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Exploring Emerging Therapies for Alopecia Areata

**Dr. Chovatiya:**
According to the National Alopecia Areata Foundation, there may be some new treatments on the horizon for patients with alopecia areata. So what therapies are being tested? And what might be coming to a clinic near you? And how exactly are they faring?

Welcome to DermConsult on ReachMD. I'm Dr. Raj Chovatiya, and joining me today to discuss the emerging therapies for patients with alopecia areata is Dr. Britt Craiglow, an Adjunct Associate Professor at the Yale School of Medicine, double board-certified Dermatologist with Dermatology Physicians of Connecticut, expert in alopecia areata, and all around amazing person.

Dr. Craiglow, welcome to the program.

**Dr. Craiglow:**
Thanks so much for having me.

**Dr. Chovatiya:**
So following the approval of baricitinib, which really was a watershed moment for all of us who treat patients with autoimmune and inflammatory diseases, what other treatment options broadly are on the horizon?

**Dr. Craiglow:**
So we have two other JAK inhibitors that have been in clinical trials, and some of the studies are still ongoing. The first is a drug called ritlecitinib. This is a JAK3/TEC inhibitor. And TEC is a tyrosine kinase that may have some impact in alopecia areata by interfering with the function of the T-cells that drive the disease process, but largely, I think of this as another JAK inhibitor. And so this was studied like the other medicines in double-blind clinical trials. They did a dose-ranging study where they looked at a variety of doses, including looking at two doses with a loading dose for the beginning of treatment, and their results were actually pretty similar to baricitinib in terms of the percent of patients that met the primary endpoint.

Now their primary endpoint was the same, SALT score of less than or equal to 20, but they looked at 24 weeks rather than 36 weeks, so a little bit shorter time point, and they had around 30 percent of patients who met that endpoint with their highest dose. And then they actually have an extension out to 48 weeks, and about 40 percent of people are meeting that. And what's interesting is actually the curves. While the patients who got loading doses had a steeper curve initially, in the end these leveled out. This medicine is at the FDA currently, and I think it will be interesting to see what gets approved, whether or not there is a loading dose included, but it didn't really affect the end game, so I think my guess is probably not. But nevertheless, it's also a daily medication and looking definitely superior to placebo in these trials.

**Dr. Chovatiya:**
It's an interesting one because of that JAK3/TEC combination because a lot of the trouble we run into with JAK inhibitors is because many of them are active ATP site inhibitors is that there is some degree of selectivity for JAK2, and that's the one that we think about often times with the hematopoietic issues related to bone marrow production of a variety of cells. And so I do wonder with this one just not even seeming to evolve that part of the pathway if we're able to actually get the same efficacy with really even more favorable safety profile, which admittedly is not a major concern in our alopecia areata patients based on what we've seen so far.

**Dr. Craiglow:**
Yeah. It is for sure more selective, and I think there is some basic science data to show that JAK3 inhibition alone is sufficient to reverse AA, and we're seeing that in the trial. But when you combine it or you're a little more broadly acting, is it more effective? And is one JAK more important than another? So the other molecule that we have is deuruxolitinib, and this is a JAK1/2, and when you see those data,

you think, “Hmm, maybe that’s really where we want to be mostly looking.”

**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 emerging therapies for alopecia areata patients.

So ritlecitinib is definitely a real interesting one, but you mentioned that there is another JAK inhibitor that looks like it may be on the way, and this one is deuruxolitinib. Maybe you can tell us a little bit more about what we should know, what’s out there, and maybe what we can expect with this one.

**Dr. Craiglow:**
Yeah. So deuruxolitinib is the third in line, but actually, there are clinical trial data. Today, it suggests it may end up being the most effective of the three medications that have been studied for alopecia areata. So their primary endpoints were looking at improvement in SALT score, so a little bit different from absolute SALT score, but patients getting a 75 percent improvement from their baseline SALT at 24 weeks, over 40 percent of patients met that on the higher dose, and we have a little while still to see more phase III data. But I think we’re all excited about something that may come later; and potentially for patients who don’t get where they want to be with the other medicines, we’ll have another option for them. There are certain phenotypes or characteristics in patients that make them respond better to one versus another, and so we’ve seen patients who fail prior to any approvals off-label tofacitinib who respond to ruxolitinib. I think in another five years hopefully, we’ll have some biomarkers or at least have some clinical characteristics to maybe guide our management or choice of molecule.

**Dr. Chovatiya:**
Are there any other therapies in the pipeline that we should have our eye on? And things that maybe have gone the way we expected? Things that haven’t gone the way we expected? Anything that you want to comment on?

**Dr. Craiglow:**
There are some other things that are being studied, different parts of this inflammatory pathway that people are thinking about targeting. We don’t have a lot of clinical trial data yet from any of those. Most of them are in phase II or even the preclinical stage. One thing I’ll mention, though is that there’s no for sure randomized clinical trial, but we do have some data about dupilumab in alopecia areata, which is interesting because mechanistically, it doesn’t really make sense that it would work, and I think if you take all-comers, it really doesn’t work very well, but there is this population of patients who have this atopic phenotype either everything or just asthma, AD, elevated IgE, and some of those patients actually do regrow hair with dupilumab.

Now on the flipside there are also several reports of patients treated with dupilumab for other indications, mostly atopic dermatitis, who have developed alopecia areata, so it’s a little bit complicated. But I think if you have a patient who maybe for one reason or another can’t take a JAK inhibitor, it is something to think about trying, and every so often you get lucky with that, so that’s a fun development that we’ve seen. And I think we’re going to be seeing more with off-label medicines and a lot of these diseases that JAK inhibitors treat co-occur in the same patient. So there are now reports of upadacitinib improving alopecia areata. So in some of these patients we have the ability to treat multiple things with one agent, and I think that is really exciting in terms of not having to make these wild recipes with different things and say, “Hey, this actually might help all three things that you have going on.”

**Dr. Chovatiya:**
I couldn’t agree more. I think that for a long time we’ve realized that there’s difficulties in delivering drugs directly the way we love to topically in dermatology, and it actually looks like there finally is some movement in this space to see if we can actually figure out the technology to appropriately deliver things deep enough into the hair follicle to maybe actually have real topical therapies as well, and so I think that’s probably the next big thing I’m excited about over the course of the next decade.

**Dr. Chovatiya:**
So before we close, Dr. Craiglow, are there any final thoughts you wanted to share with our audience today about where we are headed in alopecia areata?

**Dr. Craiglow:**
I think the landscape is changing. I really do think that there is hope for patients with this disease. And even if you’re seeing a young child and one of these medicines is not something you’re going to be giving them now, you can say, “Hey, look, there’s all this stuff that’s happening, and we’re learning so much more as we go, and there is hope in this way there really wasn’t before.”

And I think the other thing that’s important is that often in dermatology we have this feeling about treating patients with hair loss that it takes a long time; it can be hard and more difficult. But I will say that treating these patients, it’s got to be one of the most rewarding things. And yes, sometimes it does take a little bit more time, and I think now the patient interaction is changing so much because we

actually have something to offer them. A lot of that feeling about dreading the hair loss visit was because we didn't really have any treatment. And so now all of a sudden to be able to say, "Hey, there's this medicine that's actually approved for what you have," it really changes the conversation.

And I think when you see that patient back and they're doing well, it's just incredibly rewarding, and so maybe that little more investment of time in the beginning you really get it back, and we all went into this to help people. And I think it's easy to lose sight of that sometimes given all the extra things that we have to deal with, but I would say, hair loss is part of our job, it's part of what we do, and so if you can embrace it, I think many people will be surprised at how much fun it is to see people grow hair.

**Dr. Chovatiya:**
So you heard it here first. Dr. Craiglow says, "Step up your game." It's certainly encouraging to see everywhere that we've been, everywhere that we're going when it comes to treatment for alopecia areata. It is really exciting to hear it from someone who's really been on the forefront. And I just want to thank my guest, Dr. Britt Craiglow, for sharing her insights.

Thanks so much, Britt, for a great discussion.

**Dr. Craiglow:**
Thanks.

**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!