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

JAK Inhibitors vs. Biologics: Choosing the Right Atopic Dermatitis Therapy

Announcer:
You're listening to *DermConsult* on ReachMD, and this episode is sponsored by Pfizer. And now, here's your host, Dr. Raj Chovatiya.

Dr. Chovatiya:
This is *DermConsult* on ReachMD, and I'm Dr. Raj Chovatiya. I'm a Clinical Associate Professor at the Rosalind Franklin University Chicago Medical School and Founder and Director of the Center for Medical Dermatology and Immunology Research in Chicago. Joining me today to explore how JAK inhibitors compare to other systemic therapies for chronic atopic dermatitis is none other than Dr. Peter Lio. Dr. Lio is a founding partner of the Medical Dermatology Associates of Chicago and a Clinical Assistant Professor of Dermatology and Pediatrics at Northwestern University Feinberg School of Medicine. Also, Dr. Lio is a great friend. Welcome, Dr. Lio.

Dr. Lio:
Thank you for having me, it's so fun to be here.

Dr. Chovatiya:
So maybe we can start off with a little bit of background and you could tell us about some of the available systemic treatment options that we have for moderate-to-severe atopic dermatitis.

Dr. Lio:
So for a long time, as you and I both know, we had nothing FDA approved and every single thing we did was essentially off-label with the exception of systemic corticosteroids, which are sort of broadly considered okay. But in March of 2017, we got dupilumab, our first biologic. Then a couple of years later, we got tralokinumab, an IL-13 specific biologic. And then just in the last year, we have our third systemic biologic, which is lebrikizumab, also binding to IL-13, so it's very exciting to have those. And then very recently, we just got nemolizumab, one that binds to IL-31 receptor, so another biologic. So now we have four biologics and two oral JAK inhibitors, upadacitinib and abrocitinib, which have been out for a few years. So we went from zero to hero in just a couple of years. It's been really exciting.

With the oral agents—the two JAK inhibitors—I think that it is pretty clear that they work incredibly quickly. Some people can actually see improvement on the order of hours to days. Certainly, they don't hit their full stride for a few months, but many patients can see something, where the biologics in general seem to take a little bit longer, more like weeks to a few months to really kick in. But again, in particular, with nemolizumab, the newest one, that kind of neural effect seems to help some patients in just a few days, which is pretty remarkable. So we have a little bit of the speed of onset. We then have the depth of the effect—and this is tricky because we don't have a ton of head-to-head comparisons—but there were two trials that had a direct comparator between dupilumab and one of the JAK inhibitors. So one was against upadacitinib and one was against abrocitinib. And I think we can say pretty clearly that the JAK inhibitors—the oral agents—are a little bit more effective than dupilumab. Although, as we get towards the 12- and 16-week time course, there's no doubt that for many patients they start to converge. I think in part because we hit a ceiling effect. People do really well in all of these, and at some point, it's harder to differentiate. But certainly, early on, I think the oral agents are a little bit faster out of the gate and probably, as a rule, have a little bit more powerful effect, which is why I think that I and many clinicians use them as the second line. For our patients, we often will start with a biologic, and then if that's not working, we have pretty good confidence that this oral JAK inhibitor is going to help you.

Dr. Chovatiya:

Do you find yourself talking about some of these differences in terms of the endpoints that are maybe now part of our lexicon with these therapies, Dr. Lio?

Dr. Lio:
Absolutely. I think one of the things that's been so exciting is to watch the treat-to-target goal go up and up. So in other words, our expectations for how much better we can get a patient have really increased over just the past few years. And I would really attribute a lot of that credit to the JAK inhibitors. They are able to get people to that next level. So while there's no doubt that we see some hesitancy both in patients and providers, they're a little bit more powerful, but with that power really comes the ability to get new heights of both improvement on itch and that clear, or almost clear, point that is just as durable. When we look at the longer-term data, it's just as durable as we're seeing with the biologics, and that's really exciting to me. So I will bring up the JAK inhibitors from the very first visit when we're talking about systemic agents. And certainly, there are patients who say, "look, the biologics are not a good fit for me either, I don't want to deal with needles, I can't deal with an injectable that I have to keep cool, and I can't bring it if I'm traveling. The once-a-day pill is a better fit for me, and I'm okay with the slightly increased potential risk." Because the other piece of the puzzle that's really tough for us to disentangle is what are the actual risks of the JAK inhibitors in atopic dermatitis patients versus the box warning, which is honestly, a little bit off-putting for many patients. And the truth is, I think we don't know. But all the data we have so far really suggests that they're quite safe and well-tolerated in this patient population, which is why I think so many of us are comfortable saying, so long as we've discussed the other options, if we feel like this is the best fit for you, let's go.

Dr. Chovatiya:
We talked about some of these efficacy differences, but really, when thinking about safety profiles, how do you have that discussion if you're talking about the biologics as a class and oral JAK inhibitors as a class for a patient who maybe doesn't know much about what they should know related to overall safety with these drugs?

Dr. Lio:
My general approach is to first start by saying, look, there's no medicine that has absolutely zero risk. They all have some risk, otherwise they don't work. Even with a hammer, you can smash your thumb on it. It's a wonderful tool for building houses, but you can get hurt. You can even overdose on water. So I like to just set that point out. I also tell patients that the risks we're talking about, in general, are potential risks, right? Obviously if we knew something was going to cause harm to somebody, we simply wouldn't use it or we'd only use it in a very extreme kind of circumstance. But these patients are suffering. That's why they're there. So I often say the one thing I'm 100 percent sure of is that you are miserable because of your atopic dermatitis, and that's why you're here today. That I can count on. And all the other things we're worried about are really potentialities, and we're here to follow you. So I start with that. I think that kind of diffuses it a little bit.

And then I talk about the boxed warning. I think they need to hear it from us. I'm very afraid that if we don't mention it or if we brush it off, someone else will tell them about it and they'll say, "wait a minute, you didn't tell me any of these things." So I spend some time talking about where it came from, and I explain this was done in a different disease state—rheumatoid arthritis—with a JAK inhibitor that is similar but different. It's not the same. The tofacitinib is a different drug in a different population.

Dr. Chovatiya:
Even beyond efficacy and safety, just the ability to follow through with therapy is important, too. And in your experience, have you noticed any differences in terms of how individuals look at adherence for both of these approaches, oral versus injectable, and how that might impact the outcomes?

Dr. Lio:
I think that it really does depend on the individual, but there's no doubt that an injectable for some patients is simply not going to be possible. And particularly, for younger patients who have needle phobia, this can be a bit of a deal-breaker. Also, there are some issues with bringing something with you if you're traveling a lot and having to keep it refrigerated. Some of the challenge is just shipping. I have some patients who live out of the country half the year, so what do they do? They can't ship it overseas. They can't have it brought overseas. So there can be a lot of issues with that compared to a once-daily pill which makes life a little bit easier. On the other hand, some people are forgetful and don't take pills very well, and they'll say, "I actually would prefer something that I can set in my calendar every few weeks or even every month." We know tralokinumab, lebrikizumab, and nemolizumab all have a one-month dosing schedule potentially, which is pretty exciting. So once a month is a little bit easier for other people to manage, so I think it can be individualized. But there's no doubt that there's compelling reasons to pick one of these. And I wish, in an ideal world, we could pick, no matter what we wanted. We could say, "I'd like something that fits this description of a drug that is in a pill form, or this one that's in a shot form that I can do." But we're not that lucky. We don't have that. So we have to manage all of those together as a package deal.

Dr. Chovatiya:

For those just tuning in, you're listening to *DermConsult* on ReachMD. I'm Dr. Raj Chovatiya, and I'm speaking with Dr. Peter Lio about key differences between treatment options for chronic atopic dermatitis.

So given everything that we talked about—efficacy, safety, adherence—I'm going to ask you the million-dollar question now that we talk about all the time. How do you connect the right patient to the right therapy based on their individual needs, knowing that both the disease state of atopic dermatitis is so heterogeneous and the patient's experience and desire for therapy is also so heterogeneous?

Dr. Lio:
I do think at the end of the day, it depends on a couple things. First, we know some things are easy. If you are under 12, then we only have the one biologic that is approved for that age group. Particularly, for the littlest kids, we have dupilumab only. If you have multiple allergic comorbidities—like asthma or allergic rhinitis—then you might be more inclined, again, to take dupilumab, which has some of those other indications, for better or for worse. And then, for somebody who doesn't have those things and who's 12 and older, you actually have a lot of potential options.

For me, what's helpful is looking at some of the Bayesian network meta-analyses. And there's one that Aaron Drucker recently published that puts the medicines a little bit against each other, and it actually uses dupilumab as the baseline. And it really does seem that lebrikizumab is on par and maybe working slightly better, especially in the very beginning, possibly because it has that double loading dose. That's sort of compelling. And there's no doubt that our oral JAK inhibitors really do pack a wallop. They really sit significantly above the line, particularly at the higher dosing for both of them. And that's really exciting. So for the patient who's miserable, for the patient that needs fastest relief, and for the patient that maybe has failed a biologic, then it becomes a much simpler case to say, "we have the next level for you and that's an oral JAK inhibitor. It's once-daily. There is some lab monitoring. There are some things we have to discuss, but by golly, does it seem to work well even for patients like you who are really difficult and in a bad situation." So I love having those options, and I often say one other thing: this is not a permanent choice. We can try something, give it a few months, and see, and if they're not doing great, or more commonly, if they're doing better, but they're not where we want them to be, then we might say, "listen, you're better, you're sleeping a bit more, you're not bleeding and oozing and getting infected, but, gosh, you're still pretty uncomfortable. You're still having some issues. Why don't we talk about making a change?" We can always go back. Nothing is irrevocable. And I think once we open that door, patients can relax and say, "this is great. We're really trying to meet my needs, which are dynamic needs." I'm not the same person and you're not the same person each month, so we can see where we're at. And I love that idea that we can go up to something stronger for a while.

I have patients who have been on a JAK inhibitor for a couple of years and then say, "could I try to switch to something different?" And the answer is yes, we could try, and if it doesn't work out, if we say that wasn't really a good fit for you, we can easily go back. So I like to keep these options open and understand that they are dynamic systems.

Dr. Chovatiya:
Any last thoughts before we close, Dr. Lio, that you would like to leave with our audience?

Dr. Lio:
The big one is just that it is now time to reassess all of our atopic dermatitis patients and check in with them to see how they're doing because we really do have so many great new options. And while it is possible that none of these will be the right fit, there is a better chance than ever before that we now have something that is going to bring them up to that next level where they're going to be no itch, looking great, feeling great, and sleeping great—better than ever before. And I just love that idea that we can finally get patients there, particularly those who've been struggling their whole life.

Dr. Chovatiya:
Those are such great comments for us to think on as we come to the end of today's program. I really want to thank my guest, Dr. Peter Lio, for joining me to compare available treatment options for chronic atopic dermatitis. Dr. Lio, it was so wonderful having you on the program.

Dr. Lio:
Thank you so much. It was a pleasure.

Announcer:
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