Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/dermconsult/advancing-alopecia-areata-treatment-a-look-at-the-fda-approval-of-barcitinib/13949/

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

Advancing Alopecia Areata Treatment: A Look at the FDA Approval of Barcitinib

Dr. Keller:
Alopecia areata affects more than 300,000 people in the United States each year, causing hair loss to the scalp, eyebrows and eyelashes, but recent studies have shown that the Janus kinase inhibitor drug baricitinib can help significantly regrow hair for patients. This also marks the first ever FDA approval of a systemic treatment for alopecia areata, which is why today we're going to explore this treatment option.

Welcome to *DermConsult* on ReachMD. I'm Dr. Matthew Keller. And joining me today to talk about the recent FDA approval of baricitinib is Dr. Natasha Mesinkovska, Associate Professor of Dermatology and Vice-Chair for Clinical Research of Dermatology at the University of California Irvine.

Dr. Mesinkovska, welcome to the program.

Dr. Mesinkovska:
Hi, Dr. Keller. Thanks for having me.

Dr. Keller:
To start us off, Dr. Mesinkovska, can you explain the impacts of alopecia areata on patients and the treatment options that were previously available?

Dr. Mesinkovska:
Patients with alopecia areata are a special population. Unlike some other chronic diseases, it really affects people when they are younger. Right? The average age is somewhere between 25 to late 30s, around 33 to 36, depends on the study. And what is that? That's really the prime of one's life. That is the time when you go to school, get your first job, pick your partners, times when really perception is, in a way a very important factor to how things will go for you and affect your quality of life. So the psychosocial impacts of alopecia areata have really been vast, but it took for us as physicians, as a medical community, a little bit of time to catch up on it, capture it, and describe it. And thankfully we did because showing that alopecia areata is not just a cosmetic thing, that it's a medical thing, was crucial to get the pharmaceutical companies interested, to pay attention to the condition, the high prevalence and incidence of it in the population all across the world, and to start making some of the medications that they have available for clinical trials.

Really, for decades we've known that it's an autoimmune condition, that it's a condition that is chronic, that it's relapsing. What does that mean? We don't know what causes it. We know that there are genetic factors that are genetic predispositions, but what brings it on? What's that kind of a hit that brings this perfect storm when the hair falls off has not been clear.

The immunosuppressants that have been used through decades, such as prednisones, methotrexates, and cyclosporins, have worked in limited amounts of cases, or will have limited duration, or will have side effects that just precluded them to be universally used. So yes, there are cases where these medications will work but just not for everybody and not for prolonged periods of times—some of the other things, such as intralesional injections, because a lot of patients are young and many kids are affected. Doing pokes over and over every month or every 2 months is just not something that was necessarily patient-friendly, so the pain of the procedures precluded

things. Same for these things called topical sensitizers. Right? Things like DPCP where we count on the patient's body to regrow the hair as we sensitize them to one thing or another can have a lot of side effects. So although they did work for a subset of patients, when it comes to finding something that's a good and viable option long-term, we really hadn't had a lot of success until recently.

Dr. Keller:
With that in mind, let's zero in on baricitinib. How does this JAK inhibitor work in helping to regrow hair?

Dr. Mesinkovska:
So in the alopecia areata community, one of the biggest efforts both immunologically and genetically was really led by University of Columbia, Dr. Angela Christiano, Dr. Klein, and Dr. Julian. Many of these doctors really worked on the pathways and implicated JAK-STAT pathways as potential stuff and JAK inhibitors as potential medications. Then with the work of Dr.Craiglow and Dr. King, who used these medications in patients who had conditions such as psoriasis and alopecia areata, we saw that actually things that worked in the lab can work in patients too.

The family of JAK inhibitors are immunosuppressants that affect cytokine signaling that regulate immune processes, so depending on the autoimmune condition, there are different ways these JAK molecules can combine. There's 4 of them: JAK1, 2, 3 and a TYK. And depending how they can combine, then they kind of activate a separate pathway all leading to that autoimmune response that we see. So now, because of the different combinations that exist, we can use different kind of JAK inhibitors. So one, for example, may block JAK1 more preferentially, 2 and 3 less. One can be JAK2, and one can be all 3. So there are a lot of medications called JAK inhibitors that are coming out on the market who are preferentially blocking different pathways, kind of having the same outcome ultimately but probably with different efficacy.

Why is this good, and why are choices good? Because more options can serve more patients, because all patients are not alike. Different people with different kind of pathway controls may end up with the same condition. So baricitinib is one of these medications that is a great JAK inhibitor that was approved for arthritis.

Dr. Keller:
And if we take a look at the clinical trials, how were those studies designed?

Dr. Mesinkovska:
So clinical trials for alopecia areata took us a while to get to how to design them because of the relapsing and remitting nature of this condition. The episodes and the way they can happen on their own required that patients actually are enrolled in longer studies. In order for a person to qualify for the initial studies, they had to have at least 50% of their hair loss, and they had to be healthy without any infections or any malignancies within 5 years prior. They had to be 18 years and above for most of the trial, although some are now 12 years and older. And they were not allowed to have any other hair condition, hair loss, which we learned as the hair regrew, that although some people had hair gone for 30 years, when it regrew, it wasn't the hair of a 20-, 30-year-old. It was the hair of a 50-year-old with a different pattern. So we learned a lot through the trials, and I feel that every successive clinical trial is better and better. The way they were designed is that patients were taking medications or placebo, so this goes for baricitinib,ritlecitinib, CTP-543. All the medications that have been tested thus far, etrasimod and some of the others, pretty much followed that same design where people have their placebo and also have different doses of treatment.

We've been very fortunate that a lot of these medications were either approved or tested previously that have demonstrated safety for other conditions, such as rheumatoid arthritis or other things. For example, baricitinib got an emergency authorization for treating COVID in hospitalized patients, and it's also approved for arthritis, so we in the derm community for alopecia areata patients got to, in a way, benefit that we didn't have to have those early struggles to demonstrate the safety of these medications.

Dr. Keller:
That's amazing. And what are some of the key findings from those studies?

Dr. Mesinkovska:
So the key findings from the studies when it comes to the oral immunosuppressants, the oral JAK inhibitors, the safety really continued to be demonstrated throughout the trials with very low incidence of side effects, and the effectiveness really varies across different medications, but it's pretty significant. So for example, for the baricitinib trial, their endpoint was at 36 weeks, and what they wanted to show is how much people regrew hair, but it wasn't like "Oh, anyone that regrows hair is a responder." They were pretty ambitious in their goals. So in order for somebody to be a "responder" to baricitinib, they had to have a SALT of 20, meaning 80% of their hair had to regrow, so not just that you grew half of your head or like 10 hairs, 80%. It's a lot of hair to regrow on somebody. So if you look at the studies, and it says, for example, 36% of people were responders, you're like, "Oh, 1 in 3, I don't know." Well, that just means that 36 got to the 80% goal. So things that we're learning now is, as they're extending the studies to like 52 weeks and even more, the longer you are, the longer people meet that angle, so more and more people are considered responders.

Most patients I will tell you tolerate the medications pretty well. Rarely is there some nausea, but if I compare it to, for example, my doxycycline and by all means not even to isotretinoin patients, patients really tolerate it well. My number one question when I see somebody at follow-up, I'm like, "Would you know you're taking something?" Usually, the answer is pretty much, "No," so most of them are well-tolerated. I will say on average most people will start growing hair around month 2 or 3 that are responders.

Some of the early signs that I see in my experience are pimples, folliculitis on the scalp, a little bit of pimples on the face, and some of the younger ones can have full-on acne. I've had to put some people even on isotretinoin to control it.

One thing I think that we learned through the trials and is something that maybe we didn't realize before is just how much eyebrows and eyelashes mean to patients, even nose hairs, stuff that maybe we as dermatologists never thought about. And allergy is something that plagues people. Sinus infections are in alopecia areata patients. Dry eyes is more of an autoimmune condition, but we think that eyebrows, eyelashes, and nose hairs do play more of a role than we realized before as patients get better.

And through the trials, one thing I will tell you is, for people that haven't had hair for almost a decade—because that was pretty much the cutoff for an episode in all the trials—when they get their hair back, the confidence and just the overall attitude of a person changes. So although a lot of the kids, the young people, the adults are super resilient, super used to their condition, there is something that just brightens up, and the eye contact gets better. I think it's truly life-transforming when the hair comes back.

Dr. Keller:
So for those just tuning in, you're listening to *DermConsult* on ReachMD. I'm Dr. Matthew Keller, and today I'm speaking with Dr. Natasha Mesinkovska about the FDA's recent approval of baricitinib for alopecia areata.

So, Dr. Natasha, now that we know what led to the approval of baricitinib, let's turn our attention to its application in practice. Which of our patients are the right fit for this new treatment, and how would they use it?

Dr. Mesinkovska:
Probably these are going to be patients that are going to have a moderate to severe hair loss. What's moderate to severe is to each its own. Some people use, for example, 50% as the cutoff. But what if you have 20% or the patient has 20% but it's all up front and they just have a hard time covering it? So a couple articles that came out recently are trying to help people understand what's moderate and what are the psychosocial implications. So is it possible that you have 1 patch that's up front but then you have eyebrow and eyelash loss? It does give a little bit of room to a physician to figure out with the patient where they are on that severity scale so it's not just a number.

Right now it's only approved for adults. It is not for patients that are pregnant. It is not for patients that are breastfeeding. Some of the box warnings on the JAK inhibitors are serious and are things that we need to discuss with patients. So what are they? Like most immunosuppressants we're used to from psoriasis, some of the biologics, etc., patients have to be screened for infections. Right? So no infections allowed. I would say definitely no current malignancies and no malignancies in the last 5 years. And then for the JAK inhibitors in particular, I will look into cardiac and clotting factors, thrombotic event factors, what does that mean? Pretty much, if people are adults and they have issues with clotting stuff, probably not the right thing. You need to discuss this with them. And the second one, smokers. For me, smokers and heart attacks are something I will stay away from and maybe coach patients to undergo whatever it is to stop smoking. But unlike the biologics where we may not have worried about smoking as much, here I would like my patients not to have any kind of cardiac factors, or if they have any cardiac risk factors, to seriously consider it and follow them closely with primary care physicians.

Dr. Keller:
Well, that's a lot of great information and this certainly feels like a step in the right direction. But what's next? Is there more to be done in treating our patients with alopecia areata?

Dr. Mesinkovska:
I think what's next is there are going to be more JAK inhibitors. Right? There's a lot of trials right now. Another group of medications that are coming out on different pathways will be probably the etrasimod medications, and then just learning more from comorbidities. One of the things that I like a lot, especially my pediatric patients, are things that target allergies. So, for example, dupilumab, I like it. It takes a longer time to get the hair to grow back, but we don't have the same side effect profile that we have with the JAK inhibitors, so finding options as we try to figure out what are kind of the etiologies of this condition and what are the drivers of it.

I think things we'll have to figure out is right now when we have the conversation, "Okay, you're going to go on a JAK inhibitor, and we're going to talk about this being as a long-term thing." So is it for as long as you shall live, or are we going to be allowed at that take breaks? So a lot of unknowns where now we're going to tweak and figure out how much do we really need, what are going to be the side effects, because one thing about alopecia areata patients is they are relatively healthy, and most of the box warnings on all of these immunosuppressants are from arthritis patients. They are around age 50 and higher, so whether that's going to be the same thing in our population, time will tell.

Dr. Keller:
So those were all great insights into a new treatment option for our patients without alopecia areata. And as all this brings us to an end of today's program, I want to thank my guest, Dr. Natasha Mesinkovska for sharing these updates. Dr. Mesinkovska, it was great speaking with you.

Dr. Mesinkovska:
Thanks, Dr. Keller. Thanks for having me.

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