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Advances in Treatment of Moderate to Severe Psoriasis

Narrator:
Welcome to CME on ReachMD. This activity, Advances in Treatment of Moderate to Severe Psoriasis, is provided by Forefront Collaborative, and supported by an educational grant from Lilly. This activity focuses on new developments in treatment of psoriasis and monitoring of therapeutic outcomes in patients with psoriasis. The target audience for this activity is dermatologists. Other healthcare professionals, including rheumatologists, physician assistants, and nurse practitioners who treat patients with psoriasis, may also benefit from participation. Your host is Dr. John J. Russell. Dr. Russell will speak with Dr. Neil Korman, Director of Clinical Trials and Clinical Director of the Murdough Family Center for Psoriasis at University Hospitals Cleveland Medical Center. Dr. Korman will be discussing how improved understanding of psoriasis pathogenesis leads to development of new treatments and the treat-to-target concept. Also joining us is Dr. Linda Stein Gold, Director of Dermatology Clinical Research and Division Head of Dermatology at Henry Ford Health System in Detroit and West Bloomfield, Michigan. Dr. Stein Gold will be discussing practical considerations for choosing a biologic agent and monitoring for adverse reactions in psoriasis patients receiving biologic therapy.

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Dr. Russell:
Over the past two decades, research has uncovered new data on the physiopathology of psoriasis, opening doors to a host of novel therapeutic treatments. Near-complete skin clearance with minimal side effects is now a realistic treatment goal for many people living with psoriasis; yet, some patients with psoriasis receive inadequate treatment and achieve less-than-optimized therapeutic outcomes. The discussion today will address the complex decisions regarding selecting, monitoring, and modifying systemic treatments for moderate to severe psoriasis. Dr. Korman, Dr. Stein Gold, welcome to the program.

Dr. Stein Gold:
It's a pleasure to be here, thank you.

Dr. Korman:
Thanks very much for having me; looking forward to it.

Dr. Russell:
So, Dr. Korman—how has the treatment of a patient with moderate to severe psoriasis evolved, and what considerations are important prior to the initiation of any systemic therapy in these patients?

Dr. Korman:
So, if you go back to, back in the day, prior to when we had biologics, the treatment of patients with moderate to severe psoriasis was really a very challenging process since there was a lot of toxicity with all of our systemic therapies that we had. And often what was necessary was the use of rotational therapy during which the patient would be given drug A for a finite period of time, and then that

agent would be stopped before too much toxicity developed, and then a different agent would be started. And then the same scenario would occur with that patient, and then we would stop that for a period of time, and, perhaps, go to another agent. And the worry with all of these things was organ system toxicity. So, this was what we called rotational therapy, and it was really considered the state-of-the-art, unfortunately. But where we are now, today, with the current availability of 6 targeted biologics, this approach is absolutely completely obsolete. Both the American Academy of Dermatology, as well as the National Psoriasis Foundation, support the use of biologic agents as the first line for the treatment of patients with moderate to severe psoriasis, and this is really totally accepted now as the standard of care.

There are several important issues that we need to think about when we're treating patients with moderate to severe disease before initiating a systemic therapy. Probably the most important of all is to try to determine whether or not the patient might have psoriatic arthritis, as that would change how we would approach things. We'd certainly want to assess for tuberculosis with appropriate testing, assess for underlying risk of cancer or history of cancer or family history of cancer, assess for a history of demyelinating disease with multiple sclerosis being the prototypic disease. We'd certainly want to verify the patient didn't have any current or chronic infection at the time of initiation of therapy, particularly in line with screening for hepatitis B and C and for HIV. And, we'd certainly want to think about completing all of the age-appropriate immunizations before starting on a systemic biologic therapy. Some of the issues, specific issues, with that would be that in patients that we are thinking about putting a TNF inhibitor on, we'd want to be worried about congestive heart failure and multiple sclerosis. And, for patients that we're thinking about treating with an IL-17 inhibitor, we'd certainly want to think about inflammatory bowel disease and be cautious about patients who have Crohn's or ulcerative colitis.

Dr. Russell:
Dr. Stein Gold, is there anything else you'd like to add about this evolution of treatment for moderate to severe psoriasis?

Dr. Stein Gold:
Well, I really agree with Dr. Korman. The life of a psoriasis patient has just dramatically changed since I was a resident. When I was a resident, we used to have an inpatient service that would have a lot of psoriasis patients that actually had to be hospitalized for weeks or even months at a time to try to get their skin under control. And now, I'll tell you, although it does happen with maybe an erythroderma patient, it's very rare to have a psoriasis patient that needs to be admitted to the hospital. We're now able to look at psoriasis as a systemic inflammatory disease. We understand it has a lot of comorbidities. We're not just treating the skin a lot of times; we're treating the patient as a whole. And, as Dr. Korman mentioned, we're able to get these patients under control much more quickly and much more completely, I think, than we ever dreamed, maybe 20 years ago. So, it's an exciting time.

Dr. Russell:
So, Dr. Korman, with the improved understanding of psoriasis pathogenesis, what are the most important pathways that have been recently targeted, and what are some of the newer pathways to be targeted that are on the horizon, and what are some of the results of the comparator biologic trials?

Dr. Korman:
So, as Dr. Stein Gold said, we really are in a very exciting time. There are currently 3 biologic classes that are available and approved for the treatment of patients with moderate to severe psoriasis. The first group is the tumor necrosis factor inhibitors, and they include etanercept, adalimumab, and infliximab. The next group is the single IL-12/23 antagonist, ustekinumab. And then the last group is the IL-17 antagonist, which includes secukinumab, ixekizumab, and most recently approval of brodalumab. There are also 3 different IL-23 agents that are in late-stage clinical trials: guselkumab, tildrakizumab, and risankizumab. There are also short-term clinical trials of ustekinumab, secukinumab, and ixekizumab, which, when compared to etanercept, demonstrated that all 3 of these agents had superior efficacy. In addition, there are clinical trials, short-term, demonstrating that secukinumab, ixekizumab, and brodalumab all have superior efficacy to ustekinumab. And, finally, the IL-23 inhibitor, guselkumab, has been compared to adalimumab and shown to have superior efficacy in those clinical trials. So, really, we have a lot of new pathways, and we have a lot of comparative therapies, and each therapy seems to be getting better than the one before it. So, the TNF inhibitors were no slouch in terms of therapy. And then the IL-12/23 inhibitor was perhaps a little bit better than the TNF inhibitors. And now we have the IL-17 pathway that seems to be perhaps even better than the other 2 classes, and we have the IL-23 class that we don't have yet all the data on, so we have a little more time to see how well that will work.

Dr. Russell:
So, Dr. Korman, the concept of a treat-to-target—I think we've seen in hypertension and hyperlipidemia—what does that mean in the management of patients with moderate to severe psoriasis?

Dr. Korman:
Well, I think that the concept really comes from the availability now of so many different therapies that we're starting to see 90% of

patients that can be controlled at a high level with the best agents, and as many as 40% of patients that can be 100% controlled with the newest agents. So, there really has not been any consensus in the United States for treatment goals when managing patients with moderate to severe psoriasis. But I think this is a very important effort because without treatment goals, clinicians and patients have no real defined targets during the treatment course, and there's a lot of variability in treatment expectations and quality of care. The recommendation of treat-to-target is derived from the National Psoriasis Foundation. It was published last year. And at 3 months after starting a new systemic treatment for patients with moderate to severe psoriasis, we consider an acceptable response either a body surface area of 3% or less, or a body surface area improvement of 75% or more from the baseline. The target response at 3 months after starting should be 1%, but it will be happy, shall we say, with an acceptable response of 3% or less. And then during maintenance, which is typically considered every 6 months, we would prefer to see a target response that is 1% or less. So, really, what the concept of treat-to-target is, is an aspirational goal. It's not like a patient at 3 months, if they haven't reached 30% body surface area, that we should absolutely stop that agent, because if it's helped them enormously, it might be very reasonable. And it's not for the patient at 1 year who hasn't reached 1%, that we must stop the therapy. I think the reason for treat-to-target is because we now have great agents out there and we certainly want to teach patients, as well as physicians, dermatologists, that there are some amazing therapies that are available, and we can reach some really, really, really high bars in efficacy of these patients.

Dr. Russell:
Dr. Stein Gold, do you have anything else to add to this discussion?

Dr. Stein Gold:
Well, I agree with Dr. Korman. We have some agents now that actually open the expectation, and we can actually get a patient, potentially, to clear or almost-clear skin—and that can occur fairly rapidly. And I think this is a lofty goal to expect to get, potentially, to 1% body surface area or less after 3 months. It's a great goal, but it's not an absolute. And this is really a discussion between the patient and the physician. For some patients, they might have really bad arthritis and their arthritis is great, but maybe they still have some difficult plaques on their knees or elbows, or maybe a little bit on their hands, wherever, and they're happy. They're okay with it. And so, I think while it's a good goal to reach towards, it's not necessarily going to be appropriate for every single patient. We have to look at each patient, figure out what their particular goals are, what our goals are for them, and kind of come to a meeting of the minds. But, luckily, we have drugs that actually allow us now to really anticipate getting our patients to this particular goal.

Dr. Russell:
If you're just tuning in, you're listening to CME on ReachMD. I'm your host, Dr. John Russell. Today, I'm speaking with Dr. Neil Korman and Dr. Linda Stein Gold. Next, Dr. Stein Gold will continue our discussion of Advances and Treatment of Moderate to Severe Psoriasis. So, Dr. Stein Gold, both you and Dr. Korman have echoed all these great choices that you now have. So, how do you choose which biologic to prescribe in that patient who has extensive psoriasis?

Dr. Stein Gold:
And, luckily, we do have a lot of choices. And so, if a new patient walks into my office with fairly extensive disease—and that means disease probably 10% or greater, or maybe affecting sensitive areas like the palms or soles—first question I ask, similar to what Dr. Korman mentioned is, I try to figure out whether or not they have psoriatic arthritis. And I know some dermatologists are comfortable doing this themselves; others feel more comfortable involving the consultation of a rheumatologist. So, if a patient is complaining of some joint symptoms, that's something that needs to be investigated. I'll tell you, just because a patient has psoriasis doesn't mean that they can't have osteoarthritis. So, it's important to kind of figure that out. If the patient does have psoriatic arthritis, I think it's important to use a drug that treats both the psoriasis and the psoriatic arthritis. And we have that—we have a number of options available with the TNF inhibitors; ustekinumab and secukinumab are all approved. Apremilast, which is a small module, an oral agent, is also approved for not only plaque psoriasis, but also psoriatic arthritis. And it's an easy drug to use, but the efficacy results really don't come close to our newer biologic agents. So, although it's a choice, if somebody comes in with really bad psoriasis including psoriatic arthritis, I'll probably go to one of the other biologic agents. And then, as was mentioned, we have to figure out the health of the patient overall. Do they have other comorbidities that might exclude one agent or another? And, as was mentioned, if this patient has heart failure or a demyelinating disease, a TNF inhibitor wouldn't be a top choice. Also, if somebody has a history of inflammatory bowel disease, although the IL-17 drugs are not completely contraindicated, again, they probably wouldn't be a first choice. And then, other things to consider—say you have a college student who's going off to school and they don't want to get injections frequently, and they want to kind of forget about their treatments as much as possible, I might then use a drug with infrequent dosing like ustekinumab because it's dosed every 3 months. So, a lot goes into it. It's really a discussion between what the patient's expectations are, and what the options are for that particular patient. And, although we start out with good intentions, sometimes every drug does not work with every patient, and sometimes we do have to switch. And we can't necessarily predict who's going to do well on what drug, but luckily we know that if they fail one, there's a good likelihood that they're still going to respond to others.

Dr. Russell:
Dr. Korman, do you have anything else to add regarding choosing a biologic agent?

Dr. Korman:
Well, I certainly agree. It's very important to try to get a sense of their expectations and their fear factors too. So, sometimes people—they don't want the latest and the greatest. They want ones that have been around longer. They want a drug that they can be comfortable with and that they know their mother-in-law or their cousin took, and that it's been around for 10 years. And so, there are a lot of factors. You sort of have to weigh the flavor in the room to try to understand the patient better. And, I think with a lot of experience, it's relatively easy to do. And then there's the elephant in the room. Besides weighing the flavor in the room, you have to weigh the elephant in the room. The elephant in the room is the insurance company. So, it's very important that we don't overpromise to the patients what will or won't be approved. And some of the insurance companies, unfortunately, have plans, and they have their own ideas of what we may or may not be able to give any particular patient on any particular day. So, I certainly take into account what the patient wants, how severe their disease is, what their comorbidities are, what their expectations are, try to establish all those things up front, and then, I say, "Okay, well let's see, I think we've chosen this, and this sounds reasonable. Let's see if that will fly with your insurance company." And sometimes some things can fly much faster than others, and people are desperate to get started at a faster pace, and so, they don't want to wait around. So, those are all the factors that I consider.

Dr. Russell:
So, Dr. Stein Gold, when you're using these particular new biologic agents, are there some monitoring guidelines you use in your practice?

Dr. Stein Gold:
Believe it or not, there's actually no specific recommendations for the use of the biologic agents. But I think there's some consensus that a lot of dermatologists go by—especially when you're going to start a patient on a systemic medication—and the plan is to keep these patients on the medication for the long term. In general, before I start a systemic agent or biologic, I want to understand what's my baseline patient look like. Sometimes they haven't seen a doctor for a while, so they don't even know if they have any underlying illness. So, I think it's a good idea just to get a good baseline. With any of these agents, it's a great idea to check a TB at baseline, and then yearly, for really any agent that could potentially suppress the immune system. Often, I'll get a baseline CBC; I'll look at the metabolic profile; and it's also important to assess their hepatitis status. And HIV screening at baseline is not a bad thing to do as well. Now, in terms of what do you do over the long term? Well, if you ask a lot of dermatologists, you're going to get a lot of different answers. And I don't think there's any one consensus, but people often will want to just get a gauge on how patients are doing. Obviously, because these potentially can affect the immune system, you want to monitor for any type of infection, and you would do this at each visit. Ask if they've had any fevers or open sores or anything else. One might want to hold dosing if somebody has a significant infection. That's something that I would consider if they have to go on antibiotics. Obviously, if they're hospitalized for an infection, you might want to hold the biologic agent for some of the drugs. You also want to potentially monitor the IL-17 drugs. Because of their mechanism of action, there is a slightly increased risk of candidal infections. So that's something you would potentially want to ask about. Obviously, signs of malignancy over the course of time; if somebody has weight loss or just is feeling ill and weak; you might want to assess that a little more closely. In terms of monitoring the hematologic effects, some of the IL-17 drugs have had a very rare incidence of neutropenia. So, it's something that you might want to check out periodically, just to check the CBC. If you're using one of the TNF inhibitors, obviously, you're going to ask about signs of congestive heart failure. You're going to ask about any neurologic effects. And, as I mentioned earlier, inflammatory bowel disease is not an absolute contraindication, but you're going to want to ask about any new-onset GI symptoms if the patient is on an IL-17 agent. And, basically, just kind of remind patients they don't want to get live vaccine while they're on any agent that suppresses the immune system. And I think it's a good idea to keep in touch with the patient, and generally I'll do some lab monitoring, maybe at baseline, 6 months, and usually at least once a year.

Dr. Russell:
So, Dr. Korman, as a primary care doctor, one of our biggest questions with all these new medicines is, can I give my patient a flu shot?

Dr. Korman:
Well, I mean, that's a very important clinical question, and there's not a whole lot of data to really answer it from the clinical trials. But, you certainly don't ever want to give a live vaccine to any patient on a biologic; that is absolutely forbidden. But in terms of the killed vaccines, the injectable killed vaccines, I think, are absolutely very reasonable to give to patients. I do it all the time in my practice. I've never seen a problem. The data doesn't— they didn't look at it, so we don't know the answer to it. But I don't think you're at any risk of anything bad happening. It's possible that patients might not have the same level of immune response to a killed vaccine while they're on a biologic agent, and that's a risk you're going to take. It's possible that it won't work as well, but I don't think that's a whole lot of risk, so I absolutely do it routinely with all of my patients and I've seen no ill effect.

Dr. Russell:
That's terrific. Thank you. So doctors, I'd like to bring you both in for a larger discussion on psoriasis treatment. So, how do you, kind of, explain this target for patients? You're going to start patients on this. What do you tell them is this expectation that they're going to be having?

Dr. Korman:
So, what I do with patients, I see them, we talk, I examine them, we discuss things, I try to get a sense of what their expectations are, and I try to under-promise and over-deliver, for starters. So, you don't want to—or I certainly don't; this is a style thing, so it'd be interesting to hear what Dr. Stein Gold, how she handles this—but, I don't tell people, "Hey, there are some amazing drugs that we can maybe make your psoriasis go away." Especially not the first time because then you overbuild up their confidence. But, I do say things like, "Well, you have a lot of disease and I'm hopeful that we'll be able to find a way to make you significantly better," without over-promising. So, to treat to target, I don't use those words at all with the patient. I just talk about, "We're going to get you better. This is unacceptable." And many times, it's somebody who's already had disease for a long time, and they've been treated by whoever, and they're not very much better. And they still have a lot of psoriasis. I explain to them that I don't think where they are is good enough, and I would like to do more. In the past, I used to kind of leave people alone and say, "Alright, well you're happy with it, I'm happy." Not anymore. There are too many great drugs out there that we can almost always make people much better than they are with appropriate use of the appropriate agent.

Dr. Stein Gold:
I agree, Neil. I really try to under-promise, and I put it in a way that makes it a little more understandable. For instance, I'll say, "I want you to be able to wear shorts this summer. I want you to be able to put on a bathing suit and go to the pool with your kids, and not be embarrassed." And those are things for some of our psoriasis patients that they have not experienced in years. And, as you mentioned, a lot of them have been treated suboptimally for many, many, many, many years, and really haven't come to expect much more than that. So, I think, letting them know that they can have that next level of clearance and efficacy is important; but tell them, you know, this is a journey between the two of us. Not every drug works for every patient and it might take a little bit of discovering what's going to be best for that particular patient, but we'll get there.

Dr. Russell:
So, we always try to individualize care for our patients, and I'm certainly—with psoriasis, there must be some gray zones that you guys have in your practices. And what are some of the questions that you wish were answered in the research that aren't available quite yet?

Dr. Korman:
The most important question is the simplest one: What's the right agent for each patient? When can we really individualize? When will we have personalized medicine applied to psoriasis care? You turn on the television, you see all these ads for all these drugs, but which one do you pick? And we talked about this already. I pick the one that I think the patient doesn't have any contraindications or comorbidities that make that one a problem. And I pick the one that they're willing to take, and we talk about injections and how often it is. And I pick the one that hopefully their insurance will pay for. But what about if I could just take a swab of their cheek or I could get a drop of blood and put it on a slide and be able to say, "Ah, you have a 96% chance of this agent being the one that's going to make you a ton better." That's, to me, the question that I wish was answered by research to guide my day-to-day patient care.

Dr. Stein Gold:
And it's true, because we know that although the drugs work really, really well, they work differently in different people. And we haven't been able to pin that down yet. You can have two people who look exactly the same, the same amount of psoriasis, and you can give them exactly the same drug, and one person might get 90% clear and the other one might get barely, barely 50% clear. So, it would save a lot of time and money and energy if we could understand upfront how to make that best decision.

Dr. Russell:
So, as a clinician who's not intimately knowledgeable about all the new psoriasis literature, is there a study that each of you is kind of most excited about that's come out in the last year?

Dr. Korman:
That's a tough one. I think the studies that have come out that make me excited, there's not one. No, I guess, what I would say, very simply, it's not a tough question; it's an easy question. It's the endless new studies that keep coming out about new agents and that show that we're still working hard on psoriasis. We're doing an amazing job in psoriasis. However, we're not at the level of hepatitis C, where 12 weeks of treatment cures the disease. So, even though we've come a long way, baby, we still have got a long, long way to go.

Dr. Stein Gold:
And I think it's important that we continue to study these drugs year after year after year. It's great when we see a drug does well over 16

weeks. It's wonderful when we see 1-year data, but it's really important—and the pharmaceutical companies are continuing to do this—we want to see 2 years, 3 years, 4 years, and 5 years, and make sure we understand what happens when you have that patient on the drug for the long term? So, I think this really adds a lot to our understanding of these new agents.

Dr. Russell:
And just in wrapping up, have you really seen these agents really kind of change the amount of suffering your patients have?

Dr. Korman:
It changes peoples' lives. I hear stories every day about how amazing it is and, "I've never expected to get this good; and I've been this good for a month, or for 6 months, or for a year, and this is amazing." And they come back every 6 months or every year, and they continue to just rave about how thrilled they are and how much it's just dramatically changed their lives. I hear stories about patients who got married, patients who were able to go to the beach, as Dr. Stein Gold said, just so many things about the quality of their life. Psoriasis is the type of disease that just affects patients' quality of life so, so much.

Dr. Stein Gold:
Our patients are used to hiding, and the fact that they don't hide anymore and they can put themselves at the center of attention and basically reach for the stars, is something that they never thought they would do. And I think that with these newer agents, we're actually seeing that.

Dr. Russell:
I think that's a great point to end on. I'd like to thank our guests, Dr. Neil Korman and Dr. Linda Stein Gold, for helping us better understand the new psoriasis treatments and the evidence supporting individualized treatment for patients with moderate to severe psoriasis. Thank you both.

Narrator:
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