NAAF's You Are Not Alone webinar series
Novel Developments in Treating Alopecia Areata: What is Type 2 Inflammation and Why is it Important?
Emma Guttman-Yasskey, MD, PhD and Benjamin Ungar, MD
July 17, 2024

LISA ANDERSON, PHD: (00:00)
Welcome to the National Alopecia Areata Foundation's webinar, Novel Developments in Treating Alopecia Areata: What is Type 2 Inflammation and Why is it Important? Joining us today are Dr. Emma Guttman and Dr. Benjamin Ungar from the Department of Dermatology at the Icahn School of Medicine at Mount Sinai in New York. And I'm Lisa Anderson, Senior Director of Research for NAAF

Before we start the webinar, I'd like to cover a few housekeeping details. We have disabled chat for this webinar session. Please post your questions for our speakers in the Q &A section, and please keep your questions as general as possible for the benefit of all audience members. This webinar is being recorded, and all registrants will receive a link to the recording via email sometime tomorrow. And finally, please share your feedback with us. After the webinar, a link to a short survey will pop up in your browser window.

Please complete the survey there.

This webinar is part of NAAF's You Are Not Alone education and empowerment webinar series. NAAF gratefully acknowledges the support provided for this webinar series by our partners Pfizer, Eli Lilly & Company, and Sun Pharma.

Before we start the webinar, I'd like to tell you a bit about NAAF and our mission. The National Alopecia Areata Foundation is the leading advocacy organization for Alopecia Areata. NAAF's mission is to drive research to find a cure and accessible treatments for Alopecia Areata, support those impacted, and educate the public about Alopecia Areata. NAAF's vision is an empowered community with a choice to embrace or live free of Alopecia Areata. To learn more about NAAF's support resources and research and advocacy activities, or to join us as an advocate or a supporter, please visit our website at NAAF.org.

And now on to today's webinar, novel developments in treating alopecia areata. What is type two inflammation and why is it important? We are very pleased to have Dr. Emma Guttman and Dr. Benjamin Ungar with us today to talk about their exciting new research. Let me tell you a little bit about them. Dr. Guttman is considered one of the world's leading experts in inflammatory skin diseases. She is the Waldman Professor of Dermatology and Immunology and the Health System Chair of the Department of Dermatology at the Icahn School of Medicine at Mount Sinai. She is also the director of the Occupational Dermatitis

Clinic and director of the Laboratory for Inflammatory Skin Diseases. Dr. Guttman's major clinical and research focus areas are atopic dermatitis or eczema and alopecia areata. Her work has enriched the understanding of the pathophysiology of atopic dermatitis and has opened the door for novel specific drugs for eczema treatment.

Today, we're going to hear about her research on alopecia areata and how her findings are again identifying new targets for treatments. Dr. Benjamin Ungar is an assistant professor of dermatology at the Icahn School of Medicine at Mount Sinai, where he is also the director of the Alopecia Center of Excellence. Dr. Ungar graduated from Harvard University and attended medical school at the Icahn School of Medicine. From 2014 to 2016, he completed a research fellowship in the Laboratory for Investigative Dermatology at Rockefeller University, after which he graduated from medical school with distinction in research. Dr. Ungar also completed his dermatology residency at the Icahn School of Medicine at Mount Sinai, from which he graduated as a chief resident in June, 2021. We're very honored to have you both here today, and we're really looking forward to your presentation. So I'm going to stop sharing my screen now and turn it over to you.

EMMA GUTMANN-YASSKEY, MD, PHD: (03:36)
Thank you so much. This is very exciting and Benji you'll be sharing.

BENJAMIN UNGAR, MD (03:40)
Yes. Good evening, everyone. Hope that we can see the shared screen here. Yeah. OK, excellent.

EMMA GUTMANN-YASSKEY, MD, PHD: (03:49)
Yeah, it's all good. So we are super excited to talk to you about new developments in treating alopecia areata, something that is super dear to our heart. Mount Sinai, for those of you that do not know, is actually the only center in the United States that has three pillars, clinical innovation, clinical trials, and clinical research, all under one roof. we have a, that center now has many, many patients, as you can imagine, with alopecia areata because we really do it all from studying the disease in the lab to the patient and clinical trials. And we really want to make a difference in alopecia areata. And today we'll focus on our own discovery of how is type two inflammation important in alopecia areata and how does it relate to new treatments for alopecia areata. And I'm really pleased to share the stage here with Benjamin Ungar that is actually the director of the center for in Alopecia Areata at Mount Sinai.

So these are ~ disclosures. Both of us are consulting to many companies, but we don't really have any pertaining conflict for this talk today. So alopecia areata, ~ you all understand the disease, but what you may not know is that it's actually quite prevalent. It's about 2 % of the population at any given point in their life about 147 million worldwide. Usually it's the skull, but can, as you know, affect any other hairy area. The majority will have patchy alopecia, but 10 to 20 % unfortunately will progress to have alopecia totalis, so the entire skull, or alopecia universalis, the entire body. And I don't need to preach to you how much emotional distress and psychosocial morbidity it causes, not only to the patient, but to the family.

We have many times families and patients crying in our office. It really affects their entire life. And I think we need to do better, to have better treatments for alopecia areata.

Now, historical treatments for alopecia areata have many, side effects and they were also limited in terms of efficacy. I'll only mention some of them, like intralensional corticosteroids. You feel that you are chasing your tail, right? When you have extensive alopecia areata, you cannot inject the entire scalp because you inject one area, another area will appear and it's absolutely not feasible. DPCP, super messy, painful and

Of course, there are other treatments that are immune suppressants like cyclosporine, oral prednisone, but we cannot give these to patients for long term. The moment you stop, the patient will lose their hair. So what did you do? Basically nothing. It's worse than a band-aid in my view. So we really needed a better treatments for safe long-term disease control. And we really didn't have them until very recently when they start emerging.

Now, what did we start learning about alopecia areata in the last 10 years, I would say, that there is ~ an attack of immune cells called lymphocytes around the hair follicles. Think about the swarm of bees that are attacking that hair follicles. And that is happening in all the patients with alopecia areata, regardless if it's patchy or universalis.

And in all of them have that inflammation around the hair follicle. So that's really important. And this is how it looks. It's like a swarm of bees around that hair follicle, as you see on the right side as well. Now, what was relatively obscure, but there were some publications about it, but they were a little bit overlooked was the idea that among these cells that are attacking the hair follicle are cells that are involved in allergy. And look at that, cells, 87.5 % of cases. cells are one of the primary cells involved in allergic diseases. So the majority of alopecia cases will have mast cells and many alopecia cases will have eosinophils that for example are involved in asthma and in other diseases like in hypes.

Now, JAK inhibitors were shown recently, but also previously from case reports, case series to be effective in alopecia areata. There is no doubt. JAK inhibitors work in alopecia areata. But JAK inhibitors are broad, a little bit more broad agents. And it's hard with JAK inhibitors to really nail what is the pathogenesis of alopecia areata on one hand. And on the other hand, they target more than one immune pathway. And because of that, they got the black box warning. But importantly for you to know, they have a little bit broad targeting of multiple cytokines and multiple pathways. And we cannot really tease out using JAK inhibitors the molecular ~ base of alopecia areata or the pathogenesis of alopecia areata. What do we need?

We need clinical trials that will target only one single pathway or one single molecule that will be able to tease out what is the real contribution of different immune pathways to alopecia areata, very similar to what we have done in atopic dermatitis. For those of you that do not know, we were really instrumental to the therapeutic development in atopic dermatitis and we want to do the same now in alopecia areata.

So what happened, and I'll walk you through exactly what happened, because initially I was not focused or my research was not focused on alopecia areata. I got into it a little bit

through the back door and I'll walk you through the process. In our original Dupilumab studies in atopic dermatitis in the clinical trials, and Dupilumab targets only the type 2 pathway. So it's an IL-4 receptor blocker. Because of that, it targets only type 2 immunity.

So in that study, we had patients with eczema that also had alopecia areata like this patient that I'm showing you here. We of course were not focusing on alopecia areata, but you know, as a physician scientist, you are making observations. And we saw that after dupiloma, they grew hair. And that was actually an interesting thing to us. And I was scratching my head. And soon I'll tell you why I was scratching my head. Now I looked into the literature.

And it seemed that alopecia areata in many, studies, including very large studies, like the study that was done at Harvard with about 3,000 patients, it showed that atopy or allergic diseases, including eczema, asthma, allergic rhinitis are actually the number one association or comorbidity of alopecia areata, way more than thyroid disease and others that, you know, are suggested in some publications. This is like by far number one association. Also a population-based study from Israel that follows patients from the moment they are born to the day they are dying was showing that with each allergic disease that you have, like if you have asthma, you'll have increased alopecia areata. If you have asthma and atopic dermatitis, you'll have higher increase in alopecia areata rate and so on. So each one cumulatively increases your risk. And a GWAS genetic study associated IL-13 that is the key molecule of the type 2 pathway with alopecia areata. And that was an eye-opener for me. And again, I'm a physician scientist and I always tell my mentees, not accept dogmas. Dogmas are there sometimes to be broken. And at the time, the knowledge at the time was that alopecia areata is only a type one disease. And that was mostly based on ~ information coming from mouse models. That was very important, but it is very important to do, sorry, I'm going back. It's very important to do also studies in humans. So at that time, alopecia areata from that mouse work seemed to be only a type one inflammation. But allergic diseases like eczema, are type two diseases. And these are atopic dermatitis, asthma, seasonal allergies, food allergies, allergy conjunctivitis, and urticaria. And at the time, these two were considered mutually exclusive. Now, I was scratching my head, how can this be? Because patients with alopecia areata have more allergies, right? They have more eczema, more asthma, and then a hallmark of allergy is higher IgE.

Many patients with eczema, 70 to 80 % of them, and similar in asthma, will have increased IgG. Not all of them, maybe 60%. But some of them will also have increases not only in total IgG, but in some specific IgGs like dustmites or grass or pollen or one of these. And they were also reported to be increased not only in allergic diseases, but in alopecia areata patients. And even more so,

I started noticing that there were publications that antihistamines that we are giving to patients with allergies actually are used in alopecia areata, but people did not know what's the reason why they may actually help as an adjuvant. They are not helping by themselves. I mean, it's not enough, but they can help also with the disease. So, and recently a very nice publication from Dr. Angar showed that allergies increase risk for alopecia areata, and this is in a very large patient database. So having allergies, both food and seasonal allergies, will

increase the risk for alopecia areata, and in general, any allergic disease will increase that risk.

Now, all of this brought us to do a study in humans. And I'm a great believer that the secret is in human studies. That's when you really nail where the direction should be and what do we need to target. So we did a huge study, 27 patients with alopecia areata We sampled their scalp. We sampled lesional scalp with involved alopecia, but also non-lesional scalp from patients.

And we compared to atopic dermatitis, psoriasis, normal skin, and normal scalp. Why did we compare to atopic dermatitis and psoriasis? Because they are considered two poles of the immune system. One is type one, one is more type two. And we wanted to see where we fall. And what did we discover? That alopecia arreata, very similar to atopic dermatitis, it actually has type two immunity. Type two immunity is shown here by IL-13.

IL-13 is the most important product of type 2 immunity. It's very high as you see here in alopecia areata and in atopic dermatitis. Type 1 immunity is actually increased in all of these diseases. So not only in psoriasis and alopecia areata, but also in atopic dermatitis. And we linked it with the chronicity of the disease. So it's not necessarily only linked to pathogenesis, but it's linked also to the chronicity of the disease.

And we also show that IL-23, that also is important in psoriasis, is also increased in atopic dermatitis and in alopecia areata. Now what else we saw? That hair keratin can be a very good biomarker of alopecia areata in lesional scalp of patients with alopecia areata. The hair keratin are very low and with any given treatment, we want to increase this hair keratin to normal.

Now, another important thing to remember, alopecia areata very similar to atopic dermatitis, may not be a single disease across the spectrum. It may be that we have multiple phenotypes of patients, right? It may be that those that have allergic diseases, that I would say they are about half of the patients, if not more. Benji and I often discuss it and he says it may be more than half, but let's say half. It's a sizable population, right? Those that have atopic diseases or allergic diseases, and sometimes they have high IgE. And then there are other forms of alopecia areata that may have differences in terms of the immune polarization that they have. Now, another important thing for you guys to remember, and that's why it's so important to treat systemically relatively early when you have a severe disease, we and others showed

that when you see a patient with alopecia areata, right, you don't see redness on the skin. The skin appears normal, it's only bald. But believe it or not, these patients, as you see here, they have systemic inflammation. So what you see hidden, like they don't have hair, it's not red, but they do have that systemic inflammation. And we found that among the molecules that are increased in these patients are also...

in biomarkers that are linked to cardiovascular disease and atherosclerosis. So it's very, very important to treat early because you don't want to have that overt inflammation in these

patients. So that systemic treatment is very important. So we want a systemic treatment and we want a systemic treatment that is safe.

And these are the treatments that are coming into all of alopecia areata super exciting times. Who would have dreamed just a few years ago that we'll have so many molecules in development. We now have two drugs that are approved, baricitinib and ritlecitinib We are very fortunate. They work very well. Both are JAK inhibitors, baricitinib JAK1, JAK2 and ritlecitinib JAK3-TEK. And we have one that we expect approval anytime.

I cannot pronounce it, but duroxolitinib that is coming and it has also great data. It finished phase three and there are several also in development and there are some monoclonal antibodies that are being developed. And we will talk about a Dupilumab in this symposium that targets type two inflammation.

And there are some that failed clinical trials in alopecia areata, particularly topicals. So because the follicle is so deep, topicals will not work in alopecia areata.

And I want to show you few slides on ritlecitinib that targets JAK3 and TEC. And these are the results, beautiful results from the clinical trial, the mechanistic study that we were involved, but I want to show you, and my lab did the mechanistic study, that type two immunity was suppressed with ritlecitinib So type one immunity was suppressed, but also type two.

And also IL-12 and 23, I showed you that it's also involved and pay attention that hair keratin went up. And when we looked at what biomarkers are correlated with severity, at week 24, you see several type two biomarkers. IL-13 that I told you the main biomarker of type two immunity, CCL-17 and IL-9 really highlighting the importance of that type to immunity and of course the hair carotidins that went up. And now I want to show you briefly our Dupilumab study in adults. That was a preliminary study. 60 patients treated weekly with Dupilumab. mean, 40 patients treated with Dupilumab, 20 patients on placebo. The primary endpoint was 24 weeks. Now we learn better and we had the secondary endpoint at 48 weeks.

Patients in that study had to have more than 30 % scalp hair loss. And we wanted a proportion of patients to have either active atopic dermatitis or a history of atopic dermatitis. And luckily we had quite a few patients, not so much with active AD, but we had some patients with history of AD or family history of AD or increased IG. And...

That is important because we found that the baseline IgE and or a family history or personal history of atopy can predict response to Dupilumab quite well. And when we looked at the response by IgE and by atopy, we found that the good responders were those that either had high IgE or also those that had personal atopy.

or familiar lot.

And this was a hypothesis driven clinical trial. And now we are continuing with a large adult study that really hones in to the population that we think we can help them. Those that

have either high IgE or have atopy. And look at the quality of life and how it improved in that study. And what I want to say is also that dupilumab takes time to work.

It's like I tell my patients, it's not a sprinter, it's a marathon runner, but it works great in many patients. You just need to be patient and it has great, great safety. So you don't need to do blood work, great safety approved without the need to do any blood monitoring or any monitoring. And these are the results of our biomarker study.

And simply red is inflammation, blue is down regulation. And pay attention that with the pilumab you see a reversal, whereas in placebo, the blue is remaining blue, right? You don't see much change. You want to really change the phenotype. And when we want to put a number on how much we change the phenotype, 97 % of the phenotype in the scalp changed, reverted back to normal, which is impressive.

And that's at week 48. But patients with atopy had much more improvement. And that is very, very important to remember in atopic patients, the improvement was much higher. And at week 24, even before we saw any hair growth, type two immunity was downregulated. There was nothing in type one immunity. That really proves the hallmark or the pathogenesis or the

the importance of the type two immunity in alopecia areata because at 24 weeks, the only game in town is type two immunity. There is nothing going on in type one immunity. That's only happening again with disease chronicity at 48 weeks. And the hair carotines already are increased at week 24, more at week 48. you know, pictures do not lie. Benji will show you many more pictures, but these are some of the patients in the study.

The study is still ongoing. We would love ~ for you to ~ join the study, the adult study, if you have allergic diseases, you, your family, please reach out. The study is still enrolling. We see amazing hair regrowth in some patients, very similar to this. And I will end with a...very exciting news. just are starting, this month we started actually, our alopecia study with Dupilumab in children. This is an NIH funded study funded by NIAID. We also now are having a case series ~ of children with atopic dermatitis and alopecia areata treated very successfully with Dupilumab.

And I don't need to tell you that many of the children have alopecia areata and atopic dermatitis or other atopic diseases. And we are super excited to make a difference in the lives of both adults and children with alopecia areata. So to conclude on my part, alopecia areata is a very inflammatory systemic disease. Don't forget that in patients that of course have a significant disease.

was an emerging important role for type 2 immunity in addition to the type 1 immunity. And evidence is mounting that alopecia areata belongs to that atopic March or type 2 spectrum. And we want to make a difference in understanding the pathomechanisms of alopecia areata to really help propel new treatment approaches. We are very, very committed to this.

So with that, I want to thank you so much and thank first of all our ~ funders that allowed us to create this amazing alopecia areata center of excellence. We promise that we will be super laser focused in finding new treatments and thank our funding sources. And of course, thank you for your attention. makes really, it takes a village to do this science and make a difference in patients' lives.

BENJAMIN UNGAR, MD (25:18)
Thank you. All right. Thank you very much, Dr. Guttman. I'm going to pick up and discuss just a little more. Hopefully, Dr. Guttman has conveyed and convinced you of the central role, at least for many people of this type 2 or allergic inflammation, these allergic diseases that are linked to alopecia areata. With all of that evidence and backgrounds and all the studies that have been put together, ~

We wanted to push this over the finish line to really demonstrate, you know, hopefully that this is a treatment that can be, ~ or this approach to treatment is one that can be applied to ~ adults and children with alopecia areata. And so we're, you know, very excited to say that we went to NIAID, the National Institute of Allergy and Infectious Disease with exactly this proposal. And we're very excited to say that we had to

the trial accepted and is going. And so this is the information of the trial. There are going to be a few sites I'll show you that are participating. At Mount Sinai, we are already recruiting and enrolling patients. So please keep that in mind. Here's some information, both on clinicaltrials.gov and also to reach out at Mount Sinai. So one question I think

that may be fair to ask at this point, given the breadth of the background information that shows the relationship. Dr. Guttman showed a preliminary study with Dupilumab. So why even do a clinical trial to begin with? And there are a few reasons to think about it. as she mentioned, we're going to be publishing a case series of a number of children with ~ both alopecia areata and atopic dermatitis who were successfully treated and re-grew hair.

And these are some examples of those children and adolescents. And so, you can take a look at this and say, it works. Why even bother going through all this whole process? So there are a few very, very important reasons to keep in mind. So the first is that randomized controlled trials, particularly double blind randomized controlled trials, where both the people participating in the patients and also the study team

don't know who is getting a placebo or who is getting the medication is the gold standard for demonstrating that treatment is effective. It's very well documented that there are placebo responses in many cases where if someone believes that they are receiving a treatment, they will actually improve clinically. And so the gold standard is this.

The next part of why doing a clinical trial is important is that this controlled environment, this randomized comparison as well, allows us to understand alopecia areata better to lead to further treatments as well. And so the goal here is to demonstrate that dupilumab is effective. And the big picture goal is to understand the disease better so that way there are increasing numbers of treatments so that everyone can have a successful treatment.

And then lastly, and maybe this is more of a kind of a big picture of practical consideration is that FDA approvals ultimately require randomized controlled trials to demonstrate that it works. And so if this is going to be a treatment that becomes accessible and approved to treat alopecia areata, it's going to rely on randomized controlled trials and participants being involved in the trials to ultimately demonstrate its effectiveness.

So I mentioned before that this study in addition to Mount Sinai is going to be going on in a few different locations. Here's the contact information. It's also available on clinicaltrials.gov and ~ the NAAF website. Although these sites are not yet enrolling, ~ if you're potentially interested in participating, I would suggest reaching out and perhaps getting on the wait list or being in communication. So that way, once it gets to that point, you'll have that information.

Okay, so this study, just a few details to give a little more nuance to what we're doing here. these are ultimately across the study, there will be 76 participants ages six to, solicitors 18, but less than 18. So still children and adolescents. Everyone will have to have at least six months of active alopecia areata. So if it just started last month, there's potential for it to continue and kind of stabilize before participation.

~ This is going to involve people with at least a salt of 30, which is the clinical score that essentially corresponds to the percent of the scalp that's affected by alopecia areata. So 30 % or more, which would be considered that moderate to severe range of alopecia areata. And very importantly, and this again is based on all the preliminary work that was done, that everyone has to have some sort of atopic or allergic background.

There are a few specific criteria, but basically either elevated IgE levels, which are the allergic antibodies, personal history of atopic disease, or a family member with atopic disease, allergic disease, asthma, atopic dermatitis, and so on. The participants in this study are going to be enrolled two to one to receive dupilumab versus placebo, meaning that two-thirds of people from the get-go

will receive treatment, there is a one third chance that placebo will be initially administered. And based on the information that we learned in some of the earlier studies and so on, the primary endpoint, which is really the point at which we assess, does this work, will be 48 weeks of treatment. I'll note that when you look at the clinical trials that are done with JAK inhibitors, that primary endpoint that

point at which it's assessed to see if it works is earlier on, 24 or 36 weeks depending on the study and treatment. So this is, as Dr. Guttman mentioned, a slow acting medication. And so the study is now designed to allow for sufficient time for us to really see the effects that we know are likely to occur with continued treatment.

It's important to note that after those 48 weeks are up, everyone will be guaranteed to receive Dupilumab for a year. And so even the people who have initially received placebo will get treatment as part of the study. There will be blood samples provided approximately every two months. As I said earlier, part of the reason for this study is to understand the biology and the immunology of this disease better, not just in the context of this treatment,

but to allow us to develop and repurpose other treatments to lead to effective clinical responses for everyone. In addition, and this part is optional, but very strongly encourage, it's not a necessity. Very, very small biopsies, two millimeters. It's extremely small. Biopsies will be done at the start of the study and at two time points, the 48 and 96 weeks. These are small enough that stitches aren't even required.

And again, that allows us to look at with different techniques, what is happening at the level of the skin, both in terms of the disease to begin with and how that's changed with treatment and hair regrowth. So some considerations for possible participation, you if you think that your child might be someone who could be a good candidate, some things to think about. So one advantage of participating in a trial like this,

is that there's very close monitoring by a trained clinical team. Certainly it's the case that when you see someone in a kind of standard clinical practice, of course, they're going to be assessing and monitoring and so on. But the level of watchfulness in a situation and a setting like this is much, much higher. Now we know that Dupilumab is a safe treatment in many settings, atopic dermatitis, asthma, and others. It has been shown to be very safe.

as Dr. Guttman mentioned, in those diseases, there's no monitoring requirement required and so on. But nevertheless, this is being studied in a different setting and the ability to be in touch with people easily on the clinical team and the watchful eye is something that is a benefit of this as well. And as I mentioned before, studies like this are needed to move closer to possible approval for alopecia areata.

You know, it is currently the case that if someone has that moderate to severe, for example, eczema, they may be able to get treatment that may, with dupilumab that may help their alopecia areata. Our goal is to make it so that everyone with alopecia areata may have access to treatment like this that may help them. And so participation ultimately is needed to get to that point. I mentioned before, and I think it's really, really worth emphasizing and highlighting that dupilumab works slower than JAK inhibitors. So.

Ultimately, if you are looking for the fastest treatment, dupilumab is not going to be the treatment that does that. It does require some patience and commitment. And if ultimately this is the participation in this study is a consideration, then it's very important to think about this as a two-year study, really make the commitment that even if hair regrowth is not occurring three, six, even nine months in, that this is something that's worth ~ continuing with.

and it's worth sticking with the study to get to the point where it really allows the treatment to work. And again, even if there is the placebo and certainly don't want to minimize the effects of not receiving the active treatment for a year, ultimately the treatment will be given at that point. So really think about this as a two-year commitment. Dr. Guttman mentioned that

We have a similar study in adults ongoing and certainly information can be made available for that as well. And I think it's worth highlighting that, you know, that it's the preliminary

look and we don't know technically whether these people are receiving treatment or the placebo, but I think that the results kind of speak for themselves. So this was one patient and she very graciously allowed us to include her photos to demonstrate. We can see here,

hair regrowth with treatment. And again, we have every reason to believe and understand. And in fact, we know from further tracking that this is not the end point of treatment. There's a further improvement. I'm not that, know, very often there may other treatments may have been tried unsuccessfully. And this is not even necessarily the first treatment that's being administered. And she shared some photos that are more recent as well with the kind of progressive hair regrowth that's really made such a difference.

Here's another patient kind of a similar circumstance, participant in the trial where we see a tremendous amount of hair regrowth. And again, our view and kind of the preliminary data, the preliminary result and so on strongly suggest that this is not where it ends that the hair regrowth continues. And again, she very graciously shared some personal photos. You can see here the further hair regrowth that's really...

picking up and we have every reason to believe we'll continue to do so. So just to summarize and then we'll move on to the question and answer ~ portion. The newly opened Pedal, that's the clinical trial for the pediatric patients, offers an opportunity for a new approach of treating alopecia areata, again, in children with this allergic or atopic background, and maybe an option that's appropriate for your child.

So we will happily take questions. I think I'm going to stop sharing my slides in a moment. Here again is some contact information and thank you very much for your attention. And again to NAAF for inviting us to share this information and to all the funders who allow us to continue doing this work. So thank you.

EMMA GUTMANN-YASSKEY, MD, PHD: (36:56)
Thank you so much. And I just want to, just one comment to add that right now the pediatric study, the adult studies open at Mount Sinai and in the pediatric study is right now open only at Mount Sinai. The other sites will be open a little bit later. So if you want to join right now, we definitely can have you start at Sinai. We are ready for you. You saw how to reach out.

~ I'm even willing and Benji will be willing if you miss that to email either of us and we will make sure that we send you to the right place. Again, we want to make a difference. It's very important that in the time of alopecia will be within the last Benji seven years,

BENJAMIN UNGAR, MD (37:45)
Correct.

So we are looking for people who have had some hair regrowth. The disease, of course, fluctuates where people can lose hair, regrow some hair, lose it again within seven years or the initiation within seven years. Certainly, we are optimistic that people who have alopecia areata longer than that can be successfully treated as well. But we're focusing on that population.

EMMA GUTMANN-YASSKEY, MD, PHD: (38:10)
Exactly. And just to explain, you can have hair loss for longer, but if you did not have hair regrowth in the last seven years, you will not be a candidate for our study just because we want to focus on the population that maybe we can ~ show better hair regrowth at this point, because this study, if successful, we hope will lead to registration for children.

So that's the reason. And by the way, in the adult study, very similarly, again, seven years, the adult study recruited already quite a nice number of patients. It's still open. You saw two of the patients. We do not know, but we know, I mean, when you see something like that, you know they are not on placebo, right? These two patients actually were on other studies that did not grow hair. So imagine.

and they grew hair on this study. You may have seen them even speaking at some of our symposia at Mount Sinai. And we want to thank them also for their courage, sharing the pictures here. I think they want other people to know. And the important thing also to think about the fact that dupilumab is a very safe drug.

It doesn't require any blood monitoring. There is no black box. It's a biologic. So for those patients that qualify, I think it's a great option, but you need to be patient. We like to be very upfront with our patients. This will not have a fast mechanism of action like a JAK. You'll need to wait longer. Of course, it's very safe, but you'll need to wait longer for an effect.

It's like many things in life, safe but surely I think is not a bad way to go here. And with that, we'll take any questions.

LISA ANDERSON, PHD: (40:07)
We have a lot of questions. ~ Thank you both for a really interesting presentation and such a hopeful presentation. The science is really exciting. And I think everybody on here is looking forward to the day when we know more for sure about.

this treatment and other treatments. So thank you for the work that you're doing to advance the science around treatments for alopecia areata. So we have lots of questions. We'll get through as many as possible. Some are just about the allergy connection and some are more specific to Dupixin and the clinical trial. Have you seen a connection between mast cell activation syndrome and alopecia areata? I'm not sure what that is.

EMMA GUTMANN-YASSKEY, MD, PHD: (40:47)
So believe it or not, yeah, mast cell activation syndrome, it's an allergic disease. It's quite rare, but believe it or not, because I get a lot of cases referred to me from all over the globe. So I did see such a thing, but it's not something we see all the time. But the rule of thumb, if you'll have one allergic disease, you may have others. And now I think particularly after work, alopecia areata is joining that atopic or allergic march or community.

And this is part of the community. yeah, but it's a very rare condition. And I also see as part of the question somebody was asking about COVID. Yes, we see a lot of association. And I

actually was interviewed, I think for the New York Times about this, but there is a very large association between COVID. And actually that brings me also to type two immunity. COVID and not only alopecia areata, eczema as well.

The reason being, and there was an important publication during COVID time from China in Lancet showing that COVID stimulates type 2 immunity. So type 2 immunity again is eczema and alopecia areata. So we saw a huge increase in alopecia areata and in eczema. And we actually published that Dupilumab neutralizes type 2 immunity and

Believe it or not, patients on dupiliumab either don't have any manifestation when they have COVID or have much, much less manifestations. We noticed it actually during the pandemic when we had patients obese with many risk factors. They had family members that died of COVID and nothing happened to them. So we looked into that and we published a very large study. So the dupiliumab is a little bit protective of COVID.

LISA ANDERSON, PHD: (42:40)
fascinating. Thank you. There are two questions related to allergy shots. One asks, how do you feel about allergy shots for people with alopecia areata? Do you think they're beneficial? And another question is, could allergy shots contribute to developing alopecia?

EMMA GUTMANN-YASSKEY, MD, PHD: (42:54)
Yeah, great questions. I don't think it will contribute very similar to eczema. I don't think though that they are really necessary because unless there is anaphylaxis I tell my patients, if you have anaphylaxis, of course you need them. If you don't have anaphylaxis and it's just hypersensitivity, Dupilumab will actually help in that regard and, and, antihistimine So you don't need that. It's time consuming. You know, there are patients that need it.

These are the ones that really have anaphylaxis, very serious reactions. If you just have a hypersensitivity, really there is no need if you are on an agent like Dupilumab and frankly, even if you are taking antihistamines many times.

BENJAMIN UNGAR, MD (43:37)
Yeah, and I don't think ultimately we view allergy shots as a potential treatment for alopecia areata.

EMMA GUTMANN-YASSKEY, MD, PHD: (43:43)
Exactly.

LISA ANDERSON, PHD: (43:45)
Okay, thank you. Someone asked, does baricitinib have the same presumable efficacy on type two inflammation?

EMMA GUTMANN-YASSKEY, MD, PHD: (43:52)
So the difference is that baricitinib and ritlecitinib they don't target just type two immunity, right? They target type two, but they target type one and they target some type 17 and some type 22. So that led to the black box warning, right? You need to remember, these are very efficacious drugs. Both baricitinib and ritlecitinib, they are quick acting, they are very

efficacious, but they are associated. We need to monitor patients, right? We need to look into their blood.

There were some cases of increased cancers in the studies, increased lipids, liver function tests, a herpes infections. So these are drugs associated with some safety issues, right? That's important in adults and also in children and particularly in alopecia, a disease that we think that right now we need to treat patients for life. We didn't talk about that, but in alopecia, any drug we put right now.

in the mix, you need to give it all the time because the moment you take it away, you lose hair in about three months. So we need to think about a safe drug that can be given long-term that we can give it without any monitoring. So that should be our goal. And of course, in the future, we want to have drugs that we'll give for a while, we'll take them away and the hair will not shed, but we are definitely not there yet.

BENJAMIN UNGAR, MD (45:22)
Just briefly to add to that or ~ one point is that baricitinib does reduce, I mean, Dr. Guttman says it, but it does reduce type two inflammation. In fact, in Europe, it's approved to treat eczema or atopic dermatitis. The question is not does it reduce that, but what other potential effects it has as well.

LISA ANDERSON, PHD: (45:44)
~ This question is, are you seeing dupilumab effective on patients who have had alopecia universalis for more than five to 10 years? So would it be an option for someone that's had universalis for a while?

EMMA GUTMANN-YASSKEY, MD, PHD: (45:56)
So, yeah, absolutely. It's absolutely fine. For the study, only are seeking universalis or totalis is completely fine, but there needs to be some hair regrowth. Now, it doesn't have to be total hair regrowth, but we want to see that there is some activity. So within the last seven years, know, some patches of hair regrowth, whether it's in the scalp, eyebrow, something needed to happen in the last seven years.

BENJAMIN UNGAR, MD (46:22)
One thing I'll just add to that, which I think is a big picture important point is that it is the case that the longer standing the disease as a general rule, the more resistant to treatment it is. So if someone has it for longer, the treatments may not work quite as well or may not work quite as quickly. However, that's just an overall trend and we can't extrapolate to individual people based on that. So certainly there's potential for it to work.

It's just that when you design a clinical trial, there have to be specific parameters and there are a lot of considerations that go into it. So for the clinical trial, the answer is no, but in the big picture, absolutely there's a reason for optimism that it may be effective for someone who has it for longer than seven years.

LISA ANDERSON, PHD: (47:04)

Okay, very good. I see several questions on other types of alopecia. Can you address whether Dupilumab would work for someone with scarring alopecia or frontal fibrosing alopecia?

EMMA GUTMANN-YASSKEY, MD, PHD: (47:15)
So that's interesting. So we actually published a study that shows that scarring alopecia actually is mostly type 1 immunity. And I can tell you that it actually does not work in that type of alopecia. So unfortunately, dupilumab cannot fix all diseases.

LISA ANDERSON, PHD: (47:32)
Okay. This person says, based on your talk, does this mean that there are tests using biomarkers, for example, to figure out which type of treatment might be better for someone with alopecia areata before choosing one? Are we there yet?

EMMA GUTMANN-YASSKEY, MD, PHD: (47:44)
Definitely.

So first of all, this is already the beginning because if you have atopy or high IgE, then we know that the dupilumab is likely to work on you. that's already a, and dupilumab is such a safe drug, but I do think we do a lot of work now on biomarkers linked to some new drugs that are going into eczema that we think will be also beneficial for alopecia areata. And I think it will open the door for new treatments.

Definitely.

LISA ANDERSON, PHD: (48:15)
Great. Someone asks, is it possible to develop an IL-13 inhibitor?

BENJAMIN UNGAR, MD (48:20)
There are IL-13 inhibitors, yeah. One that's already approved in the US to treat eczema and one that's expected to be approved soon as well. And I think it's a very appropriate question. Could they be effective in alpaca areata for the same reasons that do come out? Probably yes.

EMMA GUTMANN-YASSKEY, MD, PHD: (48:38)
Yeah, no, absolutely. One thing to mention, the difference between IL-13 alone and Dupilumab, Dupilumab targets IL-13 and IL-4. And now we think that IL-4 may have some involvement also with the topic march. So it may be, I mean, we do not know, but right now we know that Dupilumab will work in...

the subset that has allergic diseases about the ielctin it may, like Benji says.

LISA ANDERSON, PHD: (49:07)
Interesting. Does the correlation between alopecia areata and allergies depend on how in control the allergies are? For example, if you're able to remove an allergen like a dog or seasonal allergy, would that help your hair?

EMMA GUTMANN-YASSKEY, MD, PHD: (49:20)
That's an excellent question because when I started my road in atopic dermatitis, people didn't understand that they have to treat the atopic dermatitis. They were like, ~ doctor, can you design some diet for me? Can I remove my dog, my cat? So the answer is no. Think about the fact that you have inflammation. That's the number one cause of the alopecia. The allergies are contributing, like we discussed. That's why antihistamines will help a little bit.

but it will help a little bit. That cannot be the main treatment. So do not remove the dog or the cat, but get on a good treatment that will fix your inflammation.

LISA ANDERSON, PHD: (50:00)
Okay, there's a number of questions about participating in study. How can I participate? I want to say that we will be sharing this recording so you'll have access to all this information. We'll also put up a QR code with a link to the NAAF website and please feel free to email NAAF as well. We'll share information. So people are asking, you know, if they live outside of the area where one of the sites is, can they participate or can they participate remotely?

EMMA GUTMANN-YASSKEY, MD, PHD: (50:24)
Yeah,

absolutely. We have people that fly to see us from California because right now in time is of essence, right? Right now, our site is open and you need to see us only every two months, which is not a lot.

BENJAMIN UNGAR, MD (50:40)
Unfortunately, ~ pure remote participation isn't an option because we do need to have assessments and so on in person.

EMMA GUTMANN-YASSKEY, MD, PHD: (50:47)
It's very doable. It's very doable. are very accommodating in terms of the times, know, if people need to fly in, we have that. We have even people flying in from out of the country to us. So that's not an issue. We provide a small stipend for sure people that need to fly that will not cover it. But, you know, we provide a small stipend for travel. But we have people from all over the United States flying in to see us. So no issue at all.

LISA ANDERSON, PHD: (51:15)
Great. Someone's asking you to mention how dupilumab is administered

EMMA GUTMANN-YASSKEY, MD, PHD: (51:21)
The

dupilumab is an injection and it's given in the adult study because in adults it was studied every week and every two weeks. In adults, we are giving it every week in the study. And that's very important to know because that's a dose that you'll not have, let's say you have eczema and you want to, you also have alopecia and you want to get on that drug, you'll not

be able to get on every week dosing. So for that, you really need the study. And of course it...

boosting the efficacy in children because there was only one dose studied. So we have to go for the dose studied. We are very careful and we care a lot about going for a dose that already was studied. So we are taking the eczema dose in the pediatric population.

BENJAMIN UNGAR, MD (52:06)
Just one brief addition, it's an injection that's kind of really any on the leg or the abdomen. It's not an injection into the scalp as people may be familiar with ~ steroid injections.

EMMA GUTMANN-YASSKEY, MD, PHD: (52:16)
Yeah. And by the way, we teach them, we teach people to inject themselves. And in children, we teach the parents. So only they will come. Some people actually like to come so that we teach them several times, but usually one time they come, we teach them, they take the drug home, they do the injections and they come see us every two months.

LISA ANDERSON, PHD: (52:40)
Okay, great. This question says, as a parent with alopecia and small children with extreme eczema but no alopecia yet, can the child participate or do they need alopecia

BENJAMIN UNGAR, MD (52:50)
need to

show that unfortunately they need to have at least 30 % of their scalp involved. However, you know, if they are small children with eczema. So first of all, dupilumab is approved to treat eczema as young as six months of age. So it may be appropriate for them to be on that treatment potentially. And the hope is that through these studies, by the time they're older and if they develop the disease, they'll be available, not in this kind of study setting.

EMMA GUTMANN-YASSKEY, MD, PHD: (53:14)
Definitely. I'm a great believer, listen, they can also come to see us in our Mount Sinai clinic. And I'm a great believer in starting treatment early, a treatment that is safe because now we have the belief that treating early with a systemic agent will prevent other diseases. This is actually an excellent question. And you know, treatments are getting better and better. We will have treatments that...

you'll take for a while and then you will stop and you will not have it. But Dupixent is a safe drug. have patients treated about 10 years since the approval in adults or since the studies in adults and super safe. So definitely I think that's a good question and ~ I would do that as a parent.

LISA ANDERSON, PHD: (53:58)
So you're saying it's very safe. Someone says they're still very concerned with adverse side effects. Can you describe some of the typical side effects of dupilumab

EMMA GUTMANN-YASSKEY, MD, PHD: (54:06)

Sure. you know, every drug, even aspirin, like I tell my patients, when you look at the side effects, you'll never take it, right? Tylenol, aspirin, because in a clinical trial, first of all, you guys need to know they list everything on the drug side or the placebo side together, right? So you do not really know. But for example, dupilumab decreases

~ or has a trend of decreased infections. That's a very important thing. So how do you know that the drug is safe when the FDA does not require monitoring? So even within the biologics, dupilumab is unique because this is the only biologic I know that the FDA did not place any requirement for monitoring, including in six months old babies, right? That tells you right there that that drug is super safe.

Now it shows a trend of decreased infections. Most of the drugs have increased infections, right? With Dupilumab you actually see decreased infections. The side effect that we do see in eczema, but we didn't see it at all in alopecia in neither of our studies. And that's interesting. And it was not seen in asthma either, is about 10 % of the patients with eczema treated with Dupixent 10, 15 % will have dry eyes.

It's called some conjunctivitis. But interestingly enough, it's only seen in eczema patients, not in asthma, not in the eocinophilic esophagitis patients treated with the PICS and not in alopecia patients. So very unlikely that a participant will have it. So very, very safe. We saw also very good safety in the adult study and very good safety in the children that have AD and alopecia that we treated.

We don't anticipate any issues.

LISA ANDERSON, PHD: (55:55)
I'm going to make this the last question because we're at the top of the hour. Can someone switch from a JAK inhibitor to Dupilumab as a maintenance drug?

EMMA GUTMANN-YASSKEY, MD, PHD: (56:05)
If they have, to be put on the pill right now, you need to have eczema, right? We as dermatologists need them to have eczema, moderate to severe eczema. But if that's the case, after a period when both drugs are together, it's a possibility.

BENJAMIN UNGAR, MD (56:21)
Yeah, I would say there'd have to be some overlap because we know that within basically three months of stopping a JAK inhibitor, the hair will fall out. And if dupilumab doesn't have sufficient time to work, there may be kind of a window. and in terms of participation in the trial, you can't participate if you're currently on a JAK inhibitor.

LISA ANDERSON, PHD: (56:38)
Okay. We've had a lot of questions that we won't be able to get to, but ~ it just shows the level of interest in this topic and how exciting, how excited everybody is about the research, the clinical trial and all the possibilities for the future. So I wanna thank you both for being here. I also want, will share a slide with a QR code for information about the trial. I also want to say thank you Dr. Guttman and Benji, Dr. Ungar for

your upcoming participation in the walk for alopecia. I heard that you guys are forming a Mount Sinai team and we are hoping that, you know, we appreciate your support and your participation two years in a row. So thank you for doing that. And I will share information about that as well, but maybe some folks in the audience will come and walk with you when you do your walk in New York in September.

EMMA GUTMANN-YASSKEY, MD, PHD: (57:28)
That would be lovely. We would love that.

LISA ANDERSON, PHD: (57:30)
Okay. Thank you both again. I'm going to share a few more slides to wrap up our webinar today.

EMMA GUTMANN-YASSKEY, MD, PHD: (57:38)
This was great. Thank you.

LISA ANDERSON, PHD: (57:40)
Thank you for being here. We appreciate you. Okay, so this slide has a little QR code that you can access to get more information specifically about the pediatric clinical trial that Dr. Ungar and Dr. Guttman were talking about. This will take you to the NAAF website where there's some more details about the trial and all of the contact information for the four sites is listed there. We will also share this information in our follow-up email to...

to webinar that will go out tomorrow. And of course, if you have any questions, please just email us at info at NAAF.org and we will connect you with the folks at Mount Sinai. As I just said, the walk for alopecia is coming in September and thank you Dr. Guttman and the Mount Sinai team for participating in the walk again this year. Anyone anywhere can be part of the walk for alopecia. You can join one of the walk sites like the one in New York, for example.

Or you can walk in wherever you are. So you can get more information with this QR code or visit the NAAF.org backslash walk site for more information. You can also email us at walk at NAAF.org and we'll help you get started. So let's all participate and walk for Alopecia, this Alopecia Areata Awareness Month September.

I want to thank the panelists again for being here. I want to thank our audience for being here. There were a lot of you online today. Please share your feedback on this webinar and help us plan future webinars. So a link to a short survey will pop up in your browser window at the end of the webinar. And we really appreciate your feedback. Join us for our next webinar, 504 Plan Accommodations for Alopecia Areata Preparing for Back to School. It's almost that time of year.

Embarking on a new school year can be an overwhelming experience for many students. However, the challenges can be particularly daunting for children dealing with alopecia areata. Don't miss this opportunity to hear from a panel of experienced parents, along with NAAF's support and education director, Judy Williams, as they delve into valuable resources

and effective strategies for helping students thrive in their school environments while living with alopecia areata.

gain insights from their personal journeys, and discover how these families have navigated the implementation of a 504 plan. We will be sharing our panelists' bios soon. This webinar is going to take place on Tuesday, August 20th at 7 p.m. Eastern, 4 p.m. Pacific time. And registration for this webinar is now open. You can scan this QR code to get there.

As you can tell, there's a lot happening at NAAF. And how can we help you keep up? You can subscribe to our email list and get regular updates on the breaking alopecia areata news and research, our monthly electronic newsletter, as well as notices about upcoming webinars and programs. If you're not already on our list, please scan this QR code to enter your email address to receive our emails. And don't forget.

Finally, that NAAF offers a number of resources and programs to the Alopecia Areata community, including support groups, our youth mentor and legislative liaison programs, the doctor finder, clinical trial listings, as well as news and webinar links and how to get involved. To learn more about NAAF and the resources we offer, please email us at support at NAAF.org or visit us at NAAF.org. And this concludes today's webinar program.

Thanks again, Dr. Ungar and Dr. Guttman for being here. We appreciate you and your work and we look forward to seeing you all on our next webinar. Take care, everyone.