Transcript Details
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Journal Club: Oral JAK Inhibitors in Moderate-to-Severe AD

Peter Lio, MD:
Well, that really brings us to our last piece, which it flows into very nicely, and these are the systemic JAK inhibitors. They've been exciting because they've really changed the landscape of atopic dermatitis management. Arguably, some of the most powerful treatments we've ever had, oral medicines once daily and very rapid, like a new level of rapidity.

Within really days, people are seeing improvement, which is exciting. And, I think pretty good convergence of both guidelines here, I'll read a little bit from the JTF guidelines and I want to focus particularly on what they felt from the panel, the patient panel. So they said, "The panel inferred that most well-informed patients with moderate to severe atopic dermatitis, refractory to topical and systemic treatment, including either dupilumab or tralokinumab, and possibly in the future lebrikizumab ..." They actually wrote that in, and that's part of the quote, just so you know ... "Would place a greater value on the certain benefits than the burdens and lower certainty for serious harms, but that such values could vary from patient to patient. Such variability and the low certainty for serious harms drove the conditional recommendation."

And I thought that was pretty nice. The academy was cleaner, they just said it is approved by the FDA and it is recommended. You guys were very straightforward with it. Any thoughts on the nuance? And, again, I know your pediatric focus but, of course, we have this down to age 12 for both upadacitinib and abrocitinib so you have those options. How have they fit into your practice and is it different than the topical ruxolitinib JAK?

Robert Sidbury, MD, MPH:
Yeah, I think it is, Peter. Just, in general, I think most of us, particularly pediatric providers, sort of think of topical medications and systemic medications a little bit differently and put a little bit higher burden of proof, if you will, on the evidence if we're going to recommend a systemic for a child and I think there are some huge differences here. There was actually a relatively recent network meta analysis, as you know, comparing all the systemic treatments for atopic dermatitis and the conclusion was generally that the biologics are safer but the JAK inhibitors tend to work a little better, and that was sort of where the rubber met the road. It was obviously much more complex than that and I'd encourage folks who are interested to delve into that work.

But the JAK inhibitors, prior to 2017, what did we have? The only US FDA approved systemic medication for atopic dermatitis was prednisone, the most universally disliked systemic medication for atopic dermatitis. Since 2017, we've got biologics, you mentioned three already. We've got JAK inhibitors, two approved Tier Three if you consider the EMA in Japan and other places, all systemic medications, and so it's extraordinary. The old non-steroidal systemics we had, like methotrexate for instance, I've used it, I still use it. Here's your systemic medication for your horrible eczema, it may work in about two months. Not such a lovely message to deliver.

On the other hand, JAK inhibitors, one to two days a diminution of itch, which is really quite significant, so the rapidity of onset of action as you mentioned is extraordinary, but we have to consider the boxed warning. And I think all dermatologic providers have become very savvy navigating boxed warnings because we've been doing it since 2001 with the topical calcineurin inhibitors. And there are really important things with regard to this boxed warning with systemic JAKs and the topical that we talked about, that it was generated in patient population that was much older, with rheumatoid arthritis on a different JAK entirely, tofacitinib, with a patient population enhanced for the adverse events of interest.

So lots of reasons it's apples to oranges when thinking about a healthier population of atopic dermatitis patients, but it is a real thing. It is

something that, as part of shared decision-making, we must talk about with our patients and risk stratify, right? Back in the days when we used more cyclosporine, if we had a patient with renal disease of course we're not going to choose cyclosporine over methotrexate, for instance. Now, if we've got a patient who's failed topical therapy, they're not steroid phobic and not using things, they don't have allergic contact dermatitis. We've done all the due diligence to make sure they're an appropriate candidate for systemic therapy, then we say, "Okay, this is a patient with a really strong family or personal history of cardiovascular disease. No. Clotting. No, we're not going to use a systemic JAK inhibitor, we're going to bend more towards the biologics.

Conversely, we've got a patient with horrible conjunctivitis or periocular dermatitis. We may still try a biologic, depending, and try and get around that but we might think more about a medication that doesn't have that side effect. So I think these are critical things to think about and think through as we share this decision-making process with our patients.

Peter Lio, MD:
Well, I can't thank you enough. Your knowledge is amazing but your wisdom, your wisdom is really what keeps me coming back and I love talking with you and learning from you. This has been so much fun.