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Perspectives on Psoriatic Disease & Atopic Dermatitis: The Evolving Treatment Landscapes

Announcer

Welcome to CME on ReachMD! This activity, Perspectives on Psoriatic Disease & Atopic Dermatitis: The Evolving Treatment Landscapes, is provided by Forefront Collaborative in collaboration with Interstate Postgraduate Medical Association and is supported by an educational grant from Lilly.

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Dr. Russell: As the treatment options for psoriatic diseases and atopic dermatitis continue to expand, it's becoming more and more important for clinicians to understand what the available treatment options are and how to use them appropriately. Especially since psoriasis and atopic dermatitis are two of the most common immune-mediated diseases. This is CME on Reach MD, and I'm Dr. John Russell. Joining me to help address the treatment landscape for psoriasis, psoriatic arthritis and atopic dermatitis, as well as shared decision making strategies is Dr. April Armstrong. Not only is she a Professor of Dermatology and Associate Dean at the University of Southern California, but Dr. Armstrong is also a clinician researcher, where she specializes in caring for patients with inflammatory skin diseases. So, Dr. Armstrong, thanks so much for being with us today.

Dr. Armstrong: Thank you for having me.

Dr. Russell: And, later on, we will also have with us, Heather, who will be sharing her perspective of what it's like to live with psoriasis and psoriatic arthritis. But before we hear her story, I'd like to start with you, Dr. Armstrong. So, could you provide us with an overview of how to evaluate patients with psoriasis and psoriatic arthritis for different treatment strategies?

Dr. Armstrong: Sure. Clinically, it's very important to evaluate the severity of psoriasis. We often times use a body surface area, or BSA, as a measure of psoriasis severity, as well as looking at the morphology of the skin lesions, and these include thickness, scaling, erythema, and et cetera. The National Psoriasis Foundation, or NPF, recommends consideration of mild psoriasis as less than 3% body surface area, moderate as 3 to 10%, and severe as greater than 10%. Often times for patients with facial, palmoplantar, and genital involvement, even though the area of involvement may be small, this can be disproportionately impactful for a patient, and so it's important to note that severity solely based on body surface area may not apply in these situations where patients have involvement in a sensitive area. For those with mild psoriasis, we typically consider the use of topical therapies and/or targeted phototherapy, and for those with moderate to severe psoriasis, we want to consider choosing a biologic, oral medications, or phototherapy. And in patients with psoriasis and psoriatic arthritis, often times their psoriatic arthritis will be the first consideration that will drive the ultimate treatment plan for such a patient. Dr. Russell

Dr. Russell: So, Dr. Armstrong, you just mentioned three different treatment options – biologics, oral medicines, or phototherapies – for those with moderate to severe psoriasis. Could you expand on those options?

Dr. Armstrong: Of course, so the biologics, oral medications, and phototherapies are often times considered concurrently for patients with moderate to severe psoriasis, and these days, biologics are used probably most frequently for those with moderate to severe psoriasis. And the reason being that biologics can be administered at home. Most of them are injected subcutaneously by our patients

themselves, and, on average, biologics' onset of action is a bit faster and their efficacy generally higher than phototherapy or oral medication. However, we also don't want to forget about our oral choices. For the oral options, we have apremilast, which is a PDE4 inhibitor. We also have methotrexate, cyclosporin, and acitretin. With the exception of cyclosporin, most oral options for psoriasis have a little slower onset of action compared to the biologics, and their long-term efficacy is a bit modest in comparison as well at the typically used doses. Cyclosporin is a bit of an exception because it can lead to rather quick reduction in psoriasis severity; however, we typically don't use cyclosporin for a long period of time. We often use it for a month or two months, at the most three months at a time. The reason is because long-term cyclosporin use can be associated with nephrotoxicity. Phototherapy is one of our oldest treatments for psoriasis, and these days, we use mostly narrow band UVB phototherapy, and usually patients receive 2 to 3 times per week of phototherapy, and we expect to see improvement after about three months or so. Because most phototherapy is still administered within the dermatologist's office, patients do need to go to the office to receive phototherapy, and that can be a challenge for many patients who need to go to work during the day or have other commitments.

Dr. Russell: So, Dr. Armstrong, earlier you mentioned that a patient with psoriatic arthritis kind of changes a little bit how you look at it, so how do you approach that patient who has psoriasis and psoriatic arthritis?

Dr. Armstrong: Dr. Russell, that's a great question. So, for a patient who comes in with psoriasis alone, for example, we actually screen every patient for psoriatic arthritis at every visit. And when we evaluate such a patient, often times we ask a few questions. So, in my clinic, I almost always ask two questions. One is, have you had painful or swollen joints, and number two is do you feel stiffness in your joints when you wake up? These two questions, I found in speaking with a rheumatologist, often times are helpful in terms of not diagnosing but screening patients for PsA. That is, will they have a higher likelihood of psoriatic arthritis? If they have stiffness in their joints for greater than 30 minutes or 40 minutes in the morning, and if their stiffness gets better with activity, that's more suggestive of needing to work this patient up for psoriatic arthritis. And the reason why we want to screen our patients at every visit is because about 30% of our patients will have psoriatic arthritis, at some point, among the psoriasis population and, very importantly, if a patient with psoriasis has active psoriatic arthritis, it doesn't really matter if they have just 1% body surface area, they may actually need a systemic medication, such as a biologic, in order to treat their active psoriatic arthritis and their psoriasis.

Dr. Russell: So, certainly as clinicians, we want to individualize care for our patients. And biologics seem to be a mainstream option for patients with moderate to severe psoriasis, so how do you figure out who might be a good candidate for biologic therapy, and are there guidelines from the American Academy of Dermatology or the National Psoriasis Foundation that help you make that decision?

Dr. Armstrong: The guidelines from the American Academy of Dermatology and the National Psoriasis Foundation, or AAD and NPF for short, encourage clinicians to consider biologics as among the first-line treatments for patients with moderate to severe psoriasis. This is actually a departure from the traditional notion from about a decade ago now, where patients needed to go through step-therapy, where they needed to try phototherapy first, then oral therapy, and then biologics, and that's why we do have so many options for biologics. And people, and clinicians included, just didn't understand biologics as well. So, I would say times have really changed and, obviously, before starting any biologic, we want to check to make sure that patient's certain baseline labs are normal.

Dr. Russell: So, you talked about checking labs – what do the guidelines from the AAD and the NPF say about checking labs at baseline and then ongoing in care for the patients?

Dr. Armstrong: The AAD and NPF guidelines recommend the following baseline labs for patients when we are starting them on biologics, and I would say that baseline labs are different from the labs that they recommend to check annually thereafter. So, at baseline, we should check a complete blood count, or CBC with differential, complete metabolic panel, tuberculosis testing, hepatitis B and C serology, HIV testing if the risk factors exist. And then for ongoing assessment of patients on biologics, the AAD and NPF guidelines recommend the following: The patient should be seen at quarterly or every six-month intervals, depending on their treatment response, and the patient should be assessed for infection, screened for skin cancers, and, importantly, have yearly testing for TB, if they're at risk. The guidelines specifically state that CBC with differential and CMP are actually not supported by evidence and are to be assessed at the discretion of each clinician's criteria, except if the patients are being treated with infliximab. For those on infliximab, guidelines recommend that liver function tests be repeated every three months after initiation, and if the results are normal, then every 6 to 12 months thereafter.

Dr. Russell: So, the TNF inhibitors have been around for awhile now. Can you tell me a little bit about their role in treating patients with psoriasis and psoriatic arthritis?

Dr. Armstrong: Absolutely, Dr. Russell. The TNF inhibitors that are used to treat psoriasis and psoriatic arthritis include etanercept, infliximab, adalimumab, and certolizumab. These four TNF inhibitors are approved for both psoriasis and psoriatic arthritis. Their efficacy for psoriasis is good, though not the top, though we do understand their safety profile quite well because they've been around for a while. Of note, etanercept is also approved in the pediatric and adolescent populations with psoriasis. For certolizumab, as far as we

know, it does not cross the placental barrier, and can be used throughout pregnancy. And certolizumab is also not detected in the breast milk. So, as you can see, it's a good option for patients who are pregnant and who are breastfeeding. It's important to know that for our patients with psoriasis and psoriatic arthritis, that TNF inhibitors treat psoriatic arthritis quite well. It's been shown to have high efficacy in terms of reducing the signs and symptoms of psoriatic arthritis. Now, let me just discuss adverse effect profile for patients on TNF inhibitors. So when we look at just the psoriatic arthritis population and the psoriasis population alone for the use of TNF inhibitors, what we found is that within that population there has been no increased risk of internal malignancies or serious infections associated with the TNF inhibitors that I've talked about. It is really important, in my opinion, to really interpret malignancy risk in the context of just the psoriatic disease population and be aware that some of the labeling that we see on the package inserts may not specifically pertain to this particular population. It is important to check for TB and hepatitis B for patients with psoriasis and psoriatic arthritis on TNF inhibitors and, importantly, TNF inhibitors are not suitable for those who have advanced congestive heart failure, hepatitis B, and demyelinating diseases.

Dr. Russell: So, Dr. Armstrong, how about the IL-12/23 inhibitors.

Dr. Armstrong: So, for the treatment of psoriasis, we have one agent that blocks both IL-12 and 23, and that is ustekinumab, and it is indicated for both psoriasis and psoriatic arthritis. Ustekinumab is a weight-based dosed drug and it is administered once every three months during maintenance phase. Importantly – it's important to know that it's approved not only just for adults, but also for adolescents 12 years and older. So, when we think about ustekinumab, about 70% of patients achieve PASI-75, or at least 75% improvement in their psoriasis severity at week 12. So, again, that's about 70% of the patients who will get at least 75% better by week 12, and the long-term safety record is also quite good for ustekinumab.

Dr. Russell: So, what are your thoughts about the IL-17 class of medications for psoriasis and psoriatic arthritis?

Dr. Armstrong: At the current time, we have three approved medications for psoriasis through the IL-17 class, and they are secukinumab, ixekizumab, and brodalumab. Of those three, secukinumab and ixekizumab are also approved for psoriatic arthritis. There are some mechanistic differences among those three medications. For example, secukinumab and ixekizumab block IL-17A, while brodalumab is a receptor blocker so it blocks IL-17 receptor alpha. So, overall, the IL-17 class of agents have rapid onset of action so our patients can actually see substantive difference in living even the first 2-3 weeks. The efficacy for this class overall is also quite robust with ixekizumab and brodalumab having up to about 90% of patients achieving PASI-75 by week 12. The safety record has also been reassuring for the IL-17 class. There is no increased risk of malignancy or serious infections that have been reported to be associated with IL-17 class; however, we do note that some patients with a personal history of inflammatory bowel disease – not all of them, but some of them – may experience exacerbation with these medications. So, we want to exercise caution in that particular patient population. In those patients when we have psoriasis and inflammatory bowel disease, TNF inhibitor or ixekizumab may be good options since they are indicated for both psoriasis as well as IBD.

Dr. Russell: So, Dr. Armstrong, you talked about a lot of treatment options including the TNF inhibitors in treating psoriatic diseases, but now I'd like you to focus on the IL-23 inhibitors, which are the newest class of biologics for psoriasis. So, how are they different?

Dr. Armstrong: The IL-23 class of inhibitors are different in terms of their mechanisms as well as their efficacy and safety profiles. The IL-23 inhibitors, as the name suggests, first they inhibit IL-23, which is considered a master regulator in the psoriasis pathogenesis, and also one unique feature about IL-23 inhibitors is their dosing frequency. They can often times be dosed infrequently. For example, guselkumab is dosed every eight weeks, tildrakizumab is dosed every 12 weeks, and risankizumab is also dosed every 12 weeks. So, overall, the IL-23 class of medications has a robust efficacy profile and guselkumab and risankizumab, especially, have very robust efficacy. All three of these IL-23 inhibitors have good maintenance of effect also over time among the responders. And this is important because psoriasis is a long-term disease and it's important that the medication is able to maintain their efficacy over time. At this time, I shall mention the IL-23 inhibitors are not yet approved for psoriatic arthritis but, overall, this class of biologics, IL-23 inhibitors, have a good safety profile at this time. They are not known to be associated with increased risk of malignancy or serious infections. They also are not associated with exacerbations of inflammatory bowel disease and warning labels for those with mental disorders.

Dr. Russell: For those who are just joining us, this is CME and Reach MD. I'm Dr. John Russell. Today, I'm speaking with Dr. April Armstrong about the treatment landscape for psoriatic diseases, and for our next part of our program, we're going to be speaking with Heather, a patient with psoriasis and psoriatic arthritis, to hear about her experience. Thanks so much for being with us today, Heather.

Heather: Of course. I'm glad to be here.

Dr. Russell: So, could you tell us how psoriasis and psoriatic arthritis have affected your life?

Heather: Well, sure. So, it's been a little bit of a progression for me, both in the way that I think about psoriasis and psoriatic arthritis, but also in the way that it's affected my life. So, when I was initially diagnosed with psoriasis, I was much younger. I was in my 20s, my

early 30s, and I was way more concerned, than anything else, with the way that my skin looked. Right? So, I was very self-conscious. I was always concerned about buying clothes that would cover up my psoriasis so that I didn't have to answer a lot of questions, and I didn't have people asking me all the time if it was something that they could catch. But, as I've gotten older, I've become less concerned about what people think, which, you know, obviously not everybody is like that, but I've become less concerned about it, and so now I buy clothes that are softer so that they don't scratch against my skin and I'm not as worried about the fact that people can see it – aside from the fact that it's really embarrassing that I get a lot of flakes from my scalp a lot. You know, but the other thing that's kind of changed is that I was diagnosed with psoriatic arthritis and that has impacted my life a lot more, which is part of why my skin doesn't bother me as much. So, you know, I have a lot of stiffness in the morning when I first get up, so I walk like I'm 30 or 40 years older than I actually am, and in addition I have a lot of pain in my shoulders and in my hands, and so it makes it difficult because I have two young kids and so there are times that it makes it hard to pick them up or to do crafts with them, do activities with them, and then, on top of it, I work full time and that pain also makes it difficult to do my job sometimes. Right? It makes it hard to type. It makes it hard to take notes. So, it's definitely been a progression for me.

Dr. Russell: So, Heather, what has your journey been like with different healthcare providers and treatments?

Heather: Well, so I've actually ended up having to see a number of providers over the years, and I've had really varying results with that. So, early on, when I was going to see primarily dermatologists to get treatment for my psoriasis, I ran into a lot of issues where they wanted to treat other conditions, like acne, when I was really there to have my psoriasis treated. And so, I've shopped around for doctors quite a bit, and you know, until I've landed on the combination that has worked for me. And I think the three things – there's really three things that I have decided that I care the most about when I'm looking for doctors to treat my psoriasis and my psoriatic arthritis. So one is that they really have a good understanding of the disease. It's important to me that they know the symptoms of both psoriasis and psoriatic arthritis so that when I come in with a new complaint, they can easily tell me if it's something that's just related to the conditions that I already have, or if it's something else that I need to investigate, and part of that is that – is my second thing, which is they have a really good understanding of the many treatment options that are available. You know, I think it's really easy just to say, here use topical medication, but for some patients, I don't think that's the right answer, and I think that's been one of the things for me is that I want to be more aggressive, but I also want something that's going to work with my lifestyle, and so having a doctor who can walk me through all the various things that are options for me is really important. And then the third part is that I really want someone who is going to be able to look at the whole holistic picture and work with my other doctors, so going to see a dermatologist and a rheumatologist, and other doctors, there's something that's bound to be lost in translation if I'm the one who is having to communicate everything. So, having those open lines of communication about what my treatment is, what other things might be coming up, and all of that, is really important to me and so it's been wonderful that I've been able to find that now, but it took me years of trying to get to that point.

Dr. Russell: So, thanks so much for sharing your story, Heather, and turning to you now, Dr. Armstrong, what can you tell us about the treatment landscape for atopic dermatitis?

Dr. Armstrong: Well, before I answer this question, I just really wanted to thank Heather for being with us today. Your insights and your willingness to share your journey with us is going to be really helpful for all of us who treat psoriasis and psoriatic arthritis. So, Dr. Russell, the treatment landscape for atopic dermatitis is rapidly changing and it's very exciting. It used to be that we didn't have good treatment options for patients with moderate to severe atopic dermatitis and, in fact, it can be a little bit demoralizing as clinicians when we have these patients coming to our clinic and feel like we don't have good, safe options for them. But several years ago, the FDA approved the first biologic for moderate to severe atopic dermatitis, and that has really changed the landscape for atopic dermatitis. But perhaps, let me take a step back – so, for patients with AD, they can present with different severities of AD. Those with limited atopic dermatitis, topical management is still the cornerstone. We rely on the various strengths of topical steroids, topical calcineurin inhibitors such as tacrolimus or pimecrolimus, as well as a topical PDE4 inhibitor to manage these mild cases. For those with more moderate to severe AD, we used to rely on either short courses of systemic steroids or oral agents that may have unfavorable side effect profiles when used long term, and so the traditional oral agents have included cyclosporin, methotrexate, azathioprine and mycophenolate mofetil. I would say that most traditional oral medications can be associated with significant side effects in some patients when they are used over a long period of time.

Dr. Russell: So, you mentioned biologic options for atopic dermatitis. What therapies are available for our patients?

Dr. Armstrong: Dr. Russell, in atopic dermatitis, we currently have one biologic that's approved to treat moderate to severe AD, and that is dupilumab. Dupilumab inhibits the actions of IL-4 and IL-13 by specifically blocking the IL-4 receptor alpha. Dupilumab is approved for patients who are 12 years and older, so it's approved for both the adolescent population as well as adults. In adults, approximately 38% of patients achieve clear or almost clear skin by week 16, compared to 10% for the placebo. And in adolescents, it's about a quarter of

patients who achieve clear or almost clear skin. Clinically, this has really been a game changer for our patients.

Dr. Russell: On that note, I'd like to thank Dr. April Armstrong for breaking down all of the treatment options for us, and especially you, Heather, for sharing your experience with psoriasis and psoriatic arthritis with our audience today. It was great speaking with both of you today.

Heather: Thank you for having me.

Dr. Armstrong: Thank you, Dr. Russell.

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