

CME Symposium: Clinical Update: Novel Agents for the Long-Term Management of Moderate to Severe Atopic Dermatitis

Presented by Dr. Linda Stein Gold, MD, Dr. Andrew Alexis, MD, and Dr. Peter Lio, MD

Atopic dermatitis (AD) is a difficult disease to understand because there are so many pathophysiological components involved. Inflammation drives all five pillars of AD, which are the skin barrier, psyche, inflammation, microbiome and itch. Filament aggregating protein (filaggrin) plays a number of roles in the functioning of the skin barrier. Topical steroids can increase transepidermal water loss of the skin barrier over time. Patients with AD may experience a tremendous burden on the psyche which can be exacerbated and linked to stress and a lack of sleep that becomes a vicious cycle. The microbiome may predict a skin flareup, for example staphylococcus aureus growth and toxin production in the gut are linked to flares of AD. The hallmark itch of AD can be linked to multiple molecular mediators that are increasingly being discovered.

When thinking about the approach to treatment of AD, it is important to keep in mind the heterogeneity of the disease taking into consideration age, infectious processes and location. Ongoing maintenance therapy is key in achieving better outcomes when treating AD. There is strong literature linking moisturization to improvement in AD and recent evidence shows that more frequent bathing is helpful in reducing severity. There is no evidence of increased cancer incidence in children with AD. Crisaborole is a phosphodiesterase type 4 (PDE4) inhibitor and is approved for children age 3 months and older in mild to moderate cases. There is evidence that using topical calcineurin inhibitors proactively rather than solely in exacerbations may be beneficial. Dupilumab blocks interleukin (IL)-4 and IL-13 signaling and is approved for use in children 6 years and older with AD not well controlled with topical agents. It showed improvement in itch as early as the second day of use. The AD yardstick lays out a stepwise management of AD.

There are multiple therapeutics on the horizon for treating AD. Roflumilast, another PDE4 inhibitor, is shown to be 50-300 times more potent than crisaborole and apremilast, with rapid onset of itch improvement. It is currently in phase 2 of FDA approval. Tapinarof contains a small oral hydrocarbon modulating molecule that binds to the aryl hydrocarbon receptor (AhR) transcription factor, which inhibits T helper cells (Th)17 and Th2 differentiation, upregulates skin barrier protein expression in keratinocytes (including filaggrin), and has direct antioxidant activity. In a completed phase 2b trial, patients treated with tapinarof 1% cream showed efficacy over 12 weeks. Upcoming IL-13 inhibitors include tralokinumab and lebrikizumab, which bind IL-13 at different epitopes. Nemolizumab is also an upcoming IL-31 inhibitor. Tralokinumab has completed phase III clinical trials and shows continued efficacy after 16 weeks. Lebrikizumab has completed phase 2b trials showing good efficacy as early as 12-16 weeks. Nemolizumab targets the itch-causing cytokine and is currently undergoing phase 3 clinical trials.

There are a number of janus kinase (JAK) inhibitors already approved for other conditions but that are currently being tested as treatments for AD. The function of JAK inhibitors is to phosphorylate signal transducer and activator of transcription (STAT) pathways and activate inflammatory transcription factors. JAK1, JAK2, JAK3 and TYK2 are the four main targets of novel drugs. Abrocitinib, upadacitinib, baricitinib, and ruxolitinib are some examples of new oral inhibitors under review. The advantage of JAK inhibitors over biologics is that they are small molecules that can enter the cell, and be used as oral or topical agents. Topical JAK inhibitors include delgocitinib and ruxolitinib (in phase 3 trials) with good efficacy and long-term safety data.

CME Symposium: Time to Think About Both Skin and Joint Disease: Optimizing the Diagnosis and Management of Psoriatic Arthritis Through Multidisciplinary, Patient-Centered Care

Presented by Dr. Joseph Merola, MD, MMS, Dr. Alexis Ogdie, MD, MSCE, Dr. Alice Gottlieb, MD, PhD, and Glenn Speer

Psoriatic arthritis (PsA) is common and easy to diagnose. The presence of PsA is independent of the severity of psoriasis, so providers should ask every patient about any musculoskeletal symptoms. PsA risk factors include severe psoriasis, first-degree relative with PsA and obesity. Early PsA symptoms often present as enthesitis.

The screening and diagnosis for PsA can be easily incorporated in the PsA mnemonics (**P**ain in the joints, prolonged **S**tiffness, and **A**xial spine involvement) or be diagnosed with the Psoriasis Epidemiology Screening Tool (PEST). The Psoriatic Arthritis Impact of Disease (PsAID) Questionnaire can assess symptom measures. If the patient's PsAID score is a four or less, continuation of the current therapy is suggested – if score is higher consider modifying therapy.

Comorbidities of PsA affect treatment and patient response. PsA's common comorbidities include irritable bowel syndrome, uveitis, dry eyes, depression, anxiety, cardiovascular disease and diabetes. Notably, obesity is associated with inadequate response to therapy and as a result, weight loss is essential for PsA management. It is essential to address the whole patient, identify comorbidities, communicate with the patient and their primary care provider.