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.com/programs/Practical-Dermatology-Atopic-Dermatitis-Journal-Club/journal-club-combination-therapy-with-dupilumab-and-upadacitinib/32408/

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Journal Club: Combination Therapy With Dupilumab and Upadacitinib

Dr. Neal Bhatia:
Hi. I'm Dr. Neal Bhatia, chief medical editor of Practical Dermatology, and welcome to another edition of Atopic Dermatitis Journal Club. I'm here with one of my best friends in the world, Dr. Edward Lain. Can I greet you with a warm embrace? How are you? Very good.

Dr. Ted Lain:
Most people call me Ted, but you can call me Edward. If you do, I think I might be trouble, however.

Dr. Neal Bhatia:
Yeah. Just don't call me Johnson.

Dr. Ted Lain:
That's right.

Dr. Neal Bhatia:
Yeah. So Ted is in Austin, Texas. Give us your real title.

Dr. Ted Lain:
I am a dermatologist in Austin, Texas, I am a researcher, and that's about it. I used to have more titles, but not anymore.

Dr. Neal Bhatia:
But you are the quintessential dermatologist. You're aesthetic, you're medical, you're business, and you know everything. I mean, looking at you. I'm the before picture and you're the after picture so we'll leave it at that. So we're going to talk a little bit about this article that kind of exposes the off-label issues of biologics and JAK inhibitors. It was a combination therapy study with upadacitinib and dupilumab for very severe atopic dermatitis, which we've all seen. We know what to throw at it. In this study, they actually did both. I mean, in your gut instinct, what does it say when you give someone a JAK inhibitor and a biologic? Are we breaking any rules or are we actually doing what's best?

Dr. Ted Lain:
I think we're doing what's best. I think many of us have been doing this even before this has been published because we understand that there's an extracellular component that we are dealing with with the biologic, the intracellular with JAK inhibitor. And by doing both in this of your patients, it makes a lot of sense.

Dr. Neal Bhatia:
Yeah. And you think about our colleagues, probably 20% are writing biologics, 20% are running JAKs. Everybody else is afraid.

Dr. Ted Lain:
Exactly.

Dr. Neal Bhatia:
Right?

Dr. Ted Lain:
100%.

Dr. Neal Bhatia:
And nobody's afraid of steroids or cyclosporine or anything else.

Dr. Ted Lain:
Methotrexate.

Dr. Neal Bhatia:
And yet, you look at these combos of ... Let's say you block the receptor of interleukin-4 or 13, you block the Janus kinase enzymatic pathways that has that TH2 site, and yet where is the harm? Where is the cellular suppression? Where is the dendritic cell surveillance lost? Where is it?

Dr. Ted Lain:
Absolutely. We already know from the biologic side that we are not dealing with an immunosuppressant, right? We have five-year-plus data now from the JAK inhibitor side to show safety. We absolutely know the efficacies there as well, especially the quick onset reduction in itching. So it makes a lot of sense from both efficacy and safety, in my view, to attack from both sides, use these very safely in the healthy patient in particular, whereas you really don't need to be too concerned about the safety issue that some people worry about with immunosuppressants.

Dr. Neal Bhatia:
Yeah. Now knowing the sprint effect of the JAKs, knowing the safety of the biologics, obviously there's a potential paradigm. Say, for example, you could start them both and then pull one off.

Dr. Ted Lain:
Exactly.

Dr. Neal Bhatia:
You have 12-week data, but you also have two-day data.

Dr. Ted Lain:

Right.

Dr. Neal Bhatia:
And then we have six-month-old obviously for the shots and then you have 12-years-old, but anybody could respond to this.

Dr. Ted Lain:
Absolutely. I mean, you're right, Neal. There is an opportunity here to be absolutely aggressive with their AD patient.

Dr. Neal Bhatia:
Yeah.

Dr. Ted Lain:
It doesn't have to be just the most severe patient. Perhaps there's an opportunity, especially with samples, as long as you do some preceding labs to start the JAK inhibitor with the biologic together. And then after a couple of months, after you've had the sprint effect, to your point, with the JAK, maybe you can pull that off and just keep going with the biologic. Especially with these new OX40s that'll be coming out with Q3 month dosing, it's a really interesting idea to hit it hard initially, change disease progression, and achieve some more remission with the novel injectables that will be coming up.

Dr. Neal Bhatia:
And where do you see the tweak in this? Would you maybe cut the dupilumab down to every month, would you do every other day with the pills, or maybe just let them choose after a certain timeframe?

Dr. Ted Lain:
For the severe patient, I probably would cut the pills to every other day is what I would do. I wouldn't change the dosing in the dupilumab because we know that from the data from Sanofi and Regeneron, we know that cutting back the dosing doesn't really help that much in terms of maintenance of remission.

Dr. Neal Bhatia:
Yeah.

Dr. Ted Lain:
But I do think that we could reduce the dose of the JAK inhibitor and still achieve some good control.

Dr. Neal Bhatia:
Yeah. And then still get to the point where, "Okay, are you a pill person or are you a shot person?"

Dr. Ted Lain:
Yeah, and there's that as well.

Dr. Neal Bhatia:
And figure that out. So we have case studies like this. These are case reports obviously. They're obviously well done for us being in the literature, but do we need to do something more, any more structured study? Obviously, this isn't going to be a phase four. No one's really going to take the chance, but what other research do we need?

Dr. Ted Lain:
Yeah, I think these combination therapies are really important, especially with the novel biologics that we have coming out, which allow us to go from Q4 to Q8 week dosing. For example, even starting off with Q4 is maintenance Q4. It's a change in paradigm for the biologics now in terms of injection frequency and as I mentioned with the OX40s, just right on the horizon. Absolutely, I think there's going to need to be more case theories published to allow people who may have some concern to show that, "Look, we've done 10 to 15 patients. There were no safety issues at all. We followed the product label instructions." So yes, I think combination therapy needs to be shown as we get more and more of these therapeutics.

Dr. Neal Bhatia:
And can we build this into psoriasis, for example? Can we put psoriatic arthritis patients on shots and pills? Can we think about alopecia areata? Is there a paradigm for that or hidradenitis, vitiligo? I mean, any of these could say, "Let's take the mechanism of what works, take the Legoland building blocks, and match them to the disease." But even more so, is that going to be a risk to anybody else? I don't see how.

Dr. Ted Lain:
Well, many of what we just talked about, except for psoriasis perhaps, but if you're talking about vitiligo for example, alopecia areata, you're talking about a relatively young, healthy patient. And in those patients in particular, it could be very interesting to try this aggressive combination therapy. We're already doing systemic corticosteroids for vitiligo and AA patients anyway.

Dr. Neal Bhatia:
Absolutely.

Dr. Ted Lain:
So if you are okay with doing weekly dexamethasone, in my view you should probably be okay with doing a systemic JAK.

Dr. Neal Bhatia:
Exactly.

Dr. Ted Lain:
And then combining that with a biologic, which we have so much data on in terms of safety,

Dr. Neal Bhatia:
And it shows you the common enemy is steroids.

Dr. Ted Lain:
Right.

Dr. Neal Bhatia:
Right? If we get the patients off of steroids, we can at least do something good.

Dr. Ted Lain:
Right, exactly.

Dr. Neal Bhatia:
Well, very good. Well, Kevin. Thank you.

Dr. Ted Lain:
Thank you so much. I really enjoyed it.

Dr. Neal Bhatia:
Absolutely. And again, this is good stuff. Coming from you and me, that's even better. So this is another edition of Atopic Dermatitis Journal Club and we'll see you next time.