Expert Insight on Maximizing Novel Therapeutic Strategies for Moderate to Severe Plaque Psoriasis

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Program Description
Psoriasis is a chronic inflammatory skin condition that is frequently associated with other systemic diseases. It affects about 2% of US adults and can significantly affect quality of life. The etiology includes genetic and environmental factors. Plaque psoriasis is the most common form. Join us as Dr. Alan Menter discusses current and emerging treatment strategies for managing patients with this condition, particularly moderate to severe disease.

Learning Objectives
Upon completion of this activity, participants should be better able to:

• Explain the immunopathology of moderate to severe plaque psoriasis
• Utilize knowledge of key clinical presentation and patient characteristics in treatment decision-making for patients with moderate to severe plaque psoriasis
• Implement treatment plans based upon the safety and efficacy of current anti-tumor necrosis factor alpha therapies in the long-term management of patients with moderate to severe plaque psoriasis
• Analyze emerging data on novel small molecule PDE4 and anti-interleukin 17 therapies for moderate to severe plaque psoriasis to integrate these regimens into the treatment algorithm
• Provide accurate and appropriate counsel as part of the psoriasis treatment team

Target Audience
This activity is intended for primary care physicians, dermatologists, pharmacists, rheumatologists, managed care professionals, and other health-care professionals who care for patients with moderate to severe plaque psoriasis.

Accreditation
This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of Postgraduate Institute for Medicine and AXIS Medical Education. The Postgraduate Institute for Medicine is accredited by the ACCME to provide continuing medical education for physicians.

Credit Designation
The Postgraduate Institute for Medicine designates this enduring material for a maximum of 0.25 AMA PRA Category 1 Credit(s)™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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Dr. Russell serves on the advisory board for Valeant Pharmaceuticals International and Takeda Pharmaceuticals International, Inc. and has received fees for non-CME/CE services received directly from a commercial interest or their agents (e.g., speakers’ bureaus) from Sanofi Pasteur.

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Credit Designation
Postgraduate Institute for Medicine designates this continuing education activity for 0.25 contact hour(s) (0.025 CEUs) of the Accreditation Council for Pharmacy Education. (Universal Activity Number - 0809-9999-14-197-H01-P)

Type of Activity: Knowledge

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Dr. John Russell:
Psoriasis is a chronic, proliferative, and inflammatory skin disease with reactive abnormal epidermal differentiation and hyperproliferation that affects two to three percent of the global population. Etiology includes genetic and environmental factors, and plaque psoriasis, the most common form, affecting 85 to 90 percent of people with psoriasis. Psoriasis can significantly affect quality of life, and is associated with several comorbidities, including cardiovascular disease, lymphoma, and depression. In addition, studies show that approximately 20 percent of patients suffer from moderate to severe forms of psoriasis, and psoriatic arthritis develops in between ten to 30 percent of people with psoriasis. What are effective options for these conditions, and what is still needed to improve patient outcomes? Dr. Menter, welcome to the program. Could you please elaborate a little on the key comorbid conditions physicians must be acutely aware of when managing patients with moderate to severe plaque psoriasis?

Dr. Alan Menter:
Well, epidemiological and clinical studies have shown a consistent association of psoriasis with systemic metabolic disorders, including an increased prevalence of diabetes, obesity, and cardiovascular disease. Psoriasis is indeed an independent risk factor for cardiovascular disease. It is important to screen patients for cardiovascular risk factors, and refer them to the appropriate specialist if cardiovascular disease is suspected. In addition, depression is common with psoriasis, especially the plaque form of psoriasis, given the visible appearance, longevity, and so forth.

Other conditions, such as hypertension, dyslipidemia, cancer, and inflammatory bowel disease have also been found at a high prevalence in patients with psoriasis, compared to the general population. Because of the wide range of these comorbid conditions associated with psoriasis, comprehensive screening and treatment must be implemented to most effectively manage these patients. These conditions generally and greatly impact the choice of therapy we select to treat the psoriasis as well.

Dr. John Russell:
I see. Another condition the physicians must watch for is the development of psoriatic arthritis. Could you tell us about the early clinical manifestations of psoriatic arthritis that physicians must consider in the overall management of patients with psoriasis?

Dr. Alan Menter:
Well, physicians in primary care settings generally refer patients with moderate to severe forms of plaque psoriasis on to a dermatologist. Dermatologists and rheumatologists will generally know the possibility of this condition progressing to psoriatic arthritis. As you mentioned earlier, about ten to 30 percent of patients with psoriasis also develop psoriatic arthritis, within an average of ten years. However, a small percentage of patients...
develop symptoms of arthritis prior to the development of skin disease, as much as ten to 15 years. Roughly 11 to 15 percent of patients will have simultaneous onset of arthritis and skin disease. This provides more evidence as to why treatment and overall management of patients must be individualized.

Dr. John Russell:
Thinking about effective treatments for psoriasis, how does the development of systemic and biologic therapies transform the management approach of moderate to severe plaque psoriasis?

Dr. Alan Menter:
Patients with a more severe form of the disease are typically considered for systemic therapy, including biologic therapy. The latest clinical guidelines offer recommendations for the use of the three most commonly used and approved traditional treatments, which are methotrexate, cyclosporine, and acitretin. Methotrexate is the most commonly prescribed, and has a successive use in combination with the three biologic agents in addition. Biologic therapy represents a relatively new class of drugs that are used with increasing frequency to control this chronic, systemic inflammatory disease. In spite of the overall superiority of biologic agents, the treatment response may differ substantially amongst individual patients. As with other medical conditions, a range of factors contribute to response heterogeneity observed in psoriasis. Proper identification of these factors can significantly improve the therapeutic decisions. Now, you talked earlier about the link between psoriasis and psoriatic arthritis. In the past decade, major advances in the understanding of the immunopathogenesis of psoriasis and psoriatic joint disease of common inflammatory pathways has led to the development of numerous biologic therapies that have revolutionized the treatment of moderate to severe plaque psoriasis and psoriatic joint disease. Anti-tumor necrosis factor, or what we call TNF alpha agents, are currently considered as first-line biologic therapy for the treatment of moderate to severe psoriasis and psoriatic joint disease. Currently approved anti-TNF alpha agents included etanercept, adalimumab, and infliximab for psoriasis or psoriatic arthritis. Ustekinumab, which is also approved for psoriatic arthritis, have typically seen significant improvement in their psoriasis.

Dr. John Russell:
Doctor, can you tell us what new pathways have been developed that are the rationale behind new drug development for moderate to severe plaque psoriasis?

Dr. Alan Menter:
Well, up until about five to seven years ago, the traditional pathway for psoriasis was considered the TH1 pathway, with TNF alpha central to the immunopathogenesis and understanding of psoriasis. Within the last five to seven years, the predominant new pathway, which was discovered by our immune-dermatology colleagues, is what we call the TH17 pathway, where IL-12 and IL-23 and other cytokines in addition to TNF alpha have been shown to play a prominent role in our understanding of the total pathways related to psoriasis. By having these new IL-12, IL-23 TH17 pathways available to us, it’s opened up the opportunities to develop multiple new molecules based on more specific cytokines, like IL-17, IL-23, IL-12, phosphodiesterase, there are inhibitors relating to these pathways, including the JAK kinase pathways, will enable us to develop these new molecules, and maybe have more specific therapies for more specific sub-types of psoriasis.

Dr. John Russell:
If you’re just tuning in, you’re listening to CME on ReachMD. I’m your host, Dr. John Russell, and today I’m speaking with Dr. Alan Menter. So, considering how these new biologics are expanding the pool of therapeutic options for physicians to further individualize treatment, are there any agents in late-stage clinical study for moderate to severe plaque psoriasis that are must-watch therapies?
Dr. Alan Menter:
There are several emerging therapies that target other cytokine pathways in psoriasis outside of TNF pathways that we discussed earlier. The IL-17 inhibitors, secukinumab, ixekizumab, and brodalumab, the IL-23 blocker tildrakizumab, and the small molecule kinase inhibitors, such as apremilast, which is a phosphodiesterase-4 blocker, and tofacitinib, a Janus kinase inhibitor. All these agents are fascinating Phase II clinical development programs, and have thus far demonstrated effectiveness in improving plaque psoriasis significantly in patients, based on the classic psoriasis area of severity index, or PASI score improvements form baseline, to various time points in weeks, as determined by the clinical study design, which are frequently different in these different agents. What we have seen predominantly across the board have been very manageable side effects, such as infections, including minor respiratory issues, nasopharyngitis, upper respiratory tract infection, as well as gastrointestinal issues that typically resolve within a couple of weeks of commencing therapy. So, in summation, we are seeing rapid and robust clinical improvement in skin condition, accompanied by favorable short-term safety profiles with these new emerging therapies.

Dr. John Russell:
This all sounds very promising for patients with moderate to severe plaque psoriasis. Based on current progress, what do you believe will be the impact of novel biomarkers on safety and improved care of patients with moderate to severe disease?

Dr. Alan Menter:
Well, patients with psoriasis deserve long-term control of their disease with optimal safety. Traditional systemic agents, although providing excellent short-term control, may produce acute or chronic toxicities, thus limiting their usage, particularly long-term. Dermatologists, in particular, are well-versed in combination rotational therapies for psoriasis, using these and other agents. With the advent of biologic therapies, the potential for safer long-term psoriasis control is being realized. The TH1 pathway was the original biomarker, and others have now been discovered, including IL-23, TH17, Il-17, and JAK pathways, as well as a PDE-4 blockade. There are many bio-similar agents currently in development that have eventually approved for use in the United States, will add even more complexity to overall treatment decision making. So, there’s a lot of exciting and very interesting things happening clinically that may soon further devolve the treatment landscape of moderate to severe plaque psoriasis. And research efforts will continue in many areas, including further molecular studies in patients with both psoriatic as well as psoriatic arthritis, to help us better understand the function of the various psoriasis susceptibility genes, and for us to identify novel therapeutic agents. Additionally, studies to identify a biomarker of the disease severity and treatment response will help us to optimize therapy for individual patients with moderate to severe plaque psoriasis.

“...we are seeing rapid and robust clinical improvement in skin condition, accompanied by favorable short-term safety profiles with these new emerging therapies.”
Dr. John Russell:
Dr. Menter, do you foresee pharmacogenomics playing a role in the future?

Dr. Alan Menter:
I think pharmacogenomics is the future of not only dermatology and psoriasis, but of medicine in general. I really do believe that in five years’ time, instead of saying to a patient, “Let’s try this and see how it works,” we will be able to take a genomic, genetic profile of each individual patient, and when you have a choice of five to seven to eight systemic or biologic drugs for a disease like psoriasis, we will be able to target more specifically a single agent to that individual patient’s pharmacogenomic phenotype, and then hopefully optimize the treatment, and also minimize the side effects. This, I believe, will lead not only to better treatment, but to significant cost saving to our already over-burdened health care system, making sure that there’s a higher chance of psoriasis patients responding to individual agents.

Dr. John Russell:
Thank you so much, Dr. Menter, for providing us with expert insight on current and future perspectives in the clinical management of patients with moderate to severe plaque psoriasis. Dr. Menter and a team of experts are currently giving presentations across the country on maximizing novel therapeutic strategies for moderate to severe plaque psoriasis.

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