

Advances in Dermatology: A Year in Review 2021

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Our specialty continues to advance despite the pandemic, thanks to the hard work and dedication of researchers and leaders in the field. Here is a summary of some of the biggest news from the last year.

COVID-19

COVID-19 still affects our daily lives despite widely available and effective vaccines. As dermatologists, we are tasked with counseling our patients who are treated with disease-modifying drugs. Data published this year suggests that those on methotrexate are more likely to be hospitalized for COVID-19 than those on biologics¹, apremilast (Otezla®) does not increase the risk of COVID-19 infection², and dupilumab (Dupixent®) is associated with milder infection³.

At this time, the National Psoriasis Foundation COVID-19 Task Force recommends vaccination and a booster for psoriasis patients. In general, psoriasis treatment should be continued. Those on methotrexate may consider stopping medication for 2 weeks after an mRNA vaccine dose to improve response. Ultimately these decisions are best made between individual patients and their doctor. For up-to-date or more specific recommendations, visit the NPF website at [psoriasis.org](https://www.psoriasis.org).

PSORIASIS

The FDA accepted a new drug application for tapinarof 1% cream, a novel once-daily aryl hydrocarbon receptor modulating agent (TAMA), making commercial access likely in the near future.

Oral deucravacitinib is a first-in-class tyrosine kinase 2 (TYK2) inhibitor showing superiority to apremilast in phase 3 trials⁴. Orismilast, an oral PDE4-inhibitor, is in the pipeline for not only psoriasis but also atopic dermatitis and hidradenitis suppurativa. Topical PDE4-inhibitor roflumilast cream shows promise as well⁵.

IL17-A and F inhibitor bimekizumab has performed well in trials for psoriasis⁶, and is under investigation for psoriatic arthritis, ankylosing spondylitis, and hidradenitis suppurativa⁷.

Options for pediatric patients expanded with the approval of secukinumab (Cosentyx[®]) for those six years and older. IL-23 inhibitor risankizumab (Skyrizi[®]) received approval for psoriatic arthritis in Europe this year, and approval in the US may not be far behind.

ATOPIC DERMATITIS

A victory for JAK inhibitors occurred with the recent approval of topical JAK1/2 inhibitor ruxolitinib (Opzelura[®]) for atopic dermatitis (AD) in age 12 years and up. The data is favorable for vitiligo as well⁸. Investigations into pan-JAK inhibitor delgocitinib ointment for AD for ages 2 years and up are also under way⁹.

Oral JAK inhibitors for AD remain just outside of reach at least in part due to new black box warnings. A post-marketing study of tofacitinib (Xeljanz[®]) compared to TNF inhibitors in patients with rheumatoid arthritis led to the FDA revising the warning to include increased risks of serious heart-related events, cancer, blood clots and death¹⁰. The warning applies to JAK inhibitors for RA and ulcerative colitis: tofacitinib, baricitinib (Olumiant[®]) and upadacitinib (Rinvoq[®]). The expanded approval of upadacitinib for atopic dermatitis has therefore been delayed since the summer.

Dupilumab (Dupixent[®]) appears safe and effective for patients with AD down to the age of six months in phase 3 trials¹¹. Furthermore, dupilumab shows success for prurigo nodularis¹², and chronic spontaneous urticaria¹³.

IL-13 inhibitor tralokinumab continues to do well in trials for adults and adolescent patients¹⁴. Other novel treatment targets on the horizon include transient receptor potential vanilloid subfamily V member 1 (TRPV1; asivatrep cream)¹⁵ and, sphingosine 1-phosphate receptor 1 (S1p1; oral etrasimod)¹⁶, and OX40.

CHRONIC SPONTANEOUS URTICARIA

A meta-analysis published this year suggests that ligelizumab and omalizumab (Xolair[®]) provide moderate improvement for chronic spontaneous urticaria in patients refractory to H1 antihistamine therapy, while dapsone, hydroxychloroquine, cyclosporine, and zafirlukast, showed only small beneficial effects¹⁷. Dupilumab may add another treatment option in the future based on phase 3 trial results¹².

ITCH

Difelikefalin (KorsuvaTM), an injectable kappa opioid receptor, was approved in August for pruritus in patients on hemodialysis¹⁸. Odevixibat (BylvayTM), a bile acid transporter inhibitor was also approved for pruritus in patients aged ≥ 3 months with progressive familial intrahepatic cholestasis, with investigation into other causes of cholestatic pruritus ongoing¹⁹.

SUN PROTECTION

The independent laboratory Valisure announced it detected high levels of contaminant and known carcinogen benzene in select sunscreens. More recently, benzene was found in other aerosol products, including antiperspirants and antifungal sprays. These findings have led to recalls, uneasiness among patients, and stricter regulation by the FDA.

CUTANEOUS ONCOLOGY

Non-Melanoma Skin Cancer (NMSC)

The American Academy of Dermatology published guidelines on the management of actinic keratoses (AKs) in April of this year with strong recommendations for the use of UV protection, cryosurgery, topical imiquimod, and 5-fluorouracil²⁰. The microtubule inhibitor tirbanibulin (Klisyri[®]) used once daily for five days for the treatment of AKs of the face or scalp also came to market this year.

A slight increased risk of NMSC was demonstrated in patients over age 65 on thiazide diuretics²¹, while metformin may be associated with a decreased risk of basal cell carcinoma (BCC)²². Cemiplumab was approved for advanced BCC earlier this year, for those who fail or are not candidates for hedgehog inhibitors²³.

Melanoma

Skin cancer screening came under scrutiny when an editorial in the NEJM questioned the utility, suggesting that an increase in biopsies and melanoma diagnoses have not resulted in a decrease in mortality as would be expected²⁴. Interestingly, a study showed lower overall mortality, but not melanoma-specific mortality, associated with melanoma diagnosed through routine skin checks²⁵.

Pembrolizumab (Keytruda[®]) was just approved as adjuvant treatment for patients age 12 years and up with resected stage IIB and IIC melanoma²⁶. Previously, observation alone was recommended.

Novel treatments aimed at harnessing the immune system to target melanoma are generating interest, including chimeric antigen receptor (CAR) T-cell therapies and a universal cancer vaccine in combination with immunotherapy²⁷.

Cutaneous T-cell Lymphoma (CTCL)

Overall survival for stage IA to IIA CTCL patients with **both** clonal T-cell receptor rearrangement and an abnormal T-cell population on peripheral blood flow cytometry was shown to be lower than for those with negative results for both in a retrospective cohort²⁸.

Low-dose total skin electron beam therapy with a novel rotational technique demonstrated rapid and lasting results in a cohort of 20 patients with CTCL²⁹. Positive results were also shown using the photosensitizer hypericin followed by specific wavelengths of visible light in early stage CTCL³⁰.

ACNE and ROSACEA

A combination tretinoin and benzoyl peroxide cream (Twynéo®) was approved for acne in July. Major changes in iPledge occurred as of December 13, 2021. There are now two pregnancy categories instead of three: patients who can get pregnant, and patients who cannot get pregnant. Secondly, iPledge transitioned to a fully digital enrollment and consent process that must be completed at the time of the visit.

COSMETICS

A rise in the incidence of delayed inflammatory reactions to hyaluronic acid filler after COVID-19 vaccinations and infections came as a surprise to many. Activation of angiotensin-converting enzyme receptor (ACE2) by the spike protein is one proposed mechanism for this reaction. Munavalli, et al, demonstrated effective treatment with the ACE-inhibitor lisinopril in a series of patients³¹.

Galderma's Restylane® Contour made its debut for cheek augmentation and midface contour. Restylane® Defyne also received expanded indication for chin augmentation. Additionally, Radiesse® is now indicated for the jawline.

The members of the Women's Dermatologic Society's Editorial Committee hope you find this and all editorials helpful for your practice. We wish you safe, healthy, and happy holidays, and a happy new year!

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