Transcript Details
This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/jak-inhibitor-therapy-for-alopecia-areata-expert-guidance-to-fill-in-the-gaps/16627/

Released: 01/24/2024
Valid until: 11/29/2024

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

JAK Inhibitor Therapy for Alopecia Areata: Expert Guidance to Fill in the Gaps

Announcer Open:
Welcome to CME on ReachMD. This activity titled: JAK Inhibitor Therapy for Alopecia Areata: Expert Guidance to Fill in the Gaps, is provided by Clinical Care Options, LLC, in partnership with the National Alopecia Areata Foundation, and is supported by an independent educational grant from Lilly. Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Announcer:
Hello, and welcome to JAK Inhibitor Therapy for Alopecia Areata: Expert Guidance to Fill in the Gaps, provided by Clinical Care Options, in partnership with the National Alopecia Areata Foundation. Joining us today are our expert faculty, Dr. Britt Craiglow, Associate Adjunct Professor in the Department of Dermatology at the Yale School of Medicine in New Haven, Connecticut, and Dr. Maryanne Senna, Assistant Professor of Dermatology at Harvard Medical School, and the Director at the Lahey Hair Loss Center of Excellence at the Lahey Hospital and Medical Center in Burlington, Massachusetts.

Information on faculty disclosures are listed here.

Our learning objectives today are to formulate an accurate diagnosis and classification of AA based on multiple disease and patient factors; detail factors that may predict a patient's positive or negative response to JAK inhibitor therapy for AA; and evaluate patients with AA for treatment candidacy with JAK inhibitor therapy. Our program today will include several polling questions. Some questions will be presented twice, once before, then after the content is presented. All responses will be measured in aggregate so your individual responses will not be identified. Thank you for helping us assess the impact of this educational activity. First, we'll get started with our pretest question.

Female:
How many patients with AA do you provide care for in a typical week: 1 to 4, 5 to 10, 11 to 15, 16 to 20, or more than 20?

We have a case about Claire who's 43 years old and postpartum with a history of atopic dermatitis and hypothyroidism. She has noticed round bald patches on the top and bottom right sides of her head. Physical exam notes 30% patchy scalp hair loss with ophiasis pattern. She has no eyebrow or eyelash loss, and she denies any psychosocial impact. Which of the following is consistent with her clinical presentation: Is it androgenic alopecia, limited alopecia areata, moderate alopecia areata, or severe alopecia areata? In which of the following scenarios are patients most likely to respond to JAK inhibitor therapy for alopecia areata: if they have failed other therapies, if they have a lesser severity of alopecia, if they have had a current episode of hair loss of more than 4 years, or predictors of therapy success are not yet know?

Sally is 37 years old and has had moderate alopecia areata for the past 3 months. She is interested in a JAK inhibitor today. Which of the following would preclude her from starting this therapy: concomitant use of oral minoxidil, a family history of breast cancer, uncontrolled hypertension, or a recent diagnosis of a deep vein thrombosis?

Announcer:
Now we're going to move into our presentation by starting with hearing a case in perspective on living with alopecia areata.

Patient:
I was first diagnosed with alopecia areata in 2002. I was a freshman in college, and I had started losing some eyelashes and I had a bald spot. We sort of just chalked it up to stress from college. And I went to the dermatologist, and I remember the receptionist saying to me, 'Whatever you do, don't look it up on the internet.' So of course, the first thing I did was look it up on the internet. And of course, the results that I saw were terrifying.

Socially, alopecia has really affected me in a way because it's such a visual thing that people would see the, you know, the bald spots or the regrowth and they'll say like, you know, 'Where's half your eyebrow?' Or, 'Where did your eyelashes go?' And then you always find yourself having to sort of explain, like what's wrong with you. I did have a reoccurring bald spot on the top of my head. And so, like I always had this like regrowth, and it was just sticking up all the time. And there was nothing I could do about it. But it drew a lot of attention.

But like I said it was manageable at that stage. It wasn't until I lost all my hair that it really got bad. I found that it was just - I hate to even say that it was traumatic, but it really was. By the time I lost all my hair, I mean, I was like in such denial about it that I was able to sort of put it out of my mind. But when I would look into a mirror, I would remember because I didn't look like myself anymore.

Announcer:
Now, I'm very excited to turn things over to Dr. Craiglow, who will tell us about diagnosing and classifying alopecia areata.

Dr. Craiglow:
Great, thank you so much. Thanks to those of you who are joining us and learning about AA. Maryanne and I certainly spend a lot of time thinking about it. And it's cool when other people are interested also. So, you know, if you practice dermatology, you definitely have seen alopecia areata. It's common, actually. The epidemiologic data is sort of varied, but we think it affects up to 2% of people over the course of their lifetime. And sometimes I think patients are surprised to learn that and sometimes kind of helpful to say, 'Hey, this is actually pretty common, you know, you're not alone.' But oftentimes, people have really mild disease, right, so somebody else may not notice. So, it's the most common cause of inflammation-induced hair loss. And it's largely a disease of young people. So, the onset is usually pretty early in life; we see lots of patients who have an onset in childhood. But that's not to say that you couldn't have an onset later in life. I've seen - you know, I've seen a child as young as 9 months. And I've seen somebody in her 70s, who never had a patch of alopecia areata in her whole life develop severe AA. So, it's really - it's very unpredictable and heterogeneous. And you know, classically, it affects the scalp, but importantly, it can affect any hair-bearing site, and then also fingernails.

And again, the disease course is really unpredictable. So, you know, sometimes we say the only predictable thing about it is that it's unpredictable. And that I think is really hard for us as dermatologists, but it's extra hard for patients because even if they, you know, kind of are doing okay, there's this concern. You know, it's almost like PTSD, you know, when you have an episode that's severe, or even mild honestly, like having a bald spot is a big deal, right? And that can be hard. And I think we need to recognize that for our patients.

So, there's a, you know, a huge range of severity. As we mentioned, fortunately, most cases are mild. And you know, often the classic is a little round, smooth patch of alopecia, it can become more extensive. And then we sometimes actually, I think, it's pretty common in kids, is diffuse alopecia areata, where you get this sort of more generalized thinning, which can be really mild and subtle, or it can be more severe. And then we have ophiasis pattern where basically you have a loss of the occipital scalp going up around the ears, that's a pretty classic pattern and tends to be a lot more difficult to treat. And then opposite of ophiasis, there's preservation of hair around the edge, in a sisaipho pattern. And then of course, you can go on to have complete hair loss, including loss of eyebrows, eyelashes, etcetera.

So, historically, when patients have no scalp hair, it's been called alopecia totalis. If they have no hair anywhere on their body, alopecia universalis. We're kind of trying to get away from those terms, because, you know, patients don't understand that alopecia areata is the same as alopecia universalis, it's just a spectrum of disease. But also, even among dermatologists, we don't necessarily agree what is, you know, alopecia universalis. So, if someone has five eyelashes, do they not have alopecia universalis because they have some hair? So, it's all a spectrum. We kind of call it, you know, mild, moderate, and severe AA.

So, when we look at a patient, you know, we see a patient in our clinic, you know, what are some of the things that we should be thinking about in terms of prognosticating? And again, it's very unpredictable and somebody could have none of these characteristics but some of these can sort of suggest that somebody may have a more chronic or, you know, severe course. And I think mostly these are kind of intuitive. So, early onset, that makes sense, right? Extent of hair loss or a long duration of hair loss. Again, ophiasis pattern, that can be really hard to treat. Nail involvement. Family history of alopecia areata, so about 1 in 5 people will have a first-degree family member with it, those patients tend to have, you know, worse outcomes. And then personal history of atopy also is important. So, their

numbers range but 30 to 40% of patients with alopecia areata will have associated atopic dermatitis, and those patients tend to have a more chronic course also. So, some things to kind of pay attention to when you meet a patient for the first time. So, your barometer of worry, you know, oh, they're, you know, they're 40 they have one patch, nothing else, maybe I can feel a little less concern and a 6-year-old who comes in rapidly shedding, right?

So, I think probably all patients with alopecia areata have heard over and over, 'Well it's just hair. You know, at least you're not sick,' etcetera, including from healthcare providers, which is really unfortunate, but it's just the way it is. And I think it's important to recognize that it's not just hair, you know, it's kind of just hair until it happens to you or your child or family member. And this is not something that, you know, patients are just sort of making up or saying or misinterpreting. People kind of approach people differently who have hair loss, especially extensive hair loss.

So, this was a study that basically had participants, it was done online, they showed participants, different images of the same person with complete hair, with loss of scalp hair, and then with loss of scalp hair, eyebrows, and eyelashes. And they asked different questions about sort of how they felt about this person. And so, you know, perhaps not surprisingly, about 30% of people didn't find the people to be attractive, and then also thought that the person looked sick, the person with complete scalp, eyebrows, eyelashes. And this is a really common theme; a lot of people with very severe AA are thought to have cancer, you know, undergoing chemotherapy, they get approached at the grocery store, you know, people tell them they're praying for them. And the psychology of looking sick, when you're not, is really complicated. And then I think it kind of contributes to this, people sort of start to feel bad that they feel bad, because it could be worse, etcetera. So, this is something that people are facing every day.

And we have good data to show that there's a significant impact on health-related quality of life. And importantly, that impact is very similar to atopic dermatitis and psoriasis. And I think, you know, those are diseases that we have no, you know, no problem treating, including with, you know, immunomodulatory medicines, we wouldn't think twice, even with sort of mild disease now. And you know, those diseases, especially atopic dermatitis, but oftentimes psoriasis are often marked by severe symptoms, right? Itch, difficulty sleeping, things like that. And while people with alopecia areata can have sometimes, you know, itchy, watery eyes because they don't have eyelashes, you know, things like that, it doesn't tend to have a lot of physical symptoms, right? And so, it shows that they're, you know, the emotion and social functioning actually is worse than patients who have these other diseases.

So, next, Maryanne is going to talk about classification of alopecia areata.

Dr. Makredes Senna:
Thanks, Britt, for that great introduction. And I want to just echo Britt's thanks to all of you who are joining us. As Britt said, we really get excited for people to think about this patient population because we see how impactful these new treatments can be for them.

So, I'll be talking about the classification of alopecia areata. So, for the purposes of clinical trials, we use something called the SALT, or severity of alopecia tool. And I like to flip things in my mind a lot, right, so I always have to go back and remind myself that the SALT, the L in the salt stands for hair loss, it's very easy when you're giving a SALT score to think about it as the amount of scalp coverage or hair coverage or hair present. So, always remember that in the SALT score, when we say SALT score, we're talking about the amount of hair lost on the scalp. And basically, you can think of the SALT score or the number to be more or less equivalent to the percent scalp hair that is missing. And so, a SALT score of 0 means no hair loss and a SALT score of 100 would mean complete hair loss. The only difference here is that the SALT takes into account the fact that different areas of the scalp have more hair coverage at baseline, right? So, the SALT score is basically taking that into account and weighing each of these areas a little bit differently. So, you can see here, the top of the scalp has a weight of 40%, whereas the above the ear, either on the left or right side, those each have only 18%. But more or less, you could think of it as an average of scalp hair loss.

What's important to just pause and state here, because it's going to be important later in the talk, is that for all of the clinical trials in alopecia areata that have been done for Janus kinase inhibitors, specifically, all patients had to have a minimum SALT score to enter the trial of 50, meaning that all participants in the clinical trial had to have 50% or greater scalp hair loss. In the primary efficacy endpoint, meaning the person met the initial goal of this study or the treatment expectation that was set up, is that they had to have a SALT score less than or equal to 20, or 80% scalp hair coverage or more. And SALT scores with subscripts just mean a change in the amount or the improvement from baseline. So, a SALT 30 in a subscript means that the person improved from baseline to whatever time point by 30%.

There's also the Alopecia Areata Investigator Global Assessment, which is frequently used in clinical trials, as well. And this is an ordinal measure where the investigator looks at a patient and determines if they have none, or 0%, limited alopecia areata involvement 1 to 20%, moderate 21 to 49%, severe 50 to 94%, or very severe 95 to 100% scalp hair loss. And this can be used to determine clinically meaningful treatment success, with success typically defined as hair regrowth resulting, again, in that less than or equal to 20% scalp

hair loss, or in this case, a score of 1 or 0.

Now, while these scoring tools can be really helpful in clinical trials, we know as dermatologists seeing these patients that more really plays into how patients experience the severity of their alopecia areata. And so, in an attempt to sort of get to, you know, what is severe, a group of hair loss specialists and experts around the U.S. as well as other industry and other stakeholders, got together to come up with some guidelines that could be used quickly in clinic to sort of say, you know, what patient is severe? So, just to get us thinking about this concept, you know, what is severe? So, I think all of us or anyone could look at, you know, this photo and say, 'Yeah, you know, this is a person who has severe alopecia areata, they have complete scalp hair loss.' But what about a patient like this, who has very extensive alopecia areata, who's, you know, needing to get multiple, as you can see from this photo, injections all over the scalp every 4 to 6 weeks, is this severe? And what about a patient like this with a large, very visible bald patch that's difficult to conceal, is this considered severe?

So, this expert group got together and developed the Alopecia Areata Scale or AASc, which is a clinical tool that we wanted to be able to be used quickly in the clinical setting to help practitioners determine severity. And basically, what it states is that you think about the extent of scalp hair loss first to figure out the initial category that a patient would be in. So, if we just think about the extent of scalp hair loss, the group convened and came to consensus that mild alopecia areata just considering scalp hair loss was less than or equal to 20%, moderate alopecia areata would be 21 to 49% scalp hair loss, and anything greater than 50, so 50 to 100 scalp hair loss would be severe AA.

We also through sort of a modified eDelphi process came to consensus on various clinical characteristics that would increase the AA severity rating based just on the scalp hair loss by one level, if any of the following things were present: negative impact of alopecia areata on the psychosocial functioning, right, so a patient is withdrawing from school, having difficulty doing their public-facing job, etcetera; a noticeable involvement of eyebrows or eyelashes; inadequate response after more than 6 months of treatment; or diffuse multifocal positive hair pull test consistent with rapidly progressive AA, so it's a person who might, you know, just still have a lot of hair on their head, but you know within a week or 2 weeks, they're going to be completely bald or close.

So, to put this in sort of a clinical perspective, you know, think for example, a patient comes into your clinic that has 30% scalp hair loss, you would say okay, this patient has moderate alopecia areata. And this particular patient is responding well to intralesional steroids and oral minoxidil, no involvement of eyebrows or eyelashes, and is coping well, this patient would remain as moderate alopecia areata.

Take, for example, another patient with 30% scalp hair loss. So, based on scalp hair loss alone, patient would be considered to have moderate alopecia areata. But in this case, the patient also has eyebrow loss and is avoiding social situations and finding it difficult to do his public-facing job. This would cause an increase by one level for moderate to severe AA, so that the overall severity of alopecia areata would be considered severe.

This is something that, you know, we see commonly in our clinics that it's more than just the degree of hair loss that contributes to the severity. And so, the AASc tool can be something to be helpful in trying to determine, you know, what patients might be good candidates for systemic treatments, including Janus kinase inhibitors or just to understand how the AA is sort of impacting the patient sitting in front of you.

Britt, this part of the management of alopecia areata you are going to cover.

Dr. Craigwell:
I'm going to let Maryanne take a short breath here. So, you know, pre JAK inhibitors there were lots of things, and these things continue to be used sometimes. You know, I would say the mainstay of treatment for most patients, especially adults with mild disease are intralesional corticosteroids, right? Intralesional triamcinolone often done, you know, every 4 weeks, maybe every 6 weeks and can be quite effective for, you know, for limited, patchy alopecia areata. But obviously, when somebody gets to more extensive hair loss, it's not feasible, it's not comfortable, it's not effective. Oral steroids we use sometimes, usually in sort of that setting that Maryanne described as rapidly progressing hair loss like a Hail Mary pass to try to see if we can slow things down. But obviously those are things that we can't continue indefinitely. Historically, we've used topical irritants or immunotherapy things like DPCP or squaric acid with the idea that you sort of create this inflammation, patients get an itchy rash, and maybe that inflammation, that part of the immune system kind of comes in and sort of muscles out the bad guys, like get rid of those T cells that are causing hair loss and alopecia areata. Minoxidil, you know, we used to use it more just sort of as an adjuvant treatment, thinking that it was kind of like fertilizer for hair. So, if hair was there, you know, if we're getting it from some other way, we might be able to get it to grow faster, or thicker, or longer, you know. But actually, in some patients, minoxidil orally alone can lead to improvement in alopecia areata. So, those of us who do a lot of hair loss, tend to add minoxidil to a lot of different therapies. And then of course, there's systemic immunomodulatory therapies like methotrexate, cyclosporine. And these, you know, have their own sort of set of concerns. But really, they tend to not be very effective for severe

disease. And often to get them to work, you have to combine them with chronic prednisone. So, all of a sudden, you're kind of doing a transplant-style regimen to try to maintain hair in a patient. So, you know, the bottom line is that for patients with severe disease, especially with even really moderate to severe, sometimes you can get, you know, get someone on prednisone and minoxidil or do some intralesionals. But honestly, when people get to a certain point, these do not tend to be really reliably effective. And so, a lot of patients have been told, 'Sorry, you know, there's nothing to do for you.' And I think now we're really lucky because we understand the science better. And this has sort of paved the way for these more pathogenesis-directed treatments that Dr. Senna will walk us through here.

Dr. Makredes Senna:
Thanks, Britt. I'm going to now cover the Janus kinase inhibitors, or JAK inhibitors for alopecia areata. The JAK inhibitors, you know, we know that these swarm of bees hover around the lowermost part of the hair follicle, namely the bulb, and they're cytotoxic T cells that actually penetrate the proximal antigen or growth phase of hair bulb and initiate an autoimmune attack. And the antigen for that autoimmune attack is still unrecognized, despite many decades of research. It's been shown that CD8 positive NKG2D positive T cells are the major effectors and that T helper cells also are involved in a peribulbar location.

And basically, the way the JAK inhibitors work is that these various cytokines that are proinflammatory that are implicated in alopecia areata, including interferon gamma, IL-15, IL-2, and others activate their signaling via this JAK/STAT pathway. And when that happens, the STATs then translocate to the nucleus, leading to increased gene transcription of proinflammatory cytokines, continuing this inflammatory cycling, leading to the loss of hair. And by modulating the signaling by blocking this process at the point of the JAKs, it allows this cycle of inflammation to cease and allow the hair ideally to regrow.

And so, we are really lucky in the U.S. to now have two approved agents in the management of alopecia areata. One is baricitinib, which is an oral tablet, comes in 2- and 4-mg doses, dosed once daily. And this is for adults with severe alopecia areata. We also just recently got FDA approval for ritlecitinib, and this is great because it's in those 12 years of age or older with severe alopecia areata, so includes that adolescent population. And this is an oral tablet, 50 mg that's dosed once daily. Still in investigation is deuruxolitinib, an oral tablet, 8 mg dosed twice daily, and this is being studied in adults with severe alopecia areata, or a SALT score greater than or equal to 50.

And when we look at the data for baricitinib, we can see these trials were designed to have patients either on placebo, baricitinib 2 mg, or baricitinib 4 mg once daily for 36 weeks. Again, all patients had to have at least 50% scalp hair loss to enter the trials. But most of them had very severe, somewhere around 84-85% scalp hair loss at baseline. And at 36 weeks, they looked at the proportion of patients who reached 80% scalp hair coverage. And on the 4-mg baricitinib dose, that was on average around 34% of patients, and around 20% of patients in the 2-mg dose at 36 weeks. And when you see these patients regrowing their hair, you can see just what a profound impact it has on them.

Interestingly, when you break down the efficacy data for baricitinib between those with severe alopecia areata or very severe alopecia areata, so those with 50% to 94% hair loss, to those of 95% to 100% scalp hair loss, you can see two things. One is that the proportion of patients up to 36 weeks that reached the primary efficacy endpoint goes up considerably to nearly 48% of patients on the baricitinib 4-mg dose, which suggests maybe treating these patients earlier on in the course is beneficial. But also, it shows us that we still have a good proportion of patients, even with the most severe alopecia areata, who benefit from these treatments.

If we look at long-term efficacy of baricitinib, we can see that mixed responders, or these people who had sort of reached the primary efficacy endpoint at prior visits but then sort of lost efficacy in that first initial placebo-controlled period of 36 weeks, or people who regrew eyebrows and eyelashes, but really didn't have any significant hair regrowth, if we look at those groups and follow them out to 2 years, we see that nearly 40% of those patients end up achieving that 80% scalp hair coverage if you keep them on the medication a longer period of time.

This slide looks at the most common side effects seen in patients on baricitinib versus placebo including acne, increasing creatine kinase, and hyperlipidemia. And as you can see here, the most common side effect was an elevation in both high-density and low-density lipoprotein cholesterol, so both good and bad cholesterol.

This chart shows the adverse events of special interest, namely serious infections, malignancy, major adverse cardiac events, including MI. And so, if we look at the three columns here, we see that this one in blue, the 36-week placebo-controlled trial, shows us how these rank versus placebo. And as we can see, the rates of serious infections are 0.5% and 0.2% on the 2-mg and 4-mg baricitinib arms, respectively. And there was one case of MACE in the 2-mg baricitinib arm that occurred in a male with multiple risk factors. The rates of malignancy, importantly, were similar between placebo and baricitinib. And rates of herpes zoster or shingles were 0.5% in the placebo arm, 1.4% in the 2-mg baricitinib arm, and 0.9% in the 4-mg baricitinib arm.

This middle column shows data out to 2 years for alopecia areata patients on 2 mg or 4 mg of baricitinib continuously. And we see that

the rates of these adverse events of special interest remained very low. And the column all the way to the right shows all patients on any dose of baricitinib for any length of time. And looking at data this way helps us to understand sort of the rates of rare events. And as we see here, serious infections occurred at a rate of 0.7, and other events occurred at 0.3% or lower.

And this slide shows the rates of other laboratory abnormalities, specifically high-grade neutropenia, anemia, thrombocytosis, and lymphopenia, which occur in 1.4% or less of patients on baricitinib. And importantly, even high-grade thrombocytosis above 600 was not associated with any thromboembolic events.

Looking at other laboratory changes, we see mild to moderate elevations in liver function tests were seen in 2.9% or less of individuals. Importantly, no cases of drug-induced liver injury occurred. The rate of elevated triglycerides were less than 1%. And as mentioned previously, by far the most common laboratory changes, and I see this in clinic as well, were elevations in HDL and LDL cholesterol. In the placebo-controlled trial, 42.4 had elevation in HDL and 12.2% of patients had elevation in LDL cholesterol on the 4-mg dose.

So, now if we turn to the ritlecitinib data, they had a trial where they did a bunch of different doses of ritlecitinib, but we'll focus mostly on the 50-mg daily dose, which is the one as I mentioned before that was FDA approved recently for adolescents and adults ages 12 and up. So here, what we see is that at week 24, there's a significantly higher proportion of patients with a SALT score less than or equal to 20. So, those who met that primary efficacy endpoint across almost all the ritlecitinib doses compared with placebo. And specifically, if you focus on sort of the kelly green or bright green color here, the ritlecitinib 50 mg a day arm, you see that at week 48, 43% of patients, were able to achieve the SALT score less than or equal to 20, or 80% scalp hair coverage.

And lastly, deuruxolitinib. Again, this is JAK inhibitor, as I mentioned, that's still investigational. But this data is also quite impressive. So, we see here at week 24, 29.6% and 41.5% of participants on 8 mg twice daily or 12 mg twice daily, respectively, met the primary efficacy endpoint. And we can see by looking at the data, in this fashion, that some patients even reached that primary efficacy endpoint of 80% scalp hair coverage as early as week 8.

Britt now is going to discuss with you factors that influence response to JAK inhibitors.

Dr. Craigwell:
Thanks, Maryanne. So much data, but I think the bottom line is that these drugs often are very effective. Nothing says it like those photos. And I have to say, seeing these patients back in clinic is really fun. I mean, not only do they look very different, but they feel like themselves again. There's like no better feeling as a physician, I really have to say. So, treating hair loss patients, you know, it may take a little bit more time sometimes, but it is really, really rewarding.

And I think having FDA approved treatments really changes the conversation and really makes it easier honestly. But you know, when you're in that clinic visit, you know, patients may ask, you know, 'What's my chance of responding?' And there are some clinical characteristics that may affect someone's disease course. There are some factors that, you know, may influence a patient's response to treatment. So, obviously dose, right? So, we saw with baricitinib, the 4 mg works much better than the 2 mg. And Maryanne mentioned about baseline severity, I'm going to show that just really briefly again. The idea is that patients with, you know, almost no hair, 95 to 100% hair loss, or SALT score, have a, you know, less than half of

the chance that somebody with SALT 50 and 94. So, you have somebody come in who has maybe 75% hair loss, and you're thinking about starting baricitinib, you can say, 'Well, patients like you in the clinical trial, almost half of them got to 80% or more scalp hair coverage by the end of the 36 weeks.' And I think something, you know, look at here with these trials, there's a placebo arm, right? And another thing patients ask about is like, what's the chance that they'll get better without anything, right? And so, if you have a patient with very severe alopecia areata, so SALT 95 to 100, the chance is essentially zero, right? If you have somebody more in that 50 to 94 range, it's still very low, less than 10%. Okay? So, I think that's useful data to have when you're talking to patients, especially if there's someone who's like, 'Well, maybe I want to, you know, sort of wait and see,' it's like, 'You can wait and see, but the chance that you're going to get better with doing nothing is really, really low.' That's different, obviously, for patients with mild patchy disease, but we're talking about severe here.

And then another really important sort of concept is this idea of duration of current episodes. This is the length of time since a person - for a person with very severe disease, you know, almost no hair, how long have they been like that, okay? It's not how long has it been since they got their first patch? It's how long since they lost everything, or they, you know, got to 50% plus hair loss etcetera? So, for instance, you have a 20-year-old come in, he got his first patch at 10, maybe he had waxing and waning AA over the next several years, at 15 he lost all his hair, and he hasn't had any regrowth since then, his duration of his current episode is 5 years. Okay? And that's the number that we care about: How long has it been since you've had any significant scalp hair, okay? And why do we care about that number? And that's because that influences response to treatment.

So, this is looking at the baricitinib data. So, patients here on the left, you can see patients whose duration of current episode was less than 4 years, they did much better than those who had a duration of more than 4 years. So, what this shows us is that we need to treat early and often, right? We want to try to treat when it's not very severe if we can, catch people sort of on the way, but also early. And this is something you have a patient who's had no hair, you know, for 6 years, this is the time, right? And it's not that these people who have their episode of longer than 4 years can't regrow, it's just that their chance is lower. And some of them may just take longer, but you know, this is a reason why we really want to, you know, encourage people to treat who are thinking about it.

And then the final thing that we don't have a ton of data about, but in our clinical practices have a lot of anecdotal data, and that's using oral minoxidil along with the JAK inhibitor. So, this is just a patient we published who had no regrowth on ruxolitinib 25 mg twice daily, this was used off label. And then oral minoxidil was added. And you can see, he had incredible regrowth. And so, in my clinic, and I imagine in Maryanne's also, we tend to use the two together because there really does seem to be this synergistic effect. And so, something to think about, you know, when treating your patients.

And so, when you have a patient in your room, who is a candidate, right, and I think, you know, I think the AASc, or the A-A-S-c scale is really important, because there are lots of people with, you know, less than 50% hair loss who really do have severe disease, right? People who are having a huge impact on their quality of life, that's a reason to treat, right? And I think, you know, we always talk about sort of risk and benefit, which I think is important, but we're really sort of weighing risk versus risk of not treating or consequence of not treating, right? So, other things like what have they tried in the past? How long have they had, you know, their current episode? Somebody who has had no hair for 20 years, well, it doesn't mean they can't try but their chance is going to be a lot less, right? And then comorbidities are very important. So, things that might increase their baseline risk for some of the things in the boxed warning are things to think about. And then obviously, you know, the patient's sort of level of risk tolerance and their motivation. But I would say in general, most of these patients are really looking for return to normalcy and so they're often willing to accept a small amount of risk for the chance of kind of getting their life back.

So, now we are going to see one last video.

Patient:
I went from alopecia areata to alopecia universalis. My hair started to fall out because I had just had a baby and I was expecting this. And the shedding started but it never stopped. And that was terrifying because I've been living for years and years with alopecia areata and I was pretty accustomed to it, and then when this hair loss started, this was completely different. It was actually just unbelievable. Like, I could not believe this was happening to me.

I started my treatment for alopecia universalis in July of 2021, and my dermatologist had prescribed JAK inhibitors. And it was honestly a miracle. I started the medication July 1, 2021, and 11 days after I had started taking it, I will never forget it, I was at the beach during the day and I had taken a shower and I could feel what I thought was sand on my head and I thought oh, you know, it's like not coming off. And then I quickly realized that it was like the tiniest bit of hair stubble. And it was the best thing that ever happened to me, it was such a miracle. And my hair continued to grow fuller than it had ever been before. And everything came back: my eyelashes, my eyebrows, full head of hair, it was just incredible.

Dr. Craiglow:
Okay. So, when we, you know, see our patients, obviously they're coming to us for medical treatment, but I think it's really important that we kind of acknowledge that this is hard, right? Just having somebody who kind of they feel comfortable with and gets it I think is really, really important to say this is normal, right? We have to validate their experience, because then they're going to be more comfortable opening up to us and telling us really, you know, how this is affecting their life, right? So, I often ask, is there anything that you, you know, used to do that you don't do now, etcetera? And then in terms of expectation, you know, response is really variable. It's very hard to predict. But importantly, hair growth takes time. Okay? So, you see the endpoints in these trials are 6 months and 9 months. And then when you look out longer, more people, you know, reached that endpoint. So, this is kind of a marathon and not a sprint. And I'll say these patients are patient patients, so they are willing to wait but I think just reminding ourselves that this is, you know, something that we have to kind of keep at is really important.

So, we will do the polling questions. So, back to Claire, she's 43. She has a history of atopic dermatitis. She has round bald patches on the top and bottom, right side of her head. She has 30% patchy scalp hair loss with ophiasis pattern, no eyebrows or eyelashes. And she is not having a psychosocial impact at this point. So, which of the following is consistent with her clinical presentation: does she has androgenetic alopecia, limited AA, moderate AA, or severe AA? Okay, awesome. Yes, moderate AA. And if we were looking at the Alopecia Areata Scale, versus, you know, just sort of just percentages, if she did have eyebrow and eyelash loss, or if she was having a psychosocial impact, remember, that would bump her up to severe AA.

In which of the following scenarios are patients most likely to respond to JAK inhibitor therapy, so not who's a good candidate, but who's most likely to respond: patients who have failed other therapies, if they have a lesser severity of alopecia, if they have had a current episode of hair loss of more than 4 years, or we don't have predictors of success? So, remember, patients who have, you know, a SALT 50 to 94 tend to do a lot better than those who have more severe disease. So, if this had said their current episode of less than 4 years, that would also be sort of a better predictor compared to somebody with more than 4 years. But keeping that in mind, that patients with lesser disease tend to do better, which sort of, you know, kind of makes sense.

Dr. Makredes Senna:
And Britt, I find this really helpful from a clinical perspective, like when I'm counseling patients, too, because sometimes a patient is like, 'Oh, well, I have to have like, really extensive hair loss to even be thinking about this therapy.' And it's like, 'No, actually, you know, it can work better if we start it earlier before you get there.' And so, I think it's sort of like, even as practitioners, you know, changing that sort of thinking in our minds to ensure that we give patients the best chance of responding well to these therapies.

Dr. Craigwell:
Yeah, and also remembering that regrowth takes time, right? So, you know, even starting, it's going to be a few months before we see much. So, you're, you know, waiting, and you're kind of adding that to the waiting of getting regrowth. So, it's going to be, no matter what, a long time until the patient kind of feels back to normal, especially people who wear their hair longer, right? So, I think, you know, kind of intervening earlier is oftentimes in our patient's best interest. And kind of think of, you know, when you said that it made me think of isotretinoin for acne, some people will be like, 'I don't think my acne is severe enough.' It's like, 'Oh, you've got scarring, you've got scarring, so we've got a treat,' right? And so, kind of thing with alopecia, 'You've got moderate disease, like what are we, you know, what are we waiting for?'

Dr. Makredes Senna:
Right, so sort of shifting our paradigm of how you approach it.

Dr. Craigwell:
Yeah.
This is a patient who is 37 years old, she's interested in a JAK inhibitor, which of the following would preclude her from starting, so which would be an absolute deal breaker? So, A: Concomitant use of oral minoxidil; B: Family history of breast cancer; C: Uncontrolled hypertension; or D: Recent diagnosis of a DVT. Okay, so again, in that boxed warning, you know, thrombosis is there, so somebody who has a recent DVT is probably somebody you're not going to start a JAK inhibitor on. Some of these things may make you – you know, uncontrolled hypertension, that might make you take pause and say, 'Okay, we've got to get you connected with your, you know, primary care doctor and get this under control, etcetera.' And I think, you know, a family history of breast cancer if, you know, if it was very strong and she had the, you know, BRCA mutation or something, then that would be a little bit of a different conversation, but that wouldn't - that's not a hard stop. Okay?

Announcer:
Wonderful. Well, that brings us to the end. Many thanks to our faculty, Dr. Craiglow and Senna for an excellent program. To our learners, we thank you as well. Don't forget to complete the evaluation. To find more CCO dermatology coverage, go to clinicaloptions.com. Thank you all for participating in this program.

Announcer Close:
You have been listening to CME on ReachMD. This activity is provided by Clinical Care Options LLC, in partnership with the National Alopecia Areata Foundation, and is supported by an independent educational grant from Lilly. To receive your free CME credit, or to download this activity, go to reachmd.com/cme. Thank you for listening.