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Prioritizing Itch Management in Atopic Dermatitis: A Patient-Centered Approach

Announcer:
You're listening to *DermConsult* on ReachMD, and this episode is brought to you by Galderma Laboratories. And now, here's your host, Dr. Charles Turck.

Dr. Turck:
This is *DermConsult* on ReachMD, and I'm Dr. Charles Turck. Here with me today to discuss the impact of uncontrolled itch on patients with atopic dermatitis is Dr. Christopher Bunick. He's an Associate Professor of Dermatology and Translational Biomedicine at the Yale School of Medicine in New Haven, Connecticut. Dr. Bunick, thanks for joining us.

Dr. Bunick:
Thank you, Dr. Turck. It's a pleasure to be here.

Dr. Turck:
So to start us off, Dr. Bunick, how can uncontrolled itch affect the wellbeing of patients with atopic dermatitis—particularly their mental health and overall quality of life?

Dr. Bunick:
One of the things that we have learned in the last one to two years is the really massive impact that itch has on the quality of life of atopic dermatitis patients. So the short take-home message is that itch is central to the quality of life of an atopic dermatitis patient. And this is really having profound changes in how we think about caring for the atopic dermatitis patient because now we're thinking about what are called patient-reported outcomes: what are the symptoms and the experiences that patients are feeling and having because of their atopic dermatitis?

And it turns out that there are some real key data that tell us how patients are feeling. And with itch in particular, there's a scale that we use to monitor itch. It's a 0 to 10 scale with 0 being no itch and 10 being the worst possible itch. And we generally want patients to have an itch of 0 or 1, meaning no or little itch. And in the case of some of the recent data looking at patient-reported outcomes, what we know is that for patients who have a very low itch response—meaning anywhere from 2 to 10—it dramatically reduces the quality of life of atopic dermatitis patients. Now, this quality of life can be skin pain, sleep, disturbance of daily activities, or emotional state.

And there's certain datapoints where there can be as much as a 60 percent reduction in patients' quality of life when you just go from this little to no itch—0 or 1—to itch of a 2 or 3 on that 10-point scale. That's a huge drop in quality of life because of the itch that patients are experiencing. So what we're learning is it's not just enough to have clear skin if you're an atopic dermatitis patient; you can still have decreased quality of life because of that itch. And so what we're seeing in dermatology is this changing of the standard of care in atopic dermatitis. The optimal treatment outcomes are to have minimal disease activity, clear skin, and no or little itch. This is the more big-picture treatment of the patient, the skin, and the symptoms.

Dr. Turck:
And what effect does uncontrolled itch have on the progression of atopic dermatitis?

Dr. Bunick:
So this is a very interesting question, because remember, itch is the symptom that the patient feels, but scratching is actually the activity that a patient does because of that symptom of itch. And when you scratch, you're disrupting the skin barrier, right? You're introducing

decreases in the integrity of that skin barrier. And there are consequences to that. And one of them is it alters the microbiome, or the microbial makeup of the skin. And this often leads to an increase in Staphylococcus aureus bacteria. And we often see impetiginization, which is a fancy way of saying overgrowth of the Staph aureus bacteria. And this can be triggered by that scratching from the itch.

But also, the scratching that leads to decreased barrier integrity also promotes inflammation in the skin. And when you have more inflammation, it then becomes this this feedback loop where now, all of a sudden, the decreased barrier integrity and the inflammation leads to more barrier disruption, and it leads to more itch, and then you get more scratch. People often talk about this itch-scratch cycle; well, in atopic dermatitis, you have itch, you have scratch, you have barrier disruption, you have microbiome disruption, you have inflammation, and you're back to itch.

And this cycle is something that, again, affects the patient's quality of life. And it's one of the reasons why it's so hard for atopic dermatitis patients who have moderate-to-severe disease, for their disease to just simply up and go away. Or for some of these non-advanced therapies to really tackle the disease, it's hard because of this cycle that perpetuates this moderate-to-severe itch and inflammation.

Dr. Turck:
And I was wondering what else you could tell us about the importance of a patient-centered approach that prioritizes itch relief as an end goal?

Dr. Bunick:
In the last year or so in dermatology, there's been a huge emphasis in atopic dermatitis on optimal targets and optimal outcomes for patients. And a certain task force or committee known as AHEAD—Aiming High in Eczema and Atopic Dermatitis—really emphasized the need to combine the clinician-reported outcome with the patient-reported outcome. And the most important patient-reported outcome, as we've been talking about, is itch because it has that trickle-down effect on so many aspects of quality of life.

As the clinician, yes, you're taking care of the skin, but you have to prioritize the patient's experience with itch. And what we're seeing is now the optimal treatment and the optimal outcome for patients with atopic dermatitis are little to no skin involvement and little to no itch. So there's other ways you can say that. You could say an Itch Numerical Rating Scale of 0 or 1, or an Investigator Global Assessment of 0 or 1, or an itch 0 or 1. But the layman terms are just little to no skin involvement and little to no itch. And so when you think about the patient's perspective and the itch, it's actually a key component to hitting an optimal treatment target, also known as minimal disease activity. Our goal is to have all these patients in minimal disease activity, little skin involvement, and little itch.

Dr. Turck:
For those just tuning in, you're listening to *DermConsult* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Christopher Bunick about how uncontrolled itch can impact patients with atopic dermatitis.

So now that we've discussed the benefits of a patient-centered approach, Dr. Bunick, let's dive deeper into treatment options. What evidence-based therapies that prioritize itch relief are currently available?

Dr. Bunick:
We live in a really exciting time for the treatment of atopic dermatitis because there are six advanced systemic therapies available. I'll start with the oral small molecules—these are the JAK inhibitors. So we have two approved in the United States: abrocitinib and upadacitinib. And what's really remarkable about these medications is they tend to show really fast onset, really good clearance of skin, and a really deep itch reduction in a very fast, timely manner, as I said.

And how do we know that these oral JAK inhibitors work well? Well, we've had head-to-head trials of both abrocitinib and upadacitinib with dupilumab where the JAK inhibitors beat out dupilumab, both in skin clearance and itch reduction. We also have indirect network meta-analyses that examined 22 different clinical trials and looked at how all these different medicines compare indirectly for skin clearance and itch reduction. And the JAK inhibitors tend to beat out; they have a little bit better response, both in the skin clearance and the itch, than the biologic therapies that are available—I'll touch on those in a minute. So we know that there are oral pills that patients who really don't fare well with injections, or don't want injections, can turn to, and they work very well. They're setting the standard of care.

We also have four biologic medications now available. There's dupilumab, which is an IL-4 receptor alpha blocker. There's two IL-13 inhibitors—tralokinumab and lebrikizumab—and they both work very differently in how they inhibit IL-13. And then there's the newest kid on the block, nemolizumab, which blocks IL-31, sometimes dubbed the itch cytokine. But the point is that all four of these injectable medicines are available, and it's really giving options to clinicians because not every patient in atopic dermatitis is the same. Atopic dermatitis is a very heterogeneous disease. There's many cytokines, not just IL-4 and IL-13, involved in the pathogenesis. And so

multiple therapies are needed to treat the different molecular endotypes of patients with atopic dermatitis because of that heterogeneity.

But what we do know is that the standard of care is being elevated, and so for moderate-to-severe atopic dermatitis patients, it's really important to understand that you're treating not just skin clearance, but itch reduction too, or the quality of life of the atopic dermatitis patient is not optimized.

Dr. Turck:
And what are some best practices for choosing and implementing a treatment strategy that optimizes both immediate and long-term outcomes?

Dr. Bunick:
There are now enough advanced systemic therapies between the oral JAK inhibitors and the biologics that you really should not be using long-term oral corticosteroids. They have the worst safety record. The track record of safety is the worst among the oral corticosteroids compared to all these other advanced atopic dermatitis therapies. And so we're really pushing that a dermatology provider should not be using oral corticosteroids more than 30 days, and those 30 days are really only as a bridge to an advanced systemic therapy. And if a patient has been on oral corticosteroids and is failing them, then all of the advanced therapy options are available to them—that's the oral JAK inhibitors or the biologic injectables that we discussed.

Dr. Turck:
And as we come to the end of our program, Dr. Bunick, are there any key takeaways you'd like to leave with our audience?

Dr. Bunick:
Yes, there's a few takeaways. And the first that I'd like to emphasize has to do with overcoming therapeutic inertia. And what I mean by that is, as clinicians, we tend to get stuck. We have habits of prescribing the medicines we know best and we have the most experience with, and sometimes that just isn't enough. The patient may not be responding perfectly to that medicine that we feel so comfortable with, and we have to go outside of our comfort zone and use new or innovative medicines.

And one of the examples that I'll give is in atopic dermatitis, we know that dupilumab has been around for six or more years, and it's been that grandfather medicine that was the first biologic and advanced therapy in the atopic dermatitis space, and it revolutionized how we treat atopic dermatitis. But we have to realize that in a disease that's so heterogeneous, not all patients have optimal response or minimal disease activity achieved with dupilumab therapy. And so we as clinicians have to understand the availability of other medications, whether it's other biologics or the oral JAK inhibitors, and be comfortable and confident to switch.

And that timing of that switch can be anywhere from four months to six months—four months if you're very comfortable with your decision-making, and if you're a little bit more cautious, maybe six months. But we see from clinical trial data—most recently the LEVEL UP clinical trial, which was head-to-head with dupilumab—that if a patient isn't achieving their optimal treatment target, which is skin clearance, little to no skin involvement, and little to no itch, then we can consider switching therapy in that four-to-six-month window.

And the last point I'll make is that with the biologic therapies, one of the things that is available is decreasing the frequency of dose. So for example, in the case of tralokinumab, lebrikizumab, and nemolizumab, these medicines, in contrast to dupilumab, are not always going to have to be every-two-weeks dosing. And so for some patients that want to benefit from less frequent injections, we now have some more advanced therapies. And so keeping in mind when a patient's doing really well on a biologic and taking advantage of the on-label options to dose decrease, whether it's from two weeks or four weeks, is a reasonable thing to help patients.

Dr. Turck:
Well, with those insights in mind, I want to thank to thank my guest, Dr. Christopher Bunick, for joining me to discuss how a patient-centered approach to atopic dermatitis can mitigate the impacts of uncontrolled itch. Dr. Bunick, it was great speaking with you today.

Dr. Bunick:
Alright, thank you.

Announcer:
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