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Navigating the New Atopic Dermatitis Guidelines: Advanced Treatment Approaches

Announcer:
You're listening to *DermConsult* on ReachMD, and this episode is sponsored by LEO Pharma Inc. Here's your host, Dr. Jennifer Caudle.

Dr. Caudle:
This is *DermConsult* on ReachMD, and I'm your host, Dr. Jennifer Caudle. Here with me today to discuss the latest guidelines from the American Academy of Dermatology for managing patients with moderate-to-severe atopic dermatitis is Dr. Steven Feldman. He's a Professor of Dermatology, Pathology, Social Sciences, and Health Policy at the Wake Forest University School of Medicine in Winston-Salem, North Carolina. Dr. Feldman, welcome to the program.

Dr. Feldman:
A pleasure to be with you.

Dr. Caudle:
So let's just dive right in, Dr. Feldman. Starting with phototherapy, the new guidelines conditionally recommend this approach. So what are some potential benefits but also limitations or challenges associated with phototherapy that led to this conditional recommendation?

Dr. Feldman:
Yeah, this recommendation is for people who have moderate-to-severe atopic dermatitis, people who have failed topical therapy and who have such extensive disease that they need something like phototherapy or a systemic treatment to control their disease. And all of the decisions that are in this guideline have to be made in conjunction with patients, taking into account disease severity and the impact it's having on people's lives. And because it's having a big impact on people's lives, phototherapy may be a very reasonable treatment option.

The guidelines point out that there's some big limitations. We don't have a lot of data on phototherapy. It's been used for so many centuries that there haven't been large randomized, placebo-controlled trials. So the guideline committee was working with a very limited data set: older outcomes, small sample sizes, and studies with risk of bias. But when they looked at phototherapy, they compared the risks and the benefits, risks being sunburns and possibly some increased risk of skin cancer. They decided that it's a reasonable option for people. The biggest shortcomings of phototherapy they said, and rightly so, is the inconvenience of the therapy, so adults might have to miss work or kids might have to miss school if you're doing it 2, 3 times a week. You may have copays. They did point out, and I think this was smart, that home ultraviolet light treatments – just getting a home lightbox – can address a lot of those forms of inconvenience, but they also pointed out that we have basically no data on the use of home UV for atopic dermatitis. There's some data out there now showing home UV is as good as office UV for psoriasis, maybe even better. So I think it is a reasonable treatment option for folks.

Dr. Caudle:
And after phototherapy, the guidelines zero in on systemic therapies like biologics, JAK inhibitors, and immunosuppressants. If we take a look at biologics first, the guidelines recommend dupilumab and tralokinumab for adults with moderate-to-severe atopic dermatitis. So can you tell us about the key factors that led to this recommendation and what the potential implications are?

Dr. Feldman:
We had all the drugs that were less effective and much less safe, things like methotrexate and cyclosporin. Now we have very effective

options—dupilumab and tralokinumab — and the guideline committee pointed out there was an excellent safety track record, both in clinical trials and after more than 5 years in clinical practice.

It's just remarkable, and no laboratory monitoring is required for these drugs. When they surveyed their guideline work group members, they thought dupilumab was their first-line systemic treatment for atopic dermatitis. Of course, that was before tralokinumab came out, but I think they would still say one of these biologics would be their first-line treatment. And then they also pointed out that an international expert panel also agreed: these biologics are first-line treatment. The one limitation they noted that made them say that their recommendation was not strongly supported by evidence was that there were some limitations of the safety data that were available. That said, there were a lot of good safety data.

Dr. Caudle:
Now the next recommendation involves the JAK inhibitors upadacitinib, abrocitinib, and baricitinib. According to the guidelines, upadacitinib and abrocitinib are two options for adult patients who have failed other systemic therapies or when the use of those therapies isn't advisable. It's also important to note that while baricitinib is effective, it's not FDA approved for use in atopic dermatitis. So with all this being said, Dr. Feldman, what are the key efficacy, safety, and eligibility considerations here?

Dr. Feldman:
You know, we're living in a wealth of great drugs now. The JAK inhibitors were very effective. They block the interleukins that cause atopic dermatitis, the immune signaling molecules at the root cause of the disease. They also block some unrelated immune signaling molecules, which is a limitation. They're approved for use in people with moderate-to-severe atopic dermatitis who failed other systemic therapy, and so they felt that in the guidelines, these medications are not considered to be the first-line systemic therapy for patients. But they are very effective, very high efficacy.

The limitation is the safety concern. They pointed out that tofacitinib was compared to TNF inhibitors in a high-risk rheumatoid arthritis population and couldn't be proven to be as safe as the tumor necrosis factor inhibitors. And so there ended up being a bunch of warnings placed on tofacitinib, including risk of heart disease, cancer, clots, and death. And those labels got added to other JAK inhibitors. The committee pointed out that the AD population is not a high risk as the rheumatoid arthritis population. But there's still some issues, so they felt that the safety signals warrant some caution when prescribing JAK inhibitors for atopic dermatitis. They recommend getting people up to date on vaccination, particularly for zoster. A shingles vaccine would be something I would do for patients before starting them on a JAK inhibitor. And then unlike the biologics, there was a bunch of laboratory monitoring and not enough data to say exactly when monitoring needed to be done, but ongoing monitoring was recommended.

Dr. Caudle:
And if we focus on one more recommendation, systemic corticosteroids are not recommended for atopic dermatitis due to safety risks. Can you tell us more about those concerns?

Dr. Feldman:
Yeah, so we saw for a lot of these other drugs, the guideline committee is recommending one of the forms of phototherapy, PUVA; they were saying we can't recommend it. But for steroids, they actively said don't do it. And I think they based that on one, the poor safety of long-term steroids. We know that long-term steroids have a host of side effects on people. But they also had one study—a tiny study—that was done comparing cyclosporin to prednisolone, and in that small study, the effect was so large they had to stop the study because of people having rebound flares. I think only one out of nearly 20 patients on steroids had good control of their disease; I think 6 on the cyclosporin did. The systemic steroid patients, a lot of them had rebound.

But if you look closely at the study, you see what they did was they gave the prednisolone for just 2 weeks, and then I think they gave people moisturizers after that. Well, if you give somebody with horrible atopic dermatitis just 2 weeks of maybe anything and take it away, their disease may come back. The guideline committee's conclusion was we recommend you not use systemic steroids, but if a patient needed some bridge to the next therapy or there was nothing else available, you might consider using systemic steroids.

Dr. Caudle:
For those of you who are just tuning in, you're listening to *DermConsult* on ReachMD. I'm your host, Dr. Jennifer Caudle, and I'm speaking with Dr. Steven Feldman about the updated American Academy of Dermatology guidelines for treating patients with moderate-to-severe atopic dermatitis.

So given these updated guidelines, Dr. Feldman, what are some best practices for integrating new treatment options like biologics and JAK inhibitors with existing therapies?

Dr. Feldman:

Well first, patients don't need those therapies if they have mild atopic dermatitis. If you've just got a few spots, maybe in front of the elbows or behind the knees, a topical steroid may be all they need. But when you do that, you need to really work to get them to use the medicine. I know this is going to be hard to believe, but patients aren't always fully adherent to their treatments. Adherence to topical therapy can be abysmal, so we really need for those patients, when we're using topicals, to really work to get people to use them well. Now when topicals are not practical—and that's pretty much my definition of moderate-to-severe disease, when they're not working or the disease is so extensive—then phototherapy or systemic therapy is appropriate. Of the systemic drugs, the biologics dupilumab and tralokinumab under the guidelines would be the first-line treatments. JAK inhibitors would be very reasonable and appropriate treatments when the systemic treatments have failed. The guideline committee also pointed out there may be some tendency to want to use systemic antibiotics in these patients, but those should be limited to when patients have clinically evidenced infection.

Dr. Caudle:
Now we've certainly covered a lot today, so before we close, Dr. Feldman, would you share some key takeaways on these guidelines and the management of moderate-to-severe atopic dermatitis?

Dr. Feldman:
Maybe the most important thing they pointed out is we need more data. We desperately need more data on phototherapy, and more head-to-head trials that would be helpful for determining what order to use things in. You have to use good judgment. These guidelines are not a definitive treatment algorithm that says use this first, use this next. In fact, the guidelines started with a disclaimer. Let me read it to you.

"Adherence to these guidelines will not ensure successful treatment in every situation. Furthermore, these guidelines should not be interpreted as setting a standard of care or be deemed inclusive of all proper methods of care nor exclusive of other methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding the propriety of any specific therapy must be made by the physician and the patient in the light of all the circumstances presented by the individual patient and the known variability in biologic behavior of the disease." And finally they said, and I think this reflects things well: "This guideline reflects the best available data at the time the guideline was prepared," not at the time it was published, and certainly not now. The results of future studies may require revision to the recommendations in this guideline to reflect new data.

Dr. Caudle:
And with those key takeaways in mind, I'd like to thank my guest, Dr. Steven Feldman, for sharing his insights on the updated guidelines for managing moderate-to-severe atopic dermatitis. Dr. Feldman, it was great having you on the program today.

Dr. Feldman:
It was my pleasure.

Announcer:
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