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Treating Atopic Dermatitis: A Look at the Current & Future Landscape

Announcer:
You're listening to *DermConsult* on ReachMD, and this episode is sponsored by LEO Pharma Inc. Here's your host, Dr. Raj Chovatiya.

Dr. Chovatiya:
Welcome to *DermConsult* on ReachMD. I'm Dr. Raj Chovatiya, Assistant Professor of Dermatology and Director of the Center for Eczema and Itch at Northwestern University in Chicago, Illinois. And joining me to discuss the current therapeutic landscape and novel therapies in development for atopic dermatitis are Dr. James Song and Dr. Jennifer Soung. Dr. James Song is Director of Clinical Research for Frontier Dermatology Partners in Everett, Washington. Dr. Song, thanks so much for being here today.

Dr. Song:
Thanks Raj. Great to be here with you.

Dr. Chovatiya:
And Dr. Jennifer Soung is the Director of Clinical Research at Southern California Dermatology in Santa Ana, California. Dr. Soung, it's fantastic to have us here with you.

Dr. Soung:
Thanks for having me here today.

Dr. Chovatiya:
Now to start us off, Dr. James Song, can you tell us about the inflammatory cascade and the itch-scratch cycle that occurs in atopic dermatitis?

Dr. Song:
Yeah, you know, when we think about the itch-scratch cycle, I always like to point out that in and of itself, it's not a bad thing. I mean, there's a reason this cycle has been preserved across so many different species, and there's a useful function to it. It's just that when this itch-scratch cycle is dysfunctional, that's when it becomes a problem. And that's what we're seeing in atopic dermatitis. And we see there's a lot of different players, and we sort of unravel more and more players as our understanding gets more advanced. But we know that for sure the skin is involved, but there's also this immune system, and we know that most of our conventional therapies are going to be working on this immune pathway, particularly what we call the type two pathway. So cytokines like IL-4, 13, 31, and 22 amongst others, and they all kind of signal this JAK stat pathway. And we know that they could directly have an effect on some of these itch neurons and make you itchy, but they could also make your skin barrier broken down as well. So there's a lot of crosstalk that goes behind there. And of course, you have the nervous system and the microbiome, but I think the key concept here is that there's a lot of different players and there's a lot of different crosstalk, and each of these different pathways are opportunities for us to intervene when it comes to a therapy standpoint.

Dr. Chovatiya:
Yeah, it's a really nice concept to think about that barrrier dysregulation and immune dysregulation and really that neural axis that's getting dysregulated as well, where altogether you're getting that milieu that results in atopic dermatitis. And it's kind of cool to think about our treatments targeting different aspects of that. And with that background, I want to ask you, Dr. Jenny Soung, what are the current treatment modalities available for atopic dermatitis?

Dr. Soung:
Right. I love talking about treatment because that's how we help our patients, right? And when I talk to my patients about treatments, I

think that this space is continuing to evolve, and we have so many more treatments than we've ever had before. So in terms of large categories, I think of them as topicals. And even within topicals, which are often a mainstay of treatment in atopic dermatitis, we have our traditional topical steroids and non-steroidals, like topical calcineurin inhibitors, but also our new topical JAK inhibitor. And then beyond that, we have our oral small molecule inhibitors, so just orals in general, new being the oral JAK inhibitors and being a great option in those situations where someone who has tried something else, another systemic previously, and it hasn't worked or is just not able to tolerate those therapies. And then our biologics as well. And now we have two options in the biologic class. So for an autoimmune condition of the skin like atopic dermatitis where also there's many different phenotypes and every patient has a different course, it's so nice to have a breadth of options like this.

Dr. Chovatiya:
And thinking about sort of where we were versus where we are right now, what are some of the modalities that perhaps used to be a bigger part of our armamentarium before we really started having this revolution in targeted treatment?

Dr. Soung:
When you think back, we were really using medications that were borrowed from other specialties like methotrexate and cyclosporine; I used to do a lot more light therapy. I continue to do light therapy for many other skin conditions. But really for a chronic condition like atopic dermatitis, it's really burdensome for the patient to be coming into the clinic on a regular basis. And you think about all of that lost time or the opportunity cost and time spent on taking care of their skin condition. So with really the revolution of therapies that now can possibly control disease for the long-term or we're thinking about atopic dermatitis in a different way rather than just treating that acute flare, our goal is really to prevent the next flare and maintenance of disease.

Dr. Chovatiya:
And to follow up and dig a little deeper with that, Jenny, what are some of the common challenges associated with many of these treatments?

Dr. Soung:
So when you think back to our kind of traditional treatments or before the newer treatments, we've had more than two years ago, when you think about topical steroids, our patients commonly bring up concerns such as atrophy of the skin, easy bruising, and acne, and certainly I have seen these, especially in patients who certainly have more extensive disease and persistent and chronic disease. And beyond those common concerns in topical steroids, we also have our other oral traditional systemic therapies which weren't always designed specifically for atopic dermatitis and often discovered serendipitously, such as methotrexate or cyclosporine. And remember, cyclosporine is only indicated for use for one to two years, no more than two years. So really for a chronic disease like atopic dermatitis, it can be certainly useful in situations where we want to rescue the patient with a severe flare in the short run, but really not designed for long-term treatment. As well as methotrexate. It's not always well tolerated in all of our patients. I have certainly seen a fair number of patients who cannot tolerate the GI side effects, including the nausea as well as sometimes fatigue.

Dr. Chovatiya:
Coming back to you James, are there any other barriers to effective management that we should be aware of from your perspective?

Dr. Song:
Yes, 100% agree with what's already been said. You know, with topicals, I think adherence compliance, there's a lot of misinformation out there, especially when it comes to topical steroids that we have to undo. But for some of our newer therapies, starting with injectables, because atopic dermatitis is certainly a disease of adolescence, sometimes just the idea of an injection can be a little bit hard to get over and some of these require every two week or every four-week injections, and even that could be sometimes a challenge. I also think the oral medications, you know, fair or not, it has a boxed warning on it that could be a little bit unnerving, especially for parents, but also for patients. And that could sometimes be the reason why patients don't want to escalate to a therapy like maybe an oral JAK inhibitor that has really good efficacy.

Dr. Chovatiya:
For those that are just tuning in, you're listening to *DermConsult* on ReachMD. I'm Dr. Raj Chovatiya. I'm speaking with Dr. James Song and Dr. Jennifer Soung about challenges associated with current therapies for atopic dermatitis.

So, James, back to you. Given some of those obstacles that you and Jenny so nicely discussed, I'd love to hear what you're most excited about in terms of some of the emerging therapeutic approaches that are in development for atopic dermatitis. What can we really sink our teeth into and feel jazzed about for what's going to be here in the next few years?

Dr. Song:
Yeah, this is really reminiscent of what we saw with psoriasis, even just a few years ago when we had just this explosion of therapies

almost overnight. And starting with the injections, let's talk about biologics. We have a pathway that really has not been explored until recently. We call this the OX 40 pathway, which is important for T-cell activation, but also for memory T-cell formation. And in some of the studies that we've seen, people not only stay clear, but even off the therapy, we've seen them clear for quite some time. And I think that is something we haven't really seen, at least with atopic dermatitis quite yet. So that's I think what I'm really excited about. We also have cytokine blockers, particularly IL-31 that, as you said before, is really important for itch. And then the data looks actually very promising both for itch reduction and skin clearance.

And then of course we have other biologics that are targeting cytokines that we're already familiar with, that we actually have therapies already out there, but maybe a little bit of a different tweak to it, like a 2.0 in that they're binding to different parts of the cytokine. We call those epitopes or different receptors. And that includes IL-13 and IL-4 receptor inhibitors. We also have new oral therapies, so different JAK inhibitors as well as some that are going to be targeting T-cell trafficking. And that's still fairly early in the development, but I do think there is some promise there. And then lastly, maybe I would just say topicals; you already talked about a topical JAK inhibitor that was recently approved. We have two other non-steroidal topicals that are already approved for psoriasis that shows some very promising data for atopic dermatitis as well. And so those are I think just two additional options that are certainly going to be welcome to our armamentarium.

Dr. Chovatiya:
It's exciting to think that you just mentioned a few things there, but really if we were to look across phase one, two, and three trials, we're talking about things in the hundreds actually. So even if a fraction of those really make it to our patients, it's going to be amazing the choices that we have when it comes to thinking about treatment. And maybe before we close, I can roll this one back to you, Jenny. We heard a lot about some of these novel therapies that James really nicely mentioned. What are some of the unmet needs that you see in atopic dermatitis, and how might new therapies that potentially could be here one day really address what's missing?

Dr. Soung:
I really think that because AD is such a heterogeneous disease, patients present with different types and times throughout their life, and so there are many different clinical situations that we address. Certainly there are patients who have more acute disease and need something to give them relief right away. And then certainly there are other patients who have not only acute disease, but persistent disease and need long-term control. And because of the different varieties of atopic dermatitis, we see that we have many different treatment modalities. And I think ultimately, can we find a treatment that in the long run can somehow provide long-term - I don't sometimes like to use the word disease modification - but disease quiescence or really keeping these patients under control for the long run and preventing that itch from returning. I really think it's a mind shift change since we've had these new modalities.

And that brings me back to why these new treatments have been such a relief to me. And hence for a disease like atopic dermatitis, we really need these alternative treatments to help our patients have disease control in the long run.

Dr. Chovatiya:
Given the potential impact of those treatments, it's really exciting to think about what's coming next in atopic dermatitis, and I can't wait to go on that ride with you guys. I want to thank my guests, Dr. James Song and Dr. Jennifer Soung, for sharing their viewpoints on the current and future therapeutic landscape. Dr. Song and Dr. Soung, it was fantastic having you both on the program.

Dr. Song:
Raj, what a wonderful time to be treating atopic dermatitis. You know, we really are in the golden era for AD, so it’s great to be able to discuss these exciting options for you.

Dr. Soung:
Always fun to be here discussing with both of you and excited to see what we have in the pipeline ahead.

Announcer:
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