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Alopecia Areata: Exploring New Data

Dr. Chovatiya:

For patients with alopecia areata, there's unfortunately no cure. However, we do have a few different treatment options currently available. So what can you do with your patients with alopecia areata? And how effective are these therapies at actually restoring hair loss for our patients?

Welcome to *DermConsult* on ReachMD. I'm Dr. Raj Chovatiya, and joining me today to discuss the current treatment landscape for patients with alopecia areata is the world-renowned and wonderful human being, Dr. Britt Craiglow. She's an Adjunct Associate Professor at the Yale School of Medicine and double board-certified dermatologist at Dermatology Physicians of Connecticut.

Dr. Craiglow, thanks so much for joining us.

Dr. Craiglow:

Thanks so much for having me and, for that really, really nice introduction.

Dr. Chovatiya:

Well, I mean, I'm going to put you to work here because I know that we all want to know everything there is about alopecia areata. So to jump right in, why do we need to treat alopecia areata?

Dr. Craiglow:

I think this is probably the most important piece of this whole discussion; to get people to understand that this is a medical disease, it's autoimmune, and it has a basis in science. And these people unfortunately, have been dismissed by the healthcare community. I think largely because we haven't really had reliably effective therapies, but there also is this notion that this is cosmetic or it's "just hair," and if you ask anybody who has alopecia areata, that's pretty much the farthest thing from the truth. This is a disease that has a huge negative impact on someone's quality of life. Try to imagine interacting with the world with no hair, no eyebrows, no eyelashes. You can't do it in a normal way, and so this is something I think that it's really exciting that we now have some options for people. And I will say also it's really, really rewarding. It's really fun to see these people not only look very different, but they feel really different too when we're able to help.

Dr. Chovatiya:

I think that part of the reason we've seen such limited progress over time is there were gaps and spurts in terms of our understanding of the pathophysiology of alopecia areata. Could you maybe give me a broad overview of what's really going on under the hood when you take a look at the skin for alopecia areata so we can at least understand why we treat the way we do and why that's starting to change in terms of our targeted therapies?

Dr. Craiglow:

For a long time it's been known that alopecia areata is an inflammatory disease, and in residency we learn about the swarm of bees

around the hair follicle, those lymphocytes that gather around, but it wasn't until several years ago that we really understood what those cells were and how they were communicating. And largely due to the work of Angela Christiano and Raphael Clynes, a very specific population of CD8+ T-cells were identified as a key driver of alopecia areata. And so normally, the hair follicle is the site of immune privilege, but in the setting of genetic predisposition plus "triggers," which are poorly understood and probably multifactorial and different for everybody—but nevertheless, that privilege breaks down, and these T-cells infiltrate in and around the follicle, and then they start signaling, and the key cytokines are IL-15 and interferon gamma, and those both signal via JAK/STAT. So basically, you're getting this positive feedback loop between the T-cells and the follicular epithelial cell that creates this wave of inflammation that leads to hair loss. And so because those cytokines are signaling via the JAK/STAT pathway, we can dim that down with JAK inhibitors, so this has really proven to be a truly pathogenesis-directed therapy, and for sure it's better than anything we've ever had and nothing I think that we thought we'd have really. This was a disease that has been seen as something that was largely untreatable, and now we have patients who have had not a hair on their body for five years, and it all comes back with JAK inhibition.

Dr. Chovatiya:

I really want to focus in on one of the newer therapies that we have for alopecia areata, baricitinib—not a new medication by any stretch of the imagination. But maybe you can give me a broad overview of baricitinib before we really get down to brass tacks about some of what we learned through the studies.

Dr. Craiglow:

Baricitinib is actually the first FDA-approved treatment for alopecia areata. And you're right, there is a history. Initial approval was in rheumatoid arthritis, and then outside the U.S. it's used pretty widely in atopic dermatitis. And so it's mostly a JAK-1/2 inhibition. There are two doses in alopecia areata. The four milligram really does work quite a bit better than the two milligram. It's oral. It's a once daily. And we can talk about tolerability and safety and things like that, but really exciting to finally have an approved drug.

Dr. Chovatiya:

For those of you just tuning in, you're listening to *DermConsult* on ReachMD. I'm Dr. Raj Chovatiya, and I'm speaking with Dr. Britt Craiglow about current treatment options for patients with alopecia areata.

So, Dr. Craiglow, let's explore some of the most recent data from the pivotal phase III trials, BRAVE-AA1 and -AA2, with baricitinib. Can you share at least at top level what happened? What did we see?

Dr. Craiglow:

Sure. So for basically all of the AA JAK inhibitor studies, the patient population is quite severe, so inclusion criteria was patients who had at least 50 percent scalp involvement, and many of those patients had 95 to 100 percent, so it was very skewed to the severe end of the spectrum. Patients who had had complete hair loss for more than eight years were excluded—and I think that's actually a really important point—and that was because there was some early data suggesting that the longer you have not had hair, the harder it is to regrow, so there probably is this window of opportunity. That's not universal, but for sure after a point chance of regrowth decreases.

So basically, baricitinib was studied in two randomized, double-blind, placebo-controlled trials, two doses—the two milligram and four milligram. And one thing that's different about AA trials is the timing of the primary endpoint. So we're used to atopic dermatitis or psoriasis where we may be looking at 12 or 16 weeks. With baricitinib, the endpoint was at 36 weeks, and that's because hair takes a long time to grow. And so I think that's really important clinically when we see patients because even if you see them back at three months, there may not be that much happening, but that doesn't mean they're not going to make it to where they want to be.

So what they looked at was the percent of patients who got to a SALT score of 20 or less at the end of the trial. And so SALT is the Severity of Alopecia Tool, and it's basically just a measure of what percent of the scalp is involved with hair loss. So a SALT 100 is 100 percent loss, and a SALT zero is zero percent loss, so the lower the number the better and looking at how many people got to SALT 20. So with a very conservative statistical evaluation, the patients on the four milligram dose, a little over 35 percent of patients, met that endpoint, whereas about 20 percent of patients met the endpoint with the two milligram.

Now interestingly, if you look at these patients and even if you just look at the slope of the curve, many of these patients continued to grow beyond that 36-week mark, but nevertheless definitely significant when compared to placebo, and we're having a chance to use it

in practice now and getting to see this, which is really, really exciting.

Dr. Chovatiya:

And maybe we can take a forward-facing view here with baricitinib, and I guess I want to ask where do we go from here? I think it's important to note that there is the idea of perceived risk, real risk and what was really observed during the trials. And I think that by and large the biggest question I hear is, what is going to happen one year, two years, three years down the line? Maybe you can comment on that for me.

Dr. Craiglow:

I think when it comes to JAK inhibitors, prescribers are excited about them, but also there is this level of concern. People want their patients to get better, but they are worried about causing harm. And I think the boxed warning is at the surface, very scary, but these drugs have a lot of baggage mostly from rheumatoid arthritis. And I think an understanding of where that boxed warning comes from and the patient population that informed that, which is largely really different from our patients. One thing that's really nice with these clinical trials in alopecia areata and now atopic dermatitis also is we have data in our patients. We're not looking at people with rheumatoid arthritis over 50 with at least one cardiovascular risk factor who are also taking methotrexate. I mean, most of these patients with alopecia areata, it's the only thing on their problem list; they're healthy. This is a thing that happens to very healthy people, and they tend to be on the younger side, and so it's a conversation. You certainly don't want to dismiss the warnings. And I think when you look at the rates of the scary stuff, they are very low in these clinical trials.

And I think we're not only thinking about risk and benefit, which we kind of always talk about. I think with alopecia areata it's really mostly about risk versus consequence of not treating. Like, what does your life look like without hair? And how is it changing your trajectory? And what does it mean if we don't do this now? So I think that risk or consequence of not treating is really high, and most of these patients are willing to accept some level of risk for a chance to have normalcy.

Dr. Chovatiya:

I couldn't have put it better myself, and I think the arrow is pointing up with everything we learn about baricitinib day by day when it comes to safety. Overall though, it really sounds like we have a bright future ahead for the treatment of patients with alopecia areata. And I want to thank my guest, Dr. Britt Craiglow, for her deep insights and just immense knowledge and clinical passion she brings to the field of alopecia areata.

Dr. Craiglow, thanks so much for joining me today.

Dr. Craiglow:

Thanks so much for having me.

Dr. Chovatiya:

For ReachMD, I'm Dr. Raj Chovatiya. To access this episode and others from DermConsult, visit ReachMD.com/DermConsult where you can Be Part of the Knowledge. Thanks for listening.