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Journal Club: Combining Dupilumab and Omalizumab

Dr. Neal Bhatia:
Hi, I'm Dr. Neal Bhatia, I'm chief medical editor of Practical Dermatology, and welcome to another episode of Atopic Dermatitis Journal Club. And I'm here with my best friend in the world, Dr. Brad Glick from Florida, bring it in.

Dr. Brad Glick:
Okay. It's good to see you, Neal.

Dr. Neal Bhatia:
Dr. Glick needs no introduction, but if you had to introduce yourself, what would you say?

Dr. Brad Glick:
Well, Brad Glick, South Florida, I'm a board-certified dermatologist, practice actually in Broward County, Florida, but wear several hats. I'm a program director of Dermatology Residency at Lark and Health System, have 12 residents. I also run a clinical trials unit known as GSI Clinical Research, and we do the gamut of clinical trial research in inflammatory skin diseases, and I also serve on the board of directors of the American Academy of Dermatology. Neal, I'm thrilled to be here.

Dr. Neal Bhatia:
No, it's good. Both of us are thrilled to be here. But even more so, you and I think alike in terms of being aggressive with patients, going off label if we have to, and using combinations for strategy. Let's talk a little bit about this article that combined omalizumab and dupilumab for combination of approaches for urticaria, atopic dermatitis. You gave me a case of the patient you're treating with both, tell me the story about that patient, why would you use that approach of targeted therapies?

Dr. Brad Glick:
Yeah, patients, about a quarter of our patients will come in who have atopic dermatitis, they may have background CSU and vice versa. I just think in general, a lot of the therapeutics that we have right now are very singular, they're so targeted but not going to hit the whole story. We know that atopic dermatitis, type two inflammation, perhaps for CSU too, but this is a patient who is now 85 years old, I met her 15 years ago when she was 70, she actually came to me from the University of Miami, mostly with chronic spontaneous urticaria. She was on the gamut of dapsone, and the interferon, and cyclosporine, really had to convince her to go on omalizumab and it actually helped her urticaria, but not so much her AD.

So, we'd get pretty long periods of her monthly dosing of omalizumab, but then her AD was breaking through. And I think what it spoke to me is that we weren't hitting all the targets, we were down regulating that IgE-

Dr. Neal Bhatia:
IgE.

Dr. Brad Glick:
... but we weren't hitting that IL-4, that IL-13 that we can get with some of our newer generation biologic therapies. And I think we have to think broadly, not just in the atopic dermatitis world, but even in our psoriasis patients, thinking that we're hitting very specific targets, but we're not getting the whole picture-

Dr. Neal Bhatia:
And going after the process.

Dr. Brad Glick:
And the process.

Dr. Neal Bhatia:
Which you hit on a perfect point about the process of TH2 side inhibition, IgE inhibition, but again, what's the missing link between the two, as well as... And first of all, Mazel tov for getting that Medicare patient on both drugs, which I think is a lot of work.

Dr. Brad Glick:
She's got really good insurance.

Dr. Neal Bhatia:
Well, no, that's good. And good for you to actually defend that, which is, again, a missing link in our specialty. And to that point, again, you think about dermatologists, we're all afraid of our own shadow now, everyone is not doing the work, to do the prior auths and complain about paperwork, and rightfully so. How do we get our colleagues to put their foot on the gas and take an approach like this, that says, we're not shutting cells down, we're not shutting the immune system down, we're going after the faucet that turns on the mess, how do we do that?

Dr. Brad Glick:
We've had a very long period of having broad spectrum immunosuppressive agents, then we went into the other direction and we have these highly targeted molecules, but nevertheless, we're not treating the whole patient. Whether you buy into the fact of this atopic dermatitis patient who also has background CSU, or vice versa, as we saw in the study, we have to be able to take that leap of faith that we have to hit those other targets, otherwise we're going to have patients cycling out of control.

Dr. Neal Bhatia:
Oh, completely.

Dr. Brad Glick:
In my patient, when her AD cycles out of control, ... urticaria is very transient, atopic dermatitis is every day. It's sleeplessness, it's chronic itch, and so hitting those two targets not only from a scientific perspective but from a clinical spectrum is critical. And I think that we need to be thinking this way looking forward because we can't be thinking just, let's say, like a JAK inhibitors, which are a little bit more broad spectrum.

Dr. Neal Bhatia:

More broad, exactly.

Dr. Brad Glick:
We have JAK-I inhibitors, they're somewhat targeted, but we're not hitting this whole story even there. We have to combine therapies. I think combination therapy for me is something that even at the podium, Neal, and I've been talking about for years.

Dr. Neal Bhatia:
Oh, completely. And you go after the process, we're not shutting cells down, we're not doing anything like cyclosporine, or any of the immunosuppressants do, and yet we still have our colleagues who say, well, I'm not comfortable with these drugs. It's like, how does that make any sense? More importantly, it's like how do we get dermatologists to take these diseases back from the allergist or the rheumatologist, or anybody else who's poaching medical derm from us?

Dr. Brad Glick:
Well, we need to understand what we have in our toolbox and the success. And where atopic dermatitis is concerned now, we talk about this study where we combine dupilumab and omalizumab, there's lots of opportunities for us to be artistic, and I think dermatologists are artistic. That's the point. And I think with disease states like atopic dermatitis, CSU, and the spectrum of itch diseases, or what I like to call itch-forward diseases, these therapeutics that we have, IL-4, IL-13, IgE inhibitors, they're really not immunosuppressive agents, and I think our colleagues take the word biologic and they think immune suppression, I don't want to get involved.

Dr. Neal Bhatia:
Oh, completely. Or they took anaphylaxis and said, I am not ACLS trained, I don't want to have a crash cart or whatever else. But to that point, do articles like this help us? You mentioned toolbox, you could call it arsenal, whatever we want to call it, do they help us get these drugs covered? Do they help us get patients off the ledge? And even more so, can we use this as a new paradigm to move forward?

Dr. Brad Glick:
Yeah, there's like three questions in there too, so I'll try to hit them.

Dr. Neal Bhatia:
Oh, I could ask 10 more if you'd like.

Dr. Brad Glick:
Three is plenty. I think, first of all, we have to think always out of the box. I'm being a little bit redundant, but thinking singularly when you talk about cells, these targeted cells, again, we need to be artistic. Access is always an issue too, but I think you have to fight the fight. The important thing, at least in my clinic, and in my center, what we do is we make sure that we carefully document disease states. There are patients just as in this article, Neal, that have CSU, atopic dermatitis, we have these patients in the psoriasis world that have spongiotic dermatitis.

Dr. Neal Bhatia:
Absolutely.

Dr. Brad Glick:
They might be TH17 patients, they might be a TH1 patients, they might be TH2 patients. And so, what I do is I document very carefully both disease states, and that I need to treat them at least collaboratively, dual treatment, but from an approval standpoint, we have to clearly document the need to treat both diseases.

Dr. Neal Bhatia:
Both diseases.

Dr. Brad Glick:
I think it's important that we take it back. I think we have atopic dermatitis, but we should be managing those patients with CSU.

Dr. Neal Bhatia:
So, that brings up, and actually something you brought up before. Think about that next patient you're going to see like that, would you start those drugs together? Would you address one problem at a time? Or where would you begin the process?

Dr. Brad Glick:
I think it depends on severity. And I think we do this already. Patient comes in with atopic dermatitis, moderate to severe, we're thinking biologic therapies and/or JAK inhibitors in general. But if they have background CSU, we're going to do the typical things that we do, which is dose-escalate antihistamines to their maximum, four times normal. The problem is that antihistamines are not very good for atopic dermatitis.

Dr. Neal Bhatia:
Correct.

Dr. Brad Glick:
But our target biological therapies are. So, that's my opportunity from the get-go, depending on how I'm receiving that patient, to consider dual therapy from the beginning. But I would say I will take some steps, I will start with, let's say a IL-4/13 inhibitor in dupilumab, or lebrikizumab, even nemolizumab, we have all these new drugs in the toolbox, and then consider if we cannot get a balance in the management of the underlying disease, let's say perhaps with antihistamines and dose escalation, this is the perfect opportunity to do so. Now, someone who presents to us, and I'm dermatologist number two, or number three, or number four, it's time to hit them with two drugs at one time.

Dr. Neal Bhatia:
Completely. And again, if you had your crystal ball, looking at Bruton Tyrosine Kinase inhibitors, looking at some of the newer ones for urticaria, and the JAK inhibitors for example, where do we throw all these together into the soup, right? We can put all these combinations together knowing that they don't have interactions, I make the case for dialysis patients all the time, that they should all be on these drugs because they're all going to be clearing it without any issue. But at the same time, is there a rationale to say, okay, let's put A and B together, let's put a shot and a pill together, let's make sure we're treating outside in... Where are we missing the hoop here?

Dr. Brad Glick:
Many questions, once again, Dr. Bhatia, but I love it. I like to say that not 100% of the patients get 100% clear a 100% of the time. As effective as our psoriasis therapies, and I hate to keep using that as a reference point, but that's really our biggest initial wave in these systemic therapies that have been revolutionary. But even in the setting of atopic dermatitis, most especially, and CSU, we don't clear these patients 100% of the time, we don't reduce their itch from an 8, 9, or 10 down to a numeric rating score of itch of 0, 1 or 2 all the time. So, understanding those different targets together, I think we almost are implored to use combination therapy from the get-go. Because of what I said before, which is we have such targeted therapies, we're going to miss the boat and miss some of those other inflammatory mediators of which many of them are playing a role that we don't talk about a lot of the time.

Dr. Neal Bhatia:

Absolutely. And you bring up NRS scores, we should be doing that on every patient. That should be part of their assessment. Put that in the evaluation management. It up-codes your visit anyway.

Dr. Brad Glick:
Yeah. And it helps with access as well too. In our electronic health records that we have in a couple of our different clinics, very easy to do numeric rating score for it, it's a very, very easy question to ask our patients in the clinic.

Dr. Neal Bhatia:
Completely. Even setting up the night before the visit, say, here, give us your survey, give us a DLQI, give us something for patient-reported outcomes to add to the severity of the evaluation.

Dr. Brad Glick:
Yeah, I think patient-reported outcomes are pretty critical, I think some of them are a little bit more complex. It depends on what practice model you're in. You're in an academic institution, you're doing a lot of clinical trials, those of our colleagues that are in the trenches, I think simplicity is good, BSA, IGAs are simple, they're in all the electronic health records now, and certainly the itch scores are not only important just for our ability to track itch over time, but when we track itch, we're also tracking sleeplessness.

Dr. Neal Bhatia:
Completely. And functionality.

Dr. Brad Glick:
For sure, for sure.

Dr. Neal Bhatia:
And everything else you want to know.

Dr. Brad Glick:
For sure.

Dr. Neal Bhatia:
All right, last question, did you enjoy yourself? Was this good for you today?

Dr. Brad Glick:
Dr. Bhatia, when I'm with you, I always enjoy myself. But more important, I hope that the audience enjoyed a great conversation.

Dr. Neal Bhatia:
Wonderful. They listen to me all the time, I'm glad they got to listen to you.

Dr. Brad Glick:
Thanks for having me.

Dr. Neal Bhatia:

Thank you. Dr. Glick is my, again... You want another one? All right.

Dr. Brad Glick:
We'll finish with a hug.

Dr. Neal Bhatia:
Exactly.

Dr. Brad Glick:
Thanks so much.

Dr. Neal Bhatia:
And thank you again, this is another episode of Atopic Dermatitis Journal Club, and we'll see you next time.