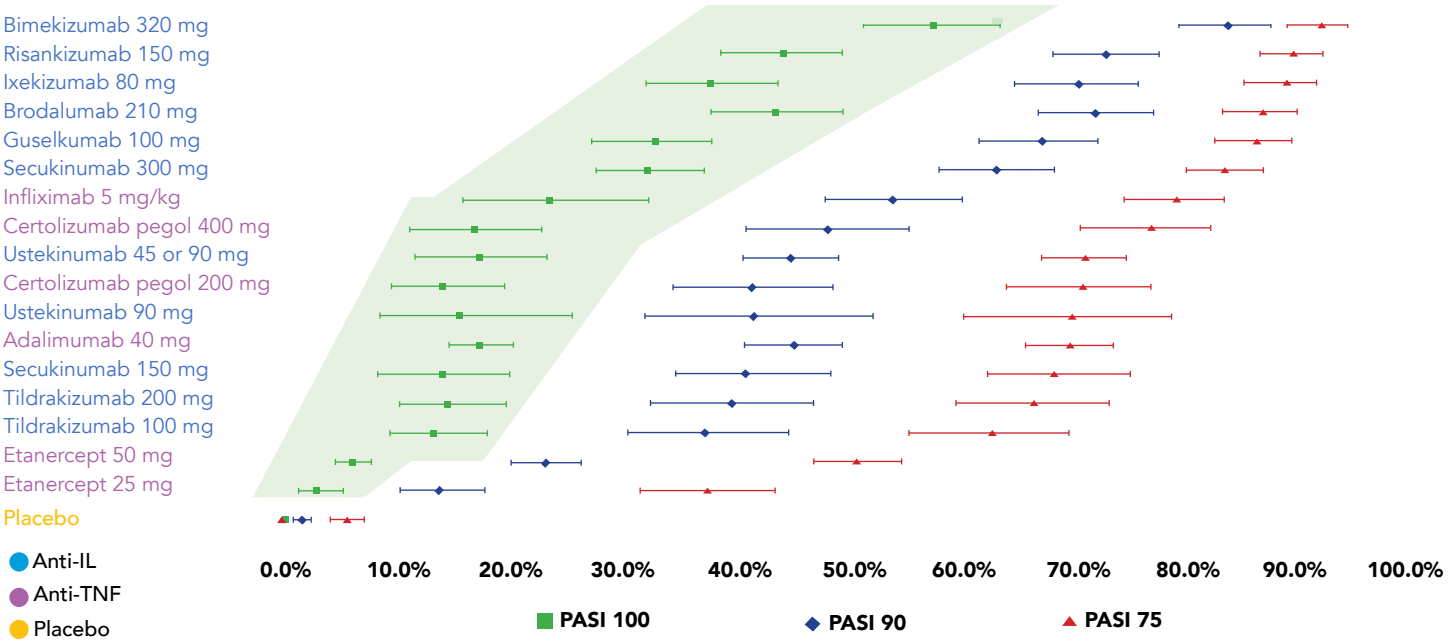


Figure 1. *Probit probabilities (95% CrI) of achieving PASI outcomes. Treatments are sorted by the highest to lowest probabilities of reaching PASI 75; Adapted from Armstrong et al., 2022; Abbr: CrI credible interval, IL interleukin, PASI Psoriasis Area and Severity Index, TNF tumour necrosis factor.*

AF: We've come a long way over the past 20 years. When I see patients in the clinic with moderate or severe psoriasis, skin clearance is a very attainable goal, and this had not been the case before the biologic era. It's also important to consider the patient's quality of life. Physicians can use the Dermatology Life Quality Index (DLQI) as a measure, or ask informal questions to understand a patient's wellbeing.

Furthermore, I prefer to choose a medication that treats a patient's psoriasis as well as potential comorbidities, such as psoriatic arthritis.

In a network meta-analysis (Figure 1.) published in *Dermatology & Therapy*, brodalumab is consistently ranked among the top three biologics in terms of the percentage of patients who achieve PASI 100. How does this compare with your real-world experience?

SP: Brodalumab is one of the most efficacious biologics that we have. There are no head-to-head studies but, in my clinical experience, bimekizumab is the only one that is more efficacious than brodalumab, and that was reflected in the 2022 meta-analysis published in *Dermatology & Therapy*. With brodalumab, patients can achieve PASI 100 in as little as eight weeks. For patients who have important upcoming events, like a wedding or holiday, and their goal is for their skin to clear quickly, brodalumab is my top choice.

AF: Absolutely, patients improve quickly on brodalumab. That's important, because many psoriasis patients have suffered with psoriasis for years and they've tried various therapies that haven't been effective. By the time they see you, they're frustrated. When you put them on the right therapy, that patient 'buy in' is immediate. Compliance is an issue in medicine, in general, so when we prescribe a medication, it really helps when it works effectively and rapidly.

I want to talk about the opposite issue now. When a patient is *not* achieving adequate response to an IL-17 or IL-23 inhibitor, do you escalate the dose?

AF: I think it depends on the biologic. For biologics that are dosed every two to three months, it's simpler to shorten the injection interval, compared to biologics already dosed more frequently. Generally, if a patient has, for example, 98% PASI clearance on a medication, I focus on managing the patient's expectations. It is often better, in these cases, to manage remaining stubborn plaques with a topical therapy. Insurance payers can challenge dose changes, so I try to optimize topical therapy as much as possible.

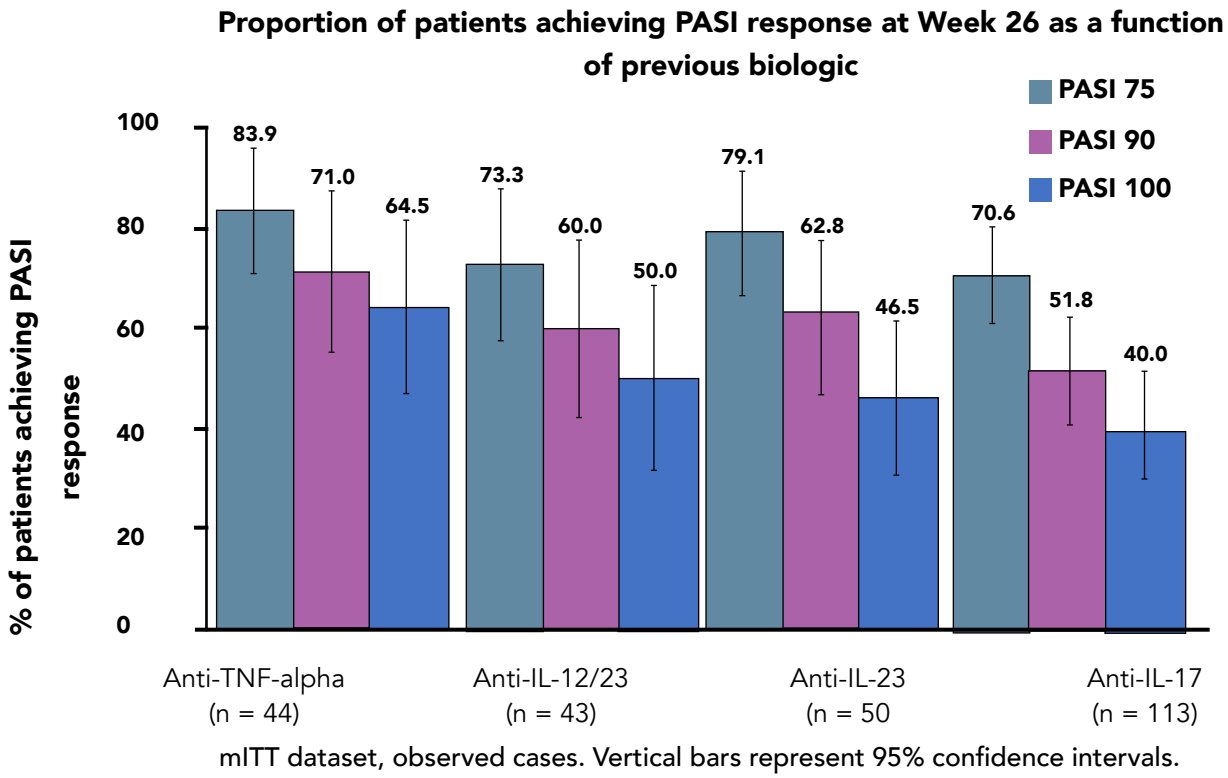


Figure 2. *Efficacy of Brodalumab in Moderate-to-Severe Plaque Psoriasis After Failure of Previous Biologic Therapies: A Phase IV, Multicentre, Open-Label Study; Papp et al, Poster presented at EADV, 2022, Milan, Italy*

SP: I commonly reduce the dosing interval of IL-23 inhibitors when patients aren't responding adequately to the biologic. I commonly increase the dosage of secukinumab, especially for patients with higher body mass index. With brodalumab, I find the standard dosage is adequate; it is very rare that patients require dose escalation.

Let's discuss some of the differences between medications within IL-17 inhibitor class. Brodalumab is the only IL-17 receptor antagonist that targets the IL-17 receptor rather than the cytokines. Is this mechanism of action meaningful to you when considering therapeutic options?

AF: When the mechanism of action is associated with differences in clinical outcomes, yes, it's relevant. Brodalumab's post-switch success, including after other IL-17 inhibitors, is likely explained by its unique mechanism of action. In the past, when a biologic failed to induce an adequate response, I would switch outside of the class. As more post-switch outcome data emerged, it's become apparent that it's possible to switch patients within the IL-17-targeting class and achieve optimal outcomes.

SP: I agree. The unique mechanism of action with brodalumab reassures me that patients will respond differently to brodalumab, if they haven't responded, or lost response, to one or more other IL-17 inhibitors.

Indeed, a study accepted for publication in the *Journal of the American Academy of Dermatology,* demonstrated a high probability of treatment success (defined as at least 50% of patients achieving PASI 90) in patients who switched to brodalumab after anti-IL-23, IL12/23, IL-17, and anti-TNF-alpha biologics failed (Figure 2.). Does this align with your clinical experience?

SP: This resonates with what I see in practice.

AF: Yes, I do see brodalumab work for patients for whom both IL-23 and IL-17 inhibitors haven't been adequately effective. It's helpful to have the background data to back it up, so as to make evidence-based switching decisions.

How do you discuss the black box warning about suicidal ideation and behavior for brodalumab and put that into context for patients?

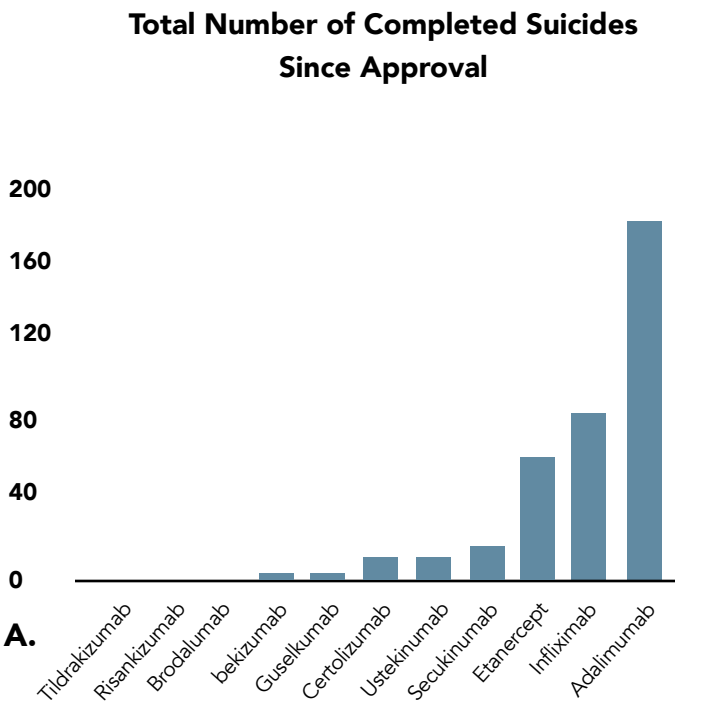
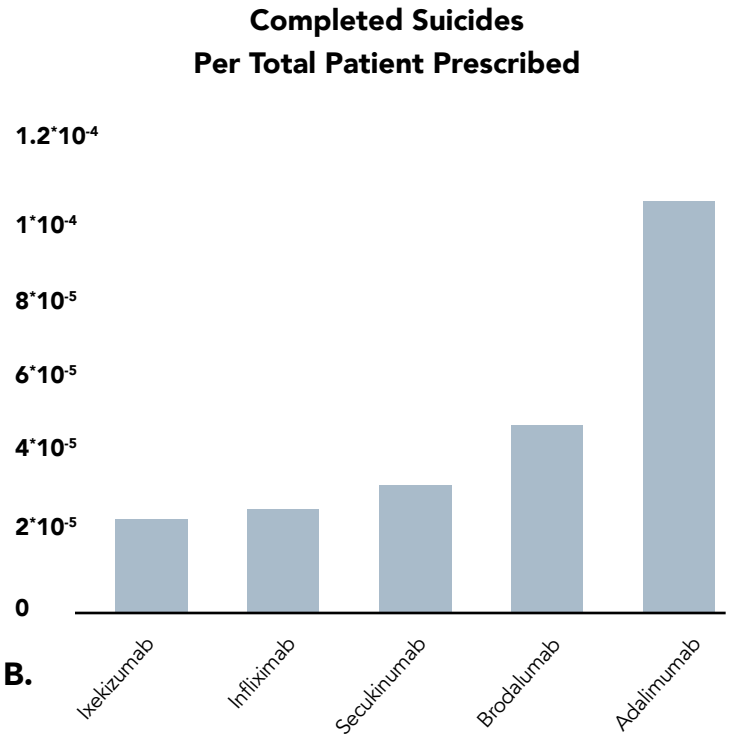


Figure 3. A, *Total number of completed suicides for all indications for each biologic since approval as of December 31, 2021 and* ***(B)*** *the number of suicides per biologic per total patients prescribed for drugs for which data were available.*



SP: Whenever I discuss brodalumab with patients, I counsel them about the black box warning, because I know there is a high likelihood they will come across the warning and not know how to interpret it. I explain that the original study included patients who were depressed, and there was a small number of completed suicides. I stress to patients that I don't think the drug increases the risk of suicide, nor do I think it makes depression worse. Instead, psoriasis itself is associated with an increased risk of suicidality. In my experience, patients often find their mood improves once they start a biologic medication, because their skin becomes clear **(see Box 2)**.

At week 12, patients receiving brodalumab experienced improvements in HADS (Hospital Anxiety and Depression Scale) scores, with statistically significant model-based treatment differences. A greater percentage of patients receiving brodalumab compared with placebo improved from 'moderate' or 'severe' anxiety or depression at baseline to less severe groups at week 12.

Box 2: *A prospective phase III, randomized, double-blind, placebo-controlled study of brodalumab in patients with moderate-to-severe plaque psoriasis, British Journal of Dermatology, 2016*

It's also reassuring for patients to know that a research letter published in *JAAD* in 2022 found that since brodalumab was launched, there has been only one completed suicide involving a patient prescribed the medication. In comparison, there have been hundreds of suicides in patients taking other biologics for psoriasis. This is simply due to the large overall number of patients who are prescribed these medications **(Figure 3)**.

AF: It was helpful for me to read the original study about the cases that led to the black box warning, as it suggested that there were outside factors rather than drug causality. However, because of the warning, I don't typically use brodalumab as a first choice for patients who have a history of depression or suicidality.

SP: I agree.

Are there special populations that you think especially benefit from brodalumab, based on your experience?

SP: I think cancer patients especially can benefit from IL-17-targeting medications, and brodalumab in particular. I had a patient with a hematologic malignancy who, after discussing with his oncologist, I treated with brodalumab, and he did very well. Brodalumab has been effective in other patients of mine who were immunocompromised as well. Furthermore, the oncologists I consult with are confident that the IL-17 medication class is very safe for cancer patients.

AF: I've used brodalumab in a wide range of psoriasis patients.

Could you share a case that highlights the benefits of brodalumab?

AF: I have a patient in his 40s who struggled with progressive psoriasis over many years. By the time I saw him, his psoriasis body surface area involvement was about 12%. He was also complaining about mild joint aches. He initially wanted to just use creams and phototherapy, but I explained to him that his disease was severe and warranted more effective therapy. Two years ago, I initiated this patient on brodalumab. In two months his skin cleared, and he also told me that he didn't realize how much joint involvement he actually had until his psoriatic arthritis resolved with brodalumab. I now see him once a year. His skin continues to stay clear, and he doesn't have any arthritis symptoms.

SP: I see a patient who is in her 70s, and she always brings baking items and a big hug for me, because I changed her life when I initiated her on brodalumab. She had recalcitrant palmoplantar psoriasis. I tried methotrexate, and then an IL-12/23 inhibitor, but neither were effective. When I tried brodalumab, the patient cleared within four weeks. She was delighted, because she was able to play with her grandchildren, crochet, play golf, and do all the activities one should be able to enjoy in retirement. I think biases about age can make some physicians think biologic medication isn't necessary for older patients, but there is a huge impact with biologic medications on quality of life at any age. It can especially be profound for someone to get clear skin when they've been suffering for so many years.

USING IL-17s FOR THE TREATMENT OF PSORIASIS IN 2024: A ROUNDTABLE DISCUSSION

Susan Poelman, MD, Anatoli Freiman, MD