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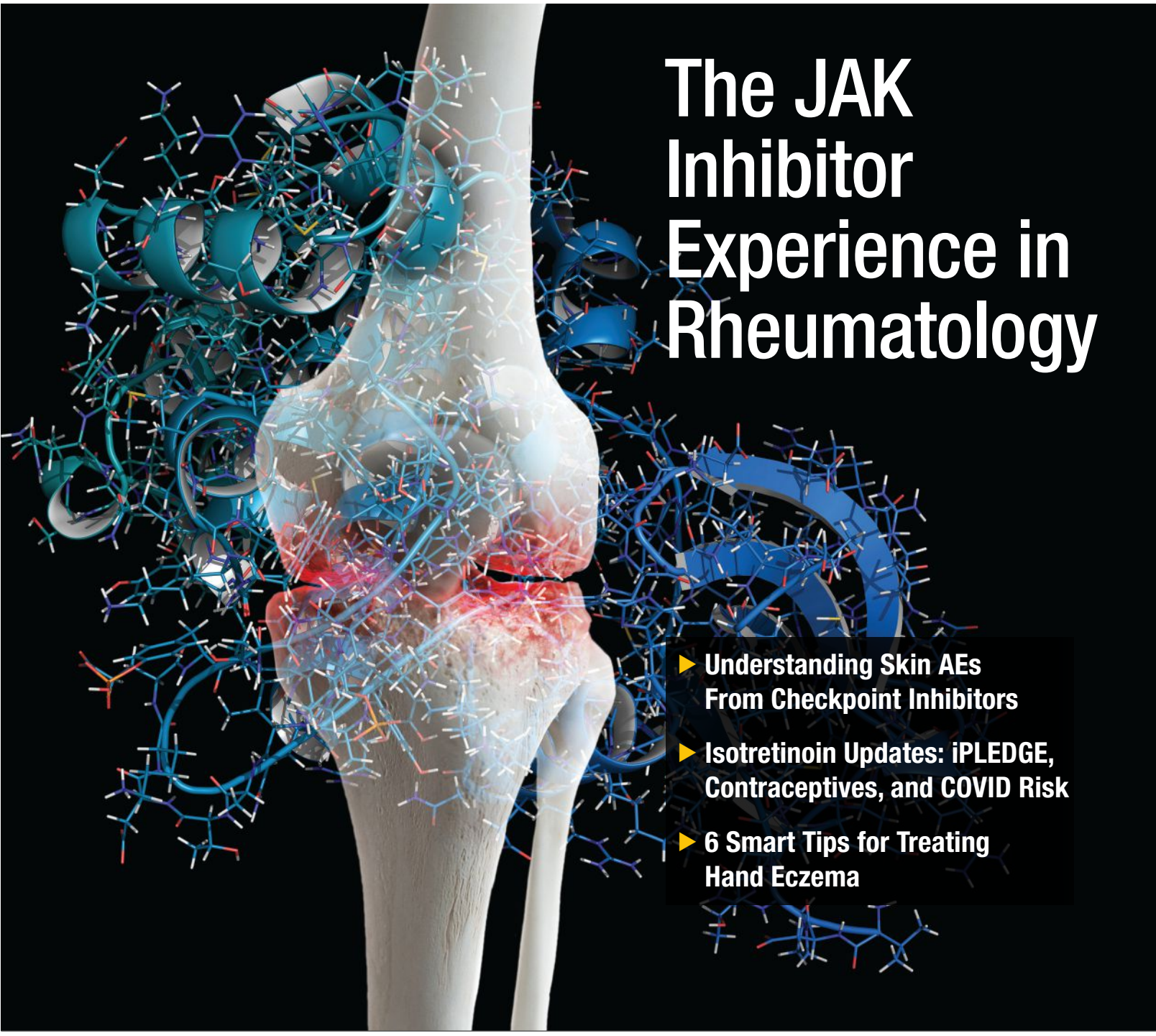
THE Dermatology Digest®

Vol. 3, No. 4 | April 2022



The JAK Inhibitor Experience in Rheumatology

- Understanding Skin AEs From Checkpoint Inhibitors
- Isotretinoin Updates: iPLEDGE, Contraceptives, and COVID Risk
- 6 Smart Tips for Treating Hand Eczema

EDUCATIONAL • INTERACTIVE • AUTHORITATIVE

ITCH-SCRATCH-
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ITCH-SCRATCH-

THE ONE-OF-A-KIND TOPICAL JAK INHIBITOR

For uncontrolled, mild to moderate atopic dermatitis in non-immunocompromised patients aged ≥12 years[1]

- **Clear or almost clear skin** (IGA 0/1)* in >50% of patients at week 8 (53.8% vs 15.1% and 51.3% vs 7.6% vehicle†; $P<0.0001$)[1,2]
- **Meaningful itch relief** (Itch NRS4) in >50% of patients at week 8 (52.2% vs 15.4% and 50.7% vs 16.3% vehicle†; $P<0.0001$)[1,2‡]
  - **Itch NRS4 response seen as early as day 3** (18.4% OPZELURA vs 4.2% vehicle and 13.2% OPZELURA vs 0% vehicle†)[3]

OPZELURA was studied in 2 identically designed, double-blind, randomized, vehicle-controlled trials (TRue-AD1 and TRuE-AD2). The 2 studies included 1249 adult and adolescent patients ≥12 years of age with an affected BSA of 3%-20% and an IGA score of 2 or 3 on a severity scale of 0-4. Patients were randomized to monotherapy with OPZELURA, ruxolitinib cream 0.75%, or vehicle twice daily for 8 weeks.[1,2]

*With a ≥2-grade improvement from baseline.[1]

†In TRuE-AD1 and TRuE-AD2, respectively.[1,2]

‡≥4-point improvement in NRS among patients with a score of ≥4 at baseline.[1]

BID=twice daily; BSA=body surface area; IGA=Investigator's Global Assessment; JAK=Janus kinase; NRS=numeric rating scale.

Discover more at OpzeluraHCP.com

Incyte Dermatology

INDICATION

OPZELURA is indicated for the topical short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in non-immunocompromised patients 12 years of age and older whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable.

Limitation of Use:

Use of OPZELURA in combination with therapeutic biologics, other JAK inhibitors or potent immunosuppressants such as azathioprine or cyclosporine is not recommended.

IMPORTANT SAFETY INFORMATION

SERIOUS INFECTIONS

Patients treated with oral Janus kinase inhibitors for inflammatory conditions are at risk for developing serious infections that may lead to hospitalization or death. Reported infections include:

- **Active tuberculosis, which may present with pulmonary or extrapulmonary disease.**
- **Invasive fungal infections, including candidiasis and pneumocystosis.**
- **Bacterial, viral, and other infections due to opportunistic pathogens.**

Avoid use of OPZELURA in patients with an active, serious infection, including localized infections.

If a serious infection develops, interrupt OPZELURA until the infection is controlled. Carefully consider the benefits and risks of treatment prior to initiating OPZELURA in patients with chronic or recurrent infection. Closely monitor patients for the development of signs and symptoms of infection during and after treatment with OPZELURA.

No cases of active tuberculosis (TB) were reported in clinical trials with OPZELURA. Cases of active TB were reported in clinical trials of oral Janus kinase inhibitors used to treat inflammatory conditions. Consider evaluating patients for latent and active TB infection prior to administration of OPZELURA. During OPZELURA use, monitor patients for the development of signs and symptoms of TB.

Viral reactivation, including cases of herpes virus reactivation (e.g., herpes zoster), were reported in clinical trials with Janus kinase inhibitors used to treat inflammatory conditions including OPZELURA. If a patient develops herpes zoster, consider interrupting OPZELURA treatment until the episode resolves.

Please see additional Important Safety Information on following page.

Please see Brief Summary of Full Prescribing Information, including Boxed Warning, on following pages.

Opzelura™
(ruxolitinib) cream 1.5%

IMPORTANT SAFETY INFORMATION for OPZELURA™ (ruxolitinib) cream 1.5% (continued)

SERIOUS INFECTIONS (continued)

Hepatitis B viral load (HBV-DNA titer) increases, with or without associated elevations in alanine aminotransferase and aspartate aminotransferase, have been reported in patients with chronic HBV infections taking oral ruxolitinib. OPZELURA initiation is not recommended in patients with active hepatitis B or hepatitis C.

MORTALITY

Higher rate of all-cause mortality, including sudden cardiovascular death, has been observed in patients treated with oral Janus kinase inhibitors for inflammatory conditions.

MALIGNANCIES

Lymphoma and other malignancies have been observed in patients treated with Janus kinase inhibitors for inflammatory conditions. Patients who are current or past smokers are at additional increased risk. Non-melanoma skin cancers, including basal cell and squamous cell carcinoma, have occurred in patients treated with OPZELURA. Perform periodic skin examinations during OPZELURA treatment and following treatment as appropriate.

MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE)

Higher rate of MACE (including cardiovascular death, myocardial infarction, and stroke) has been observed in patients treated with Janus kinase inhibitors for inflammatory conditions. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OPZELURA, particularly in patients who are current or past smokers and patients with other cardiovascular risk factors. Patients should be informed about the symptoms of serious cardiovascular events and the steps to take if these symptoms occur.

THROMBOSIS

Thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis has been observed in patients treated with oral Janus kinase inhibitors for inflammatory conditions. Many of these adverse reactions were serious and some resulted in death. Patients with symptoms of thrombosis should be promptly evaluated.

Thromboembolic events were observed in clinical trials with OPZELURA. There was no clear relationship between platelet count elevations and thrombotic events. OPZELURA should be used with caution in patients who may be at increased risk of thrombosis.

Thrombocytopenia, Anemia and Neutropenia

Thrombocytopenia, anemia and neutropenia were reported in the clinical trials with OPZELURA. Consider the benefits and risks for individual patients who have a known history of these events prior to initiating therapy with OPZELURA. Perform CBC monitoring as clinically indicated. If signs and/or symptoms of clinically significant thrombocytopenia, anemia, and neutropenia occur, patients should discontinue OPZELURA.

Lipid Elevations

Treatment with oral ruxolitinib has been associated with increases in lipid parameters including total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides.

Adverse Reactions

The most common adverse reactions (≥1%) are nasopharyngitis (3%), diarrhea (1%), bronchitis (1%), ear infection (1%), eosinophil count increased (1%), urticaria (1%), folliculitis (1%), tonsillitis (1%), and rhinorrhea (1%).

Pregnancy

There will be a pregnancy registry that monitors pregnancy outcomes in pregnant persons exposed to OPZELURA during pregnancy. Pregnant persons exposed to OPZELURA and healthcare providers should report OPZELURA exposure by calling 855-4MEDINFO or 855-463-3463.

Lactation

Advise women not to breastfeed during treatment with OPZELURA and for four weeks after the last dose (approximately 5 elimination half-lives).

Please see Brief Summary of Full Prescribing Information, including Boxed Warning, on following pages.

References: 1. Opzelura. Prescribing Information. Incyte Corporation; 2021. **2.** Papp K, Szepietowski JC, Kircik L, et al. Efficacy and safety of ruxolitinib cream for the treatment of atopic dermatitis: results from 2 phase 3, randomized, double-blind studies. *J Am Acad Dermatol.* Published online May 3, 2021. doi:10.1016/j.jaad.2021.04.085. **3.** Data on file. Incyte Corporation. 2021.

Opzelura™
(ruxolitinib) cream 1.5%

OPZELURA™ (ruxolitinib) cream, for topical use

Brief Summary of FULL PRESCRIBING INFORMATION

INDICATIONS AND USAGE: OPZELURA is indicated for the topical short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in non-immunocompromised patients 12 years of age and older whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable.

Limitation of Use: Use of OPZELURA in combination with therapeutic biologics, other JAK inhibitors or potent immunosuppressants such as azathioprine or cyclosporine is not recommended.

WARNING: SERIOUS INFECTIONS, MORTALITY, MALIGNANCY, MAJOR ADVERSE CARDIOVASCULAR EVENTS, AND THROMBOSIS

SERIOUS INFECTIONS
Patients treated with oral Janus kinase inhibitors for inflammatory conditions are at risk for developing serious infections that may lead to hospitalization or death *[see Warnings and Precautions and Adverse Reactions]*.

Reported infections include:

- **Active tuberculosis, which may present with pulmonary or extrapulmonary disease.**
- **Invasive fungal infections, including candidiasis and pneumocystosis.**
- **Bacterial, viral, and other infections due to opportunistic pathogens.**

Avoid use of OPZELURA in patients with an active, serious infection, including localized infections. If a serious infection develops, interrupt OPZELURA until the infection is controlled.

The risks and benefits of treatment with OPZELURA should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection.

Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with OPZELURA *[see Warnings and Precautions]*.

MORTALITY
Higher rate of all-cause mortality, including sudden cardiovascular death have been observed in patients treated with oral Janus kinase inhibitors for inflammatory conditions *[see Warnings and Precautions]*.

MALIGNANCIES
Lymphoma and other malignancies have been observed in patients treated with Janus kinase inhibitors for inflammatory conditions *[see Warnings and Precautions]*.

MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE)
Higher rate of MACE (including cardiovascular death, myocardial infarction, and stroke) has been observed in patients treated with Janus kinase inhibitors for inflammatory conditions *[see Warnings and Precautions]*.

THROMBOSIS
Thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis has been observed at an increased incidence in patients treated with oral Janus kinase inhibitors for inflammatory conditions compared to placebo. Many of these adverse reactions were serious and some resulted in death. Patients with symptoms of thrombosis should be promptly evaluated *[see Warnings and Precautions]*.

WARNINGS AND PRECAUTIONS

Serious Infections: Serious and sometimes fatal infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens have been reported in patients receiving oral janus kinase inhibitors. Serious lower respiratory tract infections were reported in the clinical development program with topical ruxolitinib. Avoid use of OPZELURA in patients with an active, serious infection, including localized infections. Consider the risks and benefits of treatment prior to initiating OPZELURA in patients: with chronic or recurrent infection; with a history of a serious or an opportunistic infection; who have been exposed to tuberculosis; who have resided or traveled in areas of endemic tuberculosis or endemic mycoses; or with underlying conditions that may predispose them to infection. Closely monitor patients for the development of signs and symptoms of infection during and after treatment with OPZELURA. Interrupt OPZELURA if a patient develops a serious infection, an opportunistic infection, or sepsis. Do not resume OPZELURA until the infection is controlled.

Tuberculosis: No cases of active tuberculosis (TB) were reported in clinical trials with OPZELURA. Cases of active TB were reported in clinical trials of oral Janus kinase inhibitors used to treat inflammatory conditions. Consider evaluating patients for latent and active TB infection prior to administration of OPZELURA. During OPZELURA use, monitor patients for the development of signs and symptoms of TB.

Viral Reactivation: Viral reactivation, including cases of herpes virus reactivation (e.g., herpes zoster), were reported in clinical trials with Janus kinase inhibitors used to treat inflammatory conditions including OPZELURA. If a patient develops herpes zoster, consider interrupting OPZELURA treatment until the episode resolves.

Hepatitis B and C: The impact of Janus kinase inhibitors used to treat inflammatory conditions including OPZELURA on chronic viral hepatitis reactivation is unknown. Patients with a history of hepatitis B or C infection were excluded from clinical trials.

Hepatitis B viral load (HBV-DNA titer) increases, with or without associated elevations in alanine aminotransferase and aspartate aminotransferase, have been reported in patients with chronic HBV infections taking oral ruxolitinib. OPZELURA initiation is not recommended in patients with active hepatitis B or hepatitis C.

Mortality: A higher rate of all-cause mortality, including sudden cardiovascular death was observed in clinical trials of oral Janus kinase inhibitors used to treat inflammatory conditions. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OPZELURA.

Malignancy and Lymphoproliferative Disorders: Malignancies, including lymphomas, were observed in clinical trials of oral Janus kinase inhibitors used to treat inflammatory conditions. Patients who are current or past smokers are at additional increased risk. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OPZELURA, particularly in patients with a known malignancy (other than successfully treated non-melanoma skin cancers), patients who develop a malignancy, and patients who are current or past smokers.

Non-melanoma Skin Cancers: Non-melanoma skin cancers including basal cell and squamous cell carcinoma have occurred in patients treated with OPZELURA. Perform periodic skin examinations during OPZELURA treatment and following treatment as appropriate.

Major Adverse Cardiovascular Events (MACE): Major adverse cardiovascular events (MACE) defined as cardiovascular death, non-fatal myocardial infarction (MI), and non-fatal stroke were observed in clinical trials of Janus kinase inhibitors used to treat inflammatory conditions. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OPZELURA particularly in patients who are current or past smokers and patients with other cardiovascular risk factors. Patients should be informed about the symptoms of serious cardiovascular events and the steps to take if these symptoms occur.

Thrombosis: Thrombosis, including deep venous thrombosis (DVT), pulmonary embolism (PE) and arterial thrombosis, has been observed at an increased incidence in patients treated with oral Janus kinase inhibitors for inflammatory conditions compared to patients treated with placebo. Many of these adverse reactions were serious and some resulted in death. Thromboembolic events were observed in clinical trials with OPZELURA. There was no clear relationship between platelet count elevations and thrombotic events. OPZELURA should be used with caution in patients who may be at increased risk of thrombosis.

Thrombocytopenia, Anemia and Neutropenia: Thrombocytopenia, anemia and neutropenia were reported in the clinical trials with OPZELURA. Consider the benefits and risks for individual patients who have a known history of these events prior to initiating therapy with OPZELURA. Perform CBC monitoring as clinically indicated. If signs and/or symptoms of clinically significant thrombocytopenia, anemia, and neutropenia occur, patients should discontinue OPZELURA.

Lipid Elevations: Treatment with oral ruxolitinib has been associated with increases in lipid parameters including total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides.

ADVERSE REACTIONS

Clinical Trials Experience: Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. In two double-blind, vehicle-controlled clinical trials (Trials 1 and 2), 499 subjects 12 years of age and older with atopic dermatitis were treated with OPZELURA twice daily for 8 weeks. In the OPZELURA group, 62% of subjects were females, and 71% of subjects were White, 23% were Black, and 4% were Asian. The adverse reactions reported by ≥ 1% of OPZELURA-treated subjects and at a greater incidence than in the vehicle arm through week 8 are as follows for OPZELURA (N=499) vs Vehicle (N=250), respectively: Subjects with any treatment emergent adverse event (TEAE) 132 (27%) vs 83 (33%), Nasopharyngitis 13 (3%) vs 2 (1%), Bronchitis 4 (1%) vs 0 (0%), Ear infection 4 (1%) vs 0 (0%), Eosinophil count increased 4 (1%) vs 0 (0%), Urticaria 4 (1%) vs 0 (0%), Diarrhea 3 (1%) vs 1 (<1%), Folliculitis 3 (1%) vs 0 (0%), Tonsillitis 3 (1%) vs 0 (0%), and Rhinorrhea 3 (1%) vs 1 (<1%).

Adverse reactions that occurred in Trials 1 and 2 in < 1% of subjects in the OPZELURA group and none in the vehicle group were: neutropenia, allergic conjunctivitis, pyrexia, seasonal allergy, herpes zoster, otitis externa, Staphylococcal infection, and acneiform dermatitis.

DRUG INTERACTIONS

Drug interaction studies with OPZELURA have not been conducted. Ruxolitinib is known to be a substrate for cytochrome P450 3A4 (CYP3A4). Inhibitors of CYP3A4 may increase ruxolitinib systemic concentrations whereas inducers of CYP3A4 may decrease ruxolitinib systemic concentrations.

Strong Inhibitors of CYP3A4: Avoid concomitant use of OPZELURA with strong inhibitors of CYP3A4 as there is a potential to increase the systemic exposure of ruxolitinib and could increase the risk of OPZELURA adverse reactions.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Exposure Registry: There will be a pregnancy registry that monitors pregnancy outcomes in pregnant persons exposed to OPZELURA during pregnancy. Pregnant persons exposed to OPZELURA and healthcare providers should report OPZELURA exposure by calling 1-855-463-3463.

Risk Summary: Available data from pregnancies reported in clinical trials with OPZELURA are not sufficient to evaluate a drug-associated risk for major birth defects, miscarriage, or other adverse maternal or fetal outcomes. In animal reproduction studies, oral administration of ruxolitinib to pregnant rats and rabbits during the period of organogenesis resulted in adverse developmental outcomes at doses associated with maternal toxicity.

The background risks of major birth defects and miscarriage for the indicated populations are unknown. All pregnancies carry some risk of birth defects, loss, or other adverse outcomes. The background risk in the U.S. general population of major birth defects and miscarriage is 2-4% and 15-20%, respectively.

Data

Animal Data: Ruxolitinib was administered orally to pregnant rats or rabbits during the period of organogenesis, at doses of 15, 30 or 60 mg/kg/day in rats and 10, 30 or 60 mg/kg/day in rabbits. There were no treatment-related malformations at any dose. A decrease in fetal weight of approximately 9% was noted in rats at the highest and maternally toxic dose of 60 mg/kg/day. This dose resulted in systemic exposure approximately 22 times the clinical systemic exposure at the maximum recommended human dose (MRHD); the clinical systemic exposure from ruxolitinib cream, 1.5% applied twice daily to 25-40% body surface area is used for calculation of multiples of human exposure. In rabbits, lower fetal weights of approximately 8% and increased late resorptions were noted at the highest and maternally toxic dose of 60 mg/kg/day. This dose resulted in systemic exposure approximately 70% the MRHD clinical systemic exposure. In a pre-and post-natal development study in rats, pregnant animals were dosed with ruxolitinib from implantation through lactation at doses up to 30 mg/kg/day. There were no drug-related adverse effects on embryofetal survival, postnatal growth, development parameters or offspring reproductive function at the highest dose evaluated (3.1 times the MRHD clinical systemic exposure).

Lactation

Risk Summary: There are no data on the presence of ruxolitinib in human milk, the effects on the breastfed child, or the effects on milk production. Ruxolitinib was present in the milk of lactating rats. When a drug is present in animal milk, it is likely that the drug will be present in human milk. Because of the serious adverse findings in adults, including risks of serious infections, thrombocytopenia, anemia, and neutropenia, advise women not to breastfeed during treatment with OPZELURA and for approximately four weeks after the last dose (approximately 5 elimination half-lives).

Data: Lactating rats were administered a single dose of [14C]-labeled ruxolitinib (30 mg/kg) on postnatal Day 10, after which plasma and milk samples were collected for up to 24 hours. The AUC for total radioactivity in milk was approximately 13 times the maternal plasma AUC. Additional analysis showed the presence of ruxolitinib and several of its metabolites in milk, all at levels higher than those in maternal plasma.

Pediatric Use: The safety and effectiveness of OPZELURA for the topical treatment of atopic dermatitis have been established in pediatric patients aged 12 to 17 years of age with mild-to-moderate atopic dermatitis. Use of OPZELURA in this age group is supported by evidence from Trials 1 and 2 which included 92 subjects aged 12 to 17 years. No clinically meaningful differences in safety or effectiveness were observed between adult and pediatric subjects. The safety and effectiveness of OPZELURA in pediatric patients younger than 12 years of age have not been established.

Juvenile Animal Toxicity Data: Oral administration of ruxolitinib to juvenile rats resulted in effects on growth and bone measures. When administered starting at postnatal day 7 (the equivalent of a human newborn) at doses of 1.5 to 75 mg/kg/day, evidence of fractures occurred at doses ≥ 30 mg/kg/day, and effects on body weight and other bone measures [e.g., bone mineral content, peripheral quantitative computed tomography, and x-ray analysis] occurred at doses ≥ 5 mg/kg/day. When administered starting at postnatal day 21 (the equivalent of a human 2-3 years of age) at doses of 5 to 60 mg/kg/day, effects on body weight and bone occurred at doses ≥ 15 mg/kg/day, which were considered adverse at 60 mg/kg/day. Males were more severely affected than females in all age groups, and effects were generally more severe when administration was initiated earlier in the postnatal period. These findings were observed at systemic exposures that are at least 40% the MRHD clinical systemic exposure.

Geriatric Use: Of the 1249 total subjects with atopic dermatitis in clinical trials with OPZELURA, 115 were 65 years of age and older. No clinically meaningful differences in safety or effectiveness were observed between patients less than 65 years and patients 65 years and older.

PATIENT COUNSELING INFORMATION

Advise the patient or caregivers to read the FDA-approved patient labeling (Medication Guide).

Infections: Inform patients that they may be at increased risk for developing infections, including serious infections, when taking Janus kinase inhibitors. Instruct patients to tell their healthcare provider if they develop any signs or symptoms of an infection. Advise patients that Janus kinase inhibitors increase the risk of herpes zoster, and some cases can be serious.

Malignancies and Lymphoproliferative Disorders: Inform patients that Janus kinase inhibitors may increase the risk for developing lymphomas and other malignancies including skin cancer. Instruct patients to inform their health care provider if they have ever had any type of cancer. Inform patients that periodic skin examinations should be performed while using OPZELURA.

Major Adverse Cardiovascular Events: Advise patients that events of major adverse cardiovascular events (MACE) including non-fatal myocardial infarction, non-fatal stroke, and cardiovascular death, have been reported in clinical studies with Janus kinase inhibitors used to treat inflammatory conditions. Instruct all patients, especially current or past smokers or patients with other cardiovascular risk factors, to be alert for the development of signs and symptoms of cardiovascular events.

Thrombosis: Advise patients that events of DVT and PE have been reported in clinical studies with Janus kinase inhibitors used to treat inflammatory conditions. Instruct patients to tell their healthcare provider if they develop any signs or symptoms of a DVT or PE.

Thrombocytopenia, Anemia and Neutropenia: Advise patients of the risk of thrombocytopenia, anemia, and neutropenia with OPZELURA. Instruct patients to tell their healthcare provider if they develop any signs or symptoms of thrombocytopenia, anemia or neutropenia *[see Warnings and Precautions]*.

Administration Instructions: Advise patients or caregivers that OPZELURA is for topical use only *[see Dosage and Administration]*.

Advise patients to limit treatment to 60 grams per week.

Pregnancy: Inform patients to report their pregnancy to Incyte Corporation at 1-855-463-3463 *[see Use in Specific Populations]*.

Lactation: Advise a patient not to breastfeed during treatment with OPZELURA and for four weeks after the last dose *[see Use in Specific Populations]*.

Manufactured for:
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Wilmington, DE 19803

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Contents

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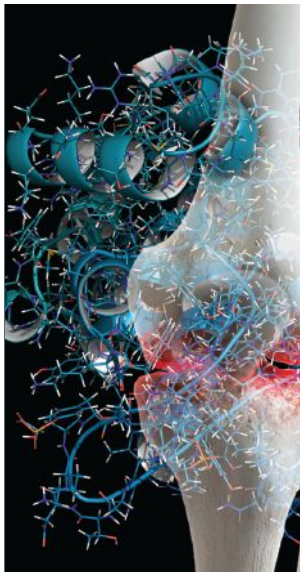
THE Dermatology Digest



***The Dermatology Digest* is Different**

Our multimedia approach delivers engaging and authoritative content in digestible bites for dermatologists overloaded with information in the emerging virtual environment. A distinct new concept, *The Dermatology Digest* filters practical and important information from industry meetings and develops original content for identified knowledge gaps in digital (video, podcast) and print formats. Concise, yet comprehensive, our content comes from the views, voices, and visions of leading dermatologists. As such, ours is an informative, educational approach thatemphasizes key details in support of safe, efficacious patient results.

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IN THIS ISSUE

The dermatology specialty has reason to be cautiously optimistic about the many drugs expanding into potential skin disease treatments. Thus, in our cover story this month, we continue to discuss the potential use of Janus kinase (JAK) inhibitors, with an in-depth interview with Dr. Roy Fleischmann, a rheumatologist who has 15 years of experience treating patients with these drugs. Dr. Fleischmann discusses the structure and function of JAK inhibitors, their pathways, and the safety and utility of these drugs across a variety of disease states.

The Dermatology Digest's (*TDD's*) signature approach to providing key meeting content is in full swing. On the pages that follow, you'll find articles with links to video or audio on valuable topics presented at Maui Derm 2022, Masterclasses in Dermatology 2022, and the recent Diversity in Dermatology Conference.

In this issue, Dr. Hilary Baldwin updates dermatologists on isotretinoin, including COVID-19 and rhabdomyolysis risk, the iPLEDGE program, and the on-going birth control dilemma. Dr. Misha Rosenbach generates awareness that dermatologists will likely see growing numbers of patients with skin reactions from immune checkpoint inhibitors and talks about how to identify and manage the many cutaneous effects from these widely used cancer drugs. Dr. Raj Chovatiya discusses the safety and efficacy of dupilumab for atopic dermatitis, asthma, and chronic rhinosinusitis as well as many other potential uses for the drug. As you'll see, there are many. Dr. Julie Harper addresses "hormonal" acne, including a relatively new hormonal treatment for men, spironolactone safety, and combination treatments. And Dr. Matthew Zirwas shares six pearls for treating hand eczema, including how to distinguish among dermatitis types, eczema interventions, and more.

In "Ted Talks," Editor-in-Chief Dr. Ted Rosen addresses loyalty (part 1)—both its importance and potential demise. (Let us know what you think.)

TDD's Literature Update tackles recent research that suggests JAK inhibitors, specifically tofacitinib, may be useful in managing refractory dermatomyositis. This month's Off-Label Pearl looks at the potential use of budesonide powder for peristomal pyoderma gangrenosum, a skin condition that currently lacks an effective, safe, and convenient treatment modality. Our Zebra will tests readers' differential diagnostic skills with the case of a 36-year-old African American male with torso lesions and a history of spontaneous keloids that become pruritic.

Enjoy this *TDD* issue, and feel free to let us know what you think or would like to see covered by reaching out to Eliza Cabana at eliza.cabana@thedermdigest.com.

The Dermatology Digest

EDITORIAL BOARD

Ted Talks

Loyalty, Part 1

"Nothing is more noble, nothing more venerable, than loyalty."

—Cicero (Roman statesman, 106-43 BC)

Ted Rosen, MD, FAAD
Editor-in-Chief

This is Ted's take.
What's yours?
ted.rosen@thedermdigest.com

The dictionary offers up many potential definitions for the word "loyalty." The one I like the most is: a strong feeling of support or allegiance.

Whether loyalty is to an ideal, an organization, a group, or an individual, it is characterized by immutable dedication, which remains steadfast even in the face of strong temptations for betrayal. Loyalty is highly prized, because it results in meaningful bonds which stand the dual tests of time and circumstance.

However, in the current age, loyalty appears to be difficult to both obtain and then maintain. Most individuals seem to be locked in a pattern of devotion—first and foremost—to their own desires and well-being. All you have to do is read, watch or listen to the news! Erstwhile political allies frequently turn on each other, often in a messy and public manner. Professional athletes demonstrate little loyalty to the organization that gave them an initial opportunity as they leap from team to team in a never-ending quest for yet an even more obscene salary. Sexual infidelity and promiscuity abound, as prominently witnessed by the lurid stories surrounding Jeffrey Epstein, Harvey Weinstein and Bill Cosby. Predatory financial gurus, like Bernie Madoff, are devoted to self-enrichment even when it leads to financial ruin for their loyal clients.

According to best-selling author and researcher, Frederick Reichheld, loyalty is nearly dead in the current business environment; companies expect to lose half their customers in five years and plan to lose up to a third of their employees in four years. To quote the Billy Joel song *My Life*: "I don't care what you say anymore, this is my life. Go ahead with your own life and leave me alone."

Nonetheless, we still instinctively seek loyalty in both our personal and professional lives.

What does loyalty have to do with medical practice? There are actually three areas of significant intersection: patient loyalty to the practice and/or the specific health care provider, employees' loyalty to the practice, and, finally, the practitioner's reciprocal loyalty to his/her patients and the practice entity.

For the sake of brevity, I will only address the first of these three herein. Unfortunately, multiple recent studies suggest that as many as 67% of practice owners and managers don't fully comprehend the vital importance of patient loyalty.

To begin, you must recognize that a practice with a tribe of loyal patients will be successful and satisfying. Know this: It costs six to seven times more to acquire a new patient than it does to retain an existing one! It is also critically important to remember that loyalty is not inherent to any relationship. A medical encounter does not automatically guarantee patient loyalty, and, therefore, patient loyalty should never be taken for granted. Rather, loyalty must be painstakingly earned by a repeated pattern of behavior. Needless to say, high quality care with consistently good clinical outcomes forms the basis for patient loyalty. A 2019 report from Press Ganey supports this assertion. However, most patients already expect to receive excellent care that addresses needs and solves problems from a board-certified specialist. Therefore, the patient

experience often makes the real difference, as "patients" morph into "health care consumers."

In the internet information era, patients have abundant choice. Research discloses that over 80% of patients will consider switching to another office if they have an unsatisfactory patient experience, regardless of a favorable medical outcome.

Attitude matters! Surveys constantly tell us that patients truly appreciate an office that "cares" and that treats them with both courtesy and respect. While that is particularly true regarding the primary provider, it is also true with reference to receptionists, medical assistants or nurses, billing personnel or the office manager. If you learn that any practice employee is having a negative impact on patient loyalty by perceived indifference, incompetence, discourtesy, disrespect or (worst of all) overt hostility, that must be addressed and rectified immediately.

Part of the patient experience equation is easy and timely access to the practice/provider. Multiple care options, simplified registration and scheduling, work-in appointments (or teledermatology visits) for urgent or emergent matters, short times spent in the waiting room, and rapid responses to questions or concerns all build patient loyalty. Patients are also likely to become loyal to practices where teamwork is on display within the office and coordination of care is standard between the specialist office and other external providers.

What else can be done to improve the patient experience and thereby help insure loyalty? Use an online presence wisely. Develop an eye-pleasing website with accurate and updated information. Savvy patients can use a portal to communicate with the practice or directly with the provider. Positive online reviews may help reinforce patients' affinity toward the practice. Online questionnaires can engage the patients so that they recognize attempts to constantly evolve and improve service. Finally, social media and/or a digital newsletter can be utilized to continue patient engagement outside the office environment. Tell the patients about

Attitude matters! Surveys constantly tell us that patients truly appreciate an office that "cares" and that treats them with both courtesy and respect.

in-office special deals or enlighten them about ground-breaking general medical or dermatology-specific developments.

A good financial experience can influence patient loyalty. Poor interactions in the financial realm can dissuade patients from continuation of care and thereby destroy any accrued loyalty. Some patient surveys suggest that over 90% of respondents would consider dropping a provider due to a distasteful financial experience. Always practice financial transparency. Surprises at the checkout desk are horrid! Consider discounts, when allowable, for patients whose economic circumstances have deteriorated.

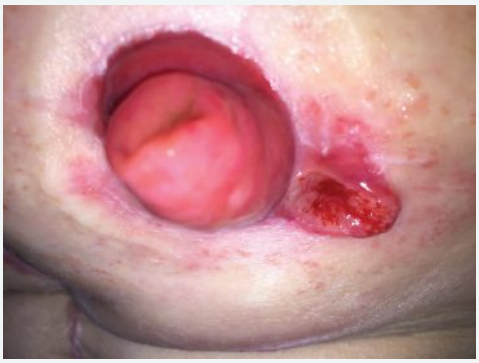
Lastly, effective marketing certainly communicates the services you provide and the reasons to trust and choose you and recommend you to others. However, do realize that high quality care delivered by an affable and approachable dermatologist, who demonstrates empathy, compassion, and concern, drives patient loyalty far more efficiently than standard marketing ploys.

Off-label Pearl

By Ted Rosen, MD, FAAD, Editor-in-Chief

Budesonide Powder for Peristomal Pyoderma Gangrenosum?

Peristomal pyoderma gangrenosum (PPG) is an uncommon variant accounting for about 15% of all pyoderma gangrenosum (PG) cases.[1]



PPG is most often associated with underlying inflammatory bowel disease (ulcerative colitis and Crohn disease) but may also be seen near ostomy sites related to treatment of gastrointestinal cancer. PPG is more frequently encountered with ileostomy sites compared to colostomy sites. Lesions are characteristically associated with excruciating pain and usually demonstrate the morphological features (ulceration, undermined and violaceous borders) encountered in the more typical form of PG. (Figure 1)

There is a wide variety of therapeutic interventions which have been proposed, testifying to the difficulty in managing this condition. Topical corticosteroids and topical calcineurin inhibitors, as well as systemic corticosteroids, cyclosporine, and dapsone are the favored recommendations. However, the use of topical agents is complicated by their propensity to interfere with the adherence of the ostomy pouch, while the various systemic agents all carry real medical risks. Thus, there is a real unmet need to identify an effective, safe, and convenient treatment modality for PPG.

A recent online publication outlined the use of generic 3mg budesonide capsules.[2] The latter are pulled open, and the budesonide powder contained within is sprinkled onto the PPG at the time of ostomy pouch changes. The dry nature of the budesonide powder protects the ostomy pouch seal, and, if needed, stoma powder can also be spread right over the medication.

Budesonide capsules are affordable and readily available, making this an attractive creative method of managing PPG.

REFERENCES

1. Afifi L, et al. Diagnosis and management of peristomal pyoderma gangrenosum: A systematic review. *J Am Acad Dermatol.* 2018;78(6):1195-1204.e1. doi:10.1016/j.jaad.2017.12.049.
2. Boettler M, et al. Budesonide capsules for peristomal pyoderma gangrenosum. *J Am Acad Dermatol.* 2022;86(2):e37-e38. doi:10.1016/j.jaad.2021.05.053.

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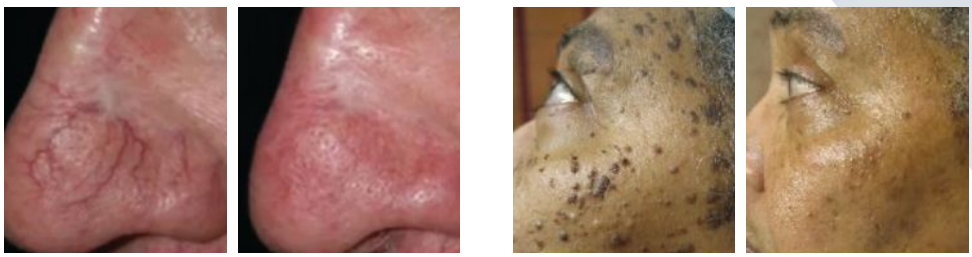

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Literature Lessons

COVID-19

Data generated by 4,666 pharmacy testing sites across 49 states was analyzed for **VACCINE EFFICACY.** Vaccination with 3 doses of mRNA COVID-19 vaccine, compared with being unvaccinated or only receiving 2 doses, was associated with protection against both the Omicron and Delta variants of the SARS CoV-2 virus. However, higher odds ratios for the association with Omicron infection suggest lower degree of protection than for Delta.

TO READ MORE: Accorsi EK, et al. Association Between 3 Doses of mRNA COVID-19 Vaccine and Symptomatic Infection Caused by the SARS-CoV-2 Omicron and Delta Variants. *JAMA*. 2022;327(7):639-651. doi:10.1001/jama.2022.0470.

(**EDITOR'S NOTE:** The "booster" shot works.)

A multicenter, open-label prospective Malaysian study of about 500 mild to moderate COVID-19 patients with risk factors for progression to severe disease were enrolled during 2021. Patients were randomized to receive either standard of care including **ORAL IVERMECTIN** (0.4mg/kg daily for five days) versus standard of care without ivermectin. There was no statistical difference between the two groups with regards to the proportion of patients who experienced disease progression (21.6% in ivermectin group, 17.3% in no ivermectin group). The study suggests that, even with early administration, ivermectin does not demonstrate significant benefit.

TO READ MORE: Lim SCL, et al. Efficacy of Ivermectin Treatment on Disease Progression Among Adults With Mild to Moderate COVID-19 and Comorbidities: The I-TECH Randomized Clinical Trial [published online ahead of print, 2022 Feb 18]. *JAMA Intern Med.* 2022;10.1001/jamainternmed.2022.0189. doi:10.1001/jamainternmed.2022.0189.

PEDIATRIC DERMATOLOGY

The authors describe a phenomenon called **"PIGMENTED TRANSVERSE NASAL BAND."** This consists of an asymptomatic 1-2mm wide band of macular pigmentation seen in children (Caucasians) and adolescents and young adults (skin of color, particularly of Indian ethnicity). This band is located at the junction of the upper two-thirds and lower one-third of the nose, just proximal to alae nasi. There is a female preponderance and a familial predilection.

TO READ MORE: Agarwal K, et al. Pigmented transverse nasal band: A review. *Indian J Dermatol Venereol Leprol.* 2022;88(2):144-147. doi:10.25259/IJDVL_820_19.

DRUGS AND DEVICES

A device emitting 20 MHz of **HIGH INTENSITY FOCUSED ULTRASOUND** was safe and effective at eliminating seborrheic keratosis.

OF 54 LESIONS TREATED

37	15	2
were completely eliminated	showed a partial response	failed to respond

On a 10-point analog scale, treatment-related pain was generally judged a 2, with an occasional 4. There was a chance of residual telangiectasia and 11% had residual mild scarring. Commercial development of this device is planned.

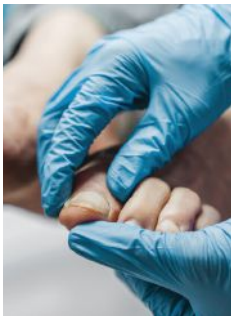
TO READ MORE: Calik J, Migdal M, Zawada T, Bove T. Treatment of Seborrheic Keratosis by High Frequency Focused Ultrasound - An Early Experience with 11 Consecutive Cases. *Clin Cosmet Investig Dermatol.* 2022;15:145-156. Published 2022 Jan 28. doi:10.2147/CCID.S348106.

While **SYPHILITIC ALOPECIA** is typically described as patchy, a case of generalized hair loss related to lues is described. The pattern closely mimicked alopecia universalis.

TO READ MORE: Sons JS, et al. A case of HIV-associated generalized syphilitic alopecia mimicking alopecia universalis. *Int J Dermatol.* 2022;61(1):e1-e2. doi:10.1111/ijd.15721.

The **LIFETIME RISK OF HIV** acquisition fell notably during the period 2017 to 2019. Overall risk fell 11%, from 1 in 106 (data from 2010 to 2014) to 1 in 120. Similar declines were seen in both men (from 1 in 68 to 1 in 76) and women (from 1 in 253 to 1 in 309). However, among Black and Hispanic populations, lifetime risk of HIV infection continued to be higher than the general population risk.

REFERENCE: Virtual Conference on Opportunistic and Retrovirus Infections. February 12-16, 2022. CROI Conference.



Although this study was done in Spain, it surprisingly revealed that among surveyed podiatrists, 86.3% considered complementary **TESTS FOR ONYCHOMYCOSIS** (KOH, culture, PCR) necessary, but only 21.4% used such tests routinely.

TO READ MORE: Aldana-Caballero A, et al. Assessment of Visual Diagnosis by Podiatrists for HPV and Onychomycosis: The Need for Complementary Tests. *J Fungi* (Basel). 2022;8(2):135. Published 2022 Jan 29. doi:10.3390/jof8020135.

(**EDITOR'S NOTE:** I really wonder what a contemporary survey study of U.S. dermatologists would show in this regard!)

The FDA has approved the first condom specifically indicated for use during **ANAL INTERCOURSE**. One Male Condom is also indicated to prevent pregnancy and to reduce incident sexually transmitted disease during vaginal intercourse. The condom failure rate (slippage, breakage, or both) during anal intercourse was only 0.68%.

TO READ MORE: FDA permits marketing of first condom specifically indicated for anal intercourse. News release. February 23, 2022. Accessed at: FDA Permits Marketing of First Condom Specifically Indicated for Anal Intercourse | FDA

A retrospective nationally representative review of 1242 adult inpatients treated for **SKIN AND SOFT TISSUE INFECTIONS**, piperacillin-tazobactam and vancomycin use was the same across all ethnic/racial groups. However, clindamycin (considered inferior and associated with a higher risk of *C. difficile* superinfection) was used almost twice as often in Black compared to White patients. Cefazolin (considered clinically superior and less risky) was administered more than twice as frequently in White compared to Black patients.

TO READ MORE: Wurcel AG, et al. Variation by Race in Antibiotics Prescribed for Hospitalized Patients With Skin and Soft Tissue Infections. *JAMA Netw Open.* 2021;4(12):e2140798. Published 2021 Dec 1. doi:10.1001/jamanetworkopen.2021.40798.

This recent Danish laboratory survey disclosed **INCREASING TERBINAFINE RESISTANCE** among clinical Trichophyton isolates. As the authors state: "Susceptibility testing is highly relevant in non-responding cases."

TO READ MORE: Astvad KMT, et al. Increasing Terbinafine Resistance in Danish Trichophyton Isolates 2019-2020. *J Fungi* (Basel). 2022;8(2):150. Published 2022 Jan 31. doi:10.3390/jof8020150.

(**EDITOR'S NOTE:** Antifungal resistance is NOT confined to places like India. It is becoming reality throughout the industrialized world.)

ATOPIC DERMATITIS

A cross-sectional survey of 240 parent-child combinations revealed that **ITCHING** in the pediatric atopic dermatitis patient occurs in the early evening and at bedtime.

TO READ MORE: Cheng BT, Patel MS, Xu M, et al. Timing of itch among children with atopic dermatitis [published online ahead of print, 2022 Feb 4]. *Ann Allergy Asthma Immunol*. 2022;S1081-1206(22)00089-8. doi:10.1016/j.anai.2022.01.042.

CONTACT DERMATITIS

Gold thread acupuncture consists of intradermal injection of multiple thin, sterile linear gold particles. This procedure may be used to relieve muscular and articular pain or to reduce wrinkles. The authors report a case reminding us that gold, while considered inert, once put into the tissue is subject to alteration over time turning it into an allergen. The patient reported development of histologically verified **FOREIGN BODY REACTIONS** at the sites of gold thread implantation. Improvement was obtained by thread removal coupled with intralesional steroid injection.

TO READ MORE: Yook H, et al. A case of foreign body granuloma developing after gold thread acupuncture. *Indian J Dermatol Venereol Leprol*. 2022;88(2):222-224. doi:10.25259/IJDVL_258_2021.

PSORIASIS

A year-long, prospective German study of 331 obese psoriasis patients found that **SECUKINUMAB** 300mg given every two weeks was more effective compared to once monthly dosing. Multiple parameters, including PASI 75, PASI 90, PASI 100, Investigator's Global Assessment scores of 0 or 1, and improved Dermatology Life Quality Index scores were all assessed. Both regimens were well tolerated. Despite more frequent dosing, there was no increase in Candida infections among the every-two-week drug recipients.

TO READ MORE: Augustin M, et al. Secukinumab dosing every two weeks demonstrated superior efficacy compared with dosing every four weeks in patients with psoriasis weighing 90 kg or more: Results of a randomised controlled trial [published online ahead of print, 2022 Jan 4]. *Br J Dermatol*. 2022;10.1111/bjd.20971. doi:10.1111/bjd.20971.

An Israeli cohort of 5,275 psoriatic arthritis patients was compared to 21,011 matched controls. The causes of death during a mean follow-up of just over 7 years was the same for both groups. After correcting for comorbid states, the crude hazard ratio for **ALL-CAUSE MORTALITY** was also the same in both groups.

TO READ MORE: Haddad A, et al. The Association of Psoriatic Arthritis With All-cause Mortality and Leading Causes of Death in Psoriatic Arthritis. *J Rheumatol*. 2022;49(2):165-170. doi:10.3899/jrheum.210159.

The fourth case of **GUTTATE PSORIASIS** associated with SARS-CoV-2 infection was reported. The eruption responded to topical corticosteroid administration.

TO READ MORE: Janodia RP, et al. Guttate psoriasis following COVID-19 infection. *Cutis*. 2022 February;109(2):101-102. doi:10.12788/cutis.0443.

A prospective Chinese study compared 152 psoriasis only patients to 136 psoriasis plus **PSORIATIC ARTHRITIS** patients. Those with arthritis had a higher age at disease onset and a greater prevalence of hypertension and hypercholesterolemia. Interestingly, methotrexate therapy was found to lower lipid levels in both groups.

TO READ MORE: Wang B, et al. The difference of lipid profiles between psoriasis with arthritis and psoriasis without arthritis and sex-specific downregulation of methotrexate on the apolipoprotein B/apolipoprotein A-1 ratio. *Arthritis Res Ther.* 2022;24(1):17. Published 2022 Jan 7. doi:10.1186/s13075-021-02715-4.

A small Egyptian study compared four different techniques (N=10 each) of preparing **PLATELET-RICH PLASMA** (PRP) for monthly injection as therapy for female pattern hair loss. It was concluded that use of a digital centrifuge, large-sized sodium citrate tubes, and a single spin with low centrifugation speed (900 rpm) was optimal for PRP preparation.

TO READ MORE: Moftah NH, et al. Different platelet-rich plasma preparation protocols in Female pattern hair loss: Does it affect the outcome? A pilot study. *J Cosmet Dermatol.* 2022; January 2.doi.10.1111/jocd.14648.

A small (N=15) U.S. open-label, single-arm, single center prospective study investigated injection of **DEOXYCHOLIC ACID** (Kybella) in the fat of upper, inner thighs. Two to four injection sessions, given 5 to 7 weeks apart, were performed. Patients received at total of 40 injections of 0.2ml at each session. At the end of a 12-week follow-up period, thigh circumference decreased an average of 2.2cm and the "thigh gap" increased by an average of 1.6cm. Overall, 13 of 15 subjects (86%) were satisfied and 11 of 15 (73%) indicated that they would undergo the treatment again.

TO READ MORE: Yuan J, et al. Safety and Efficacy of Deoxycholic Acid for Reduction of Upper Inner Thigh Fat. *J Drugs Dermatol.* 2022;21(1):66-70. doi:10.36849/JDD.2022.5919.

(**EDITOR'S NOTE:** Kybella (Allergan Aesthetics) is the only FDA approved injectable treatment for reduction of submental fat.)

A small (N=20, all women, aged 24 to 38) U.S. prospective study of same-visit **COMBINATION AESTHETIC TREATMENT** disclosed excellent patient satisfaction at 2 months post-therapy session. All patients received multi-site Botox Cosmetic injections, Juvederm Voluma into the midface, and Juvederm Volbella into the lips. Addressing all cosmetic concerns simultaneously led to decreased self-perceived age and improvement in psychosocial functioning.

TO READ MORE: Kurtti A, et al. Combination Facial Aesthetic Treatment in Millennials. *J Drugs Dermatol.* 2022;21(1):37-42. doi:10.36849/JDD.2022.6425.

Analysis of a large U.S. database showed reduced prevalence of **ANXIETY** among those who received botulinum toxin injections for cosmetic purposes (mostly glabellar rhytid reduction), for migraine management, improvement in spasticity of upper and lower limbs, and torticollis and neck pain. One theory for this finding is that relaxing facial and neck muscles, which are utilized to express negative emotions, reduces the intensity of those emotions.

TO READ MORE: Wollmer MA, et al. Postmarketing safety surveillance data reveals protective effects of botulinum toxin injections against incident anxiety. *Sci Rep.* 2021;11(1):24173. Published 2021 Dec 21. doi:10.1038/s41598-021-03713-x.

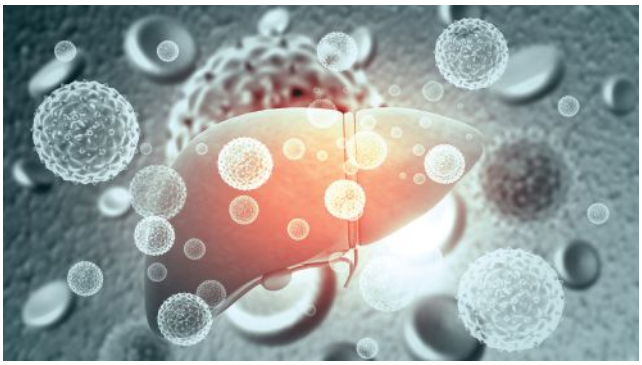
HIDRADENITIS SUPPURATIVA

Despite pain being a major feature of hidradenitis, there is no widely accepted algorithm for **PAIN MANAGEMENT** in this disorder. The authors point out the multifactorial nature of HS pain, which is worsened by underlying anxiety and depression. If oral NSAIDS, acetaminophen, and topical analgesics (such as liposomal lidocaine cream) fail, prudent use of oral opiates may be considered. Intralesional triamcinolone may relieve pain of acutely inflammatory abscesses.

TO READ MORE: Jeha GM, et al. Management of Acute and Chronic Pain Associated With Hidradenitis Suppurativa: A Comprehensive Review of Pharmacologic and Therapeutic Considerations in Clinical Practice. *Cutis*. 2021 November;108(5):281-286,E4 | doi:10.12788/cutis.0383.

A retrospective cross-sectional analysis was done using data derived from the largest managed care organization in Israel. There was an increased risk of both **HEPATITIS B AND HEPATITIS C** infection among those carrying a dermatologist-verified diagnosis of hidradenitis suppurativa. This may relate to elevated levels of IL-17.

TO READ MORE: Cohen JM, et al. Hepatitis B and C among patients with hidradenitis suppurativa: a population-based study. *Int J Dermatol*. 2022;61(1):84-88. doi:10.1111/ijd.15578.



Although self-reported postoperative recurrence occurred in 41%, patients who underwent outpatient **SURGICAL INTERVENTION** for HS were generally satisfied with the outcome. De-roofing and local tissue excision were the primary interventions done in the clinic setting at a single American academic institution.

TO READ MORE: Ravi S, Miles JA, Steele C, Christiansen MK, Sayed CJ. Patient Impressions and Outcomes After Clinic-Based Hidradenitis Suppurativa Surgery. *JAMA Dermatol*. 2022;158(2):132-141. doi:10.1001/jamadermatol.2021.4741.

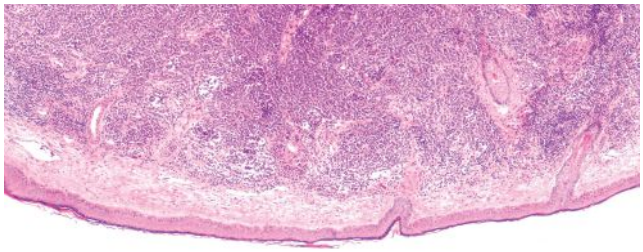
CUTANEOUS ONCOLOGY, SURGERY, AND LASERS

A systematic review and meta-analysis disclosed that smoking is not a risk factor **FOR BASAL CELL CARCINOMA**. In fact, smoking was found to be somewhat protective. This may relate to nicotine release, which reduces prostaglandin metabolism, thereby altering the cutaneous inflammatory response to UV irradiation.

TO READ MORE: Wu PC, et al. Smoking and the risk of basal cell carcinoma: a systematic review and meta-analysis. *Int J Dermatol.* 2022;61(1):e33-e37. doi:10.1111/ijd.15607.

A prospective cohort study of 618 patients with **MERKEL CELL CARCINOMA** demonstrated a higher recurrence rate (40%) following ostensibly definitive excision than that expected for both melanoma and non-melanoma skin cancer. Over 90% of the recurrences occurred within three years following treatment. Factors favoring recurrence included higher pathologic stage, male gender, older age and clinically detectable nodal disease.

TO READ MORE: McEvoy AM, Lachance K, Hippe DS, et al. Recurrence and Mortality Risk of Merkel Cell Carcinoma by Cancer Stage and Time From Diagnosis [published online ahead of print, 2022 Feb 23]. *JAMA Dermatol.* 2022;e216096. doi:10.1001/jamadermatol.2021.6096.



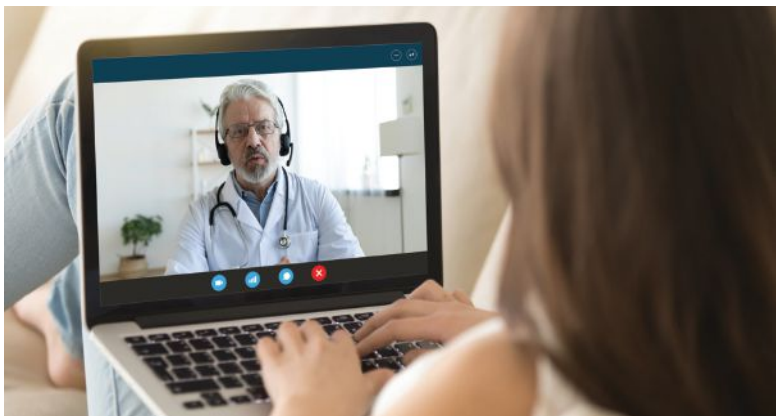
GENERAL DERMATOLOGY

A 10-year retrospective review from a single academic center revealed **VULVOVAGINAL INVOLVEMENT** in 12.7% of women with Stevens-Johnson syndrome or toxic epidermal necrolysis. To both hasten lesion involution as well as prevent long-term sequelae (mostly scarring), early intervention is recommended. Therapy may include ultrapotent topical steroids, topical estrogen-containing cream, and menstrual suppression with oral progesterone. The latter prevents the formation of premalignant vaginal adenosis. Vaginal dilation may be required.

TO READ MORE: Crowder CA, et al. Vulvovaginal involvement in Stevens-Johnson syndrome and toxic epidermal necrolysis: management and techniques used to reduce gynecologic sequelae. *Int J Dermatol.* 2022;61(2):158-163. doi:10.1111/ijd.15676.

A large survey disclosed that 70% of dermatologists predict that **TELE-DERMATOLOGY** use will continue after the COVID-19 pandemic subsides, but only 58% are planning on personally utilizing this modality. Viability of teledermatology will depend largely on fair reimbursement and continued relaxation of Federal rules. Respondents felt teledermatology was most appropriate for acne and rosacea, medication monitoring, routine follow-ups, and a small number of inflammatory conditions.

TO READ MORE: Hopkins ZH, et al. Teledermatology During the COVID-19 Pandemic: Lessons Learned and Future Directions. *Cutis.* 2022;109(1):12-13. doi:10.12788/cutis.0431.



English-speaking adults at a single New York institution were surveyed regarding their **SATISFACTION WITH TELEDERMATOLOGY** care, a modality widely expanded during the COVID-19 pandemic. It is worth noting that patients over age 55 were less satisfied than those younger, and that African-Americans expressed concerns over confidentiality. All participants preferred teledermatology for follow-up visits rather than for initial consultation.

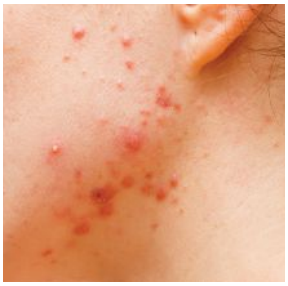
TO READ MORE: Chang LJ, et al. Disparities in telemedicine satisfaction among older and non-white dermatology patients. *J Drugs Dermatol* 2022;21:210-214

ACNE

Although the quality of the evidence was viewed as low, yet another systematic review and meta-analysis failed to show a link between **SPIRONOLACTONE** use and risk of cancer of any kind.

TO READ MORE: Bommareddy K, et al. Association of Spironolactone Use With Risk of Cancer: A Systematic Review and Meta-analysis. *JAMA Dermatol.* 2022;158(3):275-282. doi:10.1001/jamadermatol.2021.5866.

Using data from the Global Burden of Disease Study, investigators ascertained that incident cases of **ACNE VULGARIS** increased by 48% from 1990 to 2019. The age-standardized incidence rate of acne vulgaris increased from 13.5 to 15.9 per 1000 person years. Excluded from this increase in acne were the United States, Germany, Poland and New Zealand.



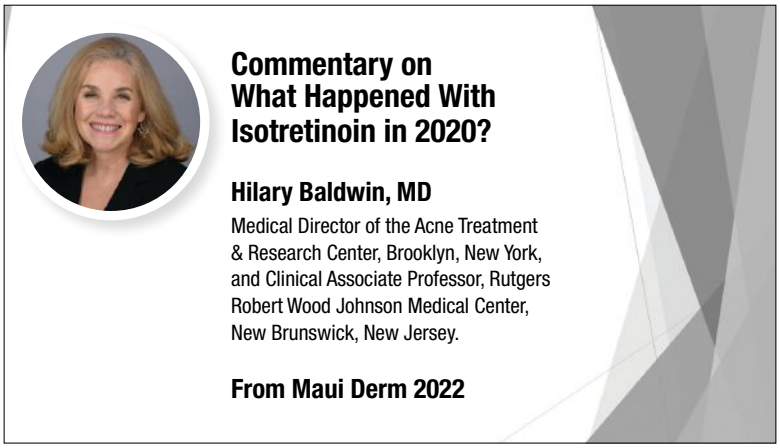
TO READ MORE: Chen H, et al. Magnitude and temporal trend of acne vulgaris burden in 204 countries and territories from 1990 to 2019: an analysis from the Global Burden of Disease Study 2019 [published online ahead of print, 2021 Nov 10]. *Br J Dermatol.* 2021;10.1111/bjd.20882. doi:10.1111/bjd.20882.

ADAPALENE has differences in basic pharmacology compared to other retinoids, likely accounting for its high degree of safety as an OTC agent. A maximal usage trial demonstrated relatively low systemic exposure. Analysis of pregnancy outcomes following known drug exposure failed to show increases in miscarriage, fetal death, or neonatal structural abnormalities.

TO READ MORE: Weiss J, et al. Safe Use of Adapalene 0.1 % Gel in a non-Prescription Environment. *J Drugs Dermatol.* 2021;20(12):1330-1335. doi:10.36849/jdd.6527.

A Recent Review of Isotretinoin

With Hilary Baldwin, MD



WATCH: https://thedermdigest.com/video/a-recent-review-of-isotretinoin

Dr. Hilary Baldwin discusses the latest with isotretinoin, including COVID-19 risk, rhabdomyolysis risk, the iPLEDGE program, and the ongoing birth control quandary.

"This is not the audience with which to discuss the use and side effects of isotretinoin. I thought, rather, I would look at the news on isotretinoin from 2020, and condense it into a few topics," said Hilary Baldwin, MD, who presented "What Happened With Isotretinoin in 2020?" at Maui Derm 2022.

"What I found in 2020 was a lot of questions regarding isotretinoin and COVID-19. Does isotretinoin increase the risk of COVID acquisition? Should we be worried about it?"

The short answer appears to be no, said Dr. Baldwin.

"About two-thirds of our patients complain of very dry nasal mucous membranes. We also know that the virus binds to the nasal mucosa and gains entry from there. So might this dry nasal mucosa mean that our patients on isotretinoin are at a higher risk of acquiring infection?"

In two studies[1,2] that looked at COVID infection rates in people on and not on isotretinoin, researchers found no difference in infection incidence, said Dr. Baldwin.

Notably, another study[3] examined repurposing 672 drugs to prevent or treat COVID. Isotretinoin ranked 1 out of 672 in its ability

to decrease binding of the virus to the nasal mucosa.

"So, there is no evidence that isotretinoin use increases the risk of COVID infection, and it appears that we can continue routine use of the drug."

iPLEDGE

Updates to the iPLEDGE program late last year disrupted patient care, creating challenges for dermatologists and their patients. But it did solve one problem, said Dr. Baldwin.

"There were many articles in 2020 regarding iPLEDGE deficiencies. Several identified inequities with the transgender public, who were forced to identify themselves as either female or male."

Fortunately, with recent changes to the website, patients are more appropriately referred to as people who can and people who cannot get pregnant, said Dr. Baldwin.

The articles identified other issues with iPLEDGE, including education and socioeconomic iniquities.

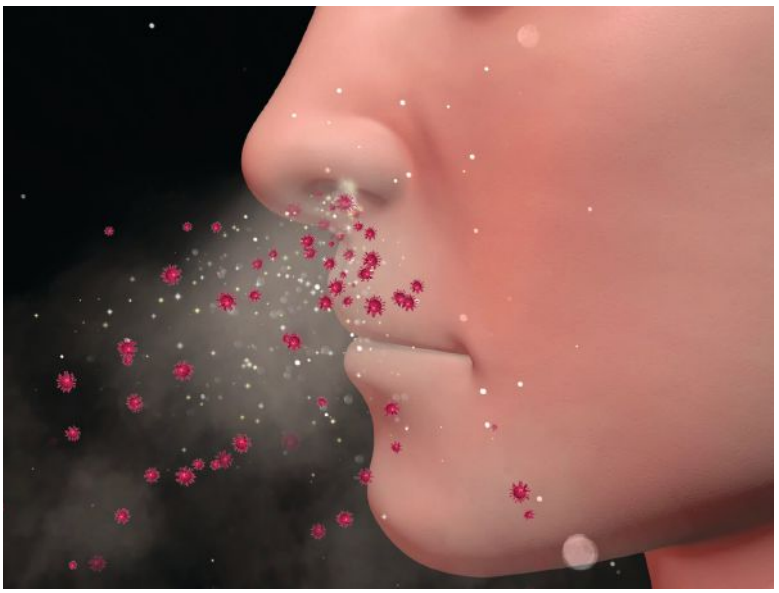
"Studies have shown that iPLEDGE marginalizes women, it marginalizes patients in poor neighborhoods, and it marginalizes those who don't have the money for computers or internet access. Language used in the iPLEDGE materials is above national literacy levels, creating issues for many of our patients."

Until the system is fixed, one solution is to provide computer access to patients in the office, said Dr. Baldwin. A dedicated computer with limited access to iPLEDGE can be used to assure that patients have completed all items before they leave the office.

A Question of CK

"Should we be checking CK [creatine kinase], especially in our athletic boys?"

It's a question that dermatologists have asked for years, said Dr. Baldwin.



"There are case reports of increased CK levels in patients on isotretinoin, but they were far and few between and most physicians do not check CK."

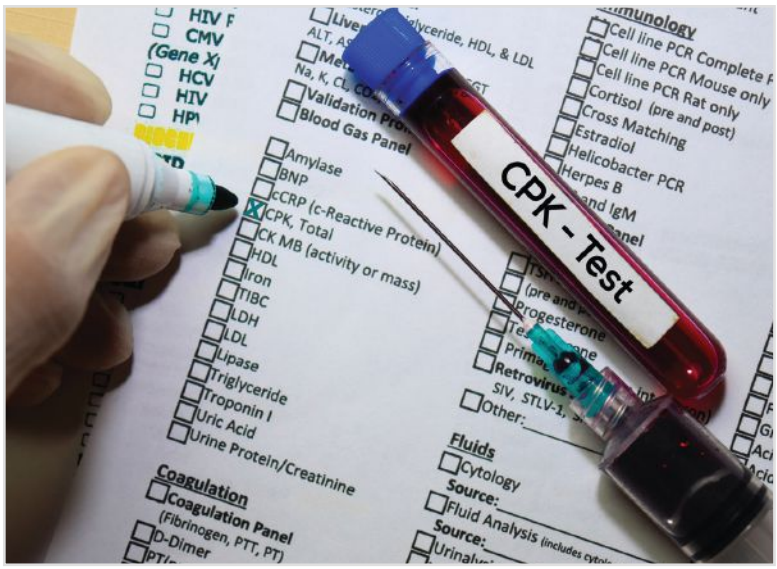
However, a study[4] published by Guy Webster, MD, PhD, in 2017 showed a frequency and magnitude of CK elevations among physically active male patients that suggested CK monitoring is warranted in this population, she said.

"Two papers in 2021 detailed several athletic males with very high CK levels, 10 to 20 times normal, on low levels of isotretinoin. Many case reports throughout the medical literature identify that athletic males are at highest risk for rhabdomyolysis. An unanswered question is whether the CK elevations are due to the at-risk population, isotretinoin use, or a combination of both. In the meantime, it seems prudent to evaluate CKs in athletic males on isotretinoin."

The Birth Control Quandary

"Over the years, I have informally queried dermatologists at educational meetings regarding their prescribing habits for oral contraceptives in patients about to start isotretinoin. Each

> "Does isotretinoin increase the risk of COVID acquisition? Should we be worried about it?"
>
> The short answer appears to be no….



> An unanswered question is whether the CK elevations are due to the at-risk population, isotretinoin use, or a combination of both. In the meantime, it seems prudent to evaluate CKs in athletic males on isotretinoin."

time the audience was evenly split between those who prescribe contraceptives and those who refer to gynecologists."

According to Dr. Baldwin, past studies have shown that dermatologists get poor marks as contraceptive counselors.

Research also shows that the counseling dermatologists provide is generally limited to oral contraceptives without any significant attention to other methods that are, in fact, more likely to result in compliant behavior with superior efficacy, namely intrauterine and subdermal implants.[5]

"Presumably this is due to the comfort level of dermatologists. We don't feel comfortable talking about implants and IUDs, and the only conversation that we have with most of our female patients is the use of oral contraceptives."

In a recent study,[6] physicians at The Ohio State's dermatology clinics were trained to administer subdermal implants.

"Once they knew how to do it, they were much more likely to have a real conversation with their patients, talking about all the various options for birth control," said Dr. Baldwin.

Of the 36 study participants on isotretinoin, 25% chose the subdermal implant. Researchers concluded that physician counseling on contraceptive options may have a significant effect on selection.

"The bottom line is that we need to be well educated in all methods of contraceptives if we are going to counsel our patients effectively. Otherwise, we should turn the job over to the gynecologists." ◈

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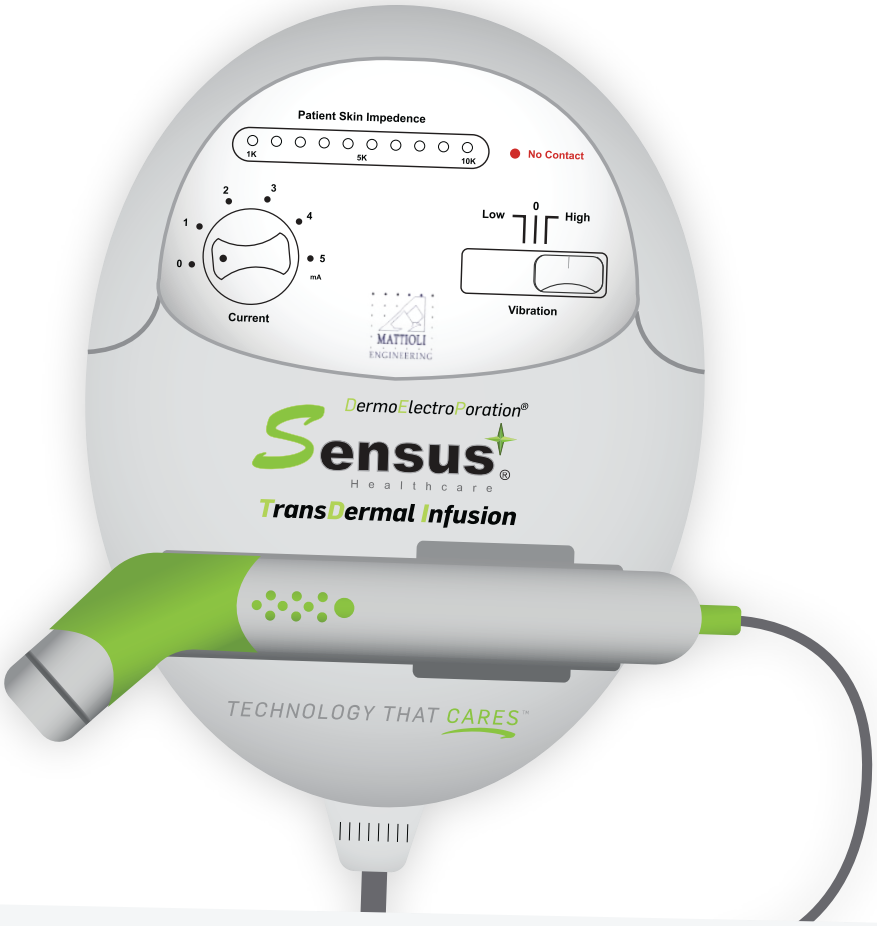
DISCLOSURE:
Dr. Baldwin is an advisor and speaker for Sun Pharma.



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The JAK Inhibitor Experience in Rheumatology

With Roy Fleischmann, MD, MACR

THIS IS PART 1 OF A 3-PART SERIES ON JAK INHIBITORS

Dr. Roy Fleischmann discusses Janus kinase (JAK) inhibitors from a rheumatologist's perspective, addressing their structure and function as well as the pathways utilizing JAKs, and the safety and utility of these drugs across a variety of disease states.

WATCH: https://thedermdigest.com/video/the-jak-inhibitor-experience-in-rheumatology

"We have had experience with all three JAK inhibitors in rheumatology and found them very efficacious and relatively safe," said Roy Fleischmann, MD, MACR, a rheumatologist who uses JAK inhibitors in practice who also has published extensively on their use, efficacy, and safety. He is an author of the ORAL Surveillance study, published in early in 2022 in the *New England Journal of Medicine*.[1]

"The Metroplex Clinical Research Center has been involved with studies of JAK inhibitors over the past 15 years. I will first address what inhibition of the JAK pathway means clinically."

JAK1, JAK2, JAK3, and tyrosine kinase (TYK2) compose the JAK family.

"And they form different combinations, usually dimers but occasionally trimers. There is only one homodimer and that is JAK2."

The combination of JAK1 and 3 affect the gamma chain cytokines interleukin-(IL-) 2, 4, 7, 9, 15, and 21. The combination of JAK2 and TYK2 is particularly interesting to dermatologists, as this dimer signals through IL-12 and IL-23. There other combinations of JAKs affecting different cytokines with resulting different biological functions, depending on the combination, said Dr. Fleischmann.

"The functions of JAK1/3 dimer, for example, are growth and maturation of lymph cells, differentiation and homeostasis of T-cells and NK cells, B-cell class switching, and inflammation. The biological function of JAK2/TYK2 are innate immunity, differentiation and proliferation of Th17 cells, and inflammation."

JAK inhibitors are oral, synthetic small molecules. They are chemicals and not proteins that have specific targets, according to Dr. Fleischmann.

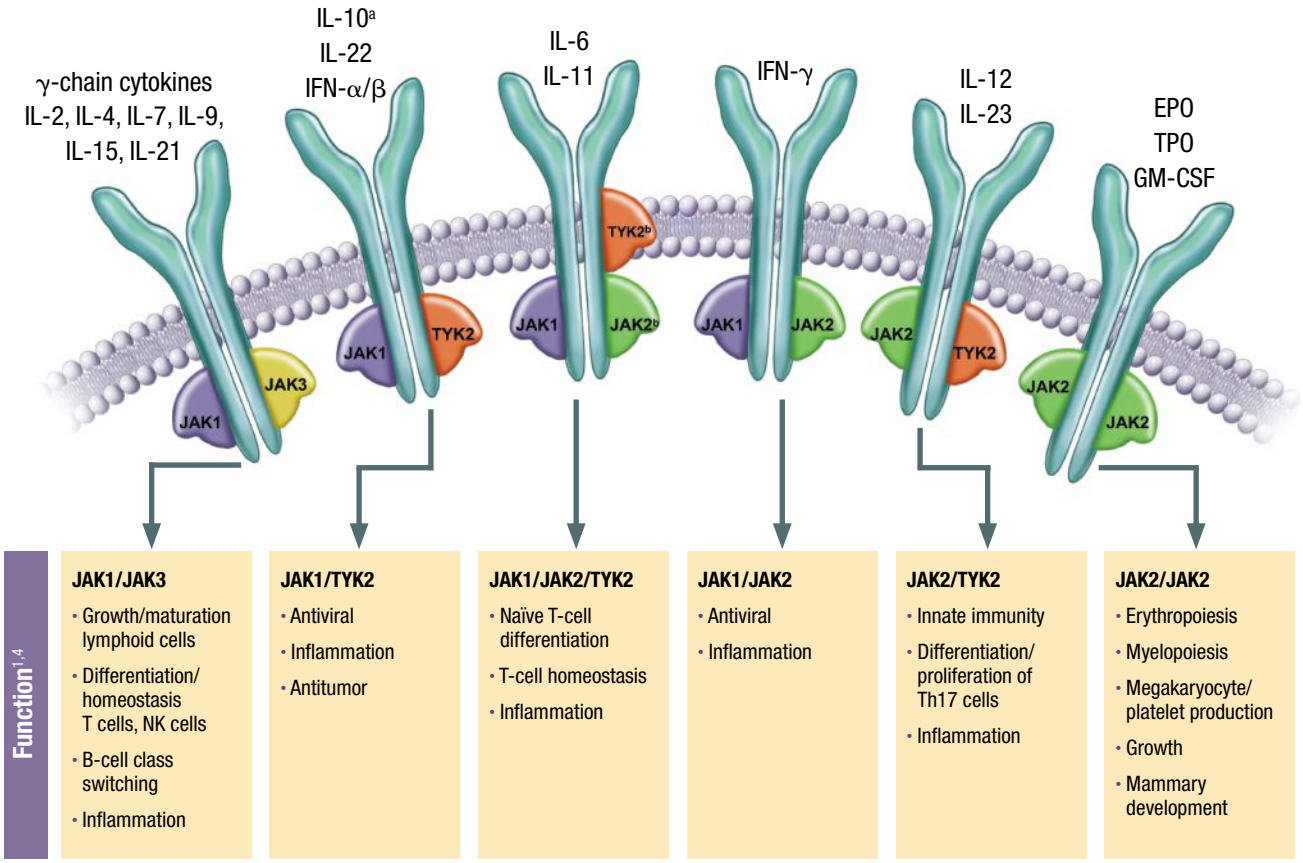
"The approved Janus kinase (JAK) inhibitors, tofacitinib (pan JAK inhibitor), baricitinib (JAK1/2 inhibitor), and upadacitinib (preferentially JAK1 inhibitor), are targeted competitive inhibitors of the adenosine triphosphate [ATP] binding site (also referred to as the 'catalytic binding site') on JAKs, while deucravacitinib, a TYK2 inhibitor, binds to the 'pseudokinase domain' of TYK2 and 'allosterically' (via conformational changes in TYK2) alters the catalytic ATP binding site preventing ATP binding."

ROY FLEISCHMANN, MD, MACR

Clinical Professor of Medicine at the University of Texas Southwestern Medical Center
Co-Medical Director of the Metroplex Clinical Research Center, Dallas, Texas.

> "By inhibiting JAK pathways, JAK inhibitors modulate signaling of multiple cytokines involved in the pathogenesis of rheumatoid arthritis and psoriatic arthritis, as well as other diseases."

Signaling Through Different JAK Combinations Has Different Biologic Functions[1-4]



[a]IL-10/IL-22 may have pro- or anti-inflammatory activities depending on the cellular environment and/or disease state.[3] [b]Type II cytokine receptors such as gp130 subunit sharing receptors for IL-6 and IL-11 I as well as IL-10, IL-19, IL-20, and IL-22, mainly signal through JAK1, but also associate with JAK2 and TYK2.[2]

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> The fact that [JAKs] inhibit the production of multiple cytokines, although not fully, is probably the reason why they are effective and relatively safe."

Cytokine signaling occurs through multiple intracellular pathways, including the JAK pathway, said Dr. Fleischmann.

"Cytokine receptor activation and JAK pathway signaling occur in the following sequence. First, a cytokine binds to type I and type II cell surface receptors followed by JAK activation and phosphorylation by ATP. Signal transducers and activators of transcriptions (STATs) then bind at the receptor and are phosphorylated by activated JAKs, which is followed by the STAT translocating to the nucleus to alter gene transcription and cytokine production."

The cytokines produced usually are a combination of both pro-inflammatory and anti-inflammatory molecules, said Dr. Fleischmann.

"JAK inhibitors target this intracellular cytokine signaling cascade by competitive inhibition of JAK1/2/3 or by binding to the pseudokinase

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THE Dermatology Digest PRESENTS

Polypodium Leucotomos for Skin Protection

Part 1

Introduction to *Polypodium leucotomos*: Current Research and Therapies

Part 2

The Role of PLE in Sun Protection

Part 3

Future Possibilities of PLE for Skin Conditions

PODCAST SERIES
FEBRUARY – APRIL 2022

FEATURING
DR. JOEL SCHLESSINGER
DR. JEANINE DOWNIE

continued from page 24

> There are no head-to-head studies of JAKs, but it appears that they have similar efficacy at least in rheumatoid arthritis."

domain of TYK2, as noted previously. As a result of the inhibition of the binding of ATP by either mechanism, the JAKs cannot phosphorylate the cytokine receptors, STATs cannot dock and are not phosphorylated or thus not activated."

The end result, according to Dr. Fleischmann, is decreased gene transcription and cytokine production.

"By inhibiting JAK pathways, JAK inhibitors modulate signaling of multiple cytokines involved in the pathogenesis of rheumatoid arthritis and psoriatic arthritis, as well as other diseases."

JAKs in Rheumatology

Three JAK inhibitors are approved in the U.S.—tofacitinib (Xeljanz, Pfizer), baricitinib (Olumiant, Lilly), and upadacitinib (Rinvoq, AbbVie). All are approved for rheumatoid arthritis. Upadacitinib and tofacitinib also are approved for psoriatic arthritis, ankylosing spondylitis, and ulcerative colitis, said Dr. Fleischmann.

"We find these drugs very useful as they are not only very effective but are also oral and patients prefer oral medications."

JAK inhibitors work by inhibiting multiple cytokines, but they don't inhibit the cytokine fully, according to Dr. Fleischmann.

"An anti-tumor necrosis factor (TNF) may inhibit 90% or 92% of TNF but the JAKs inhibit 40% or 50% of each of multiple cytokines. Published head-to-head studies have demonstrated that JAKs are at least as effective as TNFs in rheumatoid arthritis.[2,3,4] JAK inhibition has been found effective in psoriatic arthritis, ankylosing spondylitis, and ulcerative colitis. The fact that they inhibit the production of multiple cytokines, although not fully, is probably the reason why they are effective and relatively safe."

With respect to relative efficacy of the JAK inhibitors, "There are no head-to-head studies of JAKs, but it appears that they have similar efficacy at least in rheumatoid arthritis. In psoriatic arthritis (PsA) there may be a difference—there may be an advantage to upadacitinib over tofacitinib, but tofacitinib is effective. I can't comment on baricitinib because I haven't seen those studies. In ankylosing spondylitis and ulcerative colitis, both tofacitinib and upadacitinib are effective," said Dr. Fleischmann.

As for their safety profiles, although tofacitinib is a pan JAK inhibitor and upadacitinib affects primarily JAK1, their safety is actually very similar when you look at the integrated safety databases, according to Dr. Fleischmann.

"So, the differences are in the test tube but not what we see clinically."

"Prior to the FDA change[5] to the product label earlier this year, tofacitinib and upadacitinib were popular drugs that we used as first-line therapy after methotrexate. The reason for that is they are oral with a great deal of patient acceptance. And there are many patients who can take these drugs as monotherapy, many more so than with biologics which are generally more effective in combination with methotrexate," said Dr. Fleischmann.

In Part 2 of this series, Dr. Fleischmann goes in-depth into JAK inhibitor safety, the ORAL surveillance study, and the impact of the FDA's recent label change.

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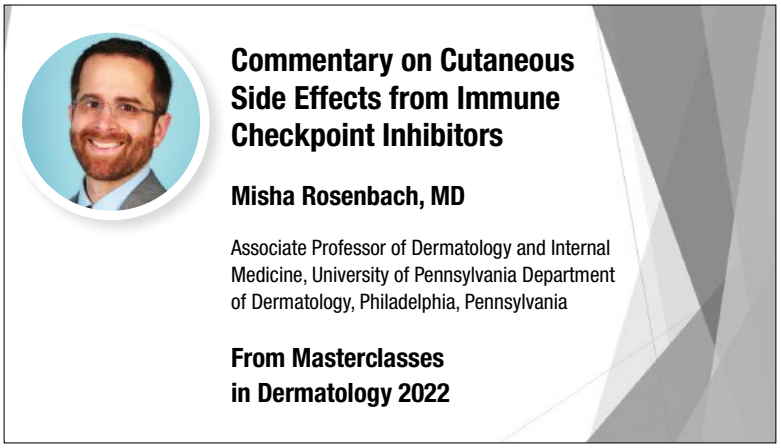
DISCLOSURES

Dr. Fleischmann is a consultant with AbbVie, Amgen, and Pfizer.

Skin Reactions from Immune Checkpoint Inhibitors

With Misha Rosenbach, MD



WATCH: https://thedermdigest.com/video/skin-reactions-from-immune-checkpoint-inhibitors

Dr. Misha Rosenbach discusses identifying and managing the broad range of cutaneous side effects from checkpoint inhibitors used to treat skin cancers and other malignancies.

"Checkpoint inhibitors cause dermatology," said Misha Rosenbach, MD, who presented "Immune Checkpoint Inhibitor-induced Autoimmunity" at Masterclasses in Dermatology 2022.

"These are drugs that dermatologists have been loosely familiar with over the past decade. Originally these cancer agents were developed and approved for treatment of advanced stage melanoma."

Checkpoint inhibitor medications as a category include CTLA-4 inhibitors, PD-1 inhibitors and PD-L1 inhibitors, said Dr. Rosenbach.

"These drugs basically work by unleashing the immune system. For melanoma patients, they are transformative."

For skin cancers alone, immune checkpoint inhibitors and combination therapies with the inhibitors have been approved for melanoma, squamous cell carcinoma, and Merkel cell carcinoma. Trials are underway for use of the drugs in basal cell carcinoma, cutaneous T-cell

For skin cancers alone, immune checkpoint inhibitors and combination therapies with the inhibitors have been approved for melanoma, squamous cell carcinoma, and Merkel cell carcinoma. Trials are underway for use of the drugs in basal cell carcinoma, cutaneous T-cell lymphoma, and other rare cutaneous neoplasms, said Dr. Rosenbach.

lymphoma, and other rare cutaneous neoplasms, said Dr. Rosenbach.

"These are drugs that dermatologists will see used to treat their patients with advanced disease. But also, these drugs are being studied for just about every type of malignancy, so the other part of this is you'll see increasing numbers of trials with monotherapy and combination therapies for increasing numbers of tumors and with increasing numbers of medication approvals," said Dr. Rosenbach.

Cutaneous AEs are Common

Patients treated with immune checkpoint inhibitors commonly experience immune-related cutaneous adverse events, according to Dr. Rosenbach.

"It's not just a rash or one skin reaction or one pattern of eruption, but the patients who get checkpoint inhibitors get a lot of side effects and get a lot of skin side effects."

Studies suggest more than 50% to nearly 90% of patients experience some sort of immune-related adverse event, according to Dr. Rosenbach.

"The skin is very commonly impacted. Depending on which drug and which combination, sometimes a quarter to almost 50% of patients will develop some sort of skin immune-related adverse event, and the skin involvement can precede other organ involvement."

There are two things that are important for dermatologists to know, according to Dr. Rosenbach: "… one, immune-related adverse events from checkpoint inhibitors can cause a wide range of eruptions. Two, that might have … prognostic implications, and that's really important for patients who are undergoing treatment for malignancies with these agents."

Patients undergoing cancer treatment often are medically complicated and seeing a skin reaction can be scary to the patient and oncologists, according to Dr. Rosenbach.

"So, it's important that dermatologists help make themselves available to help co-manage these patients and are available to see these patients quickly," he said.

Whereas oncologists may be inclined to reach for systemic corticosteroids, dermatologists, with more focus on management of skin disease, have a variety of safer, more effective tricks up their sleeves for treating some of the more common reactions from checkpoint inhibitors, including eczematous reactions, pruritic eruptions, and xerosis, said Dr. Rosenbach.

Types of Skin Reactions

Some of the more common cutaneous reactions from immune checkpoint inhibitors are morbilliform, or maculopapular reactions; itchiness or just pruritus; xerosis; psoriasiform rashes; eczematous rashes; and lichenoid reactions. Uncommon reactions may include diseases such as bullous pemphigoid, vitiligo-like depigmentation, or alopecia areata, according to Dr. Rosenbach.

"Importantly, these drugs can also cause rare, severe reactions. You can get an intense … blistering that can resemble Stevens-Johnson syndrome. You can get a drug reaction with eosinophilia and systemic symptoms (DRESS) spectrum reaction; vasculitis, diseases similar to idiopathic connective tissue diseases; granulomatous reactions; and more."

Vitiligo is one of the more interesting reactions, according to Dr. Rosenbach.

continued on page 30

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continued from page 28

"It's not just a rash or one skin reaction or one pattern of eruption, but the patients who get checkpoint inhibitors get a lot of side effects and get a lot of skin side effects."

"Patients who have advanced melanoma and are getting treated with checkpoint inhibitors sometimes will develop incidental disappearance of some other pigmented lesions…. At least in melanoma patients getting checkpoint inhibitors, when they develop some of these disease reactions, in particular when they develop vitiligo, it seems to portend a better response and better outcomes."

"Some of the more robust reactions, like lichenoid reactions, blistering eruptions or in some small studies psoriasiform eruptions, may be an indicator of potentially better treatment response. And these reactions don't necessarily happen immediately. It can be 4 to 14 days for a morbilliform reaction, or on the order of weeks to months for some severe reactions," said Dr. Rosenbach.

"There are also some studies to suggest that, if you biopsy [checkpoint inhibitor reactions] at one time point, you can see what looks like lichenoid dermatitis. But, if the rash persists and progresses over time, in some cases their clinical and pathologic picture might progress to look more like a true connective tissue disease like subacute cutaneous lupus."

According to Dr. Rosenbach, key articles can help dermatologists to become familiar with adverse events caused by immune checkpoint inhibitors,[1] as well as treatments.[2]

"I think [Nadelmann et al. is] a really nice reference for dermatologists to be aware of because it walks through what oncologists are thinking about in terms of management of these different reactions and when dermatologists should get involved. Notably for us, if you look at that table, it says 'consult dermatologist' for almost every reaction unless it's super mild."

Treatment Take-Homes

Almost any rash can be attributed to a checkpoint inhibitor, and it can occur quickly or be a delayed response. Studies are just beginning to show which reactions occur at which timepoints, according to Dr. Rosenbach.

"What's really exciting about the future for our field is that some of the work that is being done—instead of broadly using corticosteroids for the entire immune response—if we see a specific cutaneous reaction, we might soon use our dermatology skills to initiate therapy with a specific targeted inhibitor for that response. Though, this is not yet the approach, it's exciting to think about the future of less toxic, more targeted, supportive oncodermatology."

Should you stop a checkpoint inhibitor in a cancer patient because of cutaneous reactions? Not necessarily, said Dr. Rosenbach.

"First, try to suss out, is this reaction related to the drug or something else? Second, you should try to say, does this reaction portend something? Is it a sign of their immune system turning on?"

If so, have a conversation with the patient's oncologist about the benefits, risks and alternatives, said Dr. Rosenbach.

"Patients undergoing treatment for cancer have a problem list that goes: cancer, cancer, cancer… then rash; our job is to help the patient and the oncologist best manage the whole case." ◈

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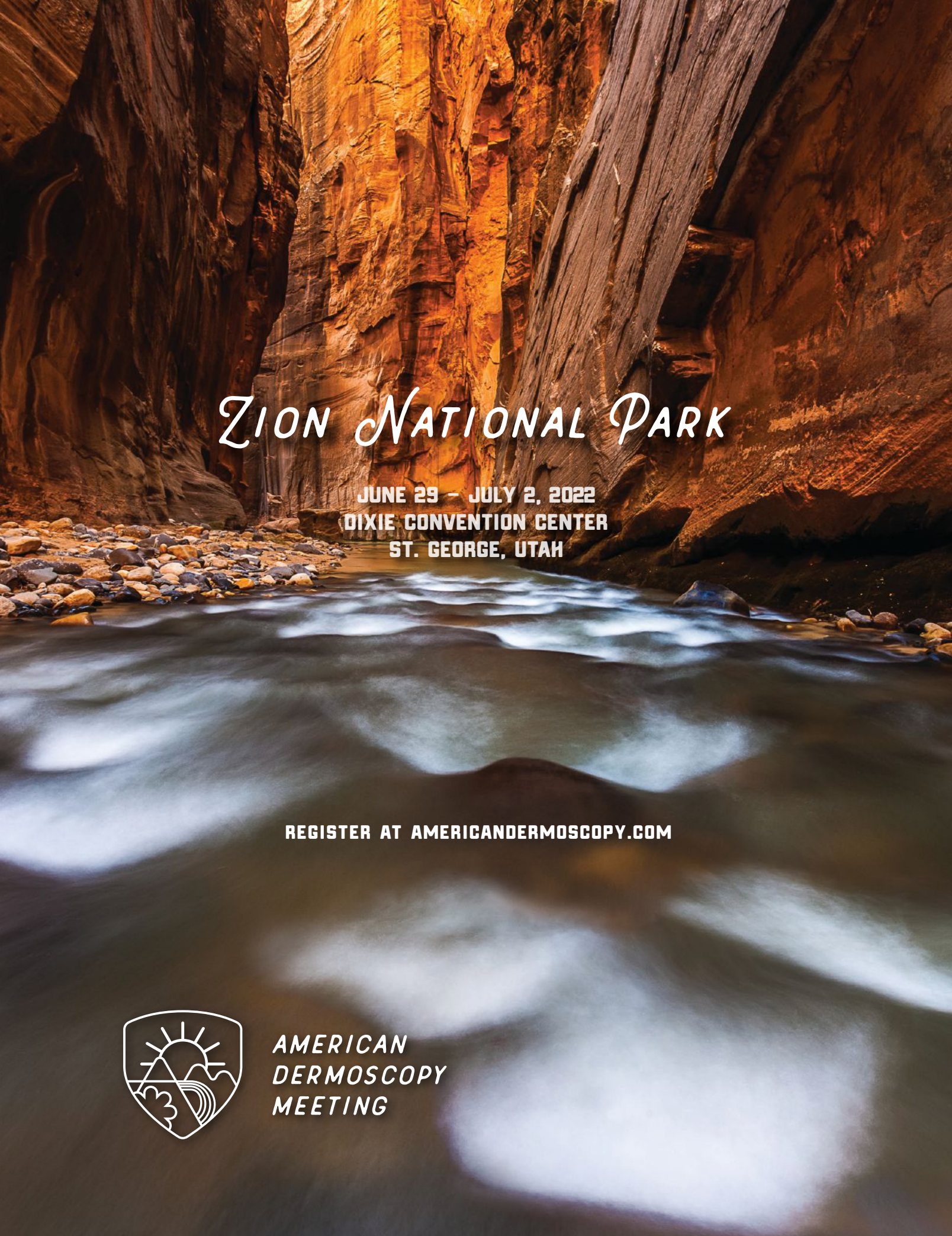
DISCLOSURES:

Dr. Rosenbach reports no relevant disclosures.



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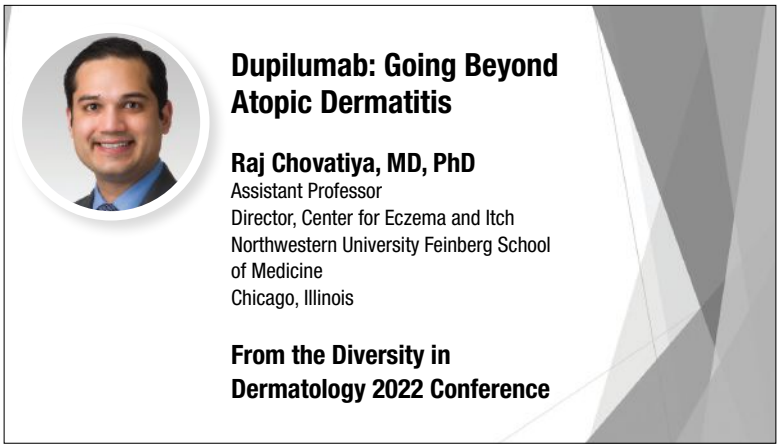
The Many Potential Uses of Dupilumab

With Raj Chovatiya, MD, PhD



LISTEN: https://thedermdigest.com/video/the-many-potential-uses-of-dupilumab

Dr. Raj Chovatiya discusses the safety and efficacy of dupilumab for atopic dermatitis, asthma, and chronic rhinosinusitis as well as its broad potential for treating other conditions affected by the IL-4/IL-13 signaling pathway.

"With atopic dermatitis, we're thinking about a pathophysiologic process that has outside-in and inside-out mechanisms. That means that there is a lot related to what's going on in the environment, the skin barrier, plus the immune system that contribute to pathophysiology of atopic dermatitis," said Raj Chovatiya, MD, PhD, who presented "Dupilumab: Going Beyond Atopic Dermatitis," at the Diversity in Dermatology 2022 Conference.

Two signaling molecules in the immune system that are important to inflammation and the acquired barrier disruption seen in atopic dermatitis are interleukin (IL)-4 and IL-13. These are two of the canonical cytokines associated with Th2-mediated immunity, called type 2 inflammation, said Dr. Chovatiya.

"Dupilumab [Dupixent, Sanofi] specifically targets the IL-4 receptor alpha subunit shared by IL-4 and IL-13 and thus blocks their downstream inflammatory signaling."

For patients with moderate to severe atopic dermatitis, dupilumab improves lesional severity, itch, quality of life, sleep, and skin pain, said Dr. Chovatiya.

"Aside from the clinical improvements that we can see, we know there is a variety of effects on both skin and systemic inflammation. The microbiome of the skin becomes more normalized. Circulating markers of inflammation decrease. We know that the skin barrier itself shows decreased proliferation with decreased markers of inflammation in the skin. Dupilumab is acting in all these ways."[1,2]

The FDA has also approved dupilumab as an add-on maintenance treatment for individuals 6 years and older with moderate to severe asthma with eosinophilic phenotype or oral corticosteroid-dependent asthma, as well as for chronic rhinosinusitis with nasal polyposis for individuals 18 and older with inadequately controlled disease, according to Dr. Chovatiya.

"Asthma and rhinosinusitis share a lot of the underlying inflammatory mechanisms of atopic dermatitis. IL-4 and IL-13 are really important in patients with these conditions and drive much of the disease severity. We also know that asthma and chronic rhinosinusitis with nasal polyposis are important comorbidities for patients with atopic dermatitis."

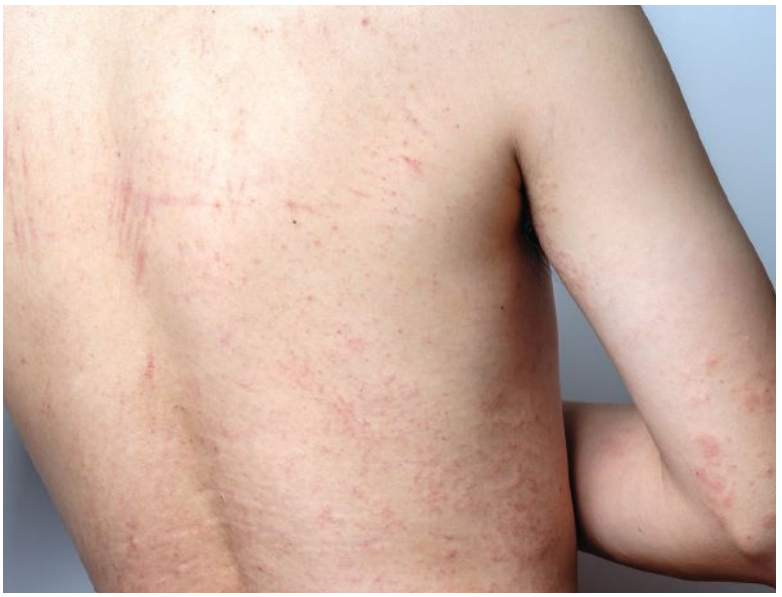
Future Dupilumab Indications

A number of trials, including phase 3, phase 2 and earlier, are looking at different dupilumab indications, according to Dr. Chovatiya.

"Dermatologically speaking, we're very close to getting approval for the indication for atopic dermatitis down to 6 months to 5 years of age."

"There are other studies that are showing promising data for prurigo nodularis and chronic spontaneous urticaria. These are the two dermatologic indications that are the furthest along. Other dermatologic indications that are relatively far along are bullous pemphigoid and other urticarias."

Prurigo nodularis, which is associated with atopic dermatitis but can occur in the absence of it, can have a similar cutaneous phenotype



For patients with moderate to severe atopic dermatitis, dupilumab improves lesional severity, itch, quality of life, sleep, and skin pain.

to atopic dermatitis, said Dr. Chovatiya.

"There are a number of reports in the literature where people with prurigo nodularis … seem to respond pretty well to dupilumab treatment. There is also the LIBERTY-PN PRIME phase 3 trial program that has shown efficacy and endpoints achieved for prurigo nodularis."[3]

There are case reports suggesting dupilumab effectively treats hand and foot dermatitis, as well as nummular dermatitis, he said.[4,5]

"We know that people can get eczematous outbreaks or just some type of eczema in the context of immunodeficiency. For example, individuals with well-controlled HIV can have eczematous outbreaks, but were excluded from the original phase 3 trials for dupilumab. There are actually some good reports in the literature showing that dupilumab is efficacious and not immunosuppressive in these patients."[6]

"Hyper IgE syndrome and CARD 11 defi-

Other conditions that anecdotally suggest dupilumab may be helpful include Grover's disease, granuloma annulare, actinic prurigo, eosinophilic granulomatosis with polyangiitis, lichen amyloidosis, and epidermolysis bullosa pruriginosa.

ciency are two rare genetic diseases that have shown promising responses to dupilumab, as well,"[7] said Dr. Chovatiya.

In his presentation, Dr. Chovatiya touched on chronic spontaneous urticaria, which he said could also be a future on-label indication for dupilumab.

"We don't understand the pathogenesis of chronic spontaneous urticaria that well, but dupilumab is helping to unravel that story.

"We don't understand the pathogenesis of chronic spontaneous urticaria that well, but dupilumab is helping to unravel that story. Results from the LIBERTY CUPID trial show … that patients treated with dupilumab actually saw significant improvement in itch and urticaria activity with very promising safety results,"[8] said Dr. Chovatiya.

"Bullous pemphigoid is another dermatologic disease that has reasonable case report data out there suggesting another use for dupilumab. Anything we can do to eliminate or reduce the use of corticosteroids in this largely older population would be great just because of the number of risks that are associated with chronic corticosteroid use. Dupilumab has been shown to reduce blisters, improve pruritis, and allow for a reduction in immunosuppression medication in dozens of case reports."[9]

Alopecia areata, which occurs in about one-third of atopic dermatitis patients and is the most common cause of auto-inflammatory hair loss, has been shown to improve with dupilumab. On the flip side, some case reports actually show new onset hair loss with dupilumab treatment, though hair loss is a rare side effect, according to Dr. Chovatiya.[10]

Dupilumab dosing studied in prurigo, urticaria, and pemphigoid trials was the same every other week maintenance regimen that dermatologists are very familiar with for atopic dermatitis. Case reports in the literature looking at many of the other indications mentioned have also used a similar dosing regimen, said Dr. Chovatiya.

Still Other Potential Approvals

A non-dermatologic indication for which dupilumab might be approved in 2022 is for treatment of eosinophilic esophagitis, which is a known comorbidity in atopic dermatitis patients, according to Dr. Chovatiya.

"Various types of allergies, keratoconjunctivitis, other eosinophilic diseases like gastritis and gastroenteritis, all are in earlier phases of investigation, and all seem to share an important type 2 inflammatory mechanism."

Other conditions that anecdotally suggest dupilumab may be helpful include Grover's disease, granuloma annulare, actinic prurigo, eosinophilic granulomatosis with polyangiitis, lichen amyloidosis, and epidermolysis bullosa pruriginosa, said Dr. Chovatiya.

"It's really important to understand the mechanism of how dupilumab works and what it's doing in atopic dermatitis. Dermatologists can then correlate this to a whole host of other diseases that share similar mechanisms. It's pretty cool to think about the number of different conditions that may all fit under this important IL-4/IL-13 signaling pathway." ◈

EDITOR'S COMMENT:

TED ROSEN, MD, FAAD
Editor-in-Chief

The Dermatology Digest thanks Dr. Chovatiya for his thoughtful and extensive review of the many exciting potential future uses of dupilumab. We believe this article highlights an interesting trend, in that it exemplifies rational investigational drug use based on known mechanisms of action and increasing understanding of disease pathogenesis. For example, any disorder with a predominantly Th2 etiology might be fair game in which to explore dupilumab use because the drug selectively blocks cornerstone Th2 cytokine activity. Still, we urge caution when using drugs off-label. Efficacy of dupilumab administration for all of the disease states enumerated in this feature remain to be verified by appropriately powered, randomized controlled trials. Likewise, while typical atopic dermatitis dupilumab dosages have been used in these exploratory case reports and case studies, that does not mean that we have determined an optimal dosing regimen; dose-ranging studies remain to be performed for each disorder.

Ted Rosen, MD, FAAD, Editor-in-Chief

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DISCLOSURES

Dr. Chovatiya has served as an advisory board member, consultant, and/or investigator for Abbvie, Arcutis, Arena, Bristol Myers Squibb, Dermavant, Incyte, National Eczema Association, Pfizer, Regeneron, Sanofi, and UCB, and speaker for Abbvie, Eli Lilly, Incyte, Pfizer, Regeneron, Sanofi, and UCB.

Mounting Evidence Supports Promise of JAK Inhibitor Treatment for Refractory Dermatomyositis

With Ted Rosen, MD, FAAD

TED ROSEN, MD, FAAD
Editor-in-Chief

Recent research suggests JAK inhibitors, specifically tofacitinib, may be useful in the management of refractory dermatomyositis.

In 2016, dermatologists from Harvard Medical School published what they described as the first report of the successful use of the Janus kinase (JAK)-1/3 inhibitor, tofacitinib, to treat refractory cutaneous dermatomyositis (DM).[1] Based on evidence suggesting that tofacitinib suppresses the interferon signaling pathway that is implicated in the pathophysiology of this rare idiopathic multisystem autoinflammatory disease, the investigators identified three patients with refractory DM, treated them with tofacitinib, and found all three patients achieved a clinically significant response as defined by the magnitude of improvement in their Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) score.

In a research letter published in the *Journal of the American Academy of Dermatology* in February 2022, the Harvard dermatologists reported their expanded experience with successful use of tofacitinib to treat refractory cutaneous DM.[2] Searching through a clinical data registry that captures patients cared for at two Harvard-affiliated hospitals, they identified 11 patients who had been diagnosed with DM, prescribed a JAK inhibitor, and had baseline and follow-up CDASI data. All of the patients received tofacitinib, and they all achieved clinically meaningful improvement as defined by change in CDASI score. In addition, all patients benefited with significant improvement in self-reported pruritus severity, and myositis resolved in the two patients who had active muscle disease.

No patients had to stop treatment because of an adverse event. During a mean treatment duration of 27.2 months, orolabial herpes simplex virus infection in a single patient

In a research letter published in the *Journal of the American Academy of Dermatology* in February 2022, the Harvard dermatologists reported their expanded experience with successful use of tofacitinib to treat refractory cutaneous [dermatomyositis].

continued on page 38

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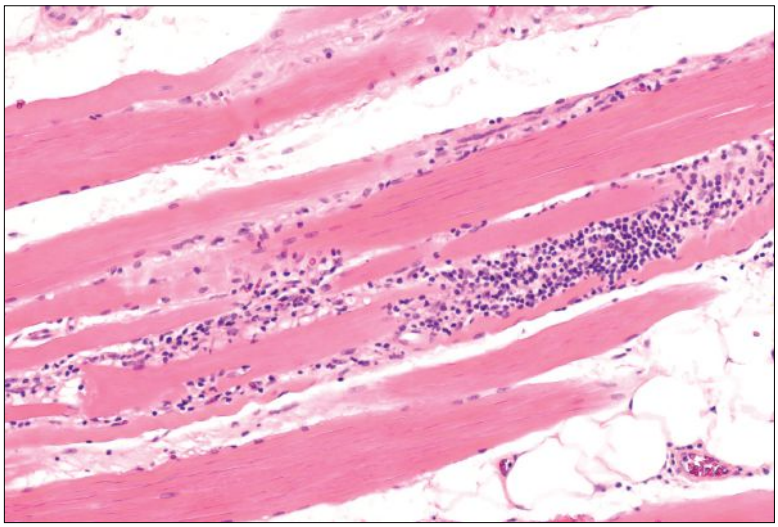
continued from page 36

was the only reported adverse event.

The investigators concluded that tofacitinib is a well-tolerated systemic treatment choice for refractory cutaneous DM, and they encouraged further investigation to help validate their findings.

Since the Harvard researchers reported their initial series, there have been several other published articles describing patients treated with tofacitinib or ruxolitinib for refractory DM.



Digging Into the Details

The 11 patients in the retrospective review comprised 10 women and one man. All of the patients were white, and they ranged in age from 19 to 74 years. Amyopathic DM was the most common subtype (n = 5); classic DM with active myositis, classic postmyopathic DM, and juvenile postmyopathic DM were equally represented among the remaining six patients.

The number of previous systemic therapies ranged from four to nine and included hydroxychloroquine, prednisone, methotrexate, mycophenolate, intravenous immunoglobulin G, lenalidomide, isotretinoin, dapsone, azathioprine, rituximab, thalidomide, quinacrine, cyclosporine, quinacrine, infliximab, and subcutaneous immunoglobulin.

Tofacitinib was administered at a dose of 5 mg or 10 mg twice a day or 11 mg extended release twice a day. Only one patient was maintained on 5 mg twice daily, while others who were started on that regimen required a dose increase. The researchers pointed out that 10 of the 11 patients required a dose of tofacitinib higher than that typically used for treating rheumatoid arthritis or psoriatic arthritis (the recommended dose for the latter two diseases is 5 mg twice a day or 11 mg extended release once a day). The JAK inhibitor was used as monotherapy in three patients and with up to three additional therapies in the remaining patients.

Mean CDASI for the group was 27.7 (range, 17 to 38) at baseline, and it improved by a mean of 17.8. All patients achieved at least an 11-point improvement in CDASI score (a change of 4 to 5 points is considered clinically meaningful). The mean improvement in CDASI score across the different DM subtypes ranged from 16.75 to 19.

Eight patients experienced clinically significant improvement within one month after starting tofacitinib, two benefited within 1.5 months, and the remaining patient improved by month two.

The patients in the series had been on tofacitinib for a duration of 11 to 40 months, and during that time, all but one patient was able to discontinue or taper concomitant therapies.

Accumulating Experience

Since the Harvard researchers reported their initial series, there have been several other published articles describing patients treated with tofacitinib or ruxolitinib for refractory DM. These additional reports include a recent systematic literature review of 14 studies en-

However, several questions remain to be answered. For example, is there a clinical advantage for using any one JAK inhibitor compared to other agents in this class of small-molecule drugs?

compassing 54 patients treated with tofacitinib or ruxolitinib and a 12-week prospective open-label clinical trial of tofacitinib conducted at Johns Hopkins University plus a follow-up report of outcomes from a long-term extension of the latter trial.[3-5]

The collective findings from this experience indicate that JAK inhibitors are a promising treatment for refractory DM with acceptable safety and durable efficacy. However, several questions remain to be answered. For example, is there a clinical advantage for using any one JAK inhibitor compared to other agents in this class of small-molecule drugs? Would there be even greater benefit from utilizing a JAK inhibitor earlier in the disease course as monotherapy or in conjunction with standard therapeutic interventions?

Some insight into these issues may come from a multicenter study that will be underway in France. Known as BIRD, it is a 24-week, quadruple-masked, placebo-controlled study investigating treatment with the JAK-1/2 inhibitor, baricitinib, in patients with relapsing or naïve DM.[6]

This prospective trial has a planned enrollment of 62 patients. Patients in both the baricitinib and placebo arms will also receive prednisone with tapering according to a predefined protocol plus one immunosuppressive drug (either methotrexate or azathioprine). The primary endpoint is evaluating prednisone-free moderate improvement at week 24, defined as a total improvement score superior or equal to 40 following ACR/EULAR definition without the need for prednisone.

The study has an anticipated start date of May 2022, but its estimated completion date is not until December 2025. ◈

By Cheryl Guttman Krader

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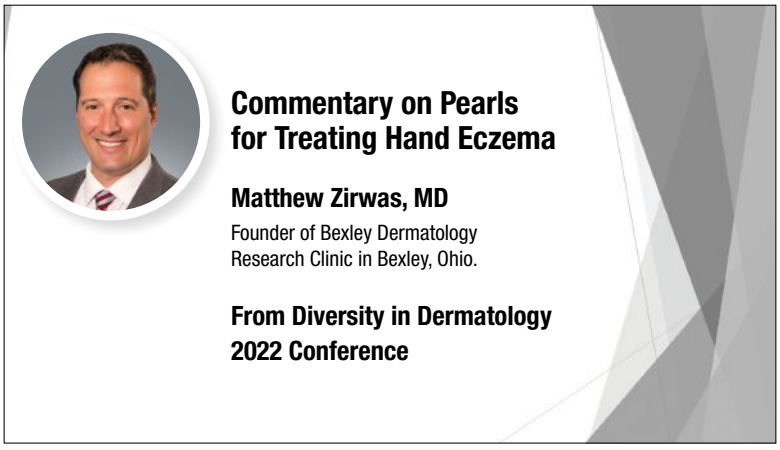
6 Pearls for Hand Eczema

With Matthew Zirwas, MD



WATCH: https://thedermdigest.com/video/6-pearls-for-hand-eczema

Dr. Matthew Zirwas shares several pearls for treating hand eczema, including distinguishing among types of dermatitis, eczema interventions, and strategies for the palms.

"I think of hand eczema primarily in etiologic terms. My main thought is, what is actually driving the hand eczema? And really there are three options. Option number one is that it's irritant contact dermatitis. Option number two is that it's allergic contact dermatitis. And option number three is that it's atopic dermatitis of the hands," said Matthew Zirwas, MD, who presented "Pearls for Treating Hand Eczema" at the Diversity in Dermatology 2022 Conference.

"…most of the things that we used to think of as just 'endogenous' hand eczema, we now think of as really being atopic dermatitis of the hands, even in a patient who has no history of childhood rashes and in a patient with no personal or family history of atopy."

Other diagnoses can also affect the hands, including lichen planus, discoid lupus, and psoriasis of the palms, said Dr. Zirwas.

"Those are things that you mainly differentiate based on biopsy, but you certainly can have a spongiotic component, especially with psoriasis of the palms and that gets to be really difficult."

Distinguishing Types of Dermatitis

Distinguishing between psoriasiform atopic dermatitis of the palms and eczematous psori-

asis of the palms can be tricky, said Dr. Zirwas.

"…as somebody who's an expert in coming up with the etiology of dermatitis, [I] frequently can't distinguish dermatitis of the palms that has psoriatic epidermal hyperplasia versus psoriasis of the palms that has a spongiotic component."

PEARL NO.1

Because the biopsy always comes back as psoriasiform spongiotic dermatitis with scattered eosinophils, which could be either atopic or psoriatic, Dr. Zirwas said he performs a diagnostic trial based on level of itch.

"The itchier it is, the more likely I am to think it's atopic dermatitis, in which case I'll give them a targeted biologic for atopic dermatitis. If that works, it confirms my diagnosis. If it doesn't work, then I'm going to switch them over to a targeted biologic for psoriasis."

By comparison, if the patient presents with less itch and more fissuring and pain, he said he begins first with a targeted biologic for psoriasis and, if necessary, moves to a targeted biologic for atopic dermatitis.

"Nobody can tell reliably (especially not dermatopathogists)…. Fortunately, we now have drugs that allow us to kind of figure out which it is."

PEARL NO.2

According to Dr. Zirwas, there are fairly reliable clues for distinguishing among irritant dermatitis, allergic contact dermatitis, and atopic dermatitis.

"Whenever I'm dealing with just a spongiotic dermatitis of the hands, usually, if it's primarily dorsal hand and more interdigital with sparing of the palm, that's most likely to be irritant contact dermatitis. If it is just the palm with complete sparing of the back of the hand and the web spaces, that is most commonly going to be atopic dermatitis of the palms, what we used to call dyshidrosis and pompholyx. If it involves both the palm and the dorsal hand, then it's most likely allergic contact dermatitis and that's really by exclusion because irritant dermatitis rarely affects the palm, and atopic dermatitis of the hands relatively rarely affects the back of the hands. And so something that affects both the palm and the dorsal is most likely going to be allergic contact dermatitis from soaps, moisturizers, things like that."

These indicators suggest but do not guarantee diagnoses, said Dr. Zirwas. Still, they are a good place to start.

Eczema Interventions

PEARL NO.3

Tell patients with hand eczema to wash their hands in cold water, said Dr. Zirwas.

"The biggest intervention you can make in terms of hand washing is not what soap they're using or even what frequency they're washing their hands. It's the temperature of the water. Good evidence came out of COVID-19 for something that we've always thought about whenever we're talking to our dermatitis patients about showering. We tell them, 'Don't take hot showers', but we never tell them, 'Don't wash your hands in hot water.'"

In a study published in late 2020,[1] water temperature affected hand dermatitis more than cleanser used or frequency of washing.

"The reason is that hot water essentially melts your cutaneous lipids—your natural protective oils—[and] lets them be rinsed away. If the water is cold, it actually hardens those intracellular lipids, makes it harder for the soap to remove them."

PEARL NO.4

Hand sanitizer is less irritating than hand washing and less likely to cause hand dermatitis, said Dr. Zirwas.

"The biggest intervention you can make in terms of hand washing is not what soap they're using or even what frequency they're washing their hands. It's the temperature of the water."

"The reason that's not widely understood is that if you already have a little bit of hand dermatitis and you try to use hand sanitizer, it burns like crazy. But if you don't already have hand dermatitis, the hand sanitizer is much better than washing your hands. And that goes with CDC recommendations."

The CDC recommends the use of alcohol-based hand sanitizers over soap and water. For a patient with hand dermatitis, there are alcohol-free benzalkonium chloride-based hand sanitizers that can be good options, said Dr. Zirwas.

For patients with allergic contact dermatitis of the hands, have them carry their own soap instead of using the fragranced, preservative-filled, antibiotic soaps in public dispensers, said Dr. Zirwas.

Allergic Contact Dermatitis

PEARL NO.5

For patients with allergic contact dermatitis of the hands, have them carry their own soap instead of using the fragranced, preservative-filled, antibiotic soaps in public dispensers, said Dr. Zirwas.

"People can carry their own small bar of soap in a little container, or we can give them a sample container of something like Cetaphil gentle hand cleanser or CeraVe gentle cleanser, and they can refill that with a low allergenicity soap for times whenever they do need to wash their hands."

Treating the Palms

The palms are the most challenging area to treat, whether it's allergic contact dermatitis, atopic dermatitis, or palmar psoriasis, because the epidermis is thicker and products do not effectively penetrate the skin, said Dr. Zirwas.

PEARL NO.6

"We do have a really good answer to that. And it's not urea… We have a much better keratolytic and it's actually the only keratolytic that is truly a keratolytic. It's thioglycolic acid."

Thioglycolic acid is hair removal cream (think Nair or Magic Shave), said Dr. Zirwas.

"What I typically tell people to do is, leave it on for about a minute, then firmly wipe it off. Wash your hands and put on your topical prescription agent after that, typically a high potency topical steroid or topical JAK inhibitor."

Pretreatment with the depilatory results in a 10- to 40-fold increase in product penetration, according to a 2008 study published in the *Journal of Investigative Dermatology,*[2] said Dr. Zirwas, who noted that this often works for patients who have failed clobetasol under occlusion overnight.

"You do the hair removal cream followed by the clobetasol or by topical ruxolitinib. You do that once a day for about a week. Then typically after a week, [patients] can change to doing the hair removal cream, followed by the prescription topical maybe once or twice a week, and it's all that they need to do."

The initial challenge for patients is withstanding the burning sensation from the depilatory, said Dr. Zirwas.

But "because high potency topical steroids and JAK inhibitors are so fast acting, the fissures actually will heal pretty quickly." ◈

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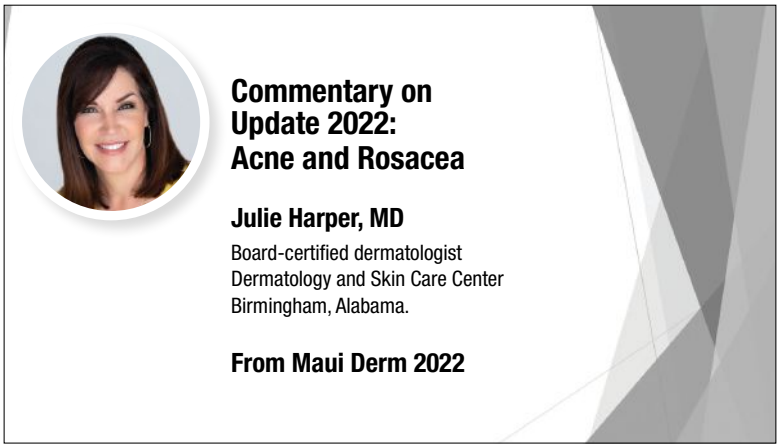
DISCLOSURE

Dr. Zirwas has no relevant disclosures.

Addressing 'Hormonal' Acne

With Julie Harper, MD



WATCH: https://thedermdigest.com/video/addressing-hormonal-acne

Dr. Julie Harper discusses adult female acne, hormonal treatment for men, spironolactone safety, and the need for combination treatments.

"It took us a long time to get people to understand that all acne is inflammatory. Even the acne that doesn't look red. Even the acne that's just blackheads. It's inflammatory by nature.... It's the same thing with hormonal acne," said Julie Harper, MD, Founding Director of the Acne and Rosacea Society, who discussed hormonal acne in the Update 2022: Acne and Rosacea session at Maui Derm 2022.

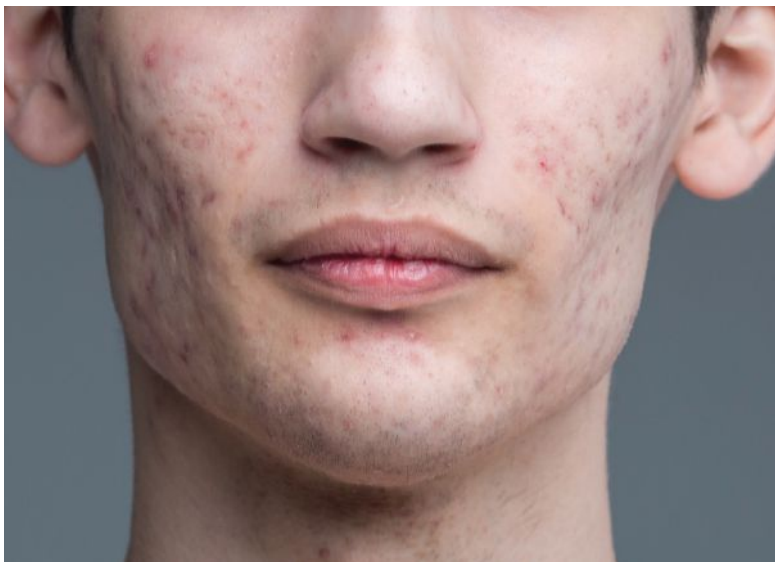
"Every hormonal treatment we've had, until recently, we can only use in women. …it's made us look at…the adult woman, and say, she has hormonal acne, because look how well it does when I use a hormonal treatment."

But hormonal acne isn't exclusive to women. The pathogenesis includes several hormonal pathways, said Dr. Harper.

"It's also comedonal acne in a 10-year-old boy. That's hormonal acne. And mixed acne in a 16-year-old boy. That's hormonal acne. So I think one huge take home is … remember that, yes, there is a subset of acne that happens in adult females, but let's just call that adult female acne."

A Hormonal Treatment for All

The FDA approved Winlevi (clascoterone) cream 1% topical (Sun Dermatology) in August



The best thing about spironolactone is that it's not an antibiotic and can be used long term, said Dr. Harper. It's also inexpensive, generic, and easy to access.

of 2020 and has somewhat equalized the acne treatment opportunities for men and women.

"Clascoterone is a topical androgen receptor inhibitor that doesn't have really any systemic effects. So we're going to get all that anti-androgen effect in the skin and none of it in the body, which now means, guess who can use this? The guys," said Dr. Harper.

In clinical trials,[1] 1400 participants were randomized into two identical vehicle-controlled studies. Nearly 40% of participants were men. Both men and women had safe and efficacious results with few adverse events.

"We've never had an anti-androgen that we could use in men, for obvious reasons. And now we do because it's topical with limited systemic exposure," said Dr. Harper.

Clascoterone (BID) is approved to treat acne in men and women 12 years of age and older. For now, twice-a-day treatment is important, said Dr. Harper.

"We're going to be using it in combinations with other things, other topicals, I realize that. We're going to be stacking things together. We don't have a lot of evidence to support that yet but that is the way most of us are going to use it in the clinic. But remember, we can use it in men and women."

Safety and Spironolactone

The best thing about spironolactone is that it's not an antibiotic and can be used long term, said Dr. Harper. It's also inexpensive, generic, and easy to access.

"[The black box warning comes from] animal studies, but we are risk-averse people. We want to do a really good job for our patients and we're aware that that's in there."

While animal studies showed tumor development in rats, human database studies by Mackenzie et al.[2] and Biggar et al.[3] did not.

"Both of those studies were big database studies where they looked at women who had been treated with spironolactone…to see if they had a higher rate of diagnosis of breast cancer. And the answer was no."

In a retrospective analysis, Wei et al.[4] examined the incidence of recurrence in breast cancer survivors who used spironolactone for hair loss. Researchers found that spironolactone was not independently associated with breast cancer recurrence, said Dr. Harper.

"People are seeing the efficacy of the drug, not seeing safety problems with it, and then we're getting good information like this that makes us feel better about things like the risk of hyperkalemia and breast cancer."

Birth Control Pills in the Background

While dermatologists don't typically prescribe birth control pills as frequently as spironolactone, many acne patients are already on birth control, said Dr. Harper.

"It doesn't mean that that doesn't help their acne. It's sitting there in the background very likely helping."

And although birth control pills come with risks, including venous thromboembolism, they don't outweigh that of an unwanted preg-

> "Probably every birth control pill, as long as it's a combination of estrogen and progestin… should help acne."

nancy, said Dr. Harper. They also offer protection for other types of cancer, including colon, uterine, ovarian, and (perhaps) cervical.

"So if you know somebody also needs contraception, you've got a really good risk-benefit ratio."

There are four brands FDA approved to treat acne: Yaz, Beyaz, Estrostep FE, and Ortho Tri-Cyclen. But that doesn't limit use, said Dr. Harper.

"Probably every birth control pill, as long as it's a combination of estrogen and progestin… should help acne. You don't want to do a progestin only minipill [or] an IUD that is only progestin…, which could make acne worse."

Importantly, birth control pills are contraindicated in smokers, said Dr. Harper.

"The definitive contraindication, I think, is somebody who's over the age of 35 [and] who smokes more than 10 cigarettes a day."

Other exclusions for Dr. Harper include a history of blood clotting or migraines.

"Pretty much everything I've said, whether it's clascoterone, spironolactone, birth control pills—these are not standalone medicines. They're working on just a part of the pathogenesis of acne. They're working on, for the most part, sebum and inflammation. And so we're going to mix them with other products that come in and help clear out that pore or that have an antimicrobial effect, so that we're really getting the best effect that we can." ◈

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DISCLOSURES:

Dr. Harper is a consultant, speaker, and/or advisory board member for Cutera, Almirall, Sun, LaRoche-Posay, Ortho, EPI, BioPharmX, Cassiopeia, Cutanea, Vyne, Galderma, Dermira, and Sol Gel.

African American with Torso Lesions, History of Spontaneous Keloids

By Ted Rosen, MD, FAAD

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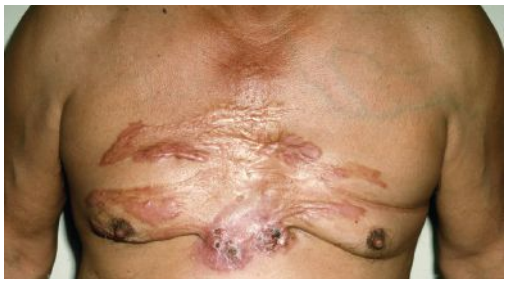

Figure 1.

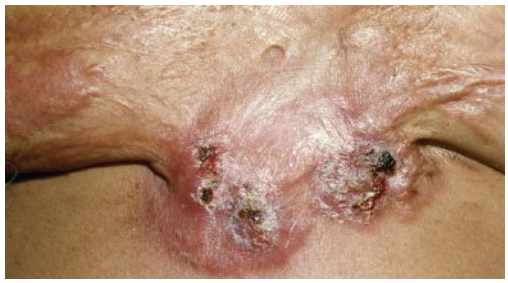

Figure 2.

CASE HISTORY

A 36-year-old African American male presented for evaluation of lesions involving the anterior torso, extending from the level of the clavicle to the uppermost abdomen, just inferior to the nipple line.

He had developed these spontaneous keloids at age 15 to 17. But other than being unsightly, the lesions had generally only been associated with mild, intermittent tenderness. Recently, a number of the keloids had become both pruritic and painful. Notably, the same symptomatic keloids had begun to exude purulent drainage. The longstanding asymptomatic lesions, however, were not demonstrating purulent discharge.

Past medical history was not contributory. Family history was positive (father and one brother) for spontaneous keloids of the chest. A recent biochemical panel and complete blood count were entirely within normal limits. Specifically, there was no leukocytosis.

Physical examination revealed at least 13 distinct keloids located only on the anterior torso. Six areas of recent purulent exudation, now inflamed and covered by crusts, were identified. (Figures 1 and 2)

Pressure on any of these areas would elicit purulent discharge. There was no axillary adenopathy. Chest radiograph was normal. The remainder of the examination was unremarkable. Specifically, the patient was (and had been) afebrile.

Biopsy revealed a few foci of folliculitis within a classic dense collagen stroma, consistent with a keloid. Aerobic, anaerobic, mycobacterial and fungal cultures of expressed purulence from several lesions yielded no growth.

What is your diagnosis and how would you help him?

For more on this case, turn to page 48 ▸

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continued from page 46

AFRICAN AMERICAN WITH TORSO LESIONS, HISTORY OF SPONTANEOUS KELOIDS

DISCUSSION

The diagnosis is suppurative keloidosis, a rare variant of spontaneous keloid formation. This entity consists of largely sterile purulence developing in previously asymptomatic keloids.

It has been estimated that about one-quarter of keloid patients may develop this phenomenon.[1,2] Patients at increased risk for suppuration to develop are typically of African ancestry, male gender, with many keloids, and with a positive family history for keloid formation.

Clinical folliculitis may precede the presence of keloid suppuration, but cultures fail to yield anything other than occasionally normal skin flora. Since this is not an infectious process, it is suggested that use of antibiotic therapy is not appropriate. It is recommended that intralesional corticosteroid injections form the basis for therapy.[1-3]

This particular patient's lesions responded nicely to intralesional injections of triamcinolone acetonide, 5-10mg/ml concentration. Because the aseptic process involved in suppurative keloidosis is likely similar to that involved in hidradenitis, it has also been suggested that use of TNF-alfa blockers might prove beneficial. In fact, one such instance has already been documented.[4]

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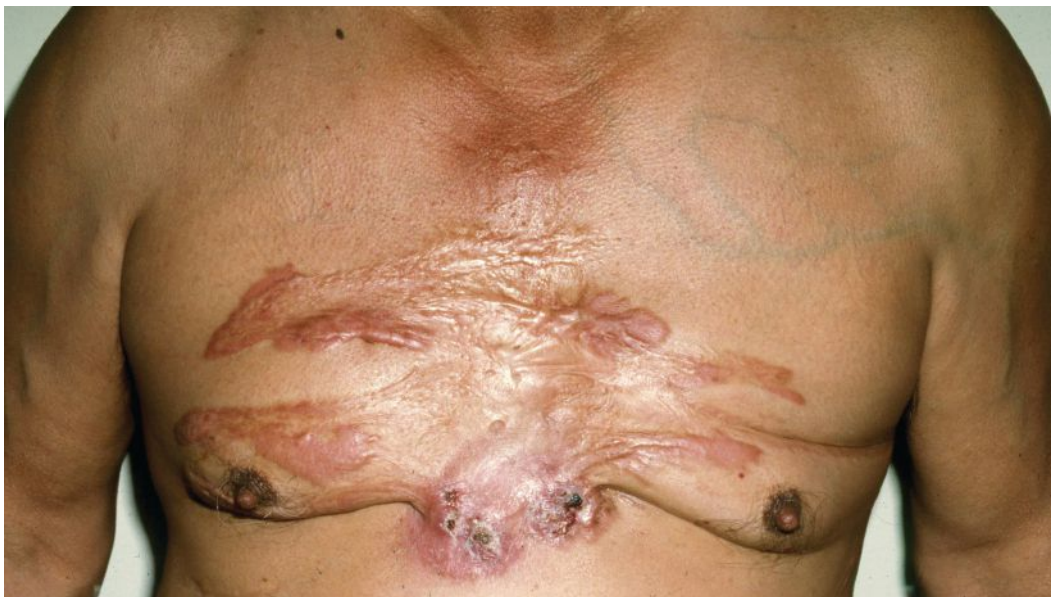

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