Transcript Details

This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.comhttps://practicaldermatology.com/series/practical-dermatology-journal-club-atopic-dermatitis/journal-club-blocking-il-4il-13-vs-jakstat/29101/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Journal Club: Blocking IL-4/IL-13 vs JAK/STAT

Dr. Neal Bhatia:
Hi, I am Dr. Neal Bhatia. I'm Chief Medical Manager of Practical Dermatology. We've all heard of artificial intelligence. I am speaking with severe intelligence, like, supreme intelligence, Dr. Peter Lio, affectionately known as Peace de Lio because the book is almost done.

Dr. Peter A. Lio:
The book is almost done. It's a book.

Dr. Neal Bhatia:
It's going to be phenomenal. The architect of pizza will be great. Speaking of architects, as the architect of atopic dermatitis, as part of the journal club, we're going to talk a little bit about some of the articles you've been a part of as well as some of those that we've all quoted. Let's talk a little bit about the IL-4 and IL-13 paths, as well as some of the other things that have been discovered.

Dr. Peter A. Lio:
Well, thank you. Thanks for having me. This is always so much fun. I love catching up with you and thinking about some of the big things happening in dermatology, and this is one of them. I think we've watched over the past, even less than a decade, went from thinking about atopic dermatitis as sort of this monolithic complex thing to now we're starting to tease apart different aspects of it. And the first really big piece was looking at IL-4 and IL-13 together. And we have one molecule that blocks them both. I think some of the thought was maybe we'd be able to subtype or separate out different responders and no responders, but most people did very well.

Now we're seeing it even more targeted with the IL-13 agents, one of which has already been approved for the last few years, another which is about to be approved. Just IL-13 seems to have a really powerful effect. But in the last couple of years, we've also now have two new options of oral JAK inhibitors that are a little broader. I love the story that when IL-4, in particular, IL-3, when it binds to that cell surface receptor, undergoes conformational change, it releases a number of different activities that can then stimulate the JAK-STAT pathway. JAK goes, it stimulates STAT, which goes in nucleus, and it changes the transcription.

What's fascinating is that a number of different cytokines will go through that JAK-STAT pathway, and thus the JAK inhibitors are a little broader and seemingly a little bit more effective when we look at the comparison. So we're now in this place where we could pick an IL-4 and IL-13, a pure IL-13, or a JAK inhibitor with a little bit more broad-spectrum activity, and this is kind of an exciting time.

Dr. Neal Bhatia:
Totally. It is imperative, like we're talking about, stopping the process and also being targeted so that cells don't have to be depleted, there's no loss of radar for anything else. But again, all these molecules that are playing in the sandbox, are they stable in one syringe? Now we hear about 4, 13, and 31 that's coming to market. We have a couple OX40, TSLPs. More importantly, are we doing the right thing by saying we're going to go after these targets and make sure that the process doesn't become the problem?

Dr. Peter A. Lio:
It's such a great point, and I think we're still learning. Part of it is, right, what do we need to block? How long do we need to block it? And what are the adverse events? We know that no medicine comes with no risk. There's always some risk. Every sword cuts both ways. But we understand there are different risks. So with our JAK inhibitors, we have a box warning that is interesting because they're more powerful, it seems, than the current biologics, and they definitely work faster.

Dr. Neal Bhatia:

Well, the sprint data is two days, a couple of weeks, et cetera.

Dr. Peter A. Lio:
Incredible.

Dr. Neal Bhatia:
And the NRS data, of course. But again, we have pill patients, we have shot patients. How do you navigate that conversation with patients?

Dr. Peter A. Lio:
And I think that's it. Now we've laid it out. I like to break it down into the word EAST, efficacy, accessibility, safety, and tolerability. We kind of go through these with the patient, and you're right, I think some patients say, "No, I'm not going to do the needles. I'm not going to do it." And other patients say, "I need to be better right away." Other patients say, "I'm afraid of doing lab monitoring. I don't want something that you have to check blood work." So I love the fact that we finally have options. And the truth is, while I think we can get almost every patient significantly better, I'm still striving to get everybody to that very high bar. I want EASI 90 or better, I want itch zero or one, and I think we can do it for a lot more than we ever could.

Dr. Neal Bhatia:
Well, you have a good point about the itch, because you think about not only the patient, but the family, the spouse, and everyone else that has to deal with the itching and the patient who's sitting there scratching maybe even out of proportion to their VSA or their EASI score. So how do you, again, navigate the conversation that says, "Look, in two days you might get better, and if not, let's go down this path." Where's the ridge that says let's change the game?

Dr. Peter A. Lio:
I love it. And it's such a journey, right? Because, yes, absolutely, the new emphasis on patient reported outcome measures is another theme, because a patient might look good or look good today when you're reading them. That one day in your office, they look pretty good, but they might not be feeling good. They might not be sleeping well. So encompassing that, but then also, when do you call it? And I think we're getting a better sense now, especially for example, with the oral JAKs. We know that after a few months, most of the patients should have seen some pretty good improvement. So if they're not better, after a few months, we have the ability to go up on the dose. So I'm not afraid anymore. I'll say, "Listen, you've done well at the starting dose, but not well enough. So let's try a little higher."

Dr. Neal Bhatia:
And, "Let's get to work." Exactly. Last thing about conjunctivitis, because you've been a big proponent about, "Let's define conjunctivitis. Let's not even make it a big dark point", but is there something new that has been in your work or something you want to bring up from the articles you put?

Dr. Peter A. Lio:
It's been fascinating because, yeah, this has been one of the most common reasons to have to stop the biologics, which is really unfortunate for the patients because they usually are really well except for this conjunctivitis. And while we don't think it's necessarily dangerous, it's certainly uncomfortable, and we know if you don't do something about it, if you let it keep going, you could eventually have scarring or damage the eye. So I think the biggest pieces are understanding that it's probably IL-13, because one hope was what if it's the IL-4, and then if we get a pure IL-13, we won't have that. But we're still seeing it with the IL-13 inhibitors.

Dr. Neal Bhatia:
Because we know IL-13 drives a lot more, whereas 4 is a lot more focused on mast cells and basal pools. But then tell me, should we be educating ourselves on identifying conjunctivitis and diagnosing it correct?

Dr. Peter A. Lio:
I think we should and I think we have to ask about that for each patient, because it is one of those things that they might not look very bad on that day, but they might be having dry eye or irritation in their eye and discomfort that we have to treat.

Dr. Neal Bhatia:
Yeah, again, ocular rosacea we don't ask about the eyes, PSA we don't ask about the joints. Maybe we're not doing our jobs as well as we should. Maybe it's just adding another topping to the pizza. So needless to say. All right, thank you as always. Thank you.

Dr. Peter A. Lio:
Pleasure as always.

Dr. Neal Bhatia:
This is another episode of Atopic Dermatitis Journal Club, and we'll see you again.