**Diagnosing and Managing Atopic Dermatitis in Individuals With Skin of Color**
Understanding Disparities in AD Diagnosis and Management:
Impacts on Individuals With Skin of Color

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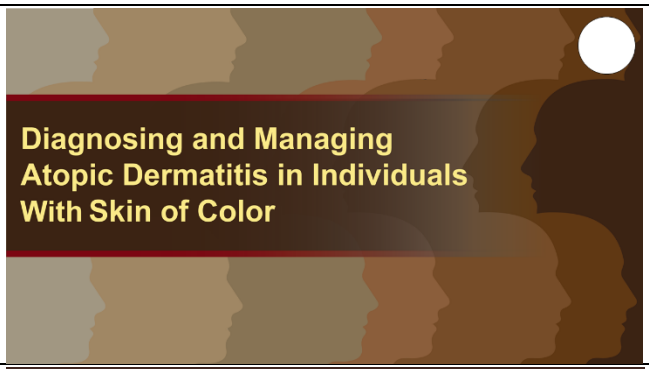
| 1. |  | Welcome to Diagnosing and Managing Atopic Dermatitis in Individuals With Skin of Color. |
| 2. |  | Dr. Jonathan Silverberg. I'm a Professor of Dermatology and Director of Clinical Research at the George Washington University School of Medicine and Health Sciences, and I'm pleased to be joined today with Doctor Susan Taylor, who is the Burnett Johnson Jr. Endowed Professor, Director of Skin of Color Research Fellowship, Vice Chair for Diversity, Equity and Inclusion in the Department of Dermatology in the Perelman School of Medicine at the University of Pennsylvania in Philadelphia; and by Doctor Prince Adotama, who's an Assistant Professor of Dermatology, Director of Diversity, Equity and Inclusion in the Department of Dermatology and the Assistant Program Director in the Department of Dermatology Residency Program and Co-Founder of Skin of Color Section at the Ronald O. Perelman Department of Dermatology, New York University Grossman School of Medicine in New York. |
| 3. |  | And the agenda for today's presentation is we'll be first addressing understanding disparities in the diagnosis and management of atopic dermatitis and the impacts on individuals with skin of color. And this will be addressed by Professor Taylor. And then there'll be a Clinical Case Challenge addressing the assessment and diagnosis of atopic dermatitis in skin of color, led by Doctor Taylor; and then Dr. Adotama will be addressing the treatment of moderate-to-severe atopic dermatitis in skin of color. And then we'll also present a Clinical Case Challenge on the treatment and ongoing assessment of atopic dermatitis in skin of color. |

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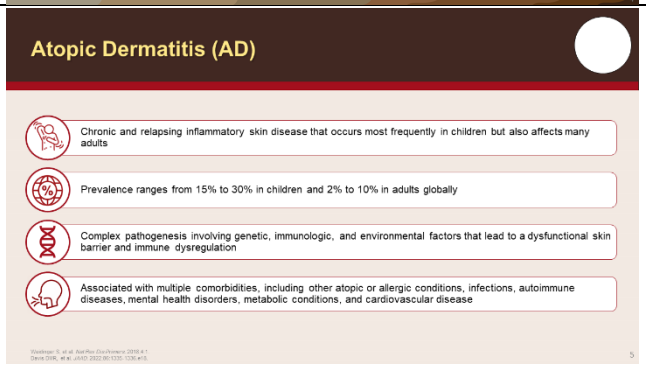
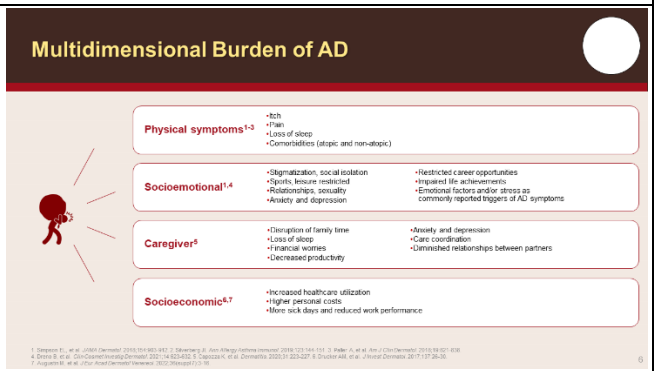
| 4. |  | And with that, I'm pleased to turn over the first presentation to Professor Taylor.<br>Thank you very much, Doctor Silverberg. And it gives me great pleasure to discuss disparities in atopic dermatitis diagnosis and management, particularly as it relates to individuals with skin of color. |
| 5. |  | We all know that atopic dermatitis is a chronic, relapsing inflammatory skin disease. Although it affects adults, it occurs much more frequently in children. The prevalence ranges anywhere between 15% and 30% in children and 2% to 10% of adults globally. It's important to point out that this is indeed a global disorder. Now, the pathogenesis of atopic dermatitis is quite complex, and it involves an interplay of genetics, immunologic, and environmental factors. And all of these lead to dysfunctional skin barrier as well as immune dysregulation. There are several comorbidities that are associated with atopic dermatitis. We're all very familiar with allergic conditions that are related to atopic dermatitis, asthma and hay fever, but also infections, autoimmune disorders, mental health disorders, metabolic conditions, and cardiovascular disease like hypertension. |
| 6. |  | So, the burden of atopic dermatitis is quite multidimensional. There are symptoms, physical symptoms that include itching, pain, loss of sleep, and, of course, the aforementioned comorbidities. You know, there are socioemotional burdens associated with atopic dermatitis. You know, there's a lot of anxiety and depression in these patients because this disorder profoundly affects quality of life. Patients can restrict their leisure activities as well as their involvement in athletics. They can restrict their ability to go outdoors, for example, in very hot weather. Their relationships are profoundly affected; these can be intimate relationships, it can be relationships with their children, if they are caregivers. You know, atopic dermatitis can restrict career opportunities and, hence, impair life achievements. And, if we think about our caregivers, there's a great deal of anxiety and depression in them. You know, they often have to coordinate care. They too, just like their |

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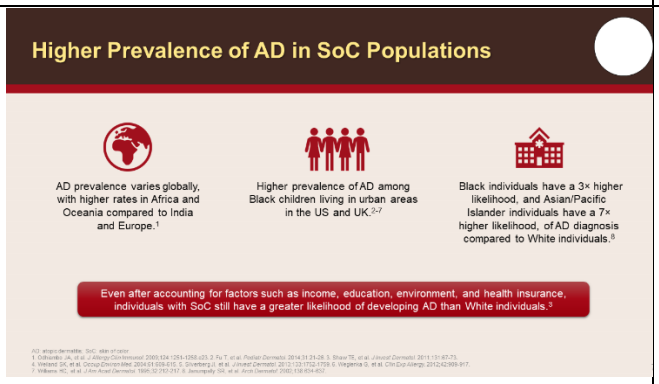
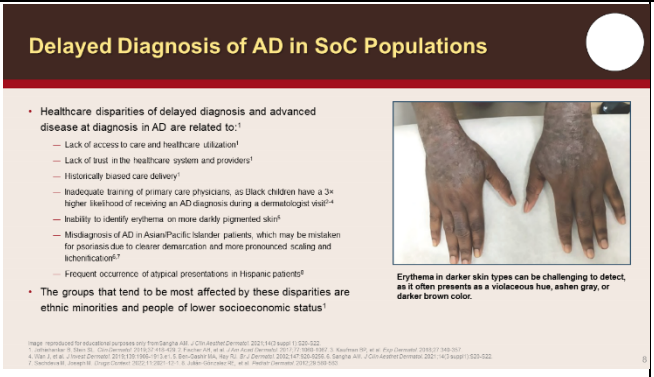
| | | child, for example, lose sleep, they miss work and can have significant financial burdens placed upon them. And the entire family structure and time spent with the family can be disrupted. Of course, there are socioeconomic considerations. There's increased utilization of the healthcare system in patients with atopic dermatitis. There are higher personal costs manifested by increased co-pays when they go to see physicians or go for treatments. And of course, with our adults, they lose more work, they take more sick days. And they have decreased work performance. So, there are profound burdens on our patients with atopic dermatitis across multiple dimensions. |
| 7. |  | We know that atopic dermatitis prevalence varies globally. There are higher rates in both Africa and Oceania, and this is in comparison to Europe as well as India. We know right here in the United States there's a higher prevalence of atopic dermatitis in Black children living in urban areas, and this trend also occurs in the United Kingdom. Black individuals have a 3 times higher likelihood, and Asian and Pacific Islanders have a 7 times higher likelihood of an atopic dermatitis diagnosis compared to White individuals. But even after accounting for factors such as income, education, environment, health insurance, individuals with skin of color still have a greater likelihood of developing atopic dermatitis than White individuals. So, this is a very special and a very important population. |
| 8. |  | Now, unfortunately, there are significant delays in diagnosis of atopic dermatitis in our skin of color populations. Now this can be due to a myriad of problems. Now the disproportionate number of atopic dermatitis cases in our skin of color populations may be due to initial decreased healthcare utilization, and this could lead to more advanced disease at the time of presentation. We know that Black children have a 3 times higher likelihood of receiving an atopic dermatitis diagnosis during dermatologic visits and that implies that, perhaps, the primary care physician is missing the diagnosis of atopic dermatitis in this population. Now, why could that be? Well, one of the primary reasons is that often erythema, which is really the hallmark of atopic dermatitis in populations of individuals with lighter skin may not be seen |

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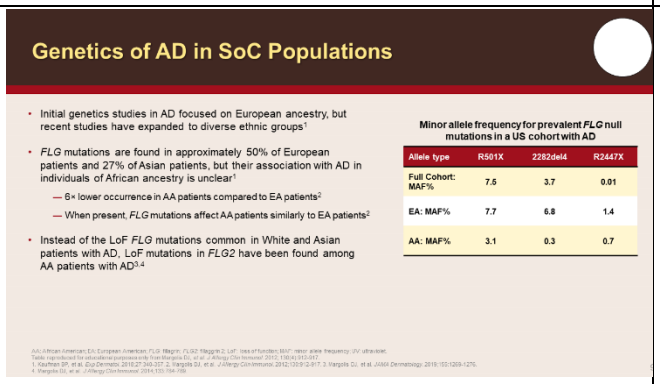
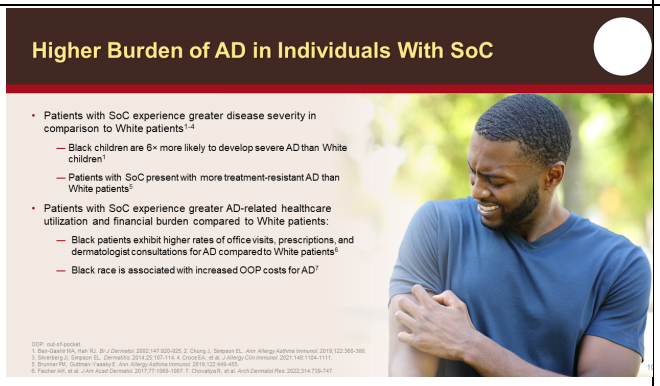
| | | or appreciated, or noted in individuals with darker skin types. And this can relate to delayed diagnosis and, unfortunately, to misdiagnosis as well. Now atopic dermatitis in our Asian and Pacific Islander patients may be just mistaken for psoriasis, and this is because, in this population, there can be differences in morphology and presentation, particularly with well-demarcated plaques as well as more pronounced scaling and lichenification, and in our Hispanic population, there can be more atypical presentations and manifestations, which again can lead to delayed or misdiagnosis. |
| 9. |  | Now, when we think about genetics of atopic dermatitis, much of the work has been done on European individuals, individuals of European ancestry. But, fortunately, more recently, we've looked at genetics in skin of color populations. Now we know that loss-of-function filaggrin mutations have been found in approximately 50% of European patients and 27% of Asian patients. But this association with atopic dermatitis in individuals of African ancestry is unclear, and, in fact, we know that individuals of African descent tend not to have loss-of-function Filaggrin mutation, but rather, a mutation in filaggrin 2. So, there are differences in gene mutations between our skin of color populations and our White population, something that's very important to know. |
| 10. |  | Now, we also know that there's a higher burden of disease in our skin of color populations. Black children, for example, are 6 times more likely to develop severe atopic dermatitis than White children. Patients with skin of color present with more treatment-resistant atopic dermatitis than White patients. Now, patients with skin of color experienced greater atopic dermatitis–related healthcare utilization as well as financial burdens compared to White patients. So, there are higher rates of office visits, prescriptions, and dermatology consultations for atopic dermatitis in our skin of color patients compared to our White patients. And Black race is associated with increased out-of-pocket costs for atopic dermatitis, and this can have a profound effect on many families. |

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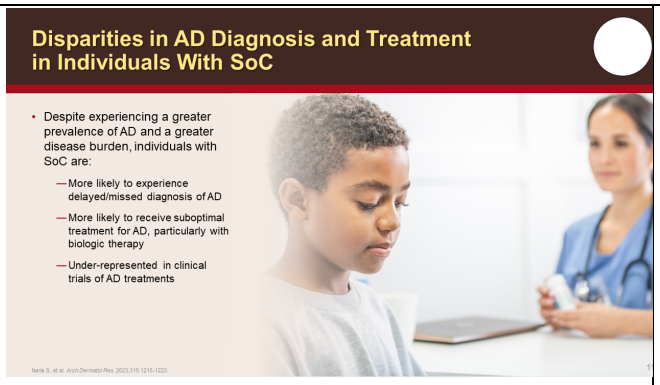
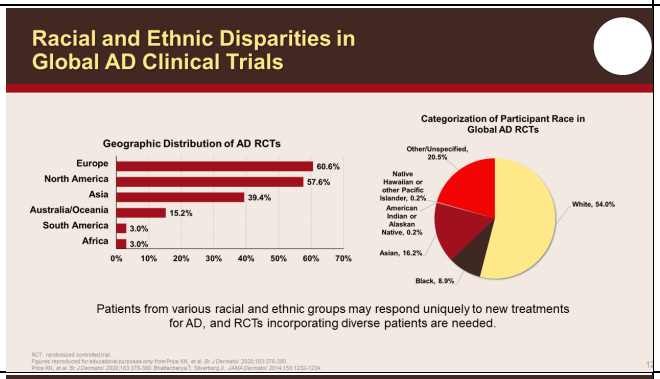
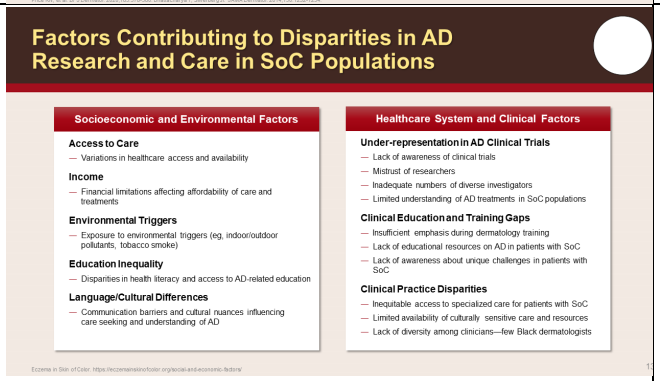
| 11. |  | Now, when we think about disparities in diagnosis and treatment, as I alluded to, they can be quite significant. Despite experiencing a greater prevalence of atopic dermatitis and a greater disease burden, individuals with skin of color are more likely to experience delayed [diagnosis] and misdiagnosis, as we said, because often the presentation of disease is different. They're more likely to receive suboptimal treatment for atopic dermatitis, and studies that have demonstrated that they are less likely to be prescribed biologic therapy, something we all need to think about. And, unfortunately, our skin of color patients are often under-represented in clinical trials for atopic dermatitis. And it's critically important for us to know if the safety and efficacy of our therapeutic modalities for atopic dermatitis, if that applies to our skin of color populations. |
| 12. |  | When we look at our racial and ethnic disparities in global atopic dermatitis clinical trials, we can see that over half of those trials occur in Europe and North America, over one-third occur in Asia, and 15% in Australia and Oceania. But if we look at areas where skin of color patients reside, particularly Africa and South America, only 3% of the randomized controlled clinical trials occur in those parts of the world. |
| 13. |  | So, there are many factors that contribute to disparities in atopic dermatitis research, as well as care in our skin of color populations. First, there's difficulties with access to care. There are various variations in healthcare access and availability. You know, we alluded to the fact that there are more financial burdens for many of our skin of color populations higher out-of-pocket co-pays that are required, you know, missed days at work, which also influences the ability of our patients to get care. We know that because of structural racism, there are significant differences and disparities in housing in many of our skin of color populations, because of a long history, particularly in the United States of redlining. Many skin of color patients live in areas where there's increased pollutants adjacent to highways, adjacent to factories, for example. There are internal indoor pollutions that they are exposed to, substandard housing with the growth of mold, for example. We know that exposure to |

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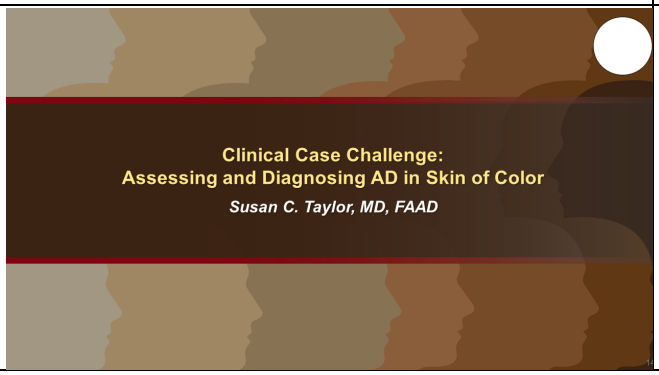
| | | tobacco smoke can exacerbate atopic diathesis in these patients. There can be inequities in education, disparities in health literacy that contribute to the overall disparities in atopic dermatitis care for our skin of color patients. Let's not forget about language and cultural differences that occur. You know, under-representation in clinical trials is a major problem, and there are many reasons that contribute to that. You know, one of which is a lack of diversity in PI's, who head up these particular studies. There can be limited understanding of atopic dermatitis treatment in skin of color populations, a lack of awareness of clinical trials, and mistrust of researchers that goes back many, many generations. When we think about clinical education and training gaps, you know there is a lack of diversity of images of atopic dermatitis in skin of color populations. So, there can be insufficient emphasis during dermatology training, lack of educational resources related to atopic dermatitis in our skin of color populations, and lack of awareness of unique challenges of patients with skin of color. And then finally, our clinical practice disparities, inequitable access to specialized care for our skin of color patients. You know, cultural sensitivity, cultural humility is critically important. You know, once our patients of color get to dermatologists, are they seeing physicians who can treat them with cultural humility, and will they return to those physicians? And of course, there's lack of diversity amongst clinicians. We know that only about 3% of dermatologists are Black and 4.2% are Hispanic, and that can impact disparities in clinical practice. We also know that under-represented-in-medicine physicians tend to serve skin of color populations significantly more than other providers. |
| 14. |  | So now I would like to take a few minutes to discuss Clinical Case Challenges, and these relate to assessing and diagnosing atopic dermatitis in skin of color patients. |

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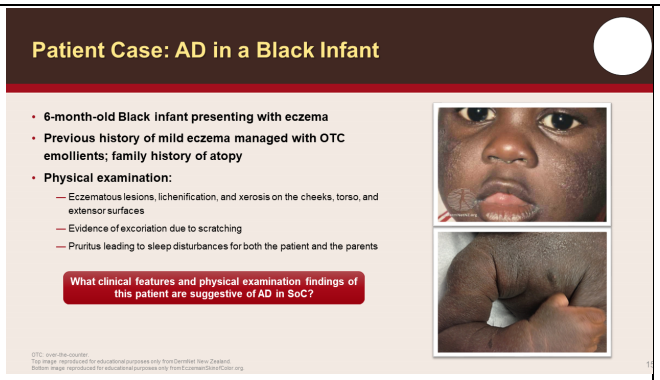
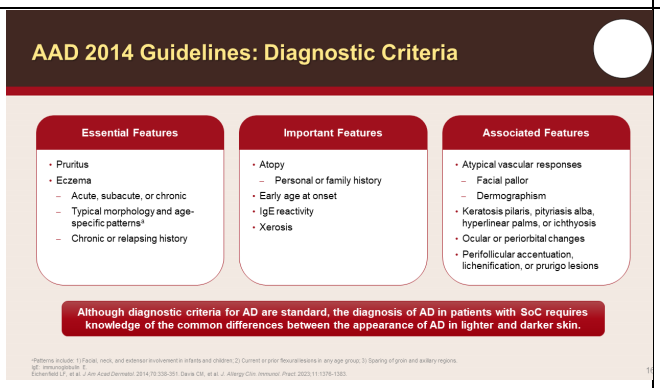
| 15. |  | So, let's start off with this Black infant who's 6 months old. This infant has a previous history of mild eczema that's been managed quite well with over-the-counter emollients. There is indeed a family history of atopy. On physical exam there are eczematous lesions, there's lichenification, there's diffuse xerosis that occurs not only on the cheeks but also the torso as well as extensor surfaces of the body. And there's evidence of excoriation due to scratching. So, the question I want to pose for you and I want you to have in the back of your mind is: What clinical features and physical examination findings of this patient are suggestive of atopic dermatitis in skin of color? |
| 16. |  | So, when we think about and look at the established diagnostic criteria from the 2014 guidelines, the essential features of the diagnosis include pruritus, and our child had pruritus, and different forms of eczema: acute, subacute, or chronic. There's typical morphology and age-specific patterns. And that morphology can differ in our skin of color patients, and we're going to go over that in the subsequent slides. We know that eczema is a chronic or relapsing disorder, and we get that history from our patients. Important features include a personal or family history of atopy [and] early age of onset; we know that most patients with atopic dermatitis are children. There's IgE reactivity and pretty widespread xerosis in most of our AD patients. Associated features can include atypical vascular responses. These can vary from facial pallor to dermographism. We often see keratosis pilaris, pityriasis alba, hyperlinear palms, or ichthyosis. There can be ocular or periorbital changes and, of course, perifollicular accentuation, particularly in our skin of color patients, lichenification [in] skin of color patients—Black and Asian, and prurigo lesions. So, although, diagnostic criteria for atopic dermatitis are standard, the diagnosis of AD in patients with skin of color requires knowledge of common differences between the appearance of atopic dermatitis in lighter and darker skin. And having that knowledge is going to help close that gap of misdiagnosis and delayed diagnosis. |

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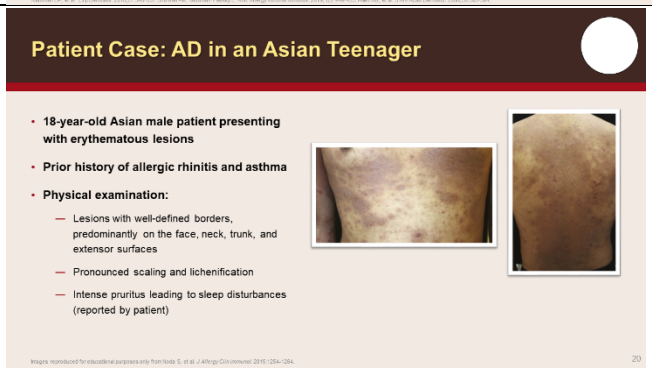
| 17. |  | So, Black patients with atopic dermatitis can present with no apparent erythema, or the erythema can be very difficult to appreciate. When present, it might not be red, but rather it can be violaceous. It can be an ashen gray or a dark brown color. There's often the presence of edema. The skin can be warm to the touch and scale may help perceive underlying erythema. |
| 18. |  | Black patients are more likely to present with diffuse xerosis. You know, we think of atopic dermatitis being present in flexor surfaces, but in skin of color patients, we must examine extensor surfaces because often that's where involvement is. Dyspigmentation is a common accompaniment of atopic dermatitis, and the dyspigmentation can be either hyper- or hypopigmentation. As I said earlier, there's often perifollicular accentuation; often we see [the] papular variant of eczema, and this can occur on the extensors as well as the trunk. |
| 19. |  | Don't forget there can be a lichen planus–like presentation of atopic dermatitis. This seems to occur almost exclusively in patients with darker skin tones. The lichen planus–like presentation can affect the extensor surfaces of the body, and it often responds quite rapidly to treatment. |
| 20. |  | Next, let's talk about an 18year-old Asian male patient who presents with erythematous lesions. There is a prior history of allergic rhinitis as well as asthma. And here you can see these lesions are well defined; they have well-defined borders. They occur primarily in this patient on the face, the neck, the trunk, as you can see here, as well as the extensor surfaces. There's often pronounced scaling and lichenification in our Asian patient[s]. And of course, intense pruritus in this particular case, leading to sleep disorders. And we see this commonly or hear this commonly in our atopic dermatitis patients. |

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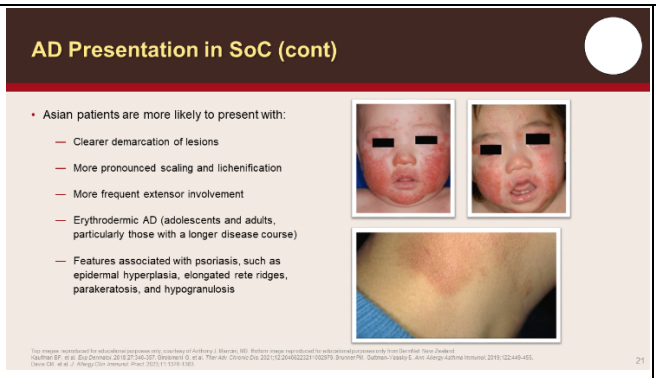
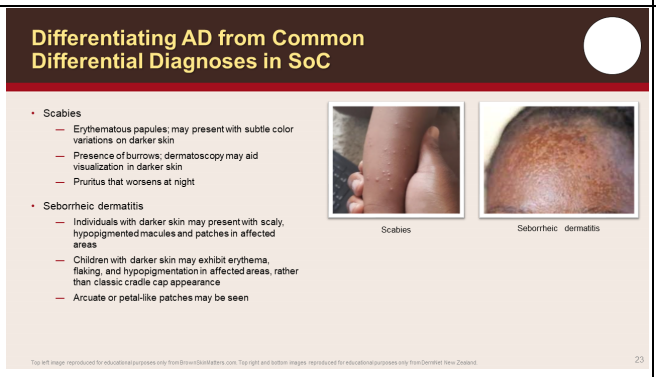
| 21. |  | Now, it's important to note that many of our Asian patients can present with clear demarcation of their lesions. There can be more pronounced scaling and lichenification; more frequent involvement of the extensor surfaces of the body. Often, we see erythrodermic atopic dermatitis in adolescents and adults, particularly those who have had a longer disease course. And we don't want to confuse atopic dermatitis in our Asian patients [with] psoriasis, and there can be histologic features on biopsy consistent with psoriasis that include epidermal hyperplasia, elongated rete ridges, parakeratosis and hypogranulosis. |
| 22. |  | Here we have a case of possible atopic dermatitis in a Filipina woman. And she is 20 years old; she presents with papular eczema; she has a long history of intermittent flares and remission since early childhood, and here we see a papular predominance. The papules can occur on the face and the perioral, and periocular area, the neck, the flexor surfaces, which we see here, as well as the hands. There can be mild erythema, subtle scaling in some areas. Definitely excoriations and secondary infections can be due to scratching. So, I want you to think, what are the differential diagnoses of this patient's presentation? And there's several things that come immediately to mind. |
| 23. |  | Well, of course you don't want to miss scabies, which can present also with erythematous papules. It may present with subtle color variations in darker skin. Don't forget, with scabies, we often see burrows. Don't forget to look into the interdigital web spaces. And dermatoscopy is a great tool. It can help in visualization in darker skin. And for scabies, typically the pruritus can be worse at night. We might also think about seborrheic dermatitis in this differential. Individuals with darker skin often present with hypopigmented macules and patches on the forehead, nasolabial fold area, the eyebrows, the hairline, often on the face, there can be arcuate-, or petaloid-type patches. And children with darker skin may exhibit erythema, flaking, hypopigmentation, in affected areas beyond the scalp and the face rather than classic cradle cap presentation. |

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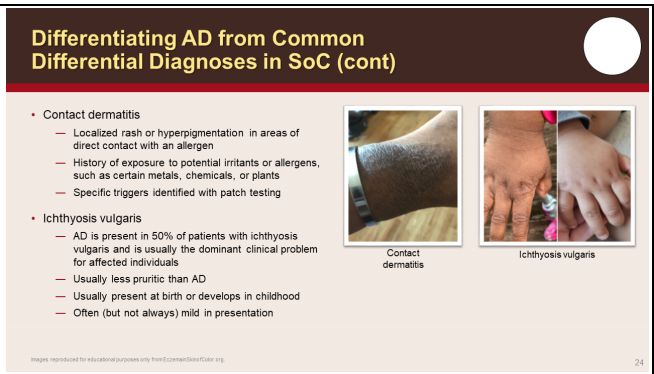
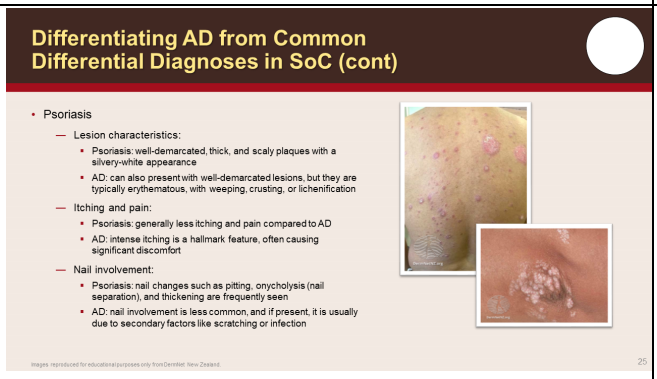
| 24. |  | Don't forget, in our differential diagnosis of atopic dermatitis is contact dermatitis. Here we see in the first picture [a] patient with a metal bracelet on. It's important to direct your history taking towards uncovering contacts. For example, you want to inquire about exposure to potential irritants or allergens, metals, chemicals, or plants. For these patients, you might consider patch testing to identify what the particular trigger is. Ichthyosis vulgaris can be a mimicker of atopic dermatitis and it can present. Atopic dermatitis is present in about 50% of patients with ichthyosis vulgaris, and this is usually the dominant clinical problem for affected patients. It's usually less pruritic than atopic dermatitis. Cosmetically, these patients are very concerned about it. Ichthyosis vulgaris often presents at birth or develops in childhood, and it's often, but not always, mild in presentation. |
| 25. |  | Psoriasis. That's often a mimicker of atopic dermatitis, and we know with psoriasis you often have very well-demarcated, thick, scaly plaques with a silvery-white appearance. But remember, atopic dermatitis can also present with well-demarcated lesions. We made that point earlier, in our Asian patients. But with atopic dermatitis, there's typically more erythema or [a] violaceous hue. There can also be weeping, crusting, or lichenification in contrast to psoriasis. In regard to symptoms of itching and pain, psoriasis tends to be less pruritic and have less pain as compared to atopic dermatitis. We know with atopic dermatitis that intense itching is a hallmark feature keeping our patients up at night, resulting in pretty significant and widely visible excoriations. And the pruritus can cause quite significant discomfort. The nail changes in psoriasis, we're all familiar with, they can range from pitting to onycholysis and thickening of the nail, whereas nail involvement in atopic dermatitis is less common, and that can be a point of differentiation between psoriasis and atopic dermatitis. |

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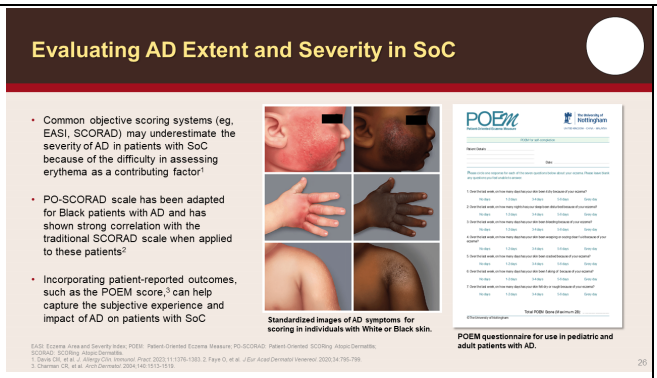
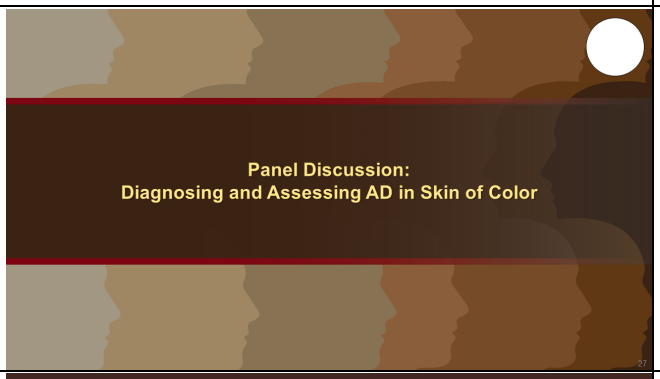
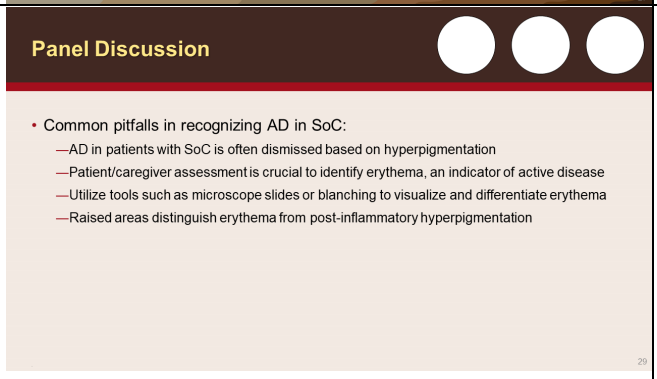
| 26. |  | Now, evaluating atopic dermatitis' extent and severity in skin of color is a very important topic and often erroneously, atopic dermatitis severity is underestimated in our skin of color patients. And that's often because the scoring system that we all utilize, the EASI score, the SCORAD really depends upon in large measure on erythema, and erythema can be more difficult to detect or underestimate in our skin of color patients. So therefore, the overall extent and severity of disease in these populations is often underestimated. Now, the patient-oriented SCORAD scale has been adapted for Black patients with atopic dermatitis. And it's actually been shown to have a strong correlation with the traditional SCORAD scale when applied to these patients. So, that's a very important and useful tool. Now, incorporating patient-reported outcomes, such as POEM score, can help to capture the subjective experience and impact of atopic dermatitis in skin of color patients. So, this is critically important if you are involved in clinical trials of atopic dermatitis for our skin of color patients, to make sure that you are being able to capture the erythema, the severity of their disease, so that they can qualify for admission into these particular clinical trials. |
| 27. |  | And with that, I'm going to turn it over to Dr. Silverberg. |
| 28. |  | Thank you, Dr. Taylor for that outstanding presentation. You know, there's a lot of, I think, practical questions that come up around these really important topics and, so, I'd love to get both of your feedback on what are some of the common pitfalls that you encounter in clinical practice. So, that you see sort of challenges that are happening most commonly in the real world related to the proper recognition and diagnosis of atopic dermatitis in skin of color.<br>Well, you know, Dr. Silverberg, a lot of my patients when they come to me, they tell me that they've really suffered for a long period of |

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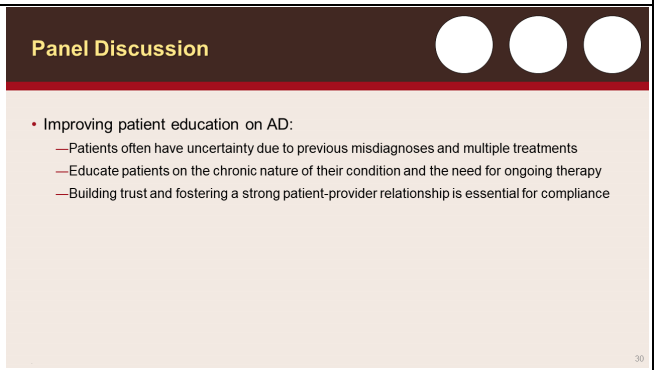
| | | time, or their child has suffered for a long period of time, and that our colleagues have sort of dismissed them and said, you know, “I don't really see much active disease,” “I see hyperpigmentation, which means it's old.” And they just give them, let's say, a topical cream to use. But if you query the patient or the caregiver, you know, “Does the skin look red to you?” that caregiver and that patient know if their skin is red and then, you know, I would love to think, my eye is trained to see the variation of red, and it's often that violaceous hue, it's a little bit different. You can use a microscope slide. You can, you know, blanch it with your fingers. You see that erythema and you see how widespread it is. And compared to post-inflammatory hyperpigmentation, the areas are raised, right? You can feel them. And then I say, “Well, this is pretty severe, moderate-to-severe disease.” I'm gonna have a discussion about systemic therapy.<br>Excellent point. |
| 29. |  | I agree. I believe patients often don't know their diagnosis. They've seen multiple doctors and I will see them and I'm like, “Oh, this looks like atopic dermatitis or eczema.” They're like, “Is that what I have.” And they're really unsure of their diagnosis, they've been on multiple treatments, and they're very unsure and they look up online and they say this– “My eczema doesn't look like what I’ve seen online.” And so, it's really important that doctors in their busy dermatology practices take the time to really sit their patients down and really explain their diagnosis, explain that this is a chronic condition, that this is not going to go away after one week of treatment. We have to maintain therapies. And so really, I think it's also really important for patients who have a discordant physician-to-patient relationship that they recognize, that there may be some, some barriers there and they may not necessarily trust you. So that means you have to take even more time to really build and foster a relationship with your patient, so they can trust what you're saying and be willing to follow your advice.<br>Excellent points. Yeah. I mean, I think, unfortunately, these problems come up all too often. You know, I've had multiple patients with phototype 5-6 who were told that they had |

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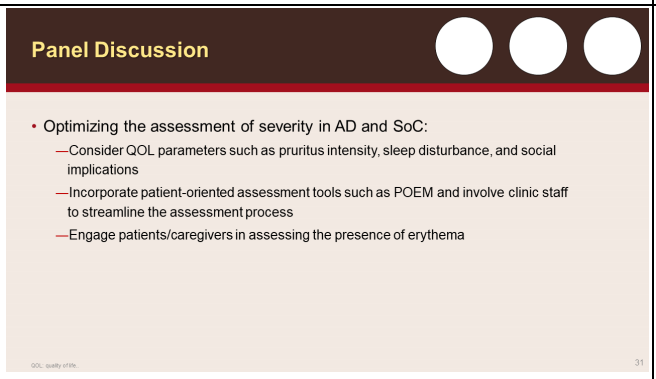
| | | psychogenic itch and that they needed to see a psychiatrist, when they were virtually erythrodermic. And I, you know, was contemplating hospitalization for wet wraps. That's how bad they were. And so, you know, that's an extreme scenario, but it should never happen. And it's something that, I think, just really needs to be more attention for. And that's the purpose of programs exactly like this, to have that attention towards really training your eye recognizing the different presentations across diverse patient populations.<br>And can I make one more other point? You know, if as a, you know, dermatologist provider, you're thinking about it, but you're not sure, you can always do a biopsy, right? And that's a very important tool. It's OK not to be sure, but it's not OK not to think about it. |
| 30. |  | Right. I think that's an excellent point. Do you have any tips or pearls around how to optimize the assessment of severity of atopic dermatitis in skin of color? You know, Susan, you did a great job, I think, outlining a lot of the clinical considerations. But, you know, for folks who don't necessarily get involved in the clinical trials, who don't necessarily do EASI score and SCORAD on a daily basis, what should they be thinking about when assessing the severity and just in the trenches in the real world.<br>Yes, so, just some of the practical things. How much pruritus does your patient have? How much is their sleep interrupted, right? Do they avoid wearing certain clothing? Do they avoid going outside, you know, if it's really hot? Do they avoid social situations? Are they embarrassed? So, those are sort of practical assessments. And when you look at their skin, you know how much involvement of anything do you see? Like any, dyspigmentation, do you see? But I would start with kind of those quality-of-life parameters.<br>That's an excellent point.<br>I am one who, in clinic, doesn't like to use EASI score and SCORAD, as I think it can be difficult in a fast-paced clinic. But I think POEM is an amazing tool. You can even have your medical assistant prior to have them fill out POEM. And POEM is a patient-oriented eczema measure and it asks seven really easy questions, and they ask questions like over the past 7 days, |

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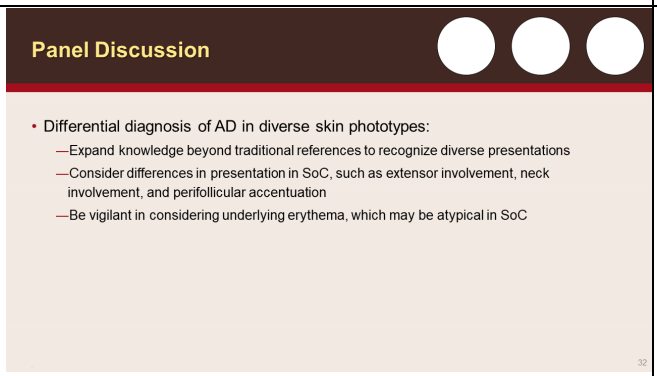
| | | over the past week, “How bothersome is this itch to you?” “How flaky is this eczema for you?” Right? And so those questions are very easy and it really pops out a severity score. So, you can kind of even, before you walk into the room have a kind of baseline idea of how severe their eczema is and know, “OK, I need to be escalating therapy for this patient,” right? So, in addition to taking a good history, I also think you can use some of those tools to be able to better assess their severity, and it could be very quick if you utilize the staff in your clinic to get that process done.<br>I love it. Yeah.<br>I love it too. And you know what? If they don't have it, they can Google it and download it off the Internet. It's like readily accessible.<br>Yep, absolutely. And I think it actually ties very nicely to something you mentioned, Susan earlier, which is—if you're not sure even how to look at the skin and the erythema, ask the patient, because they know. And I think that that's where patient-reported outcomes are so helpful because sometimes we think we know what we're looking at, but we may not be spot on. But the patient knows exactly what their experience is, and if they're super itchy and uncomfortable, or if their skin just doesn't look anything like it once did at baseline, that's going to be a really important, you know, a clue that we need to step up our game, so to speak.<br>Yeah. |
| 31. |  | And any thoughts in particular around, or things that you see most commonly with respect to differential diagnosis from the skin of color perspective versus, you know, patients with lighter phototypes? Do we, you know, are there certain things to be on the lookout more commonly or is it kind of the same broad differential diagnosis, but it just, you know, everything will look different in different skin types? Do we get fooled more with certain disorders in skin of color than we do, perhaps, in lighter skin types? For example, I feel like in lighter phototypes, you know, the erythema of psoriasis can sometimes be much more prominent. So, I think that's, like, it's easier to differentiate. But then when we go to darker phototypes, it sometimes, you don't have that clue of the erythema to help you as much. Where do you see these kinds of little things |

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| | | popping up? Like, what should we be really on the lookout for in terms of differential diagnosis to make sure we're not missing?<br>I think a lot of that is just your residency education and what you're exposed to. That's really a plug to Dr. Taylor because she's written books and textbooks on how eczema it presents in people of color, and as someone who is a person of color I make an extra effort to make sure that I'm able to identify differences in appearance in darker skin types, such as, more extensor involvement as opposed to flexor involvement, more neck involvement, more papillary or follicular accentuation, right? So it's really important that you're able to differentiate those two. And I will be able to better diagnose those patients, right? So, really look outside your usual textbooks and your references to really expand your diagnosis because things that may not look like eczema and Fitzpatrick 1-3 may be slam dunk eczema Fitzpatrick 4-6, if you have that in the back of your mind.<br>So, I totally agree. I think that almost all inflammatory disorders, which present in lighter skin tones with erythema usually don't in patients with skin of color, so all of those disorders are in jeopardy of misdiagnosis or delayed diagnosis, right? So, I think it behooves all of us to ask, could there really be erythema here and I'm not appreciating it? And that's gonna broaden and, at the same time, now you've diagnosed this. So, I think this is not a problem just for atopic dermatitis, but for almost all of the inflammatory disorders that we see.<br>Excellent point. And really just thank you for that outstanding discussion. |
| 32. |  | Alright, so I am Doctor Prince Adotama, and let's start our discussion on the treatment of moderate-to-severe atopic dermatitis in skin of color. |

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| 33. | **Question**<br>Based on available data, which treatment for moderate-to-severe AD has specifically demonstrated efficacy and safety in individuals with SoC?<br>a. Dupilumab<br>b. Tralokinumab<br>c. Abrocitinib<br>d. Baricitinib<br>e. Upadacitinib<br>The answer to this question will be discussed in detail later in the presentation. | So first, let's pose a question. Based on available data, which treatment for moderate-to-severe atopic dermatitis has specifically demonstrated efficacy and safety in individuals with skin of color? a. dupilumab, b. tralokinumab, c. abrocitinib, d. baricitinib, e. upadacitinib. And we'll discuss this in the next few slides. |
| 34. | **Biologic and JAK Inhibitor Therapies for Moderate-to-Severe AD**<br>[a] Regulatory approvals current as of June 2023.<br>EMA: European Medicines Agency; FDA: US Food and Drug Administration; IL-4Rα: interleukin receptor 4 alpha; IL-13: interleukin 13; JAK: Janus kinase; mAb: monoclonal antibody; TCS: topical corticosteroids.<br>1. Dupilumab PI. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761055s044lbl.pdf 2. Tralokinumab PI. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761180s010lbl.pdf<br>3. Abrocitinib PI. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/213871s001lbl.pdf 4. Upadacitinib PI. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/211674s010lbl.pdf<br>5. Olumiant SMPC. https://www.ema.europa.eu/en/documents/product-information/olumiant-epar-product-information_en.pdf | All right. So, let's kind of go over all the different therapies that are FDA-approved for moderate-to-severe atopic dermatitis. So, the first therapy is dupilumab, which is the subcutaneous injection. This was FDA-approved in 2017; it was the first biologic that was available for atopic dermatitis that's moderate to severe. And it was approved initially for a treatment for [patients] 18 and up, but over the years, it's expanded approval to 6 months and up. So, it's had the most broad variety, as for which patients we can treat with this condition. It can be used with or without topical corticosteroids. Our next drug is tralokinumab. This is a newer drug also for the treatment of atopic dermatitis, moderate-to-severe, and this is for patients 18 and up. And this also can be used with or without topical corticosteroids. So those are our two biologic agents. Our next two drugs are oral JAK inhibitors. This is a new class of drugs that have been FDA-approved for atopic dermatitis and that includes abrocitinib and upadacitinib. These drugs are both approved for adults and pediatric patients aged 12 and up with refractory, moderate-to-severe atopic dermatitis who do not adequately or are not adequately controlled with other systemic drug products, including biologics. And then the European Medicines Agency has an additional oral JAK inhibitor called baricitinib, and this a treatment for moderate-to-severe atopic dermatitis in adult patients.<br>So, let's go into detail on how these drugs work. |

| Therapy | Class | Mechanism of Action | Indication(s) for Patients with AD[a] |
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| **FDA-approved** | | | |
| Dupilumab subcutaneous injection[1] | Biologic (mAb) | IL-4Rα antagonist | • Treatment of adult and pediatric patients aged ≥6 months with moderate-to-severe AD whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable<br>• Can be used with or without TCS |
| Tralokinumab[2] | Biologic (mAb) | IL-13 antagonist | • Treatment of moderate-to-severe AD in adult patients (aged ≥18 years) whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable<br>• Can be used with or without TCS |
| Abrocitinib[3] | Oral small molecule | JAK1 inhibitor | • Adults and pediatric patients aged ≥12 years with refractory, moderate to severe AD whose disease is not adequately controlled with other systemic drug products, including biologics, or when use of those therapies is inadvisable |
| Upadacitinib[4] | Oral small molecule | JAK1 inhibitor | • Adults and pediatric patients aged ≥12 years with refractory, moderate-to-severe AD whose disease is not adequately controlled with other systemic drug products, including biologics, or when use of those therapies are inadvisable |
| **EMA-approved** | | | |
| Baricitinib[5] | Oral small molecule | JAK1/2 inhibitor | • Treatment of moderate to severe AD in adult patients who are candidates for systemic therapy |

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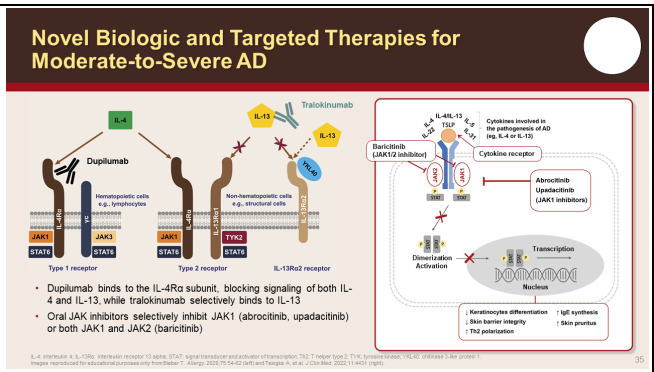
| 35. |  | So, the first drug is dupilumab and this biologic, like I had said, was FDA-approved in 2017. It actually blocks IL-4Ra. So, IL-4Ra as you can see here and here is blocked by dupilumab, and this blocks signaling for IL-4 and IL-13. IL-4 and IL-13 cytokines are extremely important in the Th2 pathway, which is responsible for things like eczema flaring, asthma, and allergies, right? So, IL-4 and IL-13 are very specific for atopic dermatitis. And so, by blocking IL-4Ra, dupilumab blocks these two very important cytokines that are important for atopic dermatitis. The other biologic is tralokinumab. Tralokinumab blocks IL-13 specifically. So as opposed to blocking the IL-4Ra, it blocks IL-13 itself and so it blocks just one of the signals and helps to improve atopic dermatitis, as a result. The next group of drugs are oral JAK inhibitors. So oral JAK inhibitors work differently. So, a lot of cytokines can theoretically bind to cytokine receptors that include IL-4 and IL-13, which we know is important for dupilumab. Also, IL-5, which is responsible for eosinophils, IL-31, which is associated with itch. Many different cytokines can be blocked with this JAK inhibitor. So, JAK is an intracellular receptor. So, typically you have a cytokine like IL-5, for example, that binds the cytokine receptor, and then dimerizes and then it goes into the nucleus and transcribes certain genes. And these genes are responsible for itch, Th2 pathway, which is responsible for eczema, and impacts the skin barrier. But, by blocking this with a JAK inhibitor such as abrocitinib, upadacitinib, or baricitinib, you actually block these downstream effects, and so you don't get increased skin pruritis and increased Th2 polarization. So, this is an intracellular small molecule that works differently and actually blocks more cytokines as a result. |
| 36. |  | So, how are we addressing the urgent need for diversity? Right. We want to know what we're doing for patients of color. Few data exist on differences in treatment efficacy and safety in patients with atopic dermatitis of different skin types. As of now, there are no standalone trials or subgroup analyses for JAK inhibitors or tralokinumab. So, we really don't know specifically how JAK inhibitors or the newer drug tralokinumab work on skin of color. However, dupilumab, the very first drug, has |

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| | | post hoc analyses that assess efficacy and safety based on race and ethnicity. |
| 37. | **Efficacy and Safety of Dupilumab in Different Racial Subgroups of Adults With Moderate-to-Severe AD in Three Randomized, Placebo-Controlled Phase 3 Trials**<br>• Post hoc analysis utilizing data from three phase 3 trials of dupilumab in AD: LIBERTY AD SOLO 1, LIBERTY AD SOLO 2, and CHRONOS<br>• Total of 2058 patients, including:<br>— 1429 White patients<br>— 501 Asian patients<br>— 128 Black/AA patients<br>• Baseline demographics and disease characteristics were generally balanced among treatment groups and racial subgroups; most patients had high disease burden at baseline<br>Clinical Trial > J Drugs Dermatol. 2019 Aug 1;18(8):804-813.<br>Efficacy of Dupilumab in Different Racial Subgroups of Adults With Moderate-to-Severe Atopic Dermatitis in Three Randomized, Placebo-Controlled Phase 3 Trials<br>Andrew F. Alexis, Marta Rendon, Jonathan I. Silverberg, David M. Pariser, Benjamin Lockshin, Christopher E.M. Griffiths, Jamie Weisman, Andreas Wollenberg, Zhen Chen, John D. Davis, Meng Li, Laurent Eckert, Abhijit Gadkari, Brad Shumel, Ana B. Rossi, Neil M.H. Graham, Marius Ardeleanu<br>Alexis AF, et al. J Drugs Dermatol. 2019;18:804-813.<br>37 | Let's go into the trial that looks at skin of color. In this post hoc analysis they looked at three different phase 3 trials, and it was a total of 2058 patients; 1429 were White, 501 were Asian, and 128 were Black or African American. And the baseline demographics and disease characteristics were generally balanced among treatment groups and racial subgroups. Most patients had high disease burden at baseline. As you know, we're looking at moderate-to-severe atopic dermatitis in these trials. |
| 38. | **Efficacy of Dupilumab in Different Racial Subgroups of Adults With Moderate-to-Severe AD in Three Randomized, Placebo-Controlled Phase 3 Trials**<br>**Change in EASI: LS Mean Change from Baseline at Week 16**<br>Subgroup / Placebo Change (SE) / Dupilumab Change (SE) / *P* Value<br>White<br>Dupilumab q2w vs Placebo: -14.91 (0.703) / -25.36 (0.693) / <.0001<br>Dupilumab qw vs Placebo: -14.91 (0.703) / -25.47 (0.651) / <.0001<br>Asian<br>Dupilumab q2w vs Placebo: -10.97 (1.664) / -24.23 (1.615) / <.0001<br>Dupilumab qw vs Placebo: -10.97 (1.664) / -25.46 (1.455) / <.0001<br>Black/AA<br>Dupilumab q2w vs Placebo: -11.88 (1.947) / -20.02 (2.722) / .0161<br>Dupilumab qw vs Placebo: -11.88 (1.947) / -19.98 (1.925) / .0028<br>Favors Dupilumab / Favors Placebo<br>-30 -20 -10 0 10 20<br>LS Mean Difference<br>LS: least squares; qw: once weekly; q2w: once every 2 weeks.<br>Image reproduced for educational purposes only from Alexis AF, et al. J Drugs Dermatol. 2019;18:804-813.<br>38 | What we want to look at is the change in EASI score. That's the Eczema Area Severity Index score. Since we looked at White patients, the change in the score for patients with dupilumab every 2 weeks was a decrease of about 25, which is a significant drop in eczema severity. For Asian patients, the change in severity was 24, also a significant drop. And for Black patients, the change the severity of every 2 weeks was 20. Not necessarily as high, but still very much a significant drop in eczema severity. So, this study kind of highlights the benefit of dupilumab for the treatment of Black patients with atopic dermatitis, moderate-to-severe. |
| 39. | **Efficacy of Dupilumab in Different Racial Subgroups of Adults With Moderate-to-Severe AD in Three Randomized, Placebo-Controlled Phase 3 Trials (cont)**<br>**Change in Peak Pruritus NRS: LS Mean Change from Baseline at Week 16**<br>Subgroup / Placebo Change (SE) / Dupilumab Change (SE) / *P* Value<br>White<br>Dupilumab q2w vs Placebo: -2.29 (0.168) / -4.12 (0.158) / <.0001<br>Dupilumab qw vs Placebo: -2.29 (0.168) / -4.24 (0.139) / <.0001<br>Asian<br>Dupilumab q2w vs Placebo: -1.41 (0.298) / -3.59 (0.285) / <.0001<br>Dupilumab qw vs Placebo: -1.41 (0.298) / -3.68 (0.261) / <.0001<br>Black/AA<br>Dupilumab q2w vs Placebo: -2.18 (0.364) / -3.82 (0.531) / .0118<br>Dupilumab qw vs Placebo: -2.18 (0.364) / -3.95 (0.389) / .0007<br>Favors Dupilumab / Favors Placebo<br>-5 0 5<br>LS Mean Difference<br>NRS: Numerical Rating Scale.<br>Image reproduced for educational purposes only from Alexis AF, et al. J Drugs Dermatol. 2019;18:804-813.<br>39 | How about the change in peak pruritus? And NRS is the numerical rating score scaled from 0 to 10 with 10 being the worst itch in your life and 0 being no itch. And as you can see, for White patients, there's a drop of 4 of itch with the dupilumab every 2 weeks. For Asian patients, a drop close to 4 as well, with dupilumab. And for Black patients it dropped once again pretty close to 4 in the overall itch. So once again, Black patients had good improvement with dupilumab for their itch scores. |
| 40. | **Safety of Dupilumab in Different Racial Subgroups of Adults With Moderate-to-Severe AD in Three Randomized, Placebo-Controlled Phase 3 Trials[1]**<br>**AEs Reported Between Baseline and Week 16**<br>White / Asian / Black/AA<br>Patients with: Placebo (n=509) / Dupilumab 300 mg q2w (n=402) / Dupilumab 300 mg qw (n=517) / Placebo (n=188) / Dupilumab 300 mg q2w (n=128) / Dupilumab 300 mg qw (n=184) / Placebo (n=53) / Dupilumab 300 mg q2w (n=27) / Dupilumab 300 mg qw (n=47)<br>≥1 TEAE, n (%)[a]: 362 (71.1) / 292 (72.6) / 372 (72.0) / 128 (68.1) / 83 (64.8) / 121 (65.8) / 24 (45.3) / 12 (44.4) / 26 (55.3)<br>≥1 TE-SAE, n (%)[a]: 22 (4.3) / 11 (2.7) / 13 (2.5) / 7 (3.7) / 1 (0.8) / 1 (0.5) / 0 / 1 (3.7) / 0<br>≥1 TEAE causing discontinuation of study drug permanently, n (%): 12 (2.4) / 6 (1.5) / 12 (2.3) / 7 (3.7) / 0 / 3 (1.6) / 1 (1.9) / 0 / 0<br>Death, n (%)[a]: 0 / 0 / 1 (0.2) / 0 / 0 / 0 / 0 / 0 / 0<br>Conjunctivitis[c]: 29 (5.7) / 45 (11.2) / 80 (15.5) / 6 (3.2) / 13 (10.2) / 15 (8.2) / 1 (1.9) / 1 (3.7) / 3 (6.4)<br>[a]AEs reported at the level of MedDRA PT. [c]Detailed description of the event is given previously.[1]<br>[c]The generic term conjunctivitis was used to summarize a cluster of MedDRA PTs that included: conjunctivitis of undetermined etiology), allergic conjunctivitis, viral conjunctivitis, bacterial conjunctivitis, and atopic keratoconjunctivitis<br>AEs: adverse events; MedDRA PT: Medical Dictionary for Regulatory Activities preferred term; TEAE: treatment-emergent adverse event; TE-SAE: treatment-emergent serious adverse event.<br>Table reproduced for educational purposes only from 1. Alexis AF, et al. J Drugs Dermatol. 2019;18:804-813.<br>2.Beck LA, et al. N Engl J Med. 2014;371:130-139.<br>40 | How about adverse effects? So, we know the efficacy has been pretty similar for Black, Asian, and White patients. How about safety? Are there any safety concerns that are worse in Black patients? And so far, none. So, we look at the number of treatment adverse events. One or more treatment adverse events, there are, about 70% of White patients had treatment adverse events, 64% of Asian patients, about 44% of Black patients. Keep in mind, there are a very small number of Black patients in this study, as I mentioned, in this post hoc analysis. |

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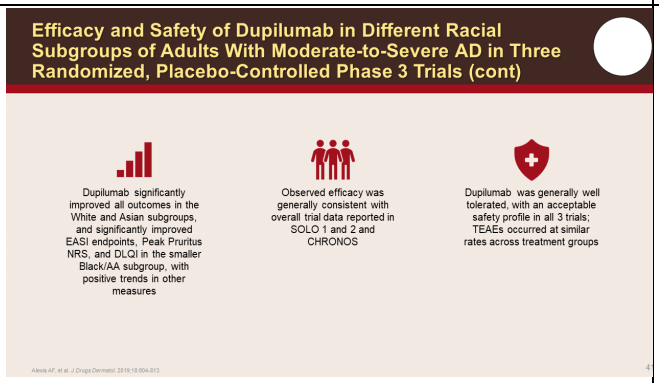
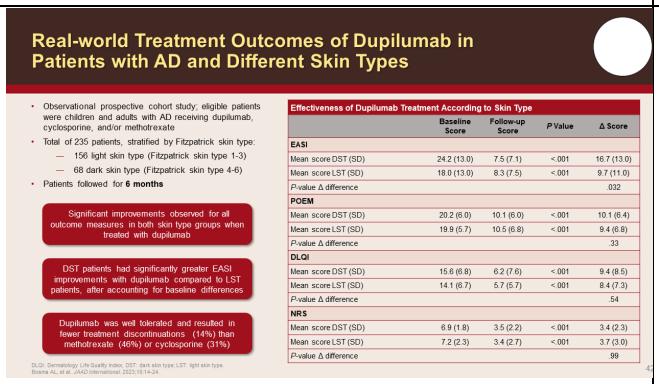
| | | As far as treatment-emergent severe adverse events, very few, only 2% in White patients, 1% in Asian patients, and about 3% in the Black patients. So very low numbers of treatment emergent severe adverse events, right? Adverse events mainly in this trial that were noted were like upper respiratory tract infections, needlestick issues, basically injection site reactions from the needle itself, and then also conjunctivitis, which is inflammation of the eye. When we compare conjunctivitis between patients of color and White patients, while 11% had conjunctivitis in the White Group, 10% in the Asian group, and 3% in the Black patient group. So, there was no marker of worse severity, of severe effects in the Black patient group or the Asian patient group. |
| 41. |  | So, overall efficacy was similar between all groups, and safety was similar. So, in conclusion, dupilumab with or without concomitant topical corticosteroids significantly improved atopic dermatitis signs and symptoms and quality of life across all racial groups, efficacy groups. And dupilumab was generally considered safe and very well tolerated in all three trials, and there was no major differences between treatment adverse events in the Black group, the Asian group, or the White group. |
| 42. |  | How about real world? So clinical trials are great, but they don't really have real world, and those patients are very specific, right? They're really in a very well-controlled environment. So, we really want to see how these patients do in a real-world environment. So, this is an observational, prospective cohort study, and they included patients that were children and adults with atopic dermatitis, moderate-to-severe, who receiving dupilumab, cyclosporine, [or] methotrexate. Cyclosporine and methotrexate are much older drugs we've been using for decades to treat atopic dermatitis. These are immunosuppressants that, they do work, but with the advent of four, now four FDA-approved drugs, biologics, and/or and small molecules for atopic dermatitis, these are falling down the wayside. What the study did was interesting, is they actually divided their patients based on Fitzpatrick skin type. And Fitzpatrick skin type is scaled 1-6, with 1-3 being lighter skin types and 4-6 being darker skin types. And in this study, 156 were light skin |

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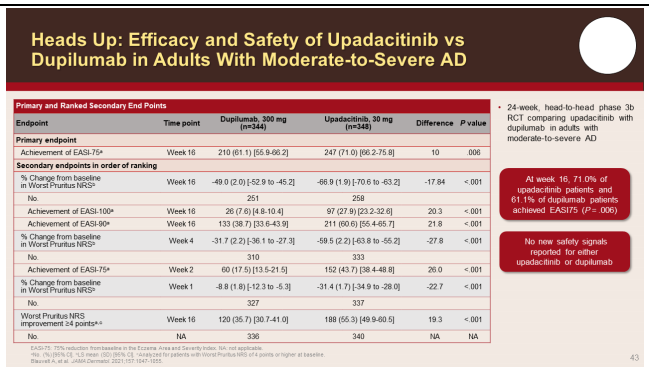
| | | types and 68 were dark skin types, and they followed these patients for 6 months. So, let's look at the EASI score, which is the Eczema Area and Severity Index. So, looking at the change, the percent change from baseline to follow-up 6 months later in patients of darker skin types, there was a decrease of 16, a very significant drop in eczema severity. And lighter skin types had a decrease of 9. So surprisingly, patients with darker skin types actually did much better and their eczema severity index dropped significantly more in the darker skin types compared to the White skin types. How about POEM? POEM is a patient-oriented eczema measure, or where the patients are asked questions, seven questions to assess the severity as the patient-reported outcome. When we look at the difference and change between darker skin types and lighter skin types, they both had a significant drop in the objective measure, patient-reported outcome. However, there is no difference between darker and White skin types. DLQI is the Dermatology Life Quality Index, and once again, both the darker skin groups and the lighter skin groups had a significant drop in their impact on their quality of life. However, there is no difference between darker skin and lighter skin types. |
| 43. |  | Next thing I wanted to do was compare upadacitinib to dupilumab. So, we noted upadacitinib, we noted dupilumab has been shown to be efficacious in patients of color, specifically Black and Asian patients. And now we just want to kind of compare dupilumab in general to upadacitinib and oral JAK inhibitors. And in this study, they compared dupilumab to upadacitinib at 30 milligrams. So, keep in mind when we start patients on upadacitinib, we usually start at 15 milligrams. So, this is a higher dose of upadacitinib. And so, when they compared the groups, their primary outcome was achieving EASI, Eczema Area and Severity Index score of 75% improvement at week 16. And 61% of dupilumab patients achieved the EASI-75 versus 71% of the upadacitinib. So upadacitinib actually outperformed dupilumab as far as the Eczema Area and Severity Index at 75. When we look at the achievement of EASI-100 and EASI-90 which is an even greater achievement, 27% of patients on upadacitinib achieved EASI-100 versus only 7% of |

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| | | dupilumab, and 60% achieved 90 versus only 38%. So, patients actually did continue to do better and better with the upadacitinib versus dupilumab 300. So, keep in mind, when you're comparing just outcomes directly, upadacitinib to the dupilumab, at least at the 30 milligrams, which is the higher dose, there is some evidence that upadacitinib may outperform dupilumab. And there were no new safety signals reported for either upadacitinib or dupilumab in this study. |
| 44. | **Question**<br>Based on available data, which treatment for moderate-to-severe AD has specifically demonstrated efficacy and safety in individuals with SoC?<br>a. Dupilumab<br>b. Tralokinumab<br>c. Abrocitinib<br>d. Baricitinib<br>e. Upadacitinib | So, based on available data, which treatment for moderate-to-severe atopic dermatitis has specifically demonstrated efficacy and safety in individuals with skin of color? And the answer would be dupilumab. This is the only drug currently on the market that has any type of post hoc analysis looking at skin of color specifically for the treatment of atopic dermatitis, moderate-to-severe. |
| 45. |  | So, what can we do to make sure that these clinical trials and these drug companies are adequately representing people of color? So, the Skin of Color Society actually had a Challenge Summit where they invited key stakeholders in various different organizations together to determine how we can kind of increase clinical trial representation. And so, this Summit actually addresses multiple different avenues. And they create recommendations for journals and how journals can, and journal editors can, purposely infuse diversity in their educational content. They reach out to community-based organizations and how community based organizations can increase outreach efforts in minoritized communities and establish patient advocacy groups. They reached out to healthcare professionals and investigators. They give recommendations on [how] investigators can ensure that their research materials include diverse populations and bilingual research staff and that their scheduling is very flexible for all patient groups. And they also had recommendations, very strong recommendations for study sponsors, pharmaceutical companies, and federal |

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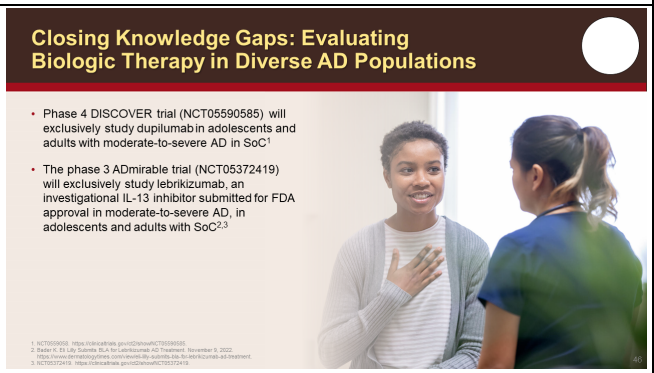
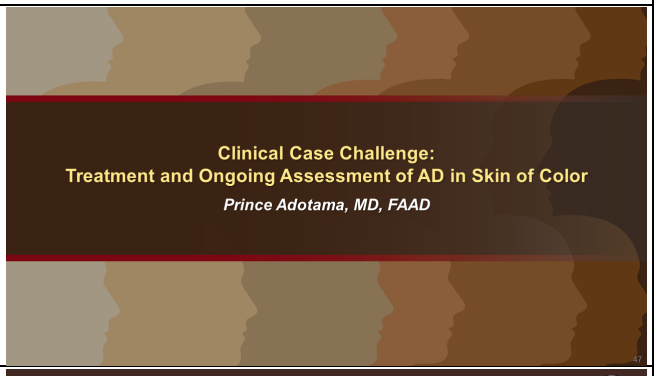
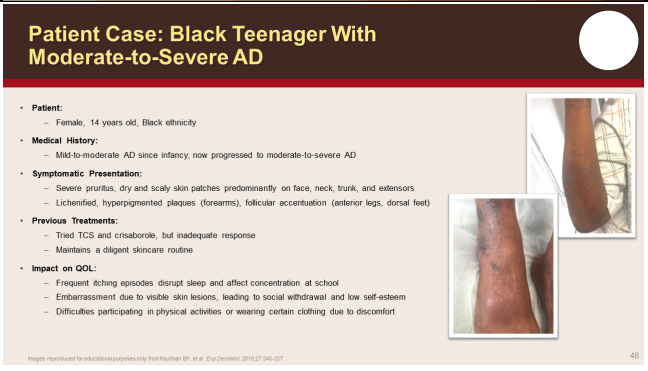
| | | agencies. So, this published study, which is available in *JAMA Dermatology*, is a great way for us to learn as a community what we can do to really increase representation of people of color in our clinical trials. That way, we don't have the situation where dupilumab is the only [agents studied in a] clinical trial to date that has patients of color represented. |
| 46. |  | So, what are we doing to close these knowledge gaps? So there now is a current phase 4 discovery trial exclusively done for dupilumab. But are we looking at adolescents and adults with moderate-to-severe atopic dermatitis and this will be specifically done for patients of color. So, when that works, this is something that we're really targeting, we're really happy that dupilumab is making this work. The next thing is the phase 3 ADmirable trial, which is an exclusive study done on lebrikizumab. This is a brand-new investigational IL-13 inhibitor, and this drug will be focusing on looking at moderate-to-severe atopic dermatitis and doing this trial in skin of color patients specifically. So now we have two trials that will be ongoing, that will be focused on skin of color. So, we can have a better idea of how skin of color patients fare with atopic dermatitis drugs. |
| 47. |  | So now I want to shift gears and talk about clinical cases. So, this clinical case challenge will be focusing on treatment and ongoing assessments for atopic dermatitis in skin of color. |
| 48. |  | So, let's talk about this first patient. This is a Black female patient, 14 years old, who initially had mild-to-moderate atopic dermatitis, nearly all her life, but recently has now progressed to moderate-to-severe atopic dermatitis. She has severe pruritus, dry and scaly skin patches predominantly on her face, her neck, trunk, and extensors. And she also has lichenification and these highly pigmented plaques on her forearms with follicular accentuation on her anterior legs and dorsal feet. And as Doctor Taylor mentioned earlier, these are typically where we see atopic dermatitis in people of |

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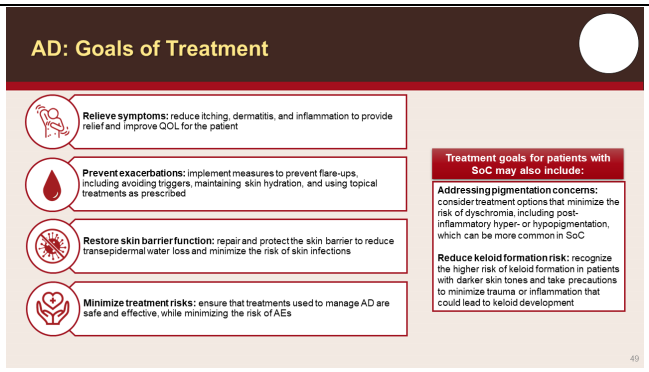
| | | color. They typically have more neck involvement, more extensor involvement, and more follicular accentuation. This patient had failed topical corticosteroids and crisaborole and had inadequate response to all of these topicals. She also maintains a very diligent skin care routine. This atopic dermatitis has a huge impact on her quality of life. She has frequent itching episodes that disrupt her sleep and affect her concentration at school. She feels very embarrassed by these skin lesions and [this] causes her to have low self-esteem and withdraw from social groups. As a result of these patches, she has a lot of difficulty participating in physical activities or wearing certain clothing due to all of the discomfort. |
| 49. |  | So, what are our goals of treatment when we have a patient with atopic dermatitis? There are four major goals of treatment. One, we want to relieve symptoms, right? We want to reduce itching, want to improve the dermatitis as a way, and this should improve their quality of life. We also want to prevent exacerbations. This is a chronic condition, so even if we treat this current flare, we want to make sure that we're able to treat them long-term so we can prevent subsequent exacerbations. We also want to make sure patients are using diligent skin care protection. So, we want to be able to restore the skin barrier function. We want to protect that skin barrier to reduce transepidermal water loss and make sure these patients are using diligent skin care and moisturization. We also want to minimize treatment adverse events, right? So, steroids potentially can cause hyperpigmentation or atrophy. We want to make sure that we're minimizing any of those treatment risks. And we also want to make sure that we're addressing pigmentation concerns when patients who have atopic dermatitis improve, specifically patients of color, they may be left with hyperpigmentation or hypopigmentation; it's important as dermatologists that we're addressing those conditions as well. And patients [with] skin of color may be at higher risk for keloid formation. So, to be cognizant of this risk for these patients, especially patients who typically scratch a lot. |

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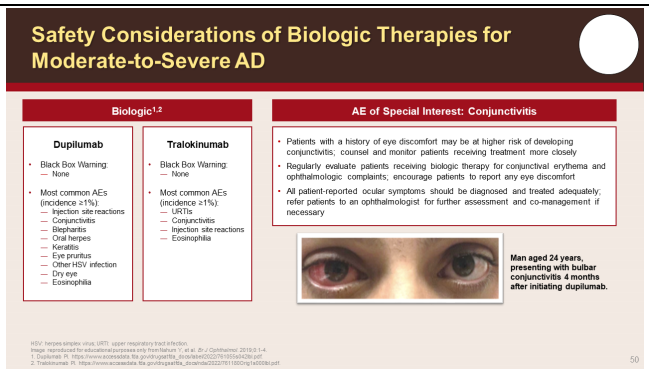
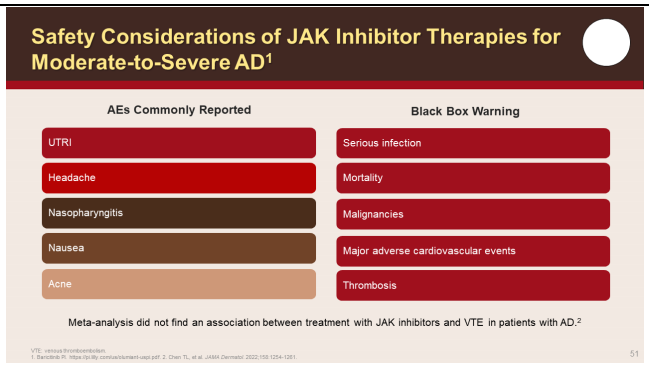
| 50. |  | So, what are the safety concerns for biologic therapies? So biologic therapies include dupilumab and tralokinumab. Both of these biologic therapies do not have black box warnings. However, they do have their own list of side effects. The most common side effect for patients with biologics is injection site reactions (as I mentioned earlier, this is an injectable drug) and conjunctivitis, which we'll talk about later. And then potentially increased risk for herpetic infections and dry eye. Tralokinumab has similar side effects, including conjunctivitis, injection site reactions, and upper respiratory tract infections.<br>I want to really focus on conjunctivitis because this is something that can come up with your patients on dupilumab and tralokinumab. And this is where you have inflammation and redness of the eyes. And patients with a history of eye discomfort at baseline may be at higher risk for developing conjunctivitis. It is really important that you are counseling your patient and monitoring them, while they're on therapy. And patients should be getting relative regular evaluations by you. And make sure they're aware that they should be discussing with you if they're having any issues with eye discomfort. Because there are, and we often will defer to our ophthalmology colleagues for assistance when treating patients who have adverse outcomes with conjunctivitis [with] dupilumab and with tralokinumab. This is a patient, for example, age 24 presenting with bulbar conjunctivitis 4 months after initiating therapy, and this is a situation where you want to be able to reach out to your patient and actually get help from your colleagues in ophthalmology to get this under better control. |
| 51. |  | How about JAK inhibitors? JAK inhibitors are oral small molecules, and these have a different host of side effects. So, the most common side effects reported include upper respiratory tract infections, headaches, nasopharyngitis, and nausea. Patients also, interestingly, can have acne. Some people will call it “JAKne,” where patients who are on oral JAK inhibitors or even topical JAK inhibitors can develop acne shortly thereafter, and oftentimes you can potentially treat through it or you may actually have to treat that acne specifically to get that under control. |

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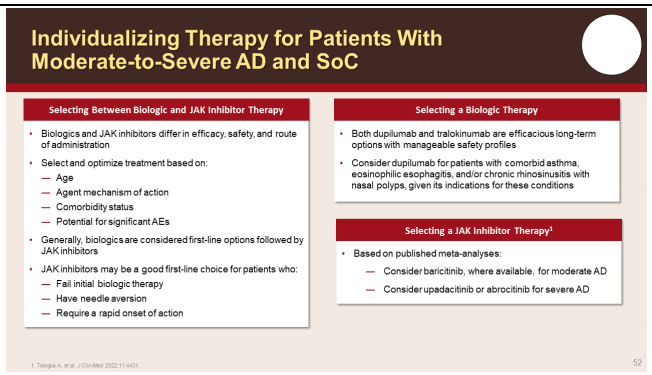
| | | There are also black box warnings. Unlike the biologics, the oral JAK inhibitors do have black box warnings and these include serious infection, increased mortality, malignancies, major adverse cardiovascular events, and thrombosis. In fact, patients who have one or more cardiovascular events, risk factors such as diabetes or hypertension [need] to be cautious when using JAK inhibitors, because of this black box warning, and patients [who] have a history of pulmonary embolism or blood clots—they should also be cautious of using oral JAK inhibitors. There was a recent meta-analysis that looked at atopic dermatitis patients specifically on oral JAK inhibitors, and in that specific cohort they did not see an increased risk of venous thromboembolism. However, keep in mind that these oral JAK inhibitors have been around for a while, and they have been used for other therapy for other conditions, such as arthritis, and in that cohort of patients, there is a higher risk of venous thromboembolism, so just keep in mind that although there is a black box warning for thrombosis in patients who have no risk factors, you wanna caution from avoiding this drug completely, thrombosis has not necessarily been found in a recent analysis to be higher risk in these atopic dermatitis patients. So, do a very thorough history of your patients and family history, social history, and all those factors to be able to determine which drug is best for your patient. |
| 52. |  | How about individualizing therapy? So, when you're trying to choose between biologics such as dupilumab and tralokinumab and oral JAK inhibitors, there's a lot of things to take into consideration. One is age, for example, if a patient is 2 years old right now, the only drug that's approved for patients 6 months and up is dupilumab. One is the mechanism of action, you want to look at the comorbidity, does someone have a lot of cardiovascular risk factors, does someone have a lot of history of blood clots? And you want to think about the potential of significant adverse events. Generally, because of the length of time these drugs have been approved, dupilumab and other drugs that inhibit IL-4 and IL-13, biologics, are typically considered first-line options. JAK inhibitors may be a good first-line option as well |

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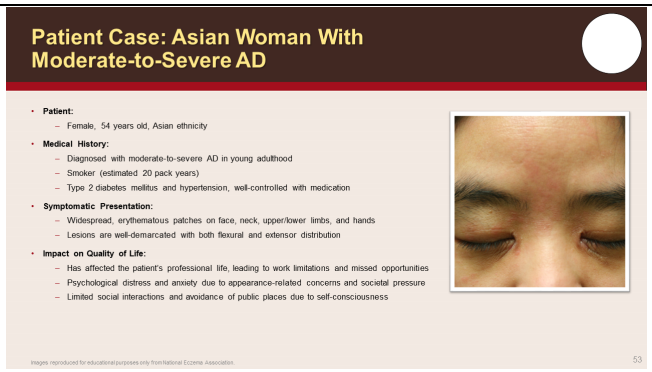
| | | in certain circumstances—if they fail initial biologic therapy, if the patient has needle aversion, or if the patient requires rapid onset. Oral JAK inhibitors work very quickly with helping to improve it, sometimes within a week or two, so patients who need really rapid onset or are needle averse, may enjoy the use of oral JAK inhibitors. And as I mentioned earlier, JAK inhibitors are approved for ages 12 and up. When you're selecting a biologic therapy, be mindful of the safety profile, and as you know, dupilumab is actually approved for asthma as well, so if someone has asthma, eosinophilic esophagitis, nasal polyps, then dupilumab might be a preferred option for those patients. As far as oral JAK inhibitors, keep in mind that baricitinib, which is not FDA approved, but it's approved by Europe. It's more likely to be used for moderate atopic dermatitis, and upadacitinib or abrocitinib can be used for severe and moderate atopic dermatitis. |
| 53. |  | Here we have another patient. This is a 54-year-old Asian female who presented with moderate-to-severe atopic dermatitis since her young adulthood. She's a smoker, estimated 20 pack-years. She also has type 2 diabetes and hypertension. But these are well controlled on medications. As far as her presentation, she has widespread, erythematous patches on her face and neck, upper and lower limbs, and her hands. Her lesions are well-demarcated with both flexural and extensor distribution. This has had a major impact on her quality of life. It's affected her professional life. She's had to take days off of work and missed opportunities for promotion as a result. She has a lot of psychological distress and anxiety due to her appearance, and she sometimes buckles under societal pressures because of the way her skin looks. She actually limits her social interactions and avoids public places due to her low self-esteem as a result of her atopic dermatitis. So, when you're deciding [on] a medication, in this case, you want to really take into consideration that she has severe atopic dermatitis involving many body surface areas, and she also has type 2 diabetes, hypertension, she's a smoker, so she has multiple cardiovascular risk factors. So, in a patient like this, you may not be jumping to oral JAK inhibitors right away. You might consider one of the biological agents. |

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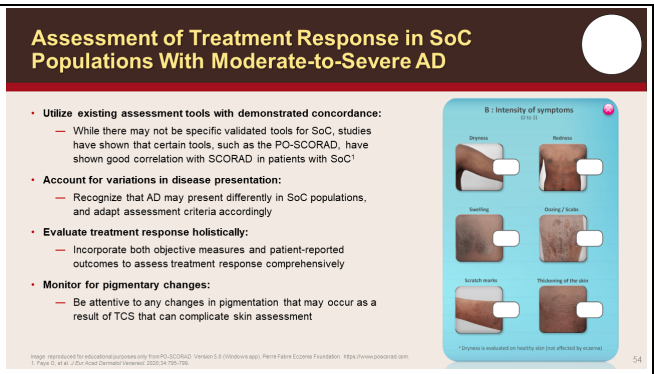
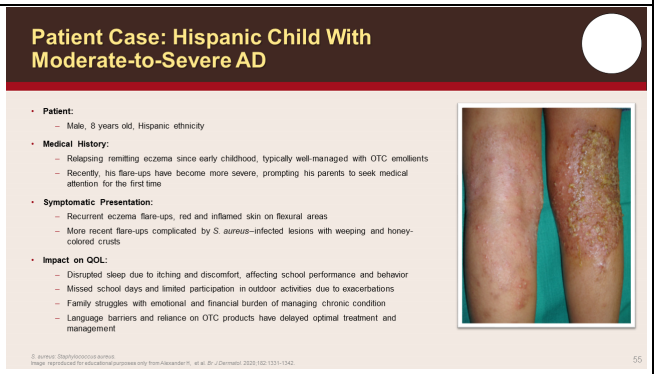
| 54. |  | When you're assessing treatment response in skin of color, there are a few tools that you can use—so you can utilize existing assessments. So, while there may not be any validated tools for skin of color, studies have shown certain tools such as the PO-SCORAD, have been shown to be just as good in people of color as they are in non–patients of color, non–people of color. You can also recognize the atopic dermatitis may present differently in skin of color populations, and Dr. Susan Taylor did an amazing job looking at the difference in presentation in people of color versus White patients. And you also want to consider viewing treatment holistically. We wanna look at objective measures, but you also want to look at patient-reported outcomes. How is this affecting them, how is this affecting their sleep, how is this affecting their job at work? You really want to be able to do a very thorough history and see how this affects the patients, not just how you see them in clinic, but how [is] it affecting their life, and it's also very, very important that we're monitoring for pigmentary changes, right? Pigmentary changes, specifically PIH can be one of the top five reasons Black patients even come to a dermatologist, so it's really important that once we treat their atopic dermatitis, they're also keeping in mind that PIH can be a very major issue for these patients and that we were actually addressing that issue as well. |
| 55. |  | This next case is a Hispanic child. This is an 8-year-old Hispanic child with atopic dermatitis. This patient has relapsing/remitting eczema since very early childhood and typically is well managed with over-the-counter emollients. Recently, however, he has been having flares-ups that have become more and more severe, prompting his parents to seek medical attention for the very first time. He presents with these recurrent eczema flares with red and inflamed skin on flexural surfaces. His most recent flares have been complicated by *Staph aureus* with *Staph aureus*–infected lesions with weeping and honey-colored crusts. As a result, his eczema has an impact on his sleep, due to all the itching and discomfort and is actually affecting his school performance and behavior. He has missed many school days and has limited participation in outdoor activities. The |

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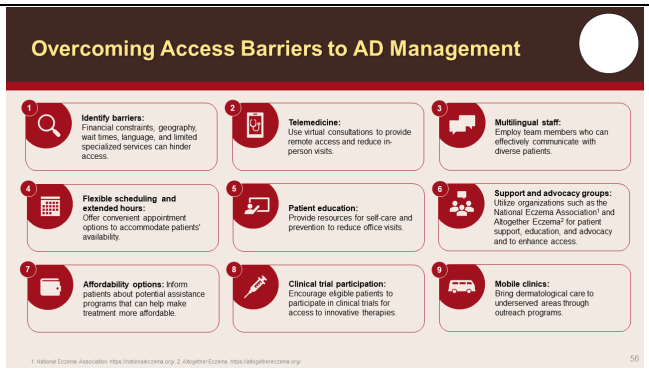
| | | family has been struggling with this condition as well. It's really impacting the entire family, and due to language barriers and difficulty connecting with doctors, he and his family have been relying more so on over-the-counter products and have delayed seeing dermatologists as a result. So, in this situation, this patient has a super infection with *Staph aureus,* and so then you might want to consider doing a wound culture or actually treating it with oral antibiotics. Keep in mind this patient is 8 years old, so you want to be careful which antibiotic you can use. Antibiotics like doxycycline are usually for 9 and up, and so once you treat this super infection then you can use potentially topicals. But depending on how severe, you may even have to escalate therapy to a biologic or JAK inhibitor. And as of now, oral JAK inhibitors are not FDA-approved for patients younger than the age of 12. So, the only biologic this patient could use, if this patient needs additional therapy, it would be dupilumab. |
| 56. |  | So how are we overcoming barriers to access to atopic dermatitis management? As I mentioned earlier, the patient before had language barrier issues, had eczema for many years, had just for the first time presented [to the] dermatologist. So, we can do better, right? What we want to do is identify barriers—are there any financial constraints, geographical wait times, are there language barriers at play, and what can we do to overcome those barriers? So we won't be able to offer flexible scheduling at times, sometimes an 8 to 4:00 PM schedule may not be enough for patients to see you. So maybe having later hours to accommodate more patients. Want to make sure that you have more affordability options, whether that be in your office or even making sure that these patients are aware of some of the options that these drug companies offer patients. Who may not be able to afford therapies? Some of these drug companies offer options, patient assistance programs as well. If patients can't come in, you want to be able to offer telemedicine services for patients. We want to also offer patient education, and patient education in culturally relevant ways and in their preferred language, right? So just getting someone a pamphlet may not work if that |

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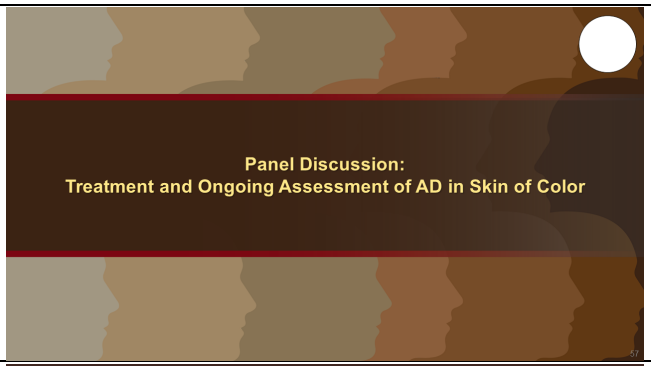
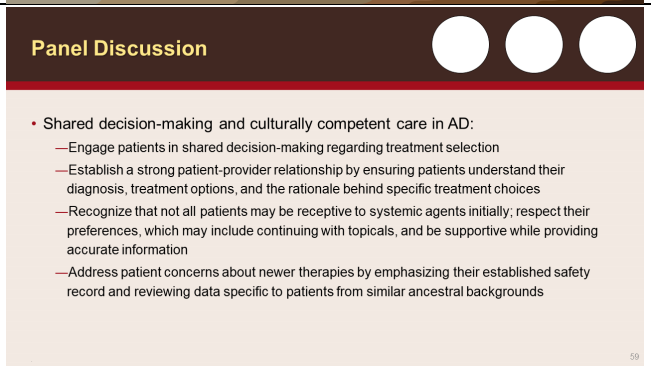
| | | pamphlet's in English and that patient doesn't speak that language. And also, if the patient is eligible, you want to be able to recommend potentially any clinical trial options for those patients. And in your actual staff in your clinic, you want to make sure you have a multilingual staff, and if you don't have multilingual staff that you have services that you can provide that allow for Spanish-speaking or any really any language-speaking. And also, these patients, as I mentioned, all three of these patients had impacts on their quality of life. So, you want to take advantage of advocacy groups or many patient support advocacy groups that do really amazing work with helping to connect patients with resources and opportunities to kind of improve their quality of life and really have a community of support for their condition. And mobile clinics are another option in really underserved areas that allow us to kind of expand our outreach. |
| 57. |  | All right. And that ends my presentation. So now I want to open the floor for panel discussion. |
| 58. |  | That was an outstanding presentation. So, I think just to start off, the question and answer really thinking about from a practical perspective, and you did such a great job reviewing all of the data and all of the options. But how do we put it all together from a shared decision-making perspective? And really, from the perspective of trying to provide culturally competent care across diverse patient populations?<br>So, I would say that patients are not just a data point, right? You can look at a patient and say, "OK, this patient has severe atopic dermatitis, they need dupilumab or they need an oral JAK inhibitor." But patients have to come, have to be on board, right? If this is your very first time seeing this patient and you're wanting to rush to dupilumab right away, they may be a little taken aback by that, they may, they want to understand their diagnosis better. They may |

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| | | want to have a better understanding of why you're choosing that, that drug specifically, right? So, it's really important that patients have buy-in and they understand their diagnosis and are comfortable with the treatment options, right? Not everyone is super keen on the idea of injections. Not everyone's super keen on the idea of lab monitoring which may be necessary for oral JAK inhibitors. Patients need lab monitoring at baseline, and sometimes they need lab monitoring a couple months thereafter, right? So, patients need to understand what their diagnosis [is], and sometimes they need to have a second meeting before you actually discuss starting a major life change like the dupilumab or tralokinumab, or any of the other oral JAK inhibitors. So really just making sure patients are aware of their condition and feel comfortable with the decisions that are being made in the room, and that will actually help to foster a better long-term relationship down the line.<br>I completely agree with that, and often, patients are not going to be receptive at the first visit with you to a systemic agent. And I think it's critically important, as we said earlier, to build that relationship. So, two things happen, a lot of times they just want to stick with topicals, right? We know they're not going to necessarily improve. But when they come back, they'll go, “Well you know, [I’m] not really much better,” and then they're open to that conversation. It might take one, it might take two, it might take three appointments, but don't judge, don't judge. Are patients going to get there? We just have to be there supportive and giving them the correct information.<br>Beautifully said, yeah, I think it's very true. I think the other thing is, you know, a lot of these therapies are pretty new, and what I found is that, for some patients, they get nervous about new treatments because they don't, they don't want to feel like they're a guinea pig or they're being experimented on. So, I think it's really important to understand the established safety record and be able to review that, know those data well and be able to provide a reassuring assessment of the data, because if you don't then, no matter how clean we think this–the drug–might be, the patient’s not going to |

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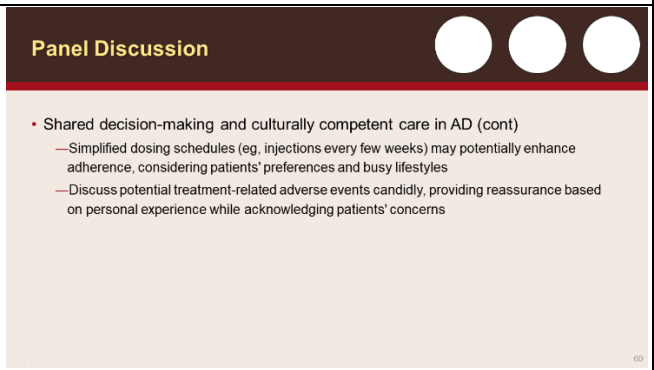
| | | necessarily see it that way, and they may be reluctant to start.<br>And when we say, you know, there's data from patients who look like you, you know, from your ancestral background, specifically looking at the safety, the efficacy–that goes really far, that particular information.<br>Patients of color, specifically Black patients, have a pretty tough history when it comes to clinical trials and experimentation. So, when you're mentioning a drug that even for some people, 2017 may not be long enough for FDA approval, some people are very nervous. So, it's really great that drug companies like the dupilumab and even newer drugs like lebrikizumab, which is not even out in the market yet, are really focusing on providing information on how these therapies work on patients of color because having that data set and having that information to provide to your patients can really go a long way to making them feel more comfortable with moving forward with that new drug. |
| 59. |  | And I think there's also practical considerations because most patients don't like the idea of using a shot, and understandably so. On the other hand, from an adherence perspective, sometimes it's a lot easier to take a shot once every 2 weeks or every 4 weeks than it is to remember to take a once-daily. And if you're, you know, if you're busy with work or at home and have other, you know, issues and psychosocial factors that are impacting your care, you know, taking a shot once every few weeks simplifies a lot for patients, and so sometimes that's just a pragmatic option that's, you know, more appropriate for them.<br>I think the other thing that's really important for these, this patient population is to go over the adverse or potential adverse events, you know, in a matter-of-fact way. Answer any questions, give percentages when we have percentages, but they're, you know, they're just really scary. I mean to really put it in plain language. I mean, they're scary for patients, they're scary for us. But if you just go through the data and be reassuring, you know, let them know this is a possibility. I tell them in my experience I have seen or I haven't seen. I think that goes a long way as well. |

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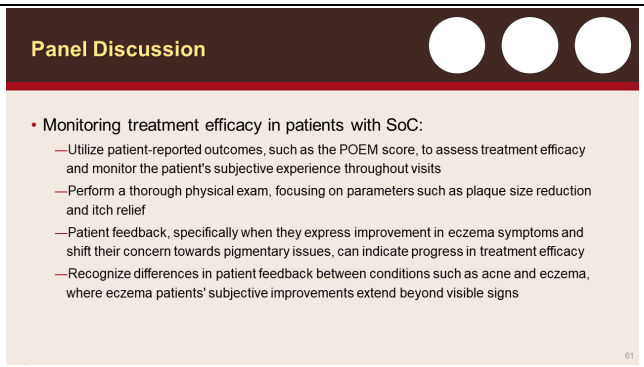
| 60. |  | And you know, this touches a little bit upon some of the, you know, the last discussion we had. And you know, once we make that decision, you know, that shared decision and patients go on to therapy. What are some of the things that you look for, particularly for just monitoring treatment effectiveness, and really considering those unique skin of color presentations?<br>So, I mentioned this earlier, but I really like patient-reported outcomes. So, I actually give that POEM score multiple times–at baseline and throughout the visit. So, I see on the second visit, the third visit, the fourth visit, that same patient-reported outcome can be done with the POEM score. That's one easy way, even before I walk into the room to know how they're doing on this condition. But you're also monitoring for the atopic dermatitis itself. Like, are their plaques decreasing in size? Are they having less itch? How is it impacting their quality of life? So really asking those questions from those patients and doing a very thorough physical exam can really help you get a better idea of how things are working. And once, and sometimes the easiest way to find out if things are working, is when a patient says, “Hey, my eczema was better—help with the darkness.” That's always a good sign. That means the eczema is almost on the back burner. Now they're focusing on pigment, so that really lets me know that we've done a lot of great service for this patient and now we're just trying to treat the pigmentary abnormality, which isn't easy, but at least we know that we're moving to a different phase of treatment.<br>Yeah, 100%. I'll see my acne patients back and they'll go “I'm no better.” And you look and there [are] no papules, you know, or comedones, but with your eczema patients, they'll say “Oh, I'm better” because their itch is better, they're sleeping, saying they're not as uncomfortable. So just apples and oranges between those two disorders.<br>Excellent points and thank you for that wonderful discussion. |

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| 61. |  | I'd like to once again thank my co-presenters really for just outstanding presentations and discussion. And I'd like to thank the audience for their participation. |