Transcript Details
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Understanding the Effect of Targeting IL-17A/F in Psoriatic Arthritis

Dr. Neal Bhatia:
But thinking in terms of, again, the therapeutic approach, now that you've outlined that immune approach, which is exactly what we needed, what do we need to, again, bring to our colleagues forward to say, "OK, not just a simple 17 approach, not just a simple 23 approach"?

And again, we have the approval of deucravacitinib for psoriatic arthritis as well, which is turning off that tyrosine kinase 2 faucet. But in the respect of targeting the major cytokines that are involved on the effector side, which is, again, 17A and F, is that an approach that should be dedicated to psoriatic arthritis, at least from the dermatology side?

Dr. Naiem Issa:
Yes, absolutely. I think a brief note on TYK2 inhibition for deucravacitinib: small molecule that has a different pharmacokinetic profile in terms of getting a small molecule into that TYK2 protein that's going to be found right below the IL-17 receptor. It has a short on and off time. While it may be beneficial, but I don't think that you're necessarily going to get the long-term deep efficacy that we're hoping for.

Now, however, when you're thinking about cytokines in of themselves, you want to have a longer-term and deeper approach where you're going to hopefully mop up those cytokines. And what we do know is that there's a significant increase in IL-17A and F in the synovium, let alone the skin, and especially in the synovium. So doing a dual blockade that's going to mop up the cytokines with good bioavailability, such as with bimekizumab, leads to great efficacy endpoints.

And specifically, what I think our colleagues may not fully realize yet is that the studies looking at PSA with bimekizumab, specifically where we have the primary endpoint being ACR50, or 50% improvement and all of those joint parameters, where classically the psoriatic arthritis data has focused on ACR20, or 20% improvement. So that alone is a shift or a milestone in PSA, especially for the dermatologists to keep that in mind.

Dr. Neal Bhatia:
No, that's important. Yeah. So thinking in terms of safety, obviously biologic safety we've gone over left and right. Everyone's familiar with them, and there's still those disbelievers who don't think these drugs are safe, or it's word association with bimekizumab and candidiasis or whatever else. And we know that the candidiasis numbers are small. We also know that it's manageable in clinical practice.

But again, thinking in terms of educating our colleagues, how do we get them off the ledge in terms of thinking, "Look at the cost of not treating these patients. Think about what's happening when these patients are slipping through, and more importantly, when we're not asking them the right questions"? What do we need to get over the hump with our patients that way?

Dr. Naiem Issa:
Sure, absolutely. So first and foremost, it is to understand that, outright, there is a small risk. We know this because IL-17, and particularly F, is actually is associated with that fungal immunity. Now, what may be lesser known is that, over time with continued usage of bimekizumab, is that the rates of candidiasis actually sharply drop after that first year. And what I believe is happening is that your immune system is regulating out to compensate for that. So we have the data that backs that up.

Not only are we able to, as dermatologists, treat candidiasis, which is our purview as dermatologists, we should be able to treat with topicals and oral antifungals, or even OTCs for that matter, such as Lamisil. But in addition, is that to have confidence in the data that

even for those patients who may have had a bout of candidiasis, those same patients do actually have a lesser risk for a repeat candidiasis over time. The data is very clear-cut in the long-term extension.

Dr. Neal Bhatia:
So that's good. So again, thinking about longevity, of course, thinking about, again, keeping patients, not just their skin health, but their joint health, on top of our minds. Again, we want to work with the rheumatologists, but again, we don't want to give these patients away. And I think that's really the key to the equation of understanding the biologic pathways.

Well, this is great. There's a great synopsis of the immunology as well, again, the clinical relevance to all this. And I know that's your background in kinase biology, but also just you see through the process, not just see what's in front of you, which is great. So thank you for all those insights, and thanks for joining us on the Journal Club today.

Dr. Naiem Issa:
It is my pleasure. Thank you so much, Neal.