2022 American Academy of Dermatology Innovation Academy Conference

Day 2 Highlights
July 21-24, 2022

The American Academy of Dermatology Innovation Academy meeting, formerly known as Summer AAD, brought top dermatologists together to learn from one another and share pearls.

Held at the Vancouver Convention Center in British Columbia, Canada, the meeting spanned four days and included a focus on new drugs in development and new uses for existing medications.

Below, we summarize some of the presentations that caught our attention during the second day of the conference. We will follow up with a postconference wrap-up report soon, so stay tuned.

Select sessions/highlights at the 2022 AAD IA Conference

New therapies for old skin diseases

Psoriasis has scored multiple new drug approvals in recent years, and now it seems that other common dermatological diseases may soon be catching up.

Janus kinase (JAK) inhibitors are undoubtedly the hottest ticket in dermatology today. These drugs interrupt the JAK-STAT (Signal Transducer and Activator of Transcription) signaling pathways that are involved in the pathogenesis of many immune-mediated and/or inflammatory diseases, including vitiligo, atopic dermatitis (AD), alopecia areata, and plaque psoriasis.

But they are not the only game in town for the treatment of many skin conditions.

What's new in vitiligo?

The U.S. Food and Drug Administration recently approved ruxolitinib cream 1.5% for nonsegmental vitiligo in adults and children 12 years and older. This is the only FDA-approved treatment for repigmentation in vitiligo and the only topical formulation of a JAK inhibitor, said David Rosmarin, M.D., a dermatologist at Tufts Medical Center in Boston.

"Ritlecitinib, a JAK3 inhibitor, and upadacitinib, a JAK1 inhibitor, are orals in development for vitiligo," Rosmarin said. "Systemic agents make sense for patients who have a large body surface area and progressive disease."

There are other new therapies in the pipeline for vitiligo, including an anti-interleukin (IL)-15 antibody and an oral drug based on blue snakeweed, said Rosmarin. "There is a lot in development, and we also need to know if some of these treatments will work better in combination such as with phototherapy," he said. "They may be synergistic, but currently most treatments are being studied as monotherapy."

What's new in AD?

Many new therapeutic agents in the AD pipeline target a variety of molecules believed to be involved in the disease process, said Benjamin Ungar, M.D., an assistant professor in the department of dermatology at the Icahn School of Medicine at Mount Sinai in New York City. "This is very exciting because even with all the significant advancements in treatments in the last few years, new safe and effective treatments are needed."

Topical steroids and a few nonsteroidal topicals have been used most commonly for mild-to-moderate AD, Ungar said. "A newly approved topical JAK inhibitor, ruxolitinib has been a significant development in expanding available topical therapies for AD," he said.

For moderate-to-severe cases, the mainstay of systemic treatment for the last few years has been dupilumab. "In recent months, FDA approval of another biologic, tralokinumab, and two oral JAK inhibitors, upadacitinib and abrocitinib, have expanded the available treatments for AD patients today," Ungar said.

The approval of dupilumab was a game changer for AD patients. Before dupilumab, systemic treatments involved broad-acting immune-suppressing medications with significant side effects, such as cyclosporine and methotrexate. “Dupilumab provides an effective treatment that is also extremely safe,” Ungar said. “Now, we're moving into an era where different treatment options will allow for more personalized and tailored approaches to treating patients.”

One promising new therapeutic target pathway under investigation involves OX40-OX40L and the C-C motif chemokine receptor 4, both of which may produce sustained responses and may even modify the disease process itself, Ungar said.

What’s new in alopecia areata?

In June 2022, the FDA approved baricitinib, an oral JAK inhibitor for adults with severe alopecia areata. This is the first systemic drug ever approved for alopecia areata, a condition that affects as many as 6.8 million people in the United States.

While baricitinib has the official FDA nod, at least two other oral JAK inhibitors – deuruxolitinib and ritlecitinib – are working their way toward FDA approval, according to Brett King, M.D., Ph.D., an associate professor of dermatology at Yale School of Medicine in New Haven, Connecticut, who helped pioneer the use of JAK inhibitors in dermatology. Topical JAK inhibitors, including delgocitinib and ruxolitinib cream, do not seem to be effective in treating alopecia areata.

What’s new in HS?

Long neglected, hidradenitis suppurativa (HS) is finally getting some attention. This immune-mediated disease causes recurring and painful boils and abscesses in the folds of the skin.

"The current understanding that we have about the pathophysiology of HS has helped us develop more targeted therapies," said Afsaneh Alavi, M.D., a dermatologist at the Mayo Clinic in Rochester, Minnesota.

In 2015, the FDA approved the tumor necrosis factor inhibitor adalimumab for the treatment of moderate-to-severe HS, making it the first and only FDA-approved therapy for HS. "This made a huge difference in the quality of life of HS patients, but there is still room for improvement," Alavi said.

Studies looking at IL-1 inhibitors, IL-17 inhibitors, IL-36 blockers, and JAK inhibitors are underway. " Research shows increased IL-7 a and c in HS patients," Alavi said.

“There's a lot of hope about JAK inhibitors, but safety is always something that requires close attention," she added. The FDA requires a black box warning for JAK inhibitors due to an increased risk for heart attack or stroke, blood clots, cancer, and death.

Still, the future is looking brighter for HS patients. As Alavi explained, “In the next few years, we will be closer to where we are with psoriasis: more treatment options, higher patient expectations, and a focus on diagnosing the condition much earlier than we do now."

What’s new in psoriasis?

Speaking of psoriasis, Jennifer Soung, M.D., director of clinical research at Southern California Dermatology in Santa Ana, California, and a clinical professor at Harbor-UCLA Medical Center, also in Santa Ana, updated attendees on existing FDA-approved treatments for psoriasis and introduced some new and emerging psoriasis options.

Multiple biologics are approved for the treatment of psoriasis, and there have been several head-to-head studies comparing these agents.

“Whether we are looking at the Psoriasis Area and Severity Index 75 (PASI75) or PASI90, these top biologics are literally within 1 to 3 percentage points of each other," Soung said. "The short-term and long-term efficacy showed brodalumab, guselkumab, ixekizumab, and risankizumab-rzaa had the highest PASI response rates at 10 to16 weeks from baseline and also at 44 to 60 weeks.”

Ixekizumab provides great skin clearance, durable efficacy, and rapid onset of action, but there is a risk for injection site pain and reaction. “A citrate-free formulation of ixekizumab proved to be bioequivalent, was associated with less injection site pain, and had no other notable differences in the safety profile compared to the original commercial formulation,” Soung said.

There are three biologics in the IL23 class. Guselkumab has an every eight-week dosing schedule, while risankizumab and tildrakizumab both are given every 12 weeks. There is an advantage to every eight-week dosing over 12-week dosing. With

12-week dosing, patients would have recurrence of their psoriasis skin lesions before the subsequent dose, so it would not be enough to keep them clear.

A new biologic that is still investigational is bimekizumab, and it will be joining the IL-17 family of biologics, Soung said. The FDA issued a complete response letter regarding the biologic's license application that indicated that certain preapproval inspection observations must be resolved.

"These are manufacturing issues, not safety issues," Soung said.

Another novel therapy, deucravacitinib, is intended to block tyrosine kinase 2 (TYK2) without inhibiting JAK1, JAK2, or JAK3, thus potentially avoiding adverse events associated with JAK inhibitors, Soung added. The FDA is expected to rule on the investigational TYK2 inhibitor in September 2022.

Moreover, the FDA approved steroid-free tapinarof 1% cream, a small-molecule topical aryl hydrocarbon receptor agonist, in June 2022. Patients were clear or almost clear at approximately four months after cessation of treatment with tapinarof cream. "This is also well tolerated in sensitive areas: face, intertriginous, genital, gluteal fold, and inframammary," Soung said.

Another exciting topical option for psoriasis is roflumilast, a potent topical PDE4 inhibitor. The Prescription Drug User Fee Act date for approval by the FDA is September 2022, Soung said.

EDP1815 is an orally delivered, anti-inflammatory, gut-restricted commensal microbe that is under investigation in psoriasis, said Soung. A Phase 2 study showed that this agent was well tolerated with no treatment-related serious adverse events and no meaningful difference in infections or gastrointestinal events compared with placebo. Another new therapy to look out for is the Janssen Phase 2 oral peptide IL23 inhibitor.

Probiotics are another hot area in psoriasis treatment, Soung said. Probiotic *Lactobacillus gasseri* KBL697 is now in ongoing Phase 3 plaque psoriasis studies.