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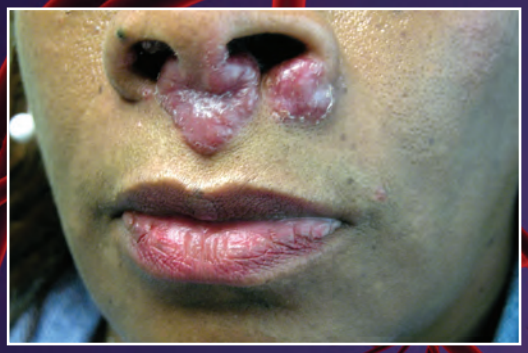
THE Dermatology Digest®

Vol. 3, No. 7 | July/August 2022

Evaluating Sarcoidosis Patients for Systemic Disease



- STD Rates on the Rise
- Cannabidiol for First-Degree Burns?
- 3 Pearls for Diagnosing, Treating Vulvar Dermatoses

EDUCATIONAL • INTERACTIVE • AUTHORITATIVE

ITCH-SCRATCH-
ITCH-SCRATCH-
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]

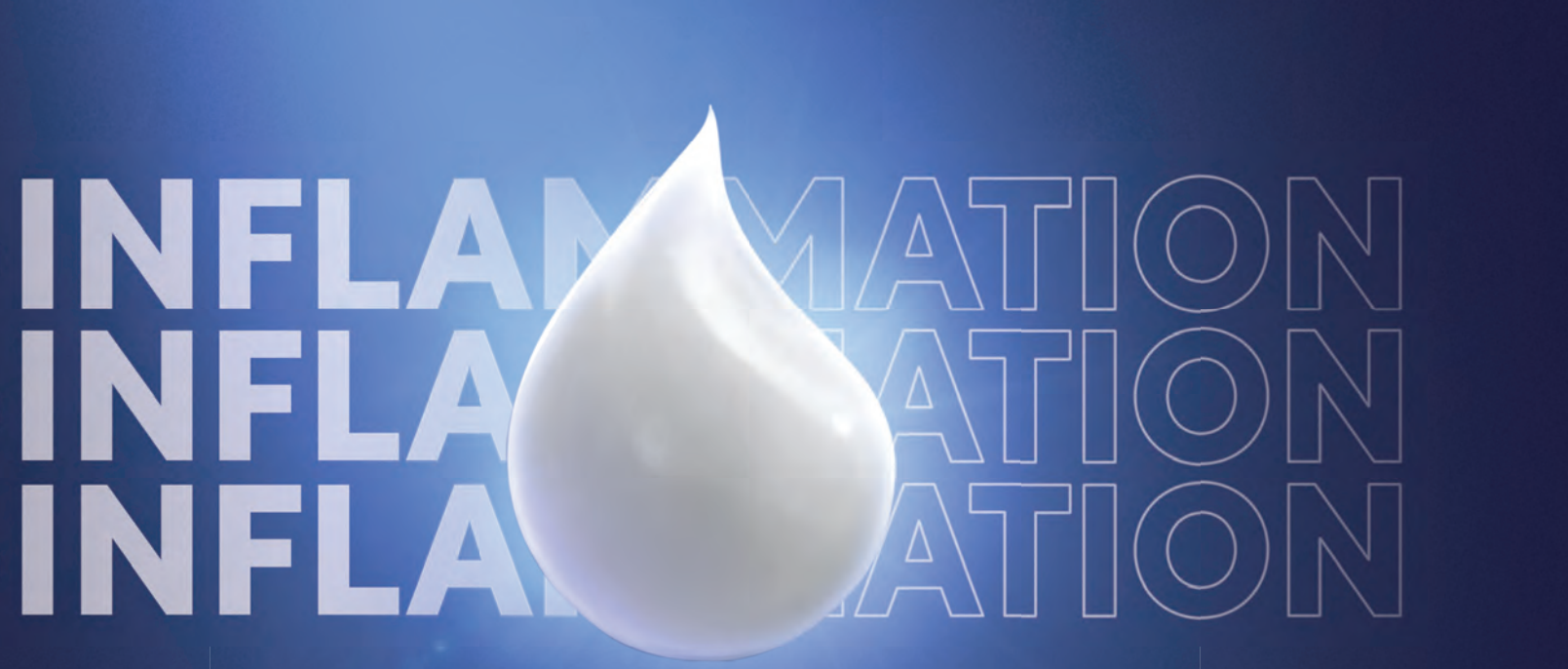
†In TRuE-AD1 and TRuE-AD2, respectively.[1,2]

‡≥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:
Incyte Corporation
1801 Augustine Cut-off
Wilmington, DE 19803

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Contents

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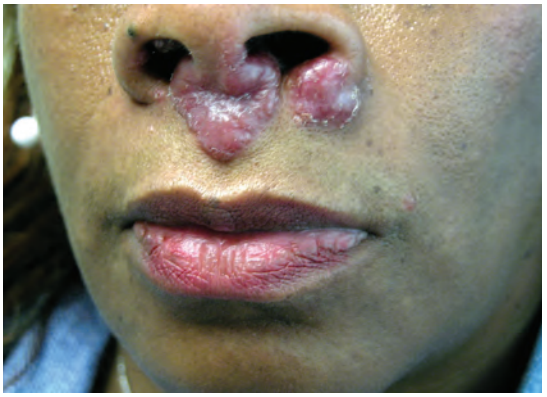

IN THIS ISSUE

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IN THIS ISSUE

Welcome to the July/August issue of *The Dermatology Digest (TDD)*, where you'll find all our regular departments—from Literature Lessons to the popular Zebra column—as well as highlights from recent and important professional meetings.

In this issue, we link you to videos, podcasts, and articles showcasing key sessions from 9 major conferences: The International Eczema Council at AAD 2022; 2022 American Academy of Dermatology (AAD) Annual Meeting; Atlantic Dermatology Conference; Innovations in Dermatology; The Mark Allen Everett, MD, Skin of Color Symposium; Music City SCALE 2022; Congress of Clinical Dermatology; Symposium for Inflammatory Skin Disease; and the 2022 Acne and Rosacea Meeting.

Among those in this issue, Dr. Robert Sidbury discusses pediatric psoriasis, including important differences in the way it can present in children and the expanded treatment armamentarium. Dr. Sidbury also shares key points from his recent presentation on pediatric atopic dermatitis including how the treatment landscape has drastically changed to include more kid-friendly therapies. Dr. John H. Joseph shares research that may make readers give pause to botulinum toxin dosing and reconstitution. Dr. Jonathan Silverberg talks about why it's important for dermatologists not to assume all forms of eczema are atopic dermatitis (AD), and how to differentiate and treat non-atopic forms of dermatitis in AD patients. Dr. Mark G. Rubin helps to answer the question, chemical peel or laser? Dr. Emmy Graber reviews the growing arsenal of lasers for treatment of acne and where they fit in today's treatment options.

The July/August cover features Dr. Sotonye E. Imadojemu's discussion on the dermatologist's role in diagnosing the multisystem disease occult systemic sarcoidosis, which researchers are finding is more likely to present at younger ages in Black patients. In another feature, Dr. Ted Rosen reviews data suggesting the alarming rise of sexually transmitted diseases.

In this issue we welcome a guest editorial by Dr. Matthew Zirwas, who shares his successful alternative approach to treating delusions of parasitosis.

Our Literature Update with Dr. Rosen looks at a recent case report describing anasarca-induced bullae and desquamation as a new variant of the edema bullae. New Drugs focuses on the dual immunotherapy Opdualag for adult and pediatric patients with unresectable or metastatic melanoma. Dr. Rosen discusses using oral acitretin for multikinase inhibitor-induced hand-foot reaction in this issue's Off-Label Pearl. And for our Zebra: A Differential Diagnosis Case by Dr. Ashfaq A. Marghoob asks readers to choose among dermoscopic images to distinguish basal cell carcinoma from melanoma.

We invite you to contribute your own ideas for content... Have a Zebra that warrants sharing? Want to make content requests or share feedback? Contact us at Editorial@thedermdigest.com.

The Dermatology Digest

High-level learning, expert insights & multi-speciality perspective

November 30th - December 3rd, 2022 | The JW Marriott Nashville, TN

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Editorial

Another Way of Looking at Delusions of Parasitosis

By Matthew Zirwas, MD
Contributing Editor

Matthew Zirwas, MD
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Ohio University Heritage College of Medicine
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For the first 10 years of my practice, I treated delusions of parasitosis (DOP) the way I was taught in residency: Listen closely to the patient's complaints; try to build a strong doctor-patient relationship; discuss the likely neuropathic cause of the sensations; do appropriate biopsies to rule out other diagnoses; and so on, in the hope that I'd eventually be able to get them to take pimozide.

Not a single patient ever took the pimozide, no matter how hard I tried to establish that relationship and do precisely what I had been taught to do.

Then, I had this conversation with a patient.

Patient: "Dr. Zirwas, why do you talk about this like I don't have an infection?"

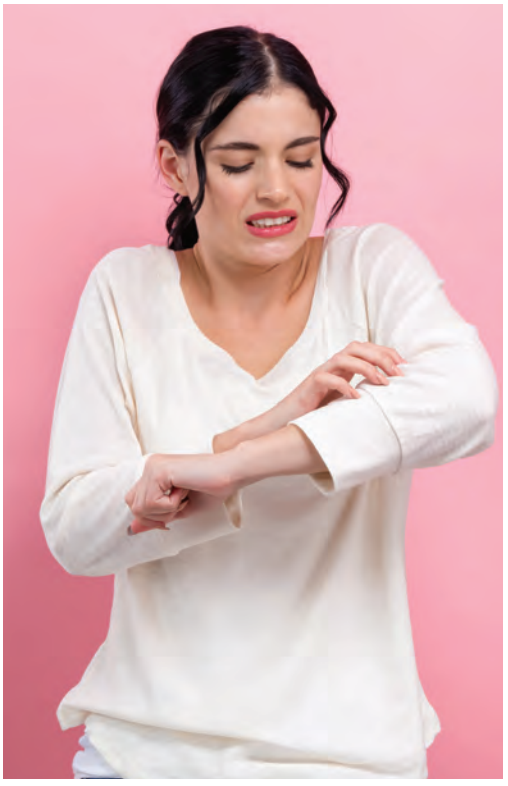
Me: "Because medical science has proven that no organism exists that causes an infection like this."

Patient: "I was a philosophy major in college. That is a fallacy. It is impossible to prove something doesn't exist."

Me: "Interesting…."

So, I went home and looked it up. And the patient was right. It is impossible to prove something doesn't exist.

I got interested enough to do some research on pimozide and its effectiveness for delusions, and it turned out that it doesn't work. In addition, microbiologic investigation had shown



that pimozide does have efficacy against intracellular infections.

Obviously, I was aware of the fact that stomach ulcers had been considered primarily a psychologically caused problem until medical science advanced to the point of being able to identify that it was actually an infection with *H. pylori*.

Not a single patient ever took the pimozide, no matter how hard I tried to establish that relationship and do precisely what I had been taught to do.

The main takeaway is that by admitting that doctors don't know everything, and that it is at least possible patients do have an infection, I've gone from not being able to help a single patient (because they wouldn't take the pimozide) to being able to literally change many lives.

The next time I saw a patient with DOP, I told [the patient] that medical science hadn't been able to find any organism that was causing [this] disease. But it is possible that medical science just hasn't advanced to the point of being able to identify it, and that I didn't know if it was an infection or not. But there was a drug that studies had shown worked really well, called pimozide, which had been shown to work as an antibiotic, even though most doctors think of it as a psychiatric medication. I told [the patient] I was willing to prescribe it and see if it would help, and if it did, we wouldn't know if it was working as an antibiotic or not. But at least [it] would be working.

[The patient] enthusiastically accepted the prescription and started on the pimozide at 1 mg bid. It was like magic. It worked so quickly and so well.

Since then, I've started calling DOP by an alternate name, "concern for non-observable infestation" and discussing it with patients as described above. In addition, I tell patients that with as rapidly and well as the pimozide works, it seems more like it is working as an antibiotic rather than as a psychiatric medication. Patients universally want to take the pimozide and it works wonderfully.

My experience has been that the possible infection is 75% less active in a month and 95% less active in 3 months.

Unfortunately, if DOP is an infection, the pimozide is only suppressing it—not eliminating it, as I generally find that stopping the drug results in the process becoming more active again. Therefore, instead of trying to stop it, I try to find the minimal dose that continues to suppress the symptoms, which is usually 1 mg a day (either 1 mg at bedtime or 0.5 mg twice daily). In some patients, I do need to continue the pimozide long term at 1 mg twice daily or the disease recurs.

The main takeaway is that by admitting that doctors don't know everything, and that it is at least possible patients do have an infection, I've gone from not being able to help a single patient (because they wouldn't take the pimozide) to being able to literally change many lives. The drug allows them to go back to being a "normal" person rather than someone consumed by a presumed infection.

Incidentally, the most common question I get is, "Can I spread this to other people if it is an infection?" To which I answer that I have never seen it spread from one person to another. So, if it is an infection, it appears that only certain people are susceptible to it.

In addition, I don't look at or send off the samples they bring in with them anymore. I tell them that thousands of patients and doctors have looked at the samples and nothing is identifiable. If it is an infection, we just don't have the tools to identify it.

I hope that this commentary on my experience gets more of my colleagues to rethink this disease and how we talk about it with our patients. ◈

References:

1. Silva H, Jerez S, Ramirez A, et al. Effects of pimozide on the psychopathology of delusional disorder. *Prog Neuropsychopharmacol Biol Psychiatry.* 1998;22(2):331-340. doi:10.1016/s0278-5846(98)00008-6
2. Lieberman LA, Higgins DE. A small-molecule screen identifies the antipsychotic drug pimozide as an inhibitor of Listeria monocytogenes infection. *Antimicrob Agents Chemother.* 2009;53(2):756-764. doi:10.1128/AAC.00607-08.

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Off-label Pearl

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

Oral Acitretin for Multikinase Inhibitor-induced Hand-foot Skin Reaction

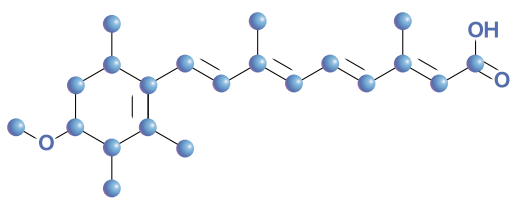
Dermatologists are increasingly being asked to suggest treatments for cutaneous adverse effects associated with an ever-expanding set of cancer chemotherapeutic agents.

The field of oncodermatology has only a few well-known experts, and therefore effective treatment of such skin disorders may prove difficult for the average dermatologist.

One such frustrating reaction is the painful, hyperkeratotic hand-foot syndrome associated with multikinase inhibitors (MKI). The latter agents are used to manage a wide variety of neoplasms, including (but not limited to) colon, kidney, and thyroid. The potentially disabling hand-foot syndrome may occur in 60% to 70% of those receiving multikinase inhibitors, especially cabozantinib, regorafenib, sorafenib, and sunitinib.[1]

We usually try the obvious: urea or lactic acid containing creams, keratolytics, and potent topical steroids. However, this condition is frequently and stubbornly refractory to such typical interventions.

A recent small-scale (N = 8) retrospective analysis may have well discovered a reasonable off-label intervention that has a chance of affording some relief: oral acitretin.[2] Given in doses of 20 to 25 mg daily, this agent provided substantial relief for 7 of 8 patients experiencing this distasteful adverse effect of multikinase chemotherapy.



Acitretin

It should be noted that the hand-foot skin reaction appeared, on average, about 17 days after initiation of MKI treatment. It took, on average, 28 days to reduce the severity of the hand-foot skin reaction, but with a wide range of 8 to 55 days. So, patience may be required and the acitretin dose may possibly need upward adjustment.

I have personally done this treatment successfully several times and hope further large-scale studies will conclusively verify this pearl.

REFERENCES

1. Belum VR, Wu S, Lacouture ME. Risk of hand-foot skin reaction with the novel multikinase inhibitor regorafenib: a meta-analysis. Invest New Drugs. 2013;31(4):1078-1086. doi:10.1007/s10637-013-9977-0
2. Said JT, Singer S, Iannattone L, et al. Outcomes of Acitretin Treatment for Refractory Multikinase Inhibitor-Induced Hand-Foot Skin Reaction [published online ahead of print, 2022 May 11]. *JAMA Dermatol.* 2022;e221425. doi:10.1001/jamadermatol.2022.1425.

Literature Lessons

GENERAL DERMATOLOGY

THE ICHTHYOSIS SCORING SYSTEM is a new, validated means of assessing the severity of either genetic or acquired ichthyosis. It takes into account the degree of erythema and scaling in several body surface areas. This should help determine who is eligible for clinical trials, as well as ongoing objective evaluation of therapeutic success.

TO READ MORE: Sun Q, et al. Development and Initial Validation of a Novel System to Assess Ichthyosis Severity. *JAMA Dermatol*. 2022;158(4):359-365. doi:10.1001/jamadermatol.2021.5917.

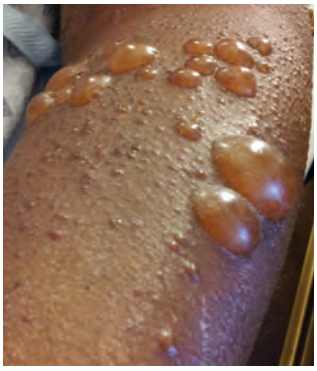
Editor's note: Like the EASI and PASI, a universal scoring system will tell us how well new drugs for ichthyosis perform.

While varicose veins are typically of cosmetic concern, they can be symptomatic. **VARICOSE VEINS** are associated with muscle cramps, peripheral edema, pain after sitting or standing for protracted periods, pruritus around one or more veins, and development of stasis ulcers at or near the ankle.

TO READ MORE: (about symptomatic varicose veins): Streed J. Could leg pain be due to varicose veins? Mayo Clinic News Network, May 3, 2022. Available at: https://newsnetwork.mayoclinic.org/discussion/could-leg-pain-be-due-to-varicose-veins.

A retrospective two-site study of almost 300 **BULLOUS PEMPHIGOID** patients seen during a 6-year period disclosed three separate clinical clusters. The first group was older, had fewer blisters, minimal to no mucosal involvement and demonstrated anti-BP230 antibodies. The second group was younger, had moderate severity (<100 blisters), mucosal involvement in 38%, and 70% had only anti-BP180 antibodies. The final cluster were younger patients with severe disease (>100 blisters), frequent (91%) mucosal involvement and 74% with only anti-BP180 antibodies. This final group was comprised of patients with the most difficult disease to control, leading to the most frequent relapses.

TO READ MORE: Guerrois F, et al. Bullous pemphigoid: three main clusters defining three outcome profiles [published online ahead of print, 2022 Apr 25]. *J Am Acad Dermatol*. 2022;S0190-9622(22)00695-8. doi:10.1016/j.jaad.2022.04.029.



OZONE can be delivered in a variety of ways, including within an aqueous or oil preparation or via a bag containing ozone placed on the skin. Ozone primarily acts as a direct anti-infective and as an antioxidant. There is some evidence that ozone may help treat primary cutaneous infections and disorders known for microbial aberrations (acne, atopic dermatitis). Ozone may also help stimulate wound healing in chronic ulcers (diabetic, stasis). However, the quality of the evidence available to date provides neither sufficient justification nor reliable procedural details to recommend ozone treatment for skin diseases. This remains an area available for additional study.

TO READ MORE: Oliveira Modena DA, de Castro Ferreira R, Froes PM, Rocha KC. Ozone Therapy for Dermatological Conditions: A Systematic Review. *J Clin Aesthet Dermatol*. 2022;15(5):65-73.

ACNE

It is worth remembering that adolescents with acne may well be highly influenced by **MISINFORMATION** derived from the internet. For example, antibiotics and isotretinoin may be characterized as poisonous. The root cause of acne may be erroneously attributed to Candida toxins or drinking fluoridated water. A vegan diet may be proposed as an acne "cure-all." Adolescent blind acceptance of information from the internet may interfere with any therapeutic plan due to non-adherence.

TO READ MORE: O'Connor C, et al. Spotting fake news: a qualitative review of misinformation and conspiracy theories in acne vulgaris [published online ahead of print, 2022 Apr 18]. *Clin Exp Dermatol*. 2022;10.1111/ced.15222. doi:10.1111/ced.15222.

ROSACEA

A systematic review and meta-analysis of 39 studies including more than 9100 patients found, not unexpectedly, that erythematotelangiectatic and papulopustular rosacea were the **MOST COMMON VARIETIES** seen in clinical practice. Phymatous rosacea accounted for only 7% of cases and was more common in men.

TO READ MORE: Barakji YA, et al. Assessment of Frequency of Rosacea Subtypes in Patients With Rosacea: A Systematic Review and Meta-analysis [published online ahead of print, 2022 Apr 6]. *JAMA Dermatol.* 2022;e220526. doi:10.1001/jamadermatol.2022.0526.

PEDIATRIC DERMATOLOGY

In a retrospective case series (N=47) of pediatric **GRANULOMA ANNULARE** at a single urban academic institution, there was a very high prevalence of atopic conditions. None of the pediatric study subjects developed diabetes. Most lesions, as expected, presented on the extremities. While topical steroids relieved pruritus, they did not hasten lesion involution.

TO READ MORE: Cruz SA, et al. The Clinical Presentation and Comorbidities Associated with Granuloma Annulare in the Pediatric Population: A Retrospective Study. *Skinmed*. 2022;20(1):24-28. Published 2022 Feb 28.

PSORIASIS

In a dose-ranging phase 2 study of **SONELOKIMAB**, an IL-17A and IL-17F blocker, clinical efficacy was demonstrated. This new agent is novel in that it is a nanobody, about one-tenth the size of a typical monoclonal antibody.

TO READ MORE: Papp KA, et al. IL17A/F nanobody sonelokimab in patients with plaque psoriasis: a multicentre, randomised, placebo-controlled, phase 2b study [published correction appears in *Lancet*. 2021 Jun 5;397(10290):2150]. *Lancet*. 2021;397(10284): 1564-1575. doi:10.1016/S0140-6736(21)00440-2.

A Korean retrospective study focusing on 800 generalized **PUSTULAR PSORIASIS** patients over a 14-year period disclosed that co-existing renal or hepatic disease, prior myocardial infarction, and concomitant diabetes mellitus put such individuals at high risk for severe disease, including admission to an intensive care unit.

TO READ MORE: Ohn J, et al. Identifying patients with deteriorating generalized pustular psoriasis: Development of a prediction model [published online ahead of print, 2022 May 2]. *J Dermatol*. 2022;10.1111/1346-8138.16383. doi:10.1111/1346-8138.16383.

Investigation of fecal samples revealed that psoriasis patients who are not systemically treated have lower **GUT MICROBIAL DIVERSITY** than carefully matched non-psoriatic controls and household cohabitants of the psoriasis study patients.

TO READ MORE: Todberg T, et al. Patients with psoriasis have a dysbiotic taxonomic and functional gut microbiota [published online ahead of print, 2022 Mar 15]. *Br J Dermatol*. 2022;10.1111/bjd.21245. doi:10.1111/bjd.21245.

Editor's note: Is this somehow etiologic or an epiphenomenon, the result of systemic inflammation?

ATOPIC DERMATITIS

An Israeli retrospective population-based cohort study involving 58,582 adult atopic dermatitis patients noted that two doses of the BNT162b2 mRNA **COVID-19 VACCINE** reduced the risk of infection, hospitalization, and death by 80%, 92%, and 96%, respectively. The most interesting thing about this study was that protection afforded by the vaccine remained the same among adult atopics who continued to receive immunosuppressive drugs, including azathioprine, mycophenolate, methotrexate, cyclosporine, and dupilumab.

TO READ MORE: Kridin K, et al. Determinants and Effectiveness of BNT162b2 mRNA Vaccination Among Patients with Atopic Dermatitis: A Population-Based Study. *Am J Clin Dermatol*. 2022;23(3):385-392. doi:10.1007/s40257-022-00672-5.

A British retrospective population-based cohort study over a 10-year period analyzed over 173,000 adult and pediatric atopic dermatitis patients. Compared to nearly 695,000 controls from the same primary care database, those with atopy had a higher baseline prevalence of **AUTOIMMUNE DISEASE** (5.8% versus 4.3%). The atopic patients also had a higher incidence of new onset autoimmune disease, especially those with severe atopic dermatitis. Specifically, those with atopic dermatitis were likely to develop psoriatic and rheumatoid arthritis, Sjogren syndrome, Crohn disease and ulcerative colitis, vitiligo, alopecia areata, pernicious anemia, and autoimmune hypothyroidism.

TO READ MORE: de Lusignan S, et al. Atopic dermatitis and risk of autoimmune conditions: Population-based cohort study [published online ahead of print, 2022 Apr 22]. *J Allergy Clin Immunol.* 2022;S0091-6749(22)00547-4. doi:10.1016/j.jaci.2022.03.030.

HIDRADENITIS SUPPURATIVA

A retrospective U.S. cohort study revealed that select **INFLAMMATORY MARKERS** can accurately reflect hidradenitis disease severity. Most reliable predictive parameters included: elevated C-reactive protein (CRP), total leukocyte and absolute neutrophil count, and counts of eosinophils, basophils, and monocytes.

TO READ MORE: Andriano TM, et al. Serum inflammatory markers and leukocyte profiles accurately describe hidradenitis suppurativa disease severity [published online ahead of print, 2022 May 11]. *Int J Dermatol*. 2022;10.1111/ijd.16244. doi:10.1111/ijd.16244.

Editor's note: I wonder if serially following CRP, for example, could be used to predict flares before they are clinically apparent, leading to more intensified intervention?

COSMETIC DERMATOLOGY

Although the metabolic syndrome was numerically more common among a cohort of patients with **MELASMA**, the difference was not statistically significant. There was no difference in metabolic parameters such as BMI between melasma patients and matched controls. Fasting insulin levels were higher in the melasma cohort, reaching statistical significance. The connection between melasma and metabolic derangement is weak, at best.

TO READ MORE: Gore Karaali M. Metabolic Syndrome in Melasma: A case-control study [published online ahead of print, 2022 May 12]. *J Cosmet Dermatol.* 2022;10.1111/jocd.15076. doi:10.1111/jocd.15076.

HAIR AND NAILS

Dermoscopic frontal and occipital scalp findings were compared between women with female pattern **ANDROGENETIC ALOPECIA, TELOGEN EFFLUVIUM**, and matched normal controls. Most notably, androgenetic alopecia was characterized by excessive hair diameter diversity, and the presence of vellus hairs and yellow dots. Telogen effluvium was more commonly associated with perifollicular scaling.

TO READ MORE: Bains P, et al. Comparison of Dermoscopic Findings in Female Androgenetic Alopecia and Telogen Effluvium and Female Controls in a Tertiary Care Center. *J Clin Aesthet Dermatol.* 2022;15(5):29-34.

An online survey disclosed that the vast majority of licensed **NAIL TECHNICIANS** had some training in detecting acral skin cancers (including acral lentiginous melanoma) and routinely referred suspicious lesions to dermatologists for evaluation. Nail professionals also were willing and eager to obtain additional training to increase their confidence and skill levels in this endeavor.

TO READ MORE: Joseph AK, et al. Knowledge, attitudes, and behaviors of nail technicians in detecting acral lentiginous melanoma [published online ahead of print, 2022 May 9]. *J Cosmet Dermatol*. 2022;10.1111/jocd.15068. doi:10.1111/jocd.15068.

CUTANEOUS ONCOLOGY, SURGERY AND LASERS

According to a recently published Swedish study, younger (18-39) and older (> 70) melanoma patients feel like they don't get enough **INFORMATION** from their health care providers. Middle-age melanoma patients (40-69) are generally satisfied with the quantity and quality of information given to them by the health care provider.

TO READ MORE: Tufvesson SH, et al. Perception of information to Swedish melanoma patients in routine clinical practice – a cross-sectional survey. *BMC Cancer* 2022;22(1):159. doi:10.1186/s12885-022-09208-w

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A fascinating case of classic **KAPOSI SARCOMA** with only transient response to radiotherapy demonstrated marked and sustained improvement following daily oral administration of 10 mg propranolol. The low dose was well tolerated.

TO READ MORE: Salido-Vallejo R, et al. Treatment With Oral Propranolol for Refractory Classic Cutaneous Kaposi Sarcoma [published online ahead of print, 2022 May 11]. *JAMA Dermatol.* 2022;10.1001/jamadermatol.2022.1278. doi:10.1001/jamadermatol.2022.1278.

Editor's note: As the authors point out, propranolol appears to be an attractive alternative in patients with thick, multiple, or symptomatic lesions when topical treatment is inadequate and/or radiotherapy and chemotherapy simply are not suitable.

A large cross-sectional study involving **ASIAN AMERICANS** from the National Health Interview Survey database disclosed that all subgroups were more likely to seek shade, wear long clothing to the ankles, and wear long-sleeved shirts but less likely to use sunscreen compared to non-Asian/non-Hispanic Whites. Those of Chinese ancestry were more likely to apply sunscreen and wear a hat compared to other Asian subgroups.

TO READ MORE: Supapannachart KJ, et al. Skin Cancer Risk Factors and Screening Among Asian American Individuals. *JAMA Dermatol.* 2022;158(3):260-265. doi:10.1001/jamadermatol.2021.5657.

A longitudinal Italian study followed a cohort of women with **VULVAR MELANOSIS** for several decades. Despite the fact that in nearly 1 out of 3 lesions increased in size or underwent color changes, no malignant degeneration was noted.

TO READ MORE: De Giorgi V, et al. Clinical and Dermoscopic Features of Vulvar Melanosis Over the Last 20 Years. *JAMA Dermatol*. 2020;156(11):1185-1191. doi:10.1001/jamadermatol.2020.2528.

DRUGS AND DEVICES

Can a patient who asserts penicillin allergy safely receive a cephalosporin? This study, based on a systematic review and meta-analysis of 77 publications (6147 patients) found that the vast majority of penicillin-allergic individuals can, indeed, receive **CEFAZOLIN** without adverse incident. Of those who were deemed penicillin allergic, only 0.7% were found to be cefazolin sensitive. Among the small group of those with a historical allergy to cefazolin, 3.7% were found to be penicillin allergic.

TO READ MORE: Sousa-Pinto B, et al. Assessment of the Frequency of Dual Allergy to Penicillins and Cefazolin: A Systematic Review and Meta-analysis. *JAMA Surg*. 2021;156(4):e210021. doi:10.1001/jamasurg.2021.0021.

National spending on drugs rose by 12% in 2021, largely related to COVID-19 vaccine and treatment costs. Despite an overall increase in **DRUG SPENDING**, the cost per prescription on average was flat or slightly declining. Out-of-pocket costs for prescription drugs increased substantially, creating a significant financial burden for select subsegments of the U.S. population.

TO READ MORE: IQVIA Institute for Human Data Science. The Use of Medicines in the U.S. 2022. April 21, 2022. Accessed at: https://www.iqvia.com/insights/the-iqvia-institute/reports/the-use-of-medicines-in-the-us-2022.

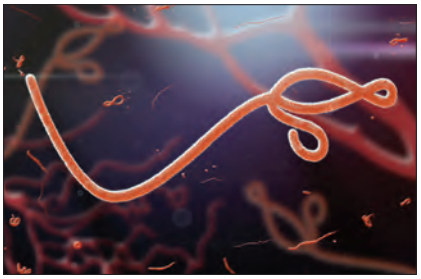
INFECTIOUS DISEASES

Even in the face of the COVID-19 pandemic, there were 2.4 million cases of **SEXUALLY TRANSMITTED DISEASE** in the U.S. during 2020, according to newly released CDC statistics. Of most interest to dermatologists, there were 133,945 cases of syphilis, up 52% from 2016. Congenital syphilis increased by 235% over 2016.

TO READ MORE: CDC. Sexually Transmitted Disease Surveillance, 2020. Released April 12, 2022. CDC.gov. Accessible at: Sexually Transmitted Disease Surveillance, 2020 (cdc.gov).

Twenty-seven **INPATIENTS WITH BODY LICE** and 81 inpatients without were included in an analysis done at University of California, San Francisco. As one might predict, those infested with the obligate blood-sucking ectoparasites had a mean 2.5 g/dL lower hemoglobin level. This may be one cause of anemia in marginalized populations, such as the homeless.

TO READ MORE: Rudd N, et al. Association of Body Lice Infestation With Hemoglobin Values in Hospitalized Dermatology Patients [published online ahead of print, 2022 Apr 20]. *JAMA Dermatol*. 2022;e220818. doi:10.1001/jamadermatol.2022.0818.



To date, **INFECTIOUS FILOVIRUSES** (such as Ebola) have only been found in Africa. However, the Lloviu virus, a very close genetic relative of Ebola, has now been found–both serologically and via direct viral isolation–from bats in both Spain and Hungary. This poses the possibility of a zoonotic spread to humans (spelunkers for example). This novel virus might logically be expected to be both lethal and contagious, based on its similarity to Ebola. Remdesivir has proven effective against Lloviu virus in-vitro.

TO READ MORE: Kemenesi G, et al. Isolation of infectious Lloviu virus from Schreiber's bats in Hungary. *Nat Commun*. 2022;13(1):1706. Published 2022 Mar 31. doi:10.1038/s41467-022-29298-1 and Görföl T, et al. Lloviu Virus in Europe is an Emerging Disease of Concern. *Ecohealth*. 2022;19(1):5-7. doi:10.1007/s10393-021-01574-4.

Investigators have discovered a new molecule, **GASDERMIN A**, which causes a specific type of programmed skin cell death, called pyroptosis, when faced with certain recognized pathogens, such a Group A Streptococci. The researchers hope to harness this novel protein to induce cell death in diseased skin (such as necrotizing fasciitis) without harming uninfected cells and eliminating the need for debilitating surgical debridement.

TO READ MORE: LaRock, D.L., Johnson, A.F., Wilde, S. et al. Group A Streptococcus induces GSDMA-dependent pyroptosis in keratinocytes. *Nature* 605, 527–531 (2022). https://doi.org/10.1038/s41586-022-04717-x.

The COVID-19 pandemic has had significant impact on the health care industry. Highlights from a detailed federal report include: More than 3600 **HEALTH CARE WORKERS** (including physicians) have died from COVID-19 infection; there currently exists a shortage of health care workers at all levels due to many retiring or leaving the field or becoming ill with lasting adverse effects; stress, anxiety, frustration and "burnout" among health care workers are at all-time highs; and both physicians and ancillary workers are increasingly subject to somatic complaints (headache, loss of appetite, abdominal complaints).

TO READ MORE: U.S. Department of Health and Human Services, Office of the Assistant Secretary for Planning and Education: Impact of the COVID-19 Pandemic on the Hospital and Outpatient Clinician Workforce. Issue Brief. May 3, 2022. Accessible at: https://aspe.hhs.gov/sites/default/files/documents/9cc72124abd9ea25d58a22c7692dccb6/aspe-covid-workforce-report.pdf.

The European experience with **"LONG COVID"** was summarized at a recent meeting. Some 9 out of 10 hospitalized COVID-19 patients have at least one symptom 60 days after illness onset, with about 55% presenting three or more symptoms. Half of those individuals have at least one symptom a full year after infection. Dyspnea may persist long after the chest radiograph clears in about 13% of COVID-19 patients. "Long COVID" is more likely to affect those 40-54 years of age. Finally, the more severe the acute illness, the greater the number of symptoms post-infection.

TO READ MORE: Gonzalez M. A COVID-19 Professional Debate. Presented at the 7th International Congress of the Spanish Society of Precision Health. May 2022.

Analysis of American "Long COVID" cases disclosed distinct patterns of hematogenous **CYTOKINES CORRESPONDING TO SYMPTOM PROFILES** in a preliminary study of 55 patients. It may well be that checking which cytokines are elevated several months after the acute phase of COVID-19 disease will soon tell us what potential "Long COVID" problems to expect.

TO READ MORE: Talla A, et al. Persistent serum protein signatures define an inflammatory subset of long COVID. *bioRxiv*. 2022; May 10.doi:10.1101/2022.05.09.491196.

University of Michigan investigators collected air samples and swabbed surfaces around the campus. Less than 2% of both types of samples were positive for SARS-CoV-2 coronavirus. When comparing sample results to actual cases of COVID-19 infection, the researchers concluded that the probability of acquiring COVID after exposure to airborne virus particles was about 1 per 100 exposures. This compares to the probability of illness acquired from a **CONTAMINATED SURFACE** at 1 for every 100,000 exposures.

TO READ MORE: Zhang X, et al. Monitoring SARS-CoV-2 in air and on surfaces and estimating infection risk in buildings and buses on a university campus [published online ahead of print, 2022 Apr 27]. *J Expo Sci Environ Epidemiol*. 2022;1-8. doi:10.1038/s41370-022-00442-9.

RHEUMATOLOGIC DISEASES

Researchers at the University of Michigan have found that both lesional and normal appearing skin of **LUPUS** patients contain elevated levels of Type 1 interferons in keratinocytes and fibroblasts compared to matched skin samples from healthy individuals. The same is true of circulating monocytes. The investigators speculate that this keeps the skin in a "primed" state so that small provocations can lead to rapid development of inflammation.

TO READ MORE: Billi AC, et al. Nonlesional lupus skin contributes to inflammatory education of myeloid cells and primes for cutaneous inflammation. *Sci Transl Med*. 2022;14(642):eabn2263. doi:10.1126/scitranslmed.abn2263.

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Beware of Occult Systemic Sarcoidosis

With Sotonye E. Imadojemu, MD, MBE

SOTONYE E. IMADOJEMU, MD, MBE

Assistant Professor of Dermatology, Harvard Medical School
Director, Cutaneous Sarcoidosis and Granulomatous Diseases Clinic, Brigham and Women's Hospital
Boston, Massachusetts

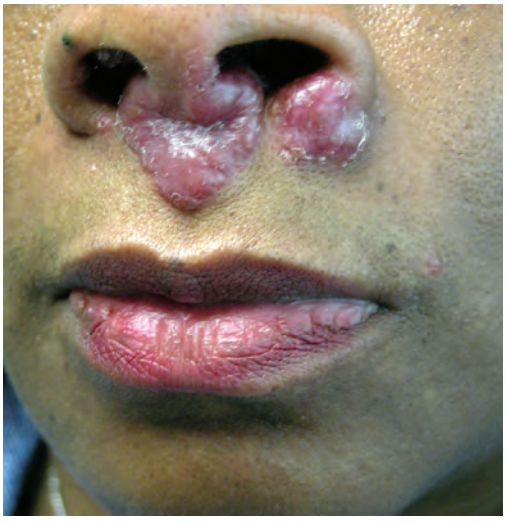
Dr. Sotonye E. Imadojemu discusses her study, which sends a cautionary signal to dermatologists who may be the first physicians to diagnose the multisystem disease occult systemic sarcoidosis.

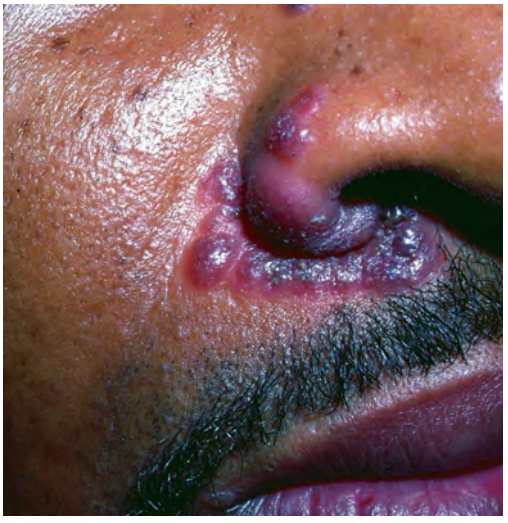
"In a study evaluating racial differences in systemic involvement among patients presenting to dermatologists for cutaneous sarcoidosis,[1] we found that Black patients are significantly younger than non-Blacks at presentation and significantly more likely to have undiagnosed extracutaneous disease," said study author Sotonye E. Imadojemu, MD, MBE.

"In particular, our results showed that Black patients were significantly more likely than non-Blacks to have cardiac involvement, and that is concerning considering that cardiac sarcoidosis is the deadliest form of this multisystem granulomatous disease."

Dr. Imadojemu continued, "While we believe our study is the first to show the increased risk for systemic disease among Black patients initially presenting with cutaneous sarcoidosis, it also highlights that any patient diagnosed with cutaneous sarcoidosis may have subclinical systemic involvement. Therefore, all patients, irrespective of race, ethnicity, or other characteristics, should be evaluated for systemic involvement."

The workup for systemic involvement should include, but is not limited to, an electrocardiogram, chest radiography, ophthalmologic examination, and baseline laboratory testing





> "In particular, our results showed that Black patients were significantly more likely than non-Blacks to have cardiac involvement, and that is concerning considering that cardiac sarcoidosis is the deadliest form of this multisystem granulomatous disease."

comprised of a complete blood count with differential and comprehensive metabolic panel.

"Additional evaluations should be dictated by the results of these initial investigations and a thorough review of systems that should be performed at each clinic visit. Any dermatologist who is not comfortable evaluating sarcoidosis patients for systemic disease should refer the individual to a pulmonologist or rheumatologist for assistance," said Dr. Imadojemu.

Commenting on the findings of the study, Ted Rosen, MD, editor-in-chief, *The Dermatology Digest* said, "Considering that Black patients presenting with cutaneous sarcoid will generally be younger and may well have asymptomatic heart disease, there may be a low index of suspicion for cardiac involvement. Nonetheless, this study highlights the need to perform a comprehensive cardiac evaluation in order to detect unsuspected cardiac disease."

He added, "Cardiac sarcoidosis often portends a bad outcome with the related fibrosis leading to congestive heart failure, arrythmias, and sudden cardiac death.[2] It should also be noted that an electrocardiogram and echocardiogram may not be sufficient to detect sarcoidosis affecting the heart. Magnetic resonance imaging and positron-emission tomography scans may be required."

Confirming a Clinical Observation

Dr. Imadojemu and colleagues were motivated to undertake the study based on an anecdotal observation that among patients with sarcoidosis. Black patients seemed to have more severe cutaneous disease and more extensive extracutaneous involvement than non-Blacks.

"Our group sought to explore the accuracy and validity of this impression by conducting a study. Our hope is that once we identified and quantified the problem, we would be better able to not only devise ways to create structures that lend the necessary support to Black patients with sarcoidosis and the physicians who care for them, but also to address and correct the roots of these health disparities," said Dr. Imadojemu.

To investigate potential racial differences in systemic involvement among patients first diagnosed with sarcoidosis by a dermatologist, Dr. Imadojemu and colleagues conducted a search of the Research Patient Data Registry of the Mass General Brigham Hospital for the years 2000 to 2019. They identified 50 patients with biopsy-proven cutaneous sarcoidosis who presented to a dermatologist without having been diagnosed with systemic disease. The largest proportion of the study population (48%) was White. Black patients and Latinx patients each accounted for 18% of the group, 4% self-identified as Asian Pacific Islander, 2% were Native American, and 10% self-identified as other.

Mean age at the time of presentation to the dermatologist was 36.9 years for Black patients and 48.4 years for non-Blacks (P =.014). A diagnostic workup identified extracutaneous involvement in 79% of Black patients versus 46% of non-Black patients (P =.044). Among patients who had a work-up for cardiac involvement, the finding was positive in 33% of Black patients

Dr. Imadojemu and colleagues were motivated to undertake the study based on an anecdotal observation that among patients with sarcoidosis, Black patients seemed to have more severe cutaneous disease and more extensive extracutaneous involvement than non-Blacks.

versus none of the non-patients (P =.032).

There was a trend for Black patients to have a higher number of extracutaneous organ systems involved (P =.049). Rates of lymph node, pulmonary, and ocular involvement were also higher among Blacks, although the differences compared to non-Black patients were not statistically significant.

Practice Performance Gap

A need to remind dermatologists that they should initiate an evaluation for systemic sarcoidosis if they are the first physician to diagnose the disorder is highlighted by another analysis in which Dr. Imadojemu and colleagues identified a significant practice gap in this area.[3] Reviewing data from the same patient cohort, the researchers found that recommendations for chest imaging and ophthalmologic examination were given to nearly all patients (97.9% and 91.7%, respectively). However, assessment for cardiac involvement was recommended to only 28 (58.3%) patients.

Future Research

Dr. Imadojemu noted that the study investigating racial differences has limitations that include its small sample size, retrospective design, and the fact that an electrocardiogram or echocardiogram may not be sufficient to identify cardiac sarcoidosis when it exists.

"Because of its limited size, our study may have lacked power to identify other potential ethno-racial differences in systemic involvement among patients with sarcoidosis initially diagnosed because of cutaneous disease. It is noteworthy that Japanese patients have been reported to have a much higher likelihood of ocular and cardiac disease than patients in the rest of the world, for reasons that remain obscure," said Dr. Imadojemu.

"Therefore, larger studies are absolutely warranted to identify broader racial/ethnic variation among patients with sarcoidosis."

Dr. Imadojemu also noted the importance of recognizing that structural racism likely plays a role in the health disparities documented in the study.

"We know that race is a social not biological category. My research explores the role that environmental exposures that vary by race due to structural racism, such as exposure to environmental toxins, housing discrimination, and racial stress, play in the pathogenesis and severity of this beguiling disease," she said. ◈

By Cheryl Guttman Krader

REFERENCES

1. Kassamali B, Villa-Ruiz C, Kus KJB, et al. Increased risk of systemic and cardiac sarcoidosis in Black patients with cutaneous sarcoidosis. *J Am Acad Dermatol.* 2022;86(5):1178-1180. doi:10.1016/j.jaad.2021.04.079.
2. Markatis E, Afthinos A, Antonakis E, et al. Cardiac sarcoidosis: diagnosis and management. *Rev Cardiovasc Med.* 2020;21(3):321-338. doi:10.31083/j.rcm.2020.03.102.
3. Villa-Ruiz C, Lo K, Desai S, et al. Practice gaps in the evaluation of systemic involvement in patients with cutaneous sarcoidosis presenting to a dermatologist: A retrospective review of 48 patients. *J Am Acad Dermatol.* 2021;85(3):794-796. doi:10.1016/j.jaad.2020.10.021.

Diagnosing Anasarca-induced Desquamation

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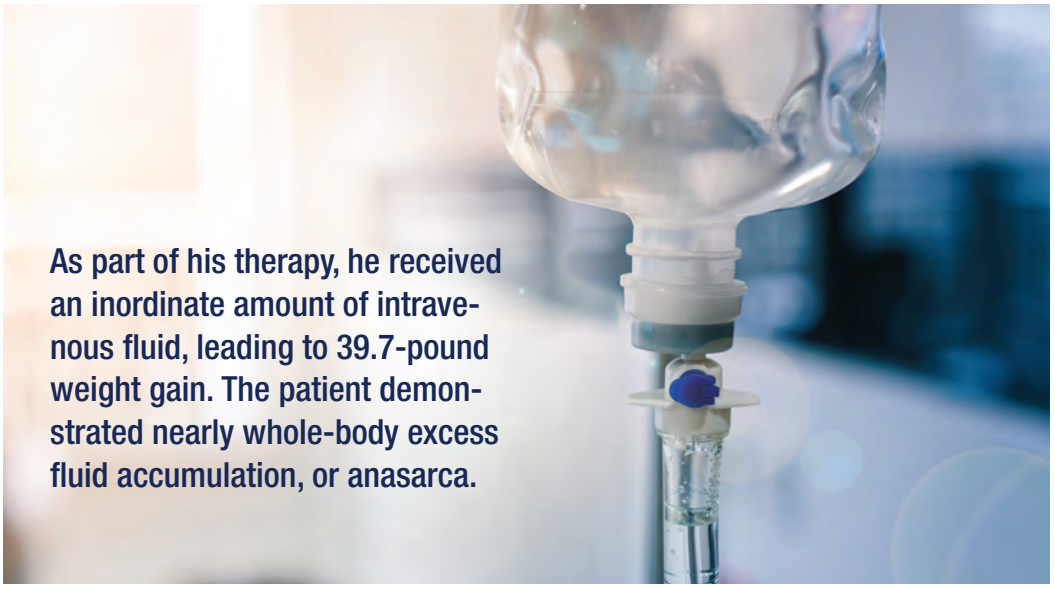
A recent case report describes anasarca-induced bullae and desquamation as a new variant of the well-known clinical phenomenon edema bullae.

In a case report recently published in *Cutis*,[1] U.S. researchers describe what they write is a new variant of a well-known clinical phenomenon of blisters and subsequent desquamation of the skin on the presence of acute edema.

"In this case report, we describe a new variant that we have termed anasarca-induced desquamation in a 50-year-old man with molting of the entire cutaneous surface after acute edema, in a setting of 40-lb weight gain over 5 days," according to the paper "The Molting Man: Anasarca-induced full-body desquamation."

The point here being that severe cutaneous edema can cause bullae followed by generalized skin sloughing.

The case report revolved around an unresponsive homeless man hospitalized due to metabolic ketoacidosis, acute renal insufficiency, hypoalbuminemia due to alcoholic liver disease, and hypothermia. As part of his therapy, he received an inordinate amount of intravenous fluid, leading to 39.7-pound weight gain. The patient demonstrated nearly whole-body excess fluid accumulation, or anasarca.



As part of his therapy, he received an inordinate amount of intravenous fluid, leading to 39.7-pound weight gain. The patient demonstrated nearly whole-body excess fluid accumulation, or anasarca.

The anasarca improved with diuretics, and as the swelling abated, nearly the entire patient's skin surface peeled off. The authors dubbed this "anasarca-induced desquamation." They opined that this is merely a more severe and generalized form of edema blisters.

Dermatology was consulted due to widespread skin sloughing without mucosal changes. A skin biopsy revealed an intracorneal split with desquamation of the stratum corneum, with very minimal perivascular lymphocytic infiltration.

"Laboratory workup for infectious causes and punch biopsies of skin lesions ruled out Stevens-Johnson syndrome and staphylococcal scalded skin syndrome, which have a similar clinical presentation to anasarca-induced desquamation. In patients with diffuse superficial desquamation in the setting of acute edema, anasarca-induced desquamation is worth investigating to avoid the use of corticosteroids and intravenous antibiotics in this inherently benign condition," the authors wrote.

In this situation, treatment is primarily aimed at reduction of the etiologic fluid accumulation (edema).

The anasarca improved with diuretics, and as the swelling abated, nearly the entire patient's skin surface peeled off. The authors dubbed this "anasarca-induced desquamation." They opined that this is merely a more severe and generalized form of edema blisters. Needless to say, the key point is to differentiate edema associated blistering and desquamation from pemphigoid, herpes zoster, toxic epidermal necrolysis, and staphylococcal scalded skin syndrome.

On a side note, while anasarca is not common, it's not really rare.

"Anasarca is a serious condition in which there is a generalized accumulation of fluid in the interstitial space. This accumulation of fluid occurs when capillary filtration exceeds the amount of fluid removed via lymphatic drainage. It is caused by a variety of clinical conditions including heart failure, renal failure, liver failure, or conditions involving the lymphatic system," according to Kattula et al.[2]

Last year, a case report in *Cureus*[3] documented the case of a 70-year-old man with a history of uncontrolled hypertension who presented to the hospital with swelling of the extremities. He was on minoxidil 10 mg twice daily, according to the authors.

"After discontinuation of minoxidil and starting intravenous diuretics, the patient showed clinical improvement. This case report reviews and explains that minoxidil-induced anasarca should be considered as a differential diagnosis in patients taking minoxidil as knowledge of this rare finding may lead to early diagnosis and management," they wrote.

REFERENCES:

1. Kou L, Kold LJ, Kelada AM, et al. The Molting Man: Anasarca-Induced Full-Body Desquamation. *Cutis*. 2022 April;109(4):221-223 | doi:10.12788/cutis.0493.
2. Kattula SRST, Avula A, Baradhi KM. Anasarca. In: StatPearls. Treasure Island (FL): StatPearls Publishing; May 8, 2022. PMID: 30085555.
3. Gbadamosi WA, Melvin J, Lopez M. Atypical Case of Minoxidil-Induced Generalized Anasarca and Pleuropericardial Effusion. *Cureus*. 2021;13(6):e15424. Published 2021 Jun 3. doi:10.7759/cureus.15424.

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Visible actinic keratoses (AKs) often indicate the presence of subclinical lesions.[1]

DANGER LURKS BELOW THE SURFACE

AMELUZ® (aminolevulinic acid HCl) topical gel, 10% with BF-RhodoLED® is the first and only combination product for photodynamic therapy (PDT) approved for field-directed treatment of AK of mild-to-moderate severity on the face and scalp,[2] which allows subclinical lesions to also be addressed.[1,3]

AMELUZ®
[aminolevulinic acid HCl] topical gel, 10%
& BF-RhodoLED®

HELP CLEAR THE FIELD

INDICATION

AMELUZ® (aminolevulinic acid hydrochloride) topical gel, 10%, in combination with photodynamic therapy (PDT) using BF-RhodoLED® or RhodoLED® XL lamp, a narrowband, red light illumination source, is indicated for lesion-directed and field-directed treatment of actinic keratoses (AKs) of mild-to-moderate severity on the face and scalp.

IMPORTANT SAFETY INFORMATION

AMELUZ® (aminolevulinic acid hydrochloride) topical gel, 10% with BF-RhodoLED® or RhodoLED® XL lamp

AMELUZ®, containing 10% aminolevulinic acid hydrochloride, is a non-sterile gel formulation for topical use only. Not for ophthalmic, oral, or intravaginal use.

AMELUZ®, in conjunction with lesion preparation, is only to be administered by a health care provider. Photodynamic therapy with AMELUZ® involves preparation of lesions, application of the product, occlusion and illumination with BF-RhodoLED® or RhodoLED® XL. The application area should not exceed 20 cm^2 and no more than 2 grams of AMELUZ® (one tube) should be used at one time. Lesions that have not completely resolved shall be retreated 3 months after the initial treatment. Refer to BF-RhodoLED® or RhodoLED® XL user manual for detailed lamp safety and operating instructions. Both patient and medical personnel conducting the PDT should adhere to all safety instructions.

AMELUZ® shall not be used by persons who have known hypersensitivity to porphyrins or any of the components of AMELUZ®, which includes soybean phosphatidylcholine. AMELUZ® should also not be used for patients who have porphyria or photodermatoses.

Hypersensitivity reactions have been reported with the use of AMELUZ® prior to photodynamic therapy (PDT). AMELUZ® should be washed off and appropriate therapy instituted. Inform patients and their caregivers that AMELUZ may cause hypersensitivity, potentially including severe courses (anaphylaxis).

Transient Amnestic Episodes have been reported during postmarketing use of AMELUZ® in combination with photodynamic therapy (PDT). If patients experience amnesia or confusion, discontinue treatment. Advise them to contact the healthcare provider if the patient develops amnesia after treatment.

Eye exposure to the red light of the BF-RhodoLED® or RhodoLED® XL lamp during PDT must be prevented by protective eyewear. Direct staring into the light source must be avoided. AMELUZ® increases photosensitivity. Patients should avoid sunlight, prolonged or intense light (e.g., tanning beds, sun lamps) on lesions and surrounding skin treated with AMELUZ® for approximately 48 hours following treatment whether exposed to illumination or not.

AMELUZ® has not been tested on patients with inherited or acquired coagulation disorders. Special care should be taken to avoid bleeding during lesion preparation in such patients. Any bleeding must be stopped before application of the gel. AMELUZ® should not be used on mucous membranes or in the eyes.

Local skin reactions at the application site were observed in about 99.5% of subjects treated with AMELUZ® and narrow spectrum lamps. The very common adverse reactions (≥10%) during and after PDT were application site erythema, pain/burning, irritation, edema, pruritus, exfoliation, scab, induration, and vesicles. Most adverse reactions occurred during illumination or shortly afterwards, were generally of mild or moderate intensity, and lasted for 1 to 4 days in most cases; in some cases, however, they persisted for 1 to 2 weeks or even longer. Severe pain/burning occurred in up to 30% of treatments.

There have been no formal studies of the interaction of AMELUZ® with other drugs. Concomitant use of the following photosensitizing medications may increase the phototoxic reactions after PDT: St. John's wort, griseofulvin, thiazide diuretics, sulfonylureas, phenothiazines, sulphonamides, quinolones, and tetracyclines.

There are no available data on AMELUZ® use in pregnant women to inform a drug associated risk. No data are available regarding the presence of aminolevulinic acid in human milk, the effects of aminolevulinic acid on the breastfed infant or on milk production. Safety and effectiveness in pediatric patients below the age of 18 have not been established as AK is not a condition generally seen in the pediatric population. No overall differences in safety or effectiveness were observed between elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Please read the US Full Prescribing Information for AMELUZ® and/or US User Manual of BF-RhodoLED® and/or RhodoLED® XL lamp available together at https://www.ameluz.com/PI.

You are encouraged to report side effects of AMELUZ®. Please contact Biofrontera Inc. at 1-844-829-7434 or FDA at 1-800-332-1088 or www.fda.gov/medwatch.

References: 1. Berman B, Amini S, Valins W, Block S. Pharmacotherapy of actinic keratosis. *Expert Opin Pharmacother.* 2009;10(18):3015-3031. **2.** AMELUZ® [prescribing information]. Woburn, MA: Biofrontera Inc; 2021. **3.** Reinhold U. A review of BF-200 ALA for the photodynamic treatment of mild-to-moderate actinic keratosis. *Future Oncol.* 2017;13(27):2413-2428.

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BRIEF SUMMARY OF PRESCRIBING INFORMATION

This Brief Summary does not include all the information needed to use AMELUZ safely and effectively. See full prescribing information for AMELUZ.

AMELUZ® (aminolevulinic acid hydrochloride) topical gel, 10% with BF-RhodoLED® lamp or RhodoLED® XL lamp

INDICATIONS AND USAGE

AMELUZ, in combination with photodynamic therapy (PDT) using BF-RhodoLED® or RhodoLED® XL lamp, a narrowband, red light illumination source, is indicated for lesion-directed and field-directed treatment of actinic keratoses (AKs) of mild-to-moderate severity on the face and scalp.

DOSAGE AND ADMINISTRATION

AMELUZ, in conjunction with lesion preparation, is only to be administered by a health care provider.

AMELUZ, containing 10% aminolevulinic acid hydrochloride, is a non-sterile gel formulation for topical use only. Not for ophthalmic, oral, or intravaginal use.

Photodynamic therapy with AMELUZ involves preparation of lesions, application of the product, 3h occlusion and illumination with BF-RhodoLED or RhodoLED XL. The application area should not exceed 20 cm^2 and no more than 2 grams of AMELUZ (one tube) should be used at one time. Lesions that have not completely resolved shall be retreated 3 months after the initial treatment. Refer to BF-RhodoLED or RhodoLED XL user manual for detailed lamp safety and operating instructions. Both patient and medical personnel conducting the PDT should adhere to all safety instructions.

CONTRAINDICATIONS

AMELUZ is contraindicated in patients with:
- Known hypersensitivity to porphyrins.
- Known hypersensitivity to any of the components of AMELUZ, which includes soybean phosphatidylcholine.
- Porphyria. AMELUZ use may cause uncontrolled phototoxic effects.
- Photodermatoses. PDT may worsen the phototoxic or photoallergic reactions.

WARNINGS AND PRECAUTIONS

Hypersensitivity

Several cases of hypersensitivity were reported during postmarketing use of AMELUZ prior to PDT illumination. If allergic reactions occur, clean the area of skin where the product was applied and institute appropriate therapy. Inform patients and their caregivers that AMELUZ may cause hypersensitivity, potentially including severe courses (anaphylaxis).

Transient Amnestic Episodes

Transient amnestic episodes have been reported during postmarketing use of AMELUZ in combination with photodynamic therapy. Inform patients and their caregivers that AMELUZ in combination with photodynamic therapy may cause transient amnestic episodes. Advise them to contact the healthcare provider if the patient develops amnesia after treatment.

Risk of BF-RhodoLED or RhodoLED XL Lamp Induced Eye Injury

BF-RhodoLED or RhodoLED XL lamp may cause eye irritation, glare, or injury. Before operating the lamp, personnel must refer to the user manual for specific warnings, cautions, and instructions. Eye exposure to the BF-RhodoLED or RhodoLED XL light must be prevented. Protective eye equipment must be used by patient, healthcare providers and any person present during the illumination period. Avoid staring directly into the light source.

Increased Photosensitivity

AMELUZ increases photosensitivity. Avoid sunlight, prolonged or intense light (e.g., tanning beds, sun lamps) on lesions and surrounding skin treated with AMELUZ for approximately 48 hours following treatment, whether exposed to illumination or not. Concomitant use of AMELUZ with other known photosensitizing agents may increase the risk of phototoxic reaction to PDT.

Risk of Bleeding in Patients with Coagulation Disorders

AMELUZ has not been tested on patients with inherited or acquired coagulation disorders. Special care should be taken to avoid bleeding during lesion preparation in such patients. Any bleeding must be stopped before application of the gel.

Ophthalmic Adverse Reactions

Eyelid edema has occurred with AMELUZ application. AMELUZ can cause ophthalmic adverse reactions. AMELUZ is intended for topical use only. Do not apply AMELUZ into the eyes. Rinse eyes with water in case of accidental contact.

Risk of Mucous Membrane Irritation

AMELUZ can cause mucous membrane irritation. AMELUZ is intended for topical use only. Do not apply AMELUZ to the mucous membranes. Rinse with water in case of accidental contact.

ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections [see Warnings and Precautions]: Hypersensitivity, Transient Amnestic Episodes, Risk of BF-RhodoLED or RhodoLED XL Lamp Induced Eye Injury, Increased Photosensitivity, Risk of Bleeding in Patients with Coagulation Disorders, Ophthalmic Adverse Reactions, Risk of Mucous Membrane Irritation.

Clinical Trial 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.

The clinical program for AMELUZ included three double-blind and placebo-controlled trials (Trials 1, 2, and 3), enrolling a total of 299 subjects that were treated with narrow band light. Trial subjects were adults greater than or equal to 49 years of age, and the majority had Fitzpatrick skin type I, II, or III. No subjects had Fitzpatrick skin type V or VI. Approximately 86% of subjects were male, and all subjects were Caucasian.

For all trials, the enrolled subjects had mild to moderate AKs (Olsen grade 1 and 2) with 4 to 8 lesions on the face and scalp. Overall, 87 placebo-treated subjects (n=16, n=32, n=39) and 212 AMELUZ-treated subjects (n=32, n=55, and n=125) were illuminated with BF-RhodoLED or similar narrow spectrum lamps.

Local skin reactions at the application site were observed in about 99.5% of subjects treated with AMELUZ and narrow spectrum lamps. The most frequent adverse reactions during and after PDT were application site erythema, pain, burning, irritation, edema, pruritus, exfoliation, scab, induration, and vesicles.

Most adverse reactions occurred during illumination or shortly afterwards, were generally of mild or moderate intensity, and lasted for 1 to 4 days in most cases; in some cases, however, they persisted for 1 to 2 weeks or even longer. Severe pain/burning occurred in up to 30% of subjects. In one case, the adverse reactions required interruption or discontinuation of the illumination.

The incidence of common (≥1%, <10%) and very common (≥10%) adverse reactions in randomized, multicenter trials at the application site are presented in Table 1.

Table 1: Incidence of Adverse Reactions Occurring at ≥1% of the AMELUZ Group and More Frequently than the Vehicle Group in the Actinic Keratosis Trials at the Application Site

Adverse reaction	Vehicle n=87	AMELUZ n=212
Adverse reactions at the application site		
Erythema	34 (39%)	195 (92%)
Pain/Burning	26 (30%)	195 (92%)
Irritation	17 (20%)	153 (72%)
Edema	3 (3%)	75 (35%)
Pruritus	14 (16%)	72 (34%)
Exfoliation	4 (5%)	41 (19%)
Scab	2 (2%)	41 (19%)
Induration	0 (0%)	26 (12%)
Vesicles	1 (1%)	25 (12%)
Paresthesia	2 (2%)	18 (9%)
Hyperalgesia	0 (0%)	13 (6%)
Reaction	2 (2%)	8 (4%)
Discomfort	0 (0%)	7 (3%)
Erosion	0 (0%)	6 (3%)
Discharge	0 (0%)	4 (2%)
Bleeding	0 (0%)	3 (1%)
Pustules	0 (0%)	3 (1%)

Common (≥1%, <10%) adverse reactions not at the application site for AMELUZ were headache, skin exfoliation, chills and eyelid edema. Less common (≥0.1%, <1%) adverse reactions at the application site for AMELUZ were hemorrhage and swelling. The adverse reactions not at the application site were blister, feeling hot, pruritus, pyrexia, scab, nervousness, pain, petechiae, rash pustular, skin erosion and ulcer. In a clinical trial designed to investigate the sensitization potential of aminolevulinic acid with 216 healthy subjects, 13 subjects (6%) developed allergic contact dermatitis after continuous exposure for 21 days with doses of aminolevulinic acid that were higher than doses normally used in the treatment of AK.

Postmarketing Experience

The following adverse reactions have been reported during post-approval use of AMELUZ. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Skin and subcutaneous tissue disorders: allergic dermatitis, application site inflammation, application site discoloration.
Eye disorders: eye irritation, diplopia, ocular hyperemia, photophobia, and blurred vision.
General disorders and administration site conditions: fatigue.
Immune System disorders: hypersensitivity.
Nervous system disorders: dysaesthesia, transient amnestic episodes.

DRUG INTERACTIONS

There have been no formal studies of the interaction of AMELUZ with other drugs. It is possible that concomitant use of other known photosensitizing agents such as St. John's wort, griseofulvin, thiazide diuretics, sulfonylureas, phenothiazines, sulphonamides, quinolones and tetracyclines may enhance the phototoxic reaction to PDT.

USE IN SPECIFIC POPULATIONS

Pregnancy

There are no available data on AMELUZ use in pregnant women to inform a drug associated risk. Animal reproduction studies were not conducted with aminolevulinic acid. Systemic absorption of aminolevulinic acid in humans is negligible following topical administration of AMELUZ under maximal clinical use conditions. It is not expected that maternal use of AMELUZ will result in fetal exposure to the drug. The estimated background risk of major birth defects and miscarriage for the indicated population are unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Lactation

No data are available regarding the presence of aminolevulinic acid in human milk, the effects of aminolevulinic acid on the breastfed infant or on milk production. However, breastfeeding is not expected to result in exposure of the child to the drug due to the negligible systemic absorption of aminolevulinic acid in humans following topical administration of AMELUZ under maximal clinical use conditions. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for AMELUZ and any potential adverse effects on the breastfeeding child from AMELUZ or from the underlying maternal condition.

Pediatric Use

Safety and effectiveness in pediatric patients below the age of 18 have not been established. AK is not a condition generally seen in the pediatric population.

Geriatric Use

Of the 384 subjects exposed to AMELUZ in randomized, multicenter clinical trials, 83% (318/384) of the subjects were 65 years old and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, but greater sensitivity of some older individuals cannot be ruled out.

Please read the US Full Prescribing Information for AMELUZ® and/or US User Manual of BF-RhodoLED® and/or RhodoLED® XL lamp available together at https://www.ameluz.com/PI.

You are encouraged to report side effects of AMELUZ®. Please contact Biofrontera Inc. at 1-844-829-7434 or FDA at 1-800-332-1088 or www.fda.gov/medwatch.

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Continued Explosion of Sexually Transmitted Diseases

By Ted Rosen, MD

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Data from 2019 collected by the Centers for Disease Control and Prevention (CDC) indicated that, for the sixth consecutive year, the incidence of sexually transmitted disease (STD) continued to increase.

STD data for any given year is typically available in September or October of the following year. However, 2020 data collection, collation and reporting were delayed due to the justifiable CDC preoccupation with the COVID-19 pandemic.

The 2020 data was eagerly anticipated because nobody knew exactly what to expect. Would shelter/work at home recommendations and requirements, social distancing rules, mask-wearing mandates, bar closures, increased depression and anxiety, and the virtual death of large group gatherings going to lead to a decrease in STDs?[1] Or, would fewer overall visits for health care, closure or severe restrictions of STD clinics nationwide, more available idle time due to layoffs or curtailed work schedules, and worldwide condom and antibiotic shortages lead to a continuing increase in STDs?[1]

The wait is finally over, and the picture is bleak.

Of course, the statistics need to be interpreted with caution. The COVID-19 pandemic led to major disruptions in STD-specific services. Only about 8% of all STD clinics operated normally; many others were periodically or completely closed due to lack of personal protective equipment or due to a configuration and/or size which was not conducive to social distancing.[2,3] Other STD clinics limited or entirely eliminated preventative testing and prophylactic treatment, only caring for those who presented with acute signs and symptoms suggestive of STDs.[2,3] There was also a shortage of trained STD health care intervention personnel, as many were reassigned to COVID-related tasks.

Thus, if anything, incomplete STD case report collection may have led to a significant underestimate of the 2020 U.S. STD burden.

Nonetheless, the CDC press release of April 12, 2022, was a grim reminder that STDs have not disappeared in the middle of the pandemic.[4] While cases of chlamydia decreased slightly, the other reportable STDs increased compared to 2019. For example, reported cases of gonorrhea increased by at least 10%, going from 616,392 to 677,769; reported cases of syphilis (all stages) increased at least 3.2%, going from 129,813 to 133,945 – with the largest gain coming in primary and secondary syphilis of 7%.[4]

Most tragically, reported 2020 cases of congenital syphilis rose nearly 15%, going from 1870 to 2148.[4] The number of 2020 cases of congenital syphilis represents a remarkable increase of 235% compared to 2016.

Epidemiologic trends noted in previous years continued. Fifty-three percent of all reported STD cases were diagnosed in adolescents and young adults, aged 15 to 24.[4,5]

Some racial and ethnic groups remain harder hit than non-Hispanic Whites. Thirty-two percent of all reported cases of chlamydia, gonorrhea, and primary and secondary syph-

ilis (the most contagious form) occurred in non-Hispanic Black individuals, even though that group only comprises about 12% of the U.S. population.[5]

Men who have sex with men (gay, bisexual) are also disproportionally impacted by STDs, particularly syphilis and all forms of uncomplicated gonorrhea.[5] These disparities likely reflect a number of factors, such as: lack of access to regular medical care or difficulty in obtaining sexual health care, some element of discrimination, stigmatization of those with known STDs, and differences in the individuals' sexual network (ie. partners often drawn from a social pool characterized by high STD prevalence).

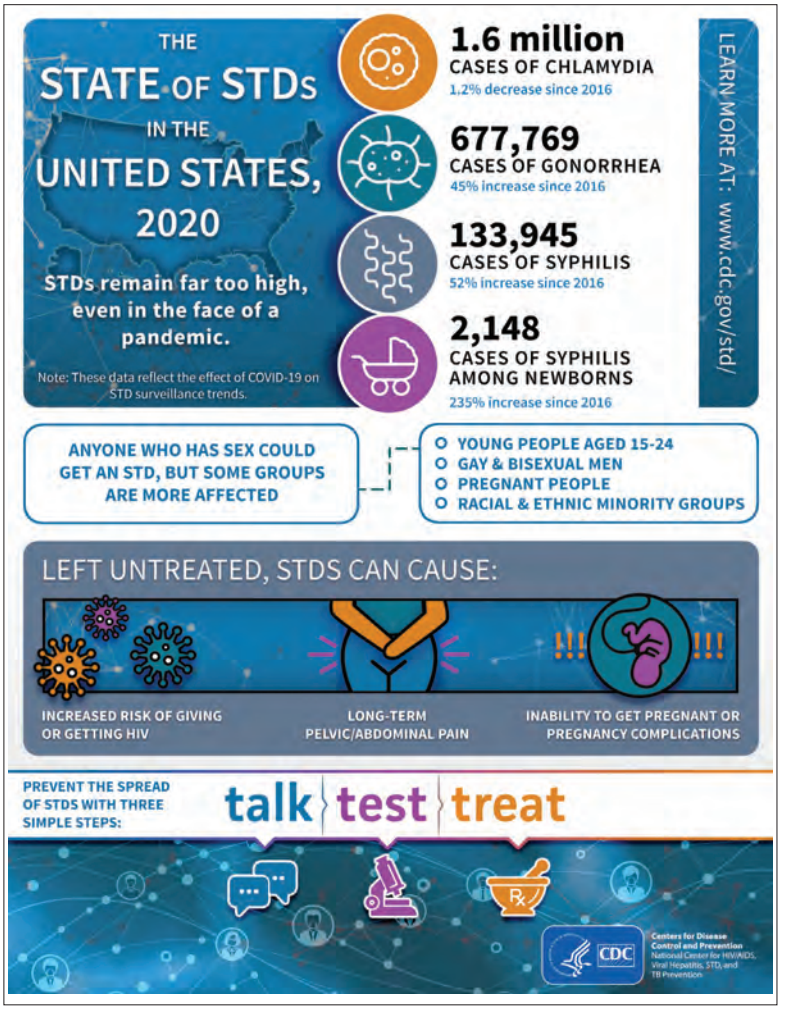
It wasn't that long ago when the CDC was talking about syphilis eradication in America! Sadly, this goal seems farther away than ever.

The CDC press release and the accompanying full report[6] reinforce the need for dermatologists to refresh their skills with regard to diagnosis and treatment of STDs that predominantly manifest on the cutaneous surface.

By the way, preliminary statistics for 2021 don't look any better. Even as delayed case reports are still being submitted, there is already a 34% increase among women and a 9% increase among men of primary and secondary syphilis, and a 6% increase in congenital syphilis![7]

Historically, dermatologists were highly involved in the STD world. Now is not the time to ignore these disorders, as they are resurgent. Now is not the time to abrogate STD diagnosis and therapy to other specialties who do not have the training or skill sets to accurately diagnose STDs, and offer up treatment in a timely fashion.

Now is the time to recommit to being the expert, the community resource, regarding these most important diseases.



REFERENCES:

1. Wiggins CJ, Rosen T. Sexually Transmitted Diseases in the COVID-19 Era. *Skinmed.* 2020;18(4):210-212. Published 2020 Aug 1.
2. Wright SS, Kreisel KM, Hitt JC, et al. Impact of the COVID-19 Pandemic on Centers for Disease Control and Prevention-Funded Sexually Transmitted Disease Programs. *Sex Transm Dis.* 2022;49(4): e61-e63. doi:10.1097/OLQ.0000000000001566.
3. CDC. Impact of COVID-19 on STDs. Sexually Transmitted Disease Surveillance 2020. Accessible at: www.cdc.gov/std/statistics/2020/impact.htm. Accessed June 15, 2022.
4. CDC. New data suggest STDs continued to increase during first year of the COVID-19 pandemic. 2022; April 12. Press Release. Accessible at: 2020 STD Surveillance Report Press Release | Newsroom | CDC. Accessed June 15, 2022.
5. CDC. Disparities in STDs. Sexually Transmitted Disease Surveillance 2020. Accessible at: www.cdc.gov/std/statistics/2020/overview.htm#Disparities. Accessed June 15, 2022.
6. CDC. New Data Show that STDs Remain Far Too High. Sexually Transmitted Disease Surveillance 2020. Accessible at: www.cdc.gov/std/statistics/2020/default.htm. Accessed June 15, 2022.
7. CDC. Preliminary 2021 Data: Syphilis. Sexually Transmitted Disease Surveillance 2020. Accessible at: www.cdc.gov/std/statistics/2020/preliminary2021.htm

… the CDC press release of April 12, 2022, was a grim reminder that STDs have not disappeared in the middle of the pandemic.

A Dual Immunotherapy for Metastatic Melanoma

By Ted Rosen, MD

TED ROSEN, MD, FAAD

Professor of Dermatology
Baylor College of Medicine
Houston, Texas

Opdualag is a fixed-dose combination of the LAG-3-blocking antibody relatlimab and the programmed death receptor-1 blocking antibody nivolumab to treat adult and pediatric patients with unresectable or metastatic melanoma.

The FDA recently approved a dual immunotherapy drug for the treatment of adult and pediatric patients 12 years of age or older with unresectable or metastatic melanoma. The new drug, marketed under the brand name Opdualag (Bristol-Myers Squibb), consists of nivolumab (a widely used PD-1/PD-L1 inhibitor) and a novel agent known as relatlimab. Relatlimab is a lymphocyte-activation gene 3 (LAG-3) blocking agent.

Efficacy was evaluated in a randomized (1:1), double-blinded trial in 714 patients with previously untreated metastatic or unresectable Stage III or IV melanoma (NCT03470922). The trial excluded patients with active autoimmune disease, medical conditions requiring systemic corticosteroid or immunosuppressive treatment, uveal melanoma, and active or untreated brain or leptomeningeal metastases.

Patients were randomized to receive Opdualag (nivolumab 480 mg and relatlimab 160 mg) by intravenous infusion every 4 weeks or only nivolumab 480 mg by intravenous infusion every 4 weeks until disease progression was noted or unacceptable toxicity occurred. The primary efficacy outcome measure was progression-free survival, as determined by blinded independent central review. Median progression-free survival was 10.1 months (95% CI: 6.4-15.7) in the Opdualag arm and 4.6 months (95% CI: 3.4-5.6) in the nivolumab arm.[1]

Progression-free survival at 12 months was 47.7% in the Opdualag arm compared to 36% in the nivolumab-only arm of the pivotal study.[1]

As might be expected, significant treatment-related adverse events were more common in combination therapy than with nivolumab alone (18.9% versus 9.7%). The most common adverse reactions associated with Opdualag administration were hypothyroidism or thyroiditis, musculoskeletal pain, fatigue, nonspecific drug rash (9.3%), pruritus, and diarrhea/colitis.[1] The most com-

Progression-free survival at 12 months was 47.7% in the Opdualag arm compared to 36% in the nivolumab-only arm of the pivotal study.

As might be expected, significant treatment-related adverse events were more common in combination therapy than with nivolumab alone (18.9% versus 9.7%).

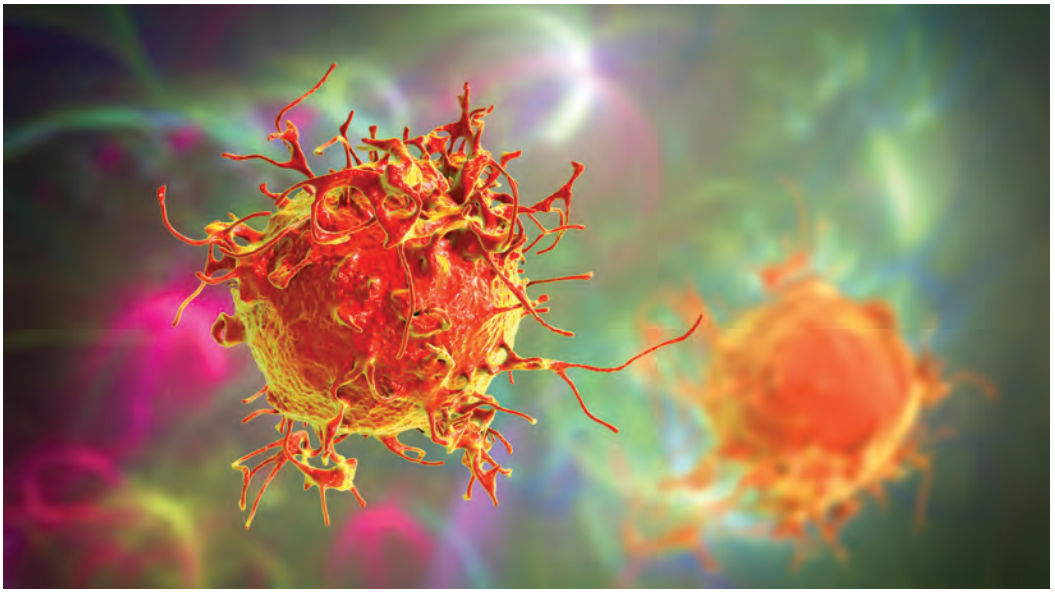
mon laboratory abnormalities (≥20%) were decreased hemoglobin, decreased lymphocytes, increased aspartate aminotransferase (AST) and alanine aminotransferase (ALT), and decreased sodium.[1]

Aside from the obvious clinical benefit, this new drug puts into play a new target for checkpoint inhibition: LAG-3. This is a receptor found on a variety of immune effector cells, including activated T- and B-lymphocytes and natural killer cells.[2] LAG-3 functions as a signaling inhibitor; thus, LAG-3 blockade restores anti-tumor effects, particularly of T-cells. Relatlimab is a monoclonal antibody directed against LAG-3. Tumor infiltrating lymphocytes with high LAG-3 expression, and thus best subject to blockade, include ovarian and colorectal cancer, melanoma, and some hematological malignancies (e.g., Hodgkin disease).

As noted by Heymann,[3] many questions remain. For example, how does this new combination drug compare to the current standard of care nivolumab plus ipilimumab? It would also be interesting to see if relatlimab itself can function as a salvage drug when/if primary checkpoint inhibition fails. Finally, can relatlimab be utilized successfully concurrent to or after BRAF or MEK targeted therapy for advanced melanoma? ◈

REFERENCES

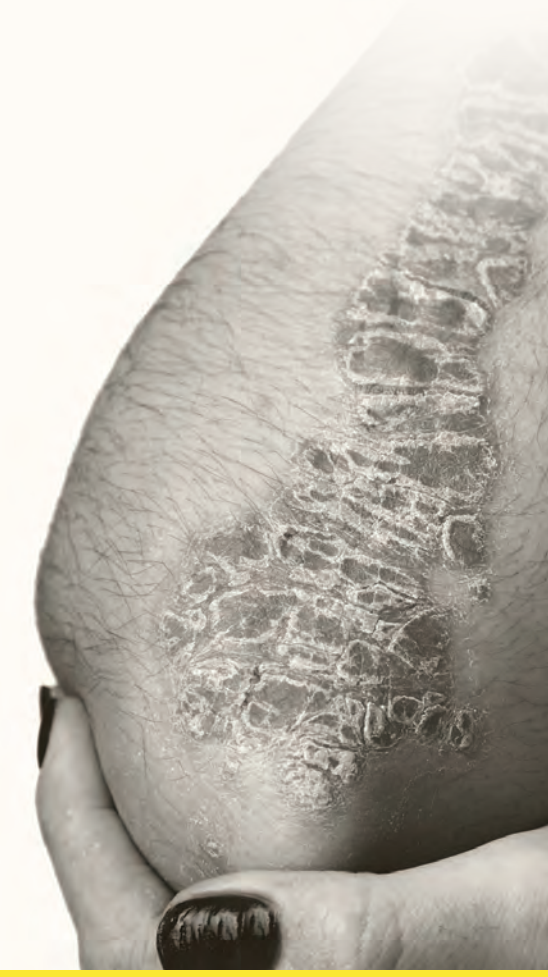
1. Tawbi HA, Schadendorf D, Lipson EJ, et al. Relatlimab and Nivolumab versus Nivolumab in Untreated Advanced Melanoma. *N Engl J Med.* 2022;386(1):24-34. doi:10.1056/NEJMoa2109970.
2. Lythgoe MP, Liu DSK, Annels NE, et al. Gene of the month: lymphocyte-activation gene 3 (LAG-3). *J Clin Pathol.* 2021; 74(9):543-547. doi:10.1136/jclinpath-2021-207517.
3. Heymann WR. Lagging Ahead: LAG-3 Checkpoint Inhibition for Advanced Melanoma. Dermatology World Insights and Inquiries, May 11, 2022. Lagging ahead: LAG-3 checkpoint inhibition for advanced melanoma (aad.org).



THE Dermatology Digest
thedermdigest.com
PRESENTS

VIDEO EDUCATION SERIES

Innovations in Topical Treatments for Pruritic Medical Conditions



Video 1: **The Neurobiology of Itch in Cutaneous Immunology**

Video 2: **Topical Itch Treatments: Unmet Needs and Innovations**

Video 3: **Beyond Diagnosis and Treatment of Itch in Skin of Color**

Supported by ARCUTIS BIOTHERAPEUTICS

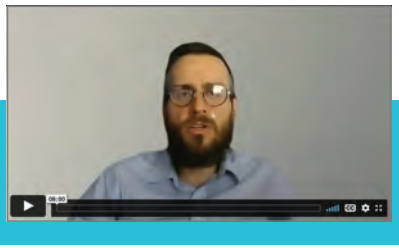
International Eczema Council at AAD 2022

March 24, 2022

Non-Atopic Dermatitis in Atopic Dermatitis Patients

"Dermatitis in the broadest sense or even eczematous morphology is just that—morphology. It's a visual pattern, something that we see either with the naked eye or looking under a microscope at histological patterns," said Jonathan Silverberg, MD, PhD, MPH, who presented "Diagnosis and Management of Non-Atopic Forms of Dermatitis in Atopic Dermatitis Patients" at the International Eczema Council satellite meeting at AAD 2022. "But there are many different etiologies for eczematous disorders. And we certainly should not assume that all forms of eczema are atopic dermatitis."

Jonathan Silverberg, MD, PhD, MPH
Professor of Dermatology
Director of Clinical Research and Patch Testing
George Washington University School of Health Sciences
Washington, DC



thedermdigest.com/video/non-atopic-dermatitis-in-atopic-dermatitis-patients

EDUCATIONAL PROGRAM

AD Diagnosis and Assessment

Atopic dermatitis is a complex condition with both typical and atypical clinical presentations. In Part 2 of this video series, Drs. Larry Eichenfield and Eric Simpson discuss making an accurate diagnosis, including tips for recognizing uncommon manifestations, as well as a comprehensive approach to disease assessment for pediatric and adult patients.

Sponsored by Sanofi

Lawrence Eichenfield, MD
Rady Children's Hospital
San Diego, California

Eric Simpson, MD, MCR
Oregon Health & Science University
Portland, Oregon

thedermdigest.com/video/ad-toolbox-part-2-diagnosis-and-assessment

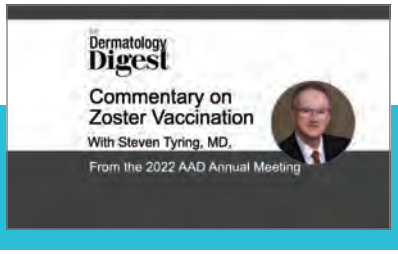
2022 American Academy of Dermatology (AAD) Annual Meeting

March 25–29, 2022

Reducing Shingles Risk

"Vaccines have been around for a couple hundred years, since the advent of the smallpox vaccine, but usually the vaccines are to prevent something that a person doesn't already have," said Stephen K. Tyring, MD, PhD, who presented "Zoster Vaccination" as part of the panel "Herpes Zoster: Controversies and Conundrums in Treatment and Prevention" at the 2022 American Academy of Dermatology (AAD) Annual Meeting. "[Almost] all of us who grew up in the 20th century have the chickenpox virus, or at least the DNA sitting in the nerve root, the dorsal root ganglion."

Steven Tyring, MD, PhD
Board-certified dermatologist
Houston Skin Associates
Houston, Texas

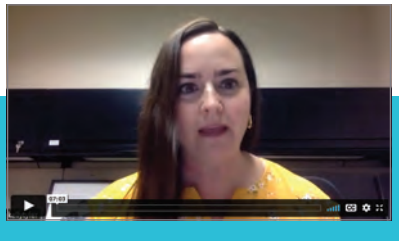


thedermdigest.com/video/reducing-shingles-risk

3 Pearls for Diagnosing and Treating Vulvar Dermatoses

"Amongst dermatologists there is the misconception that patients with genital skin disease are very challenging to treat. That's really not the case," said Kelly Tyler, MD, who co-presented the session "A Guide to Treating and Diagnosing Vulvar and Penile Dermatoses" at the 2022 American Academy of Dermatology (AAD) Annual Meeting.

Kelly Tyler, MD
Assistant Professor
Ohio State Dermatology
Columbus, Ohio



thedermdigest.com/video/3-pearls-for-diagnosing-and-treating-vulvar-dermatoses

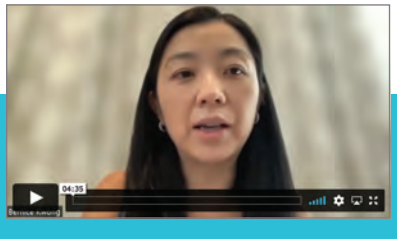
Healing Nutrient-Starved Skin in Hospitalized and Cancer Patients

"In sick and hospitalized patients, one of the most important lessons we have learned is that mixed nutritional deficiencies or deficiencies in multiple vitamins are more common than solitary vitamin deficiencies," said Bernice Kwong, MD, who co-presented "Nutritional Deficiencies in Hospitalized and Cancer Patients," at the 2022 Annual American Academy of Dermatology (AAD) meeting in Boston.

Bernice Kwong, MD
Clinical Professor of Dermatology
Stanford University School of Medicine
Stanford, California

Rob Novoa, MD
Clinical Associate Professor of Pathology and Dermatology
Stanford University School of Medicine
Stanford, California

Silvinia Pugliese, MD
Clinical Assistant Professor of Dermatology
Stanford University School of Medicine
Stanford, California



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EDUCATIONAL PROGRAM

The Disease State of Mature Skin

Skin aging is more than cosmetic. In addition to overall thinning, wrinkles, and pigmentary changes, skin becomes fragile and can bruise and tear more easily. In this, the first of three podcasts that address aging skin and improving skin health, board-certified dermatologists, Dr. Joel Schlessinger and Dr. Roger Ceilley discuss the characteristics and causes of aging skin, including an overview of options for intervention.

Sponsored by Ferndale

Joel Schlessinger, MD
Schlessinger MD Skin Research Center
Omaha, Nebraska

Roger Ceilley, MD
Dermatology PC
West Des Moines, Iowa

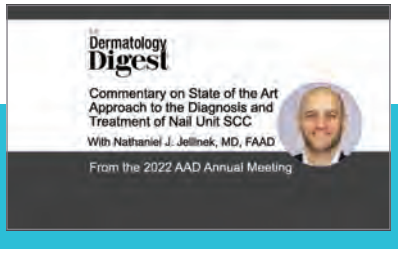
thedermdigest.com/the-disease-state-of-mature-skin-listing

2022 American Academy of Dermatology (AAD) Annual Meeting (continued)

Diagnosing and Treating Nail Unit SCC

"[We know] that squamous cell carcinoma in the nail unit is fraught with delays in diagnosis. That is because it can mimic several other diagnoses, including common diagnoses such as chronic paronychia. Because of that and… a general unease with biopsying, nail unit tumors tend to have delays in diagnosis, and that's something we see also in the literature," said Nathaniel J. Jellinek, MD, FAAD, who presented "State of the Art Approach to the Diagnosis and Treatment of Nail Unit Squamous Cell Carcinoma" at the 2022 American Academy of Dermatology (AAD) Annual Meeting.

Nathaniel J. Jellinek, MD, FAAD
Assistant Clinical Professor
Department of Dermatology Warren Alpert Medical School
Brown University, Providence, Rhode Island



thedermdigest.com/podcast/diagnosing-and-treating-nail-unit-scc

EDUCATIONAL PROGRAM

Core Concepts and Treatment Modalities in Non-Melanoma Skin Cancer

Not all treatment modalities for non-melanoma skin cancer are the same. In Part 1 of this video series, Dr. Mark Nestor reviews the essentials of radiation oncology for the dermatologist, including available modalities as well as innovation in superficial radiation therapy (SRT).

Sponsored by Sensus

Mark Nestor, MD, PhD
Center for Clinical and Cosmetic Research
Adventura, Florida

thedermdigest.com/video/core-concepts-and-treatment-modalities-in-non-melanoma-skin-cancer

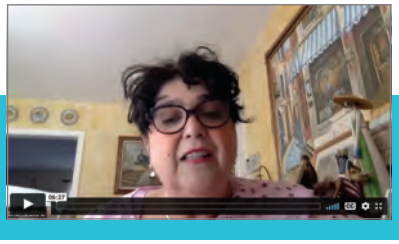
Atlantic Dermatology Conference

April 22–24, 2022

4 Lessons From Cosmetic Dermatology

"Many times, my colleagues who are focused on medical dermatology ignore or poopoo cosmetic dermatology. We have to learn that what helps one, can help the other," said Cherie M. Ditre, MD, who presented "Lessons Learned from Cosmetic Patients" at the Atlantic Dermatology Conference virtual meeting.

Cherie M. Ditre, MD
Associate Professor of Clinical Dermatology
University of Pennsylvania School of Medicine
Philadelphia, Pennsylvania



thedermdigest.com/video/4-lessons-from-cosmetic-dermatology

EDUCATIONAL PROGRAM

Introduction to *Polypodium leucotomos*: Current Research and Therapies

Polypodium leucotomos extract is derived from a South American fern known to provide protection against solar UV radiation exposure. In this, the first of three podcasts, board-certified dermatologists Dr. Joel Schlessinger and Dr. Jeanine Downie discuss the history of polypodium leucotomos, including current formulations and applications.

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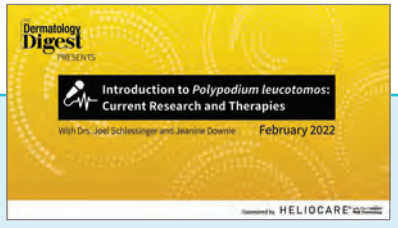
Joel Schlessinger, MD
Schlessinger MD Skin Research Center
Omaha, Nebraska

Jeanine Downie, MD
Image Dermatology PC
Montclair, New Jersey



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Innovations in Dermatology

April 27–30, 2022

Tips for Non-surgical Skin Tightening

"Some of my favorite nonsurgical skin tightening devices are radiofrequency and micro-focused ultrasound devices. One of the commercially available radiofrequency devices is called Thermage [Solta Medical], which uses radio waves to create heat in the skin, which causes new collagen formation and collagen contraction. And I think especially on the lower face it can lead to some good skin tightening," said Jacqueline Watchmaker, MD, FAAD, who presented "Nonsurgical Skin Tightening: Who, What, Where, and When?" at the Innovations in Dermatology meeting in Scottsdale, Arizona.

Jacqueline Watchmaker, MD, FAAD
Cosmetic dermatologist
Southwest Skin Specialists
Scottsdale, Arizona

thedermdigest.com/podcast/tips-for-non-surgical-skin-tightening

Current Status and Future Role of AI in Dermatology

"In health care, we have seen a proliferation of artificial intelligence (AI) applications. Currently there are no FDA-approved AI applications in dermatology but there are many different groups working on that pathway. In the next decade or so, we will see clinical applications likely coming down the pipeline to be applied to the field of dermatology," said Roxana Daneshjou, MD, PhD, FAAD who presented "AI in Dermatology" at the Innovations in Dermatology conference in Scottsdale, Arizona.

Roxana Daneshjou, MD, PhD, FAAD
Clinical Scholar, Dermatology
Stanford School of Medicine
Stanford, California

thedermdigest.com/video/current-status-and-future-role-of-ai-in-dermatology

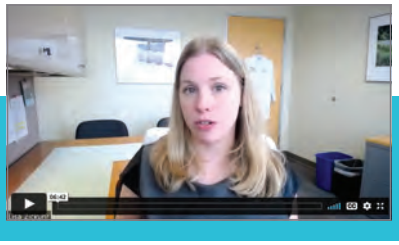
The Mark Allen Everett, MD, Skin of Color Symposium

May 6, 2022

Cutaneous Lupus in Skin of Color

"When you talk about lupus, there are really two main categories. There is systemic lupus where patients have symptoms in any organ system and then there is cutaneous lupus where the manifestations are limited to the skin," said rheumatologist Lisa Zickuhr, MD, MHPE, who presented "Cutaneous Lupus across Skin Tones" at the Mark Allan Everett, MD, Skin of Color Symposium at The University of Oklahoma.

Lisa Zickuhr, MD, MHPE
Assistant Professor of Rheumatology
Washington University School of Medicine
Saint Louis, Missouri



thedermdigest.com/video/cutaneous-lupus-in-skin-of-color

EDUCATIONAL PROGRAM

The Role of PLE in Sun Protection

Polypodium leucotomos extract (PLE) is derived from a South American fern known to provide protection against solar UV radiation exposure. In the second podcast in this series, board-certified dermatologists Dr. Joel Schlessinger and Dr. Jeanine Downie discuss in detail the benefits of PLE supplementation for preventing skin damage from sun exposure.

Sponsored by Ferndale

Joel Schlessinger, MD
Schlessinger MD Skin Research Center
Omaha, Nebraska

Jeanine Downie, MD
Image Dermatology PC
Montclair, New Jersey

thedermdigest.com/video/the-role-of-ple-in-sun-protection

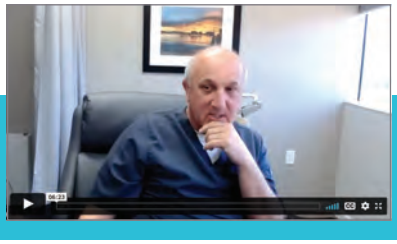
Music City SCALE 2022

May 11–15, 2022

The Evolution of Botulinum Toxin Injections

"Darwin will tell you if you don't evolve you die. And on some level, you have to evolve eventually to being able to customize [neurotoxin] volumes of reconstitution and doses for the indication to get the best result," said John H. Joseph, MD, who presented "State of the Art Neurotoxins and a Paradigm Shift in Reconstitution" at Music City Scale 2022.

John H. Joseph, MD
Double board-certified plastic surgeon
Encino, California

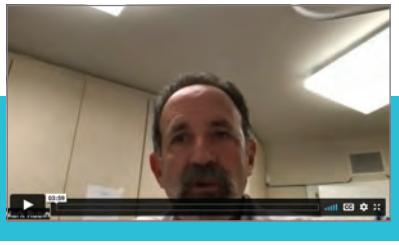


thedermdigest.com/video/the-evolution-of-botulinum-toxin-injections

Chemical Peel or Laser?

"So the whole concept of chemical peels in the age of lasers is that everybody's become infatuated, obviously, with laser technology because it's new, exciting, [and] it's what patients want. But…you could use older therapies and still do just as well," said Mark G. Rubin, MD, who presented "Chemical Peels in the Age of Lasers" at the Symposium for Cosmetic Advances & Laser Education (SCALE) 2022.

Mark G. Rubin, MD
Board-certified dermatologist
Lasky Clinic
Beverly Hills, California



thedermdigest.com/video/chemical-peel-or-laser

CBD Holds Promise for Treating First-Degree Burns

"I primarily do research—a lot of alopecia research, but [I] … connected with a company [that] asked me to do a clinical study on a cannabidiol and aspartame combination for eczema. We published this paper and the results were really impressive," said Andy Goren, MD, who presented "Novel Cannabidiol Treatment Against the Development of Burns" at the Symposium for Cosmetic Advances and Laser Education (SCALE) 2022.

Andy Goren, MD
Professor of Dermatology (contratto)
University of Rome G. Marconi
Rome, Italy
President and Chief Medical Officer of Applied Biology
Irvine, California

thedermdigest.com/video/cbd-holds-promise-for-treating-first-degree-burns

EDUCATIONAL PROGRAM

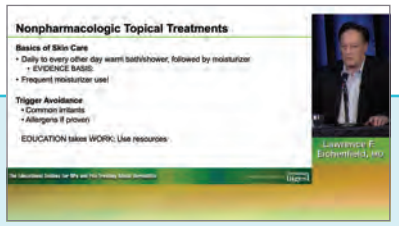
Non-Pharmacological and Topical Therapies for AD

Topical therapies are the mainstay treatment for patients with atopic dermatitis. In Part 3 of this video series, Drs. Larry Eichenfield and Eric Simpson discuss the basics of skin care, trigger avoidance, and fundamental and maintenance topical treatments for mild, moderate, and severe atopic dermatitis, including an algorithm for step-up care.

Sponsored by Sanofi

Lawrence Eichenfield, MD
Rady Children's Hospital
San Diego, California

Eric Simpson, MD, MCR
Oregon Health & Science University
Portland, Oregon



thedermdigest.com/video/ad-toolbox-part-3-non-pharmacological-and-topical-therapies

Congress of Clinical Dermatology

June 2–5, 2022

SCAR Updates

"Drug eruptions are by far and away the most common single entity that are seen by dermatologists in the hospital setting but are also seen in the outpatient setting too," said Benjamin Kaffenberger, MD, who presented "Severe Cutaneous Adverse Reactions" at the Congress of Clinical Dermatology presented by the Georgia Society of Dermatology and Dermatologic Surgery.

Benjamin Kaffenberger, MD, MS
Clinical Associate Professor of Dermatology
The Ohio State University, Columbus, Ohio

thedermdigest.com/video/scar-updates

EDUCATIONAL PROGRAM

Medical Interventions for Mature Skin

With age, skin becomes thinner, wrinkles, fragile and can bruise and tear more easily. In the final podcast in this 3-part series that addresses aging skin and improving skin health, board-certified dermatologists, Dr. Joel Schlessinger and Dr. Roger Ceilley discuss medical interventions for mature skin, including specific ingredients and topical formulations designed to reduce the incidence and duration of bruising.

Joel Schlessinger, MD
Schlessinger MD Skin Research Center
Omaha, Nebraska

Roger Ceilley, MD
Dermatology PC
West Des Moines, Iowa

Sponsored by Ferndale

thedermdigest.com/podcast/medical-interventions-for-mature-skin

CONFERENCE

Symposium for Inflammatory Skin Disease

June 10–12

Pediatric Psoriasis Considerations

"Psoriasis is often thought of as an adult disease. But kids definitely get psoriasis, and kids can get psoriasis sometimes in ways that can easily be mistaken for other things," said Robert Sidbury, MD, MPH, who presented "Treating Psoriasis in Children," during the virtual Symposium for Inflammatory Skin Disease meeting.

Robert Sidbury, MD, MPH
Professor of Pediatrics and Chief of Dermatology
Seattle Children's Hospital
University of Washington School of Medicine
Seattle, Washington

thedermdigest.com/video/pediatric-psoriasis-considerations

EDUCATIONAL PROGRAM

The Pathogenesis of Psoriasis and Comorbidities

In the first video of this educational series, Dr. April Armstrong discusses key concepts of mild-to-moderate psoriasis, including epidemiology, pathogenesis, comorbidities, and related guidelines and screening recommendations

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April Armstrong, MD
Keck School of Medicine, USC
Los Angeles, California

thedermdigest.com/video/examining-psoriasis-pathogenesis-and-comorbidities

Symposium for Inflammatory Skin Disease (continued)

Updates in Pediatric AD Treatment

"It was interesting because literally days before I gave this talk, dupilumab was approved for the treatment of atopic dermatitis down to 6 months of age. This was really a fundamental change," said Robert Sidbury, MD, MPH, who presented "Treating Atopic Dermatitis in Children," during the virtual Symposium for Inflammatory Skin Disease meeting.

Robert Sidbury, MD, MPH
Professor of Pediatrics and Chief of Dermatology
Seattle Children's Hospital
University of Washington School of Medicine
Seattle, Washington

thedermdigest.com/video/updates-in-pediatric-ad-treatment

EDUCATIONAL PROGRAM

Atopic Dermatitis and Itch: A Pediatric Perspective

Dr. Robert Sidbury discusses special considerations of atopic dermatitis and skin itch in the pediatric population, including common misconceptions, etiological factors, and impact on quality of life. This is the third video in part 1 of this video series on the science of chronic itch and inflammation.

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Robert Sidbury, MD, MPH
Professor of Pediatrics and Chief of Dermatology
Seattle Children's Hospital
University of Washington School of Medicine
Seattle, Washington

thedermdigest.com/featured/atopic-dermatitis-and-itch-a-pediatric-perspective

CONFERENCE

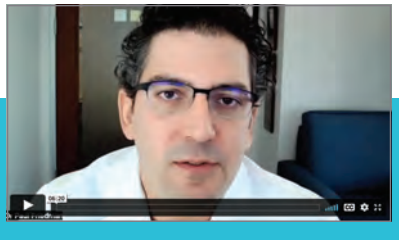
2022 Acne and Rosacea Meeting (ARM)

June 23–26, 2022

Tips for Treating Rosacea With Devices

"In terms of our practice, what we're most commonly utilizing for the treatment of rosacea is the pulsed dye laser… it's yellow light, and it's been shown to safely and effectively reduce both facial erythema and telangiectasias and has been the standard of care for years," said Paul M. Friedman, MD, who presented "Treating Rosacea with Devices: How I Do It" at the 2022 Acne and Rosacea Meeting, held in partnership with the Cosmetic Bootcamp meeting in Aspen, Colorado.

Paul M. Friedman, MD
Director
Dermatology & Laser Surgery Center
Houston, Texas



thedermdigest.com/video/tips-for-treating-rosacea-with-devices

EDUCATIONAL PROGRAM

Treatment of Mild to Moderate Psoriasis: Current Options and Unmet Needs

In the second video in this educational series, Dr. Linda Stein Gold examines current treatment options for mild-to-moderate psoriasis, including topical and combination therapies, efficacy, and vehicle opportunities.

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Linda Stein Gold, MD
Director of Dermatology
Clinical Research
Head, Division of Dermatology
Henry Ford Health System
Detroit, Michigan

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3 Lasers for Acne Treatment

"I was excited to give this talk because in the past I've given talks about acne and lasers and there really wasn't much new to present. In the past year, this has really changed," said Emmy Graber, MD, MBA, who presented "Lasers and Acne: What's in the Pipeline," at the 2022 Acne and Rosacea Meeting, held in partnership with the Cosmetic Bootcamp meeting in Aspen, Colorado.

Emmy Graber, MD, MBA
President, The Dermatology Institute of Boston
Affiliate Clinical Instructor, Northeastern University
Boston, Massachusetts

thedermdigest.com/video/3-lasers-for-acne-treatment/

EDUCATIONAL PROGRAM

Future Possibilities of PLE for Skin Conditions

Polypodium leucotomos extract (PLE) is derived from a South American fern known to provide protection against solar UV radiation exposure. In the third and final podcast in this series, board-certified dermatologists Dr. Joel Schlessinger and Dr. Jeanine Downie discuss the benefits of PLE supplementation for inflammatory skin conditions, including polymorphous light eruption, rheumatoid arthritis, vitiligo, psoriasis, and more.

Joel Schlessinger, MD
Schlessinger MD Skin Research Center
Omaha, Nebraska

Jeanine Downie, MD
Image Dermatology PC
Montclair, New Jersey

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thedermdigest.com/podcast/future-possibilities-of-ple-for-skin-conditions

Leaf-like Areas vs Streaks and Pseudopods

By Zaeem Nazir, MD, and Ashfaq A. Marghoob, MD

ASHFAQ A. MARGHOOB, MD
Dermatology Service,
Department of Medicine
Memorial Sloan Kettering
Cancer Center
New York, New York

CASE HISTORY

A patient in her 40s presents to the clinic for a new mole on her lower back, which she first noticed 2 years ago. She was planning to see a dermatologist but was unable to once the COVID pandemic started. She has no personal or family history of melanoma or non-melanoma skin cancer.

On clinical and dermoscopic exam, you observe the following:

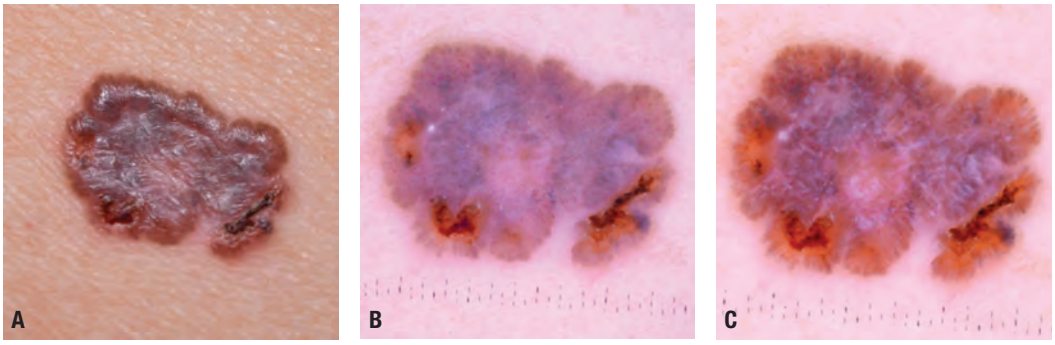

FIGURE 1. Clinical and Dermoscopic Images of the Lesion: **A.** Clinical, **B.** Non-polarized dermoscopy, **C.** Polarized dermoscopy.

QUESTION:

For this lesion, which dermoscopic feature is most diagnostic?

A. Streaks
B. Ulceration
C. Shiny white blotches and strands
D. Leaf-like areas

(Don't look to your right at the answer!)

ANSWER:

D. Leaf-like areas

This patient has a lesion clinically suspicious for superficial spreading melanoma with variegated color, border irregularity, and asymmetry. While the initial impression has been a crucial driver for triage and diagnosis in medicine for centuries, anchoring bias can affect one's subsequent judgement, even with evidence to the contrary. With a diagnosis of melanoma in mind, one may appreciate shiny white structures, radial streaks, blue-white veil, and regression structures on dermoscopy—all features associated with the diagnosis of melanoma.

What is your diagnosis?

For more on this case, turn to page 48 ▸

DISCUSSION

A broader differential would also include pigmented basal cell carcinoma (BCC), as it can present similarly to melanoma. However, differentiating the two can be challenging as they are both associated with shiny white blotches and strands, brown dots, and atypical vascular structures. While the morphology of shiny white structures found in both have been hypothesized to help differentiate the two, present literature has confirmed that shiny white blotches and strands are associated with both BCC[1] and nodular melanoma >2mm in thickness.[3] On this particular case, the presence of a rolled border in this lesion provides strong evidence the lesion may be a pigmented BCC and not melanoma.

The key to this diagnosis is not to confuse the streaks associated with melanoma for the leaf-like structures associated with pigmented BCC. Streaks are defined as bulbous projections which must not be disconnected from the tumor or have an obtuse angle (>90) to the tumor edge[4]; they appear to radiate away from the tumor core and commonly point to the hyperpigmented center of a lesion (Figure 2). In contrast, leaf-like structures or spoke wheels are brown to gray-blue discrete bulbous extensions[2] which converge focally, often towards the periphery of lesions which commonly have a hypopigmented center (Figure 3). The latter are highly diagnostic for BCC, with a specificity of 100%.

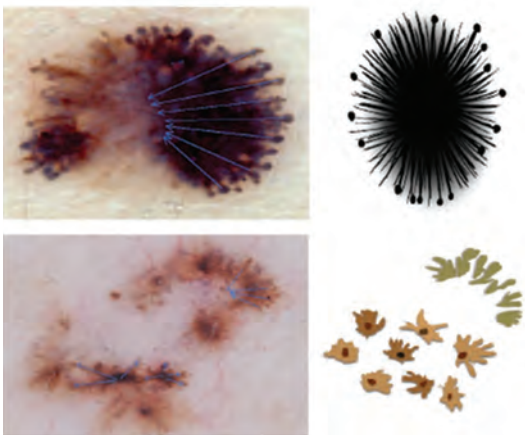

FIGURE 2. (Top) Example of streaks in melanoma pointing to tumor center. (Bottom) Example of leaf-like structures and spoke wheels in BCC pointing to the periphery of the tumor center.

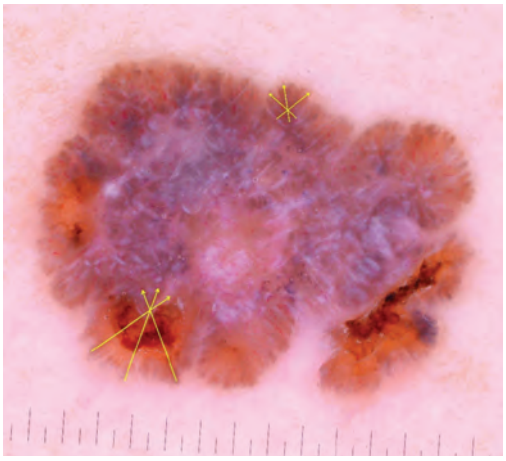

FIGURE 3. Illustration of leaf-like structures found on dermoscopy of our patient's lesion.

This lesion was excised, and pathology confirmed the diagnosis of a nodular, pigmented basal cell carcinoma with uninvolved margins.

Appreciation for this key finding may help us identify other diagnostic structures for BCC, such as ulceration and shiny white blotches/strands which both have specificities of 95%.[1,2] Other diagnostic structures to look for include blue-gray ovoid nests (specificity 99%), arborizing telangiectasia (92%), and spoke-wheel-like structures (100%).[1]

REFERENCES

1. Navarrete-Dechent C, Bajaj S, Marchetti MA, Rabinovitz H, et al. Association of shiny white blotches and strands with nonpigmented basal cell carcinoma: evaluation of an additional dermoscopic diagnostic criterion. *JAMA Dermatol.* 2016;152(5):546. doi:10.1001/jamadermatol.2015.5731.
2. Menzies SW, Westerhoff K, Rabinovitz H, et al. Surface Microscopy of Pigmented Basal Cell Carcinoma. *Arch Dermatol.* 2000;136(8). doi:10.1001/archderm.136.8.1012.
3. Sgouros D, Lallas A, Kittler H, et al. Dermatoscopic features of thin (≤2 mm Breslow thickness) vs. thick (>2 mm Breslow thickness) nodular melanoma and predictors of nodular melanoma versus nodular non-melanoma tumours: a multicentric collaborative study by the International Dermoscopy Society. *J Eur Acad Dermatol Venereol.* 2020;34(11):2541-2547. doi:10.1111/jdv.16815.
4. Menzies SW, Crotty KA, McCarthy WH. The Morphologic Criteria of the Pseudopod in Surface Microscopy. *Arch Dermatol.* 1995;131(4):436-440. doi:10.1001/archderm.1995.01690160064010.
5. Tavoloni Braga JC, Scope A, Klaz I, Mecca P, et al. Melanoma mimicking seborrheic keratosis: An error of perception precluding correct dermoscopic diagnosis. *J Am Acad Dermatol.* 2008;58(5):875-880. doi:10.1016/j.jaad.2007.12.011.

DISCLOSURES:
Dr. Marghoob reports no relevant disclosures.

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