Biologics and Systemic Therapies for Psoriasis: Treat the Patient, Not the Disease

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In this era of bountiful psoriasis treatments, dermatologists generally can work with patients to provide satisfactory results, particularly with biologics. However, in some patients, especially those with psoriatic arthritis, there may be other factors that drive us to use systemic therapies. The skin manifestations of psoriasis are, in essence, a window into an underlying state of inflammation, and treating psoriasis with a systemic medication may yield dividends in other areas of the patient's health. Herein, treatment recommendations are provided with the adage "treat the patient, not the disease" in mind.

What do patients need to know initially about psoriasis treatment?

It is important to set expectations with the patient based on the treatment selected, not only for patient satisfaction but to forge an enduring bond with the patient so he/she will trust you to guide the treatment plan if the first therapy does not work as well as anticipated. Because psoriasis is a longitudinal disease process, the patient-physician relationship should be, too. Certainly, these principles generally apply among all patient groups and demographics; however, one may take into account a few special circumstances when dealing with psoriasis. In a pediatric patient, I may try to see if topical therapy including calcipotriene can adequately treat the skin disease before pursuing systemic treatment. The rationale is 2-fold: (1) this patient would be committed to an extended period on immunomodulatory therapy if he/she truly requires it, and (2) some of the forms of psoriasis in children, such as guttate psoriasis, may be self-limited, so it is reasonable to see if it will persist before forging ahead with a long-term systemic medication. In patients with a recent history of cancer, I would likely choose an oral medication such as apremilast before a biologic; even though there are no real data to suggest biologics are associated with higher rates of solid-organ malignancy, most practitioners would err on the side of being more conservative. For patients with human immunodeficiency virus, the tendency is to use the agents with more data (eg, tumor necrosis factor α inhibitors) due to safety concerns with an immunomodulatory medication.

What are your go-to treatments?

I tend to be as aggressive as the patient wants to be with therapy. I regularly see patients in whom multiple systemic treatments have failed and a more creative regimen is needed, such as combining a biologic medication with an oral antipsoriatic treatment (eg, apremilast, acitretin). However, I do have patients with moderate to severe psoriasis who have not seen a dermatologist before. I do not find it necessary to have topical treatments fail before starting a biologic; after all, the sequelae of long-term topical steroid use are notable.

With the newer biologics on the market, such as the IL-17 and IL-23 inhibitors, the sky's the limit for psoriasis area and severity index clearance, but the true benefit is that these medications are much more targeted toward the pathogenesis of psoriasis. Unfortunately, we have to be mindful of insurance and formulary restrictions, but when faced with choosing a broad-acting immunomodulatory agent or a more specific/targeted immunomodulatory agent for an inflammatory disease, most dermatologists would choose the more targeted medication. The data support that the newer agents have better psoriasis area and

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severity index responses and a much greater proportion of clearance, but there is something to be said about biologics such as etanercept, adalimumab, and ustekinumab, which have been on the market for much longer and have shown durable response with a longer track record of safety and efficacy. Recent head-to-head comparisons can help guide treatment. For instance, patients who achieved suboptimal clearance on ustekinumab can safely and reasonably be switched to guselkumab based on the findings of the NAVIGATE study, which looked at this exact situation. More of these studies looking at specific prior treatment failures and improvement upon switching to a newer agent are needed to underscore the efficacy of these drugs and also to help argue for their placement on insurance formularies.

For a new patient with psoriasis, I will screen for psoriatic arthritis, look at involvement (eg, body surface area, individual plaque severity/thickness, locations such as scalp and extremities), and assess patient attitudes toward different treatments. Two patients with the exact same clinical appearance might have completely different strategies, one wanting to be as aggressive as possible to get rid of the psoriasis and the other not believing in systemic treatments and wanting to be as "natural" as possible.

For patients with only cutaneous involvement, the dosing frequency and efficacy of the newer IL-17 and IL-23 classes of medications are hard to beat. If a patient has notable psoriatic arthritis, I still tend to reach for a tumor necrosis factor α inhibitor first. For patients with limited involvement, especially those with scalp and/or palmoplantar psoriasis, I have found that apremilast works quite well. Apremilast, in general, would be a good first-step medication for patients wary of systemic therapy, and with its relatively benign side-effect profile, it has almost completely supplanted methotrexate in my practice. We also have a few newer topical medicines such as a calcipotriene 0.005%–betamethasone dipropionate 0.064% foam and a betamethasone dipropionate spray 0.05% that have proven useful, with more products in the pipeline.

How do you keep patients compliant with treatment?

Setting expectations is most important, and letting patients know what to expect from their first visit really helps to keep them satisfied with the plan and progress. Giving the patient a say in guiding the treatment and perhaps coming up with a rough treatment plan with a defined timeline also helps, such as starting with a topical regimen but moving on to an oral medicine if the topical does not work within 2 to 3 months, and then a biologic if oral therapy does not work well within 3 to 6 months. It is important not to push the patient to pursue a more aggressive therapy unless he/she wants to, otherwise the patient might not be compliant or may stop altogether.

What do you do if they refuse treatment?

If the patient is in your office, clearly he/she does want some help. Try to figure out what is at the root of the treatment refusal. Is the patient refusing topical steroids because he/she is afraid of them? Is the patient unable to stomach having to inject himself/herself? Finding the basis of their reticence may take more time, but we usually can find a mutually agreeable plan of action. Even if the first step is to watch and wait, you want the patient leaving your office knowing that if things do not progress as expected or get worse, they can have faith in you to come back and get more help.

What resources do you recommend to patients for more information?

The National Psoriasis Foundation is a great resource for patients. They have numerous outreach programs and a wealth of patient information. Also, the American Academy of Dermatology is a good resource, not just for patients but for providers; for example, the academy offers appeals letters that can be sent to insurance companies to try to advocate for a specific medication for patients.

SUGGESTED READINGS

Help patients appeal denial of psoriasis drugs. American Academy of Dermatology website. https://www.aad.org/members/publications/member-to-member/2017/jan-27-2017/help-patients-appeal-denial-of-psoriasis-drugs. Accessed February 9, 2018.

Langley RG, Tsai TF, Flavin S, et al. Efficacy and safety of guselkumab in patients with psoriasis who have an inadequate response to ustekinumab: results of the randomized, double-blind, phase III NAVIGATE trial [published online October 10, 2017]. *Br J Dermatol.* 2018;178:114-123.