Acne Updates

Pearls on treating acne from a recent Maui Derm Conference

NICHOLAS BROWNSTONE, MD

Acne is an extremely common skin disease and while particularly prevalent in adolescents, it can persist into adulthood as well. Most dermatology providers are very familiar with treating acne, as approximately 15% of the US population has suffered from acne and, by some estimates, nearly 9 out of 10 adolescents have also suffered from this condition. Julie Harper, MD, a board-certified dermatologist in private practice in Birmingham, Alabama a founding director and past president of the American Acne and Rosacea Society, gave a presentation on acne treatment updates at the Maui Derm NP+PA Summer 2022 conference.

ACNE UPDATES CONTINUES ON PAGE 22
An IL-23 inhibitor for adults with moderate to severe plaque psoriasis (Ps)

**DURABLE, RAPID & CLEAR IN Ps**
Significantly Higher PASI 90 and PASI 100 Response Rates vs Placebo at Week 16

**SKYRIZI EFFICACY:**
IN Ps AT WEEK 16 IN TWO PIVOTAL PHASE 3 STUDIES (NRI)

<table>
<thead>
<tr>
<th>Co-primary Endpoints (P&lt;0.0001)</th>
<th>Secondary Endpoint (P&lt;0.001)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PASI 90 at Week 16</td>
<td>PASI 100 at Week 16</td>
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<tr>
<td>SKYRIZI</td>
<td>PLACEBO</td>
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<tr>
<td>ULTIMMA-1</td>
<td>ULTIMMA-2</td>
</tr>
<tr>
<td>75% (229/304)</td>
<td>75% (220/294)</td>
</tr>
<tr>
<td>5% (5/102)</td>
<td>2% (2/98)</td>
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<td>sPGA 0/1 at Week 16</td>
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<tr>
<td>SKYRIZI</td>
<td>PLACEBO</td>
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<tr>
<td>ULTIMMA-1</td>
<td>ULTIMMA-2</td>
</tr>
<tr>
<td>88% (267/304)</td>
<td>84% (246/294)</td>
</tr>
<tr>
<td>8% (8/102)</td>
<td>5% (5/98)</td>
</tr>
<tr>
<td>PASI 100 at Week 16</td>
<td></td>
</tr>
<tr>
<td>SKYRIZI</td>
<td>PLACEBO</td>
</tr>
<tr>
<td>ULTIMMA-1</td>
<td>ULTIMMA-2</td>
</tr>
<tr>
<td>36% (109/304)</td>
<td>51% (149/294)</td>
</tr>
<tr>
<td>0% (0/102)</td>
<td>2% (2/98)</td>
</tr>
</tbody>
</table>

NRI=Non-Responder Imputation.

**Maintenance of Response**
In the randomized psoriasis trials, among patients who received SKYRIZI and achieved PASI 90 or PASI 100 at Week 16

- **88% MAINTAINED PASI 90 AT WEEK 52 (n=398/450)**
- **80% MAINTAINED PASI 100 AT WEEK 52 (n=206/258)**

**Study Design**
UltIMMa-1 (N=506) and UltIMMa-2 (N=491) were replicate phase 3, randomized, double-blind, placebo- and active-controlled studies to evaluate the efficacy and safety of SKYRIZI (150 mg) vs placebo over 16 weeks and biologic active control over 52 weeks in adult patients with moderate to severe plaque psoriasis. SKYRIZI (150 mg) was given as 2 subcutaneous injections at Weeks 0, 4, and 16, and every 12 weeks thereafter. Co-primary endpoints were PASI 90 and sPGA 0/1 at Week 16 vs placebo in each study (assessed by non-responder imputation).
**CONSISTENT PASI 90 AND 100 RATES AT ~4.5 YEARS**

**PASI 90 AND 100 ACHIEVEMENT AT WEEK 232 IN THE OPEN-LABEL EXTENSION (OLE)**

Integrated results from UltIMMa-1 and -2 — all data are as observed and, therefore, cannot be determined to be statistically significant.

![Graph showing PASI 90 and 100 achievement over time](image)

**KEY VARIABLES (AS MEASURED EVERY 12 WEEKS THROUGH WEEK 232) OF OLE:**
- sPGA 0/1
- PASI 75
- PASI 90
- PASI 100

**OLE LIMITATIONS:**
In an open-label extension, there is potential for enrichment of the long-term data in the remaining patient populations, because patients who are unable to tolerate or do not respond to the drug often drop out.

**STUDY DESIGN:**
The data presented here are a sub-analysis of the LIMMitless OLE and include only patients from UltIMMa-1 and -2 who were originally randomized to SKYRIZI, completed the RCT, and enrolled in the OLE. LIMMitless is an ongoing OLE study for which patients who completed either UltIMMa trial, IMMvent, or IMMhance were eligible to participate.

**STATISTICAL METHODOLOGY:**
Regardless of how missing data were handled, results were consistent at timepoints evaluated.

**INDICATION**
SKYRIZI is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy.

**IMPORTANT SAFETY INFORMATION**

- **Hypersensitivity Reactions**
  SKYRIZI® (risankizumab-rzaa) is contraindicated in patients with a history of serious hypersensitivity reaction to risankizumab-rzaa or any of the excipients. Serious hypersensitivity reactions, including anaphylaxis, have been reported with the use of SKYRIZI. If a serious hypersensitivity reaction occurs, discontinue SKYRIZI and initiate appropriate therapy immediately.

- **Infection**
  SKYRIZI may increase the risk of infection. Do not initiate treatment with SKYRIZI in patients with a clinically important active infection until it resolves or is adequately treated. In patients with a chronic infection or a history of recurrent infection, consider the risks and benefits prior to prescribing SKYRIZI. Instruct patients to seek medical advice if signs or symptoms of clinically important infection occur. If a patient develops such an infection or is not responding to standard therapy, closely monitor and discontinue SKYRIZI until the infection resolves.

**Learn more by visiting www.SkyriziHCP.com/dermatology**

- Through 232 weeks: interim analysis of the LIMMitless open-label extension study. Poster presented at: Fall Clinical Dermatology Conference; October 21-24, 2021; Las Vegas, NV; hybrid.

**Please see the Brief Summary of the Full Prescribing Information on the following page.**

**References:**

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US-SKZD-220313 May 2022
Printed in U.S.A.
Table 1. Adverse Drug Reactions Occurring in ≥ 1% of Subjects on SKYRIZI through Week 16

<table>
<thead>
<tr>
<th>Adverse Drug Reactions</th>
<th>SKYRIZI</th>
<th>Placebo</th>
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<tbody>
<tr>
<td>Upper respiratory tract infection*</td>
<td>22.1%</td>
<td>14.7%</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>19.6%</td>
<td>15.7%</td>
</tr>
<tr>
<td>Dermatologic</td>
<td>22.1%</td>
<td>14.7%</td>
</tr>
<tr>
<td>Asthma exacerbation</td>
<td>11.3%</td>
<td>5.4%</td>
</tr>
<tr>
<td>Eczema</td>
<td>11.3%</td>
<td>5.4%</td>
</tr>
<tr>
<td>Onychomycosis</td>
<td>11.3%</td>
<td>5.4%</td>
</tr>
<tr>
<td>Hepatic enzyme increased</td>
<td>11.3%</td>
<td>5.4%</td>
</tr>
<tr>
<td>Injection site bruising</td>
<td>11.3%</td>
<td>5.4%</td>
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<tr>
<td>Injection site reaction</td>
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<td>5.4%</td>
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</tbody>
</table>

* Includes: injection site bruising, erythema, extravasation, hematoma, hemorrhage, inflammation, infection, reaction, Stevens-Johnson syndrome, toxic epidermal necrolysis, pyoderma gangrenosum, transient synovitis, viral exanthem

Adverse drug reactions listed in bold occurred in > 1% and ≤ 3.1% of subjects in the SKYRIZI group and at a higher rate than in the placebo group through Week 16 and were defined as Serious Adverse Events.

Table 2. Adverse Drug Reactions Occurring in ≥ 0.1% of Subjects on SKYRIZI Through Week 16

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Adverse drug reactions listed in bold occurred in ≤ 3.1% of subjects in the SKYRIZI group and were defined as Serious Adverse Events.

Table 3. Adverse Drug Reactions Occurring in ≥ 0.1% of Subjects on Placebo Through Week 16

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Table 4. Other Adverse Drug Reactions Occurring in ≥ 0.1% of Subjects on Placebo Through Week 16

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Table 5. Other Adverse Drug Reactions Occurring in ≥ 0.1% of Subjects on SKYRIZI Through Week 16

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Table 7. Other Adverse Drug Reactions Occurring in ≥ 0.1% of Subjects on SKYRIZI Through Week 16

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Two (or more) is better than one

AS THE PRESIDENT AND CEO of a life sciences company whose mission is to improve the quality of life through health care communications, education, and research, I thought I would devote this month’s letter to the importance of collaboration, both internally and externally, here at MJH Life Sciences™.

Years ago, MJH Life Sciences™ started, with great success, a Strategic Alliance Program (SAP) program to align specific brands, such as Dermatology Times®, with partners that would make for good, mutually collaborations. These SAPs are usually nonprofits, charities, educational summits, or other organizations with which we envision a mutual benefit of raising awareness for one another’s missions and objectives. These partnerships offer both parties virtually endless opportunities to elevate visibility, whether sharing content, introducing key thought leaders, creating partner webinars, promoting one another’s conferences, and much more.

Currently, our partners include the Science of SkinCare Summit, SCALE (the Symposium for Cosmetic Advances and Laser Education), the Cosmetic Bootcamp, New Frontiers in Cosmetic Medicine & Medical Dermatology, the National Infusion Center Association, the Dermatology Research and Education Foundation, the Society for Pediatric Dermatology, and the Skin Cancer Foundation. Most recently, we have inked a partnership with the American Hair Loss Association, whose mission includes educating and improving the lives of those affected by hair loss. You can find more information on these partners at https://www.dermatologytimes.com/sap-partner.

Furthermore, if you know of an organization that might be a good fit for a strategic partnership, please feel free to reach out to our associate editorial director, Lois Levine, at llevine@mjhlifesciences.com. For now, continue to enjoy these last few weeks of summer, and thank you for continuing to be, as readers, our most important partners! 

Mike Hennessy Jr. is the President and CEO of MJH Life Sciences®

Visit our SAP partners!
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Legal Eagle

He Is my Covering Physician. Why Am I Being Sued?

By David J. Goldberg, MD, JD

Goldberg is medical director of Skin Laser and Surgery Specialists of New York and New Jersey; director of cosmetic dermatology and clinical research at Schweiger Dermatology Group in New York, New York; and clinical professor of dermatology and past director of Mohs Surgery and Laser Research at the Icahn School of Medicine at Mount Sinai in New York, New York.

Dr. Jones, an oculoplastic surgeon, performed a bilateral transconjunctival blepharoplasty procedure on Mrs. Smith. Smith is a healthy 50-year-old woman and is on no medications. Her visual acuity, prior to the procedure, was corrected easily with contact lenses. The blepharoplasty procedure went smoothly and lasted less than an hour. The patient left the ambulatory surgical facility without any difficulty at 11 AM. At 4 PM, Jones called Smith to check on her postoperative course. She reported some ecchymoses but otherwise no difficulties. At 6 PM, Jones called his covering cosmetic dermatologic surgeon—Dr. Owens, who does not perform blepharoplasties—and signed out to him. He discussed Smith’s surgery with Owens.

At 8 PM, Smith called Jones’ office with a concern about her surgery. Jones’ answering service immediately paged Owens, the covering physician. Owens returned the page within 15 minutes. In their discussion, Smith described the ecchymoses. She also noted significant blurring of the vision in her right eye. When she tried to correct her vision with an old pair of glasses, she found no improvement. Owens discussed the situation with Smith and reassured her that such findings are not unusual. He suggested she try to sleep and call Jones in the morning.

The next morning, Smith awoke to find she had no vision in her right eye. She immediately returned to Jones’ office and he noted that she had evidence of a retrobulbar hemorrhage. Although he immediately performed surgery to correct the problem, the blindness was permanent. Had Owens made the correct diagnosis and performed immediate surgery, the blindness would have been prevented.

Smith brought a negligence cause of action against both Jones and the covering physician, Owens. The basis of her case against Jones was that he was in a “joint venture” with Owens. After all, they cover each other’s practices on a regular basis. It should be noted that there were no payments made for the cross coverage and the 2 practices shared neither staff nor facilities.

Is Dr. Jones liable?

The answer will generally depend on the acts of the on-call physician who allegedly committed the act negligence as well as applicable law. Imputing of Jones’ liability in this situation will generally turn on the degree to which the actions of the on-call physician were influenced or controlled by Jones. For example, if the on-call physician consulted with Jones and, in reliance on his judgment, injured Smith, liability might be attached to both physicians. However, the mere fact that at various times different physicians are on call for the same patients will not typically expose them to liability for the acts of a physician who was allegedly negligent during his or her on-call shift.

A joint venture is typically defined as 2 or more parties combining property and/or services in a joint undertaking for profit with the rights of mutual control. All joint ventures may be held liable for actions of individual venturers. Physicians who share an on-call arrangement are not usually considered to be engaged in a joint venture that would subject them to liability for each other’s actions.

In Rossi v Oxley, 495 SE2d 39 (Ga 1998), a patient sued a physician who participated in an on-call arrangement with other independent physicians. Each on-call physician billed patients directly for any services provided. The Georgia Supreme Court held that a joint venture did not exist between the physicians. Liability could not be extended on the basis of a simple on-call arrangement. The court noted that the mutual control element was not satisfied because the patient’s physician could not control the on-call physician’s judgment in treating the patient.

In addition, the court noted, even if it could be argued that both physicians “controlled” the patient, it would reject any vicarious liability for sharing of on-call duties for public policy reasons. A finding of liability, the court noted, would discourage the practice of on-call arrangements and therefore decrease the availability of quality care, increase costs, or both.

Had Jones chosen Owens, a general surgeon, as the on-call physician, a cause of action in negligence may be present against the general surgeon. In this case, the question becomes one of Jones’ duties in providing on-call coverage for his patients. Jones had a duty to provide a covering physician who understood the blepharoplasty procedure and its potential complications. If a cosmetic dermatologist would not generally be expected to understand the surgical procedure and its complications, Jones may have breached his duty of reasonable care to Smith by providing Owens as a covering physician. If that breach in duty led to the blindness, then Jones would also be liable for the negligence.

The same precarious situation could occur in a dermatology practice. A typical “group practice” situation might have a cosmetic surgical dermatologist, several general dermatologists, and a dermatopathologist/dermatologist. On a typical day, the surgical dermatologist might perform a liposuction procedure under tumescent anesthesia. The “partner” dermatopathologist/dermatologist on call that evening might not know anything about liposuction. If the patient developed complications from the procedure, the significance of which would have been minimized by early detection, then liability would be divided between the covering dermatologist and the surgical dermatologist. The surgeon would not be able to suggest that it was not his turn for coverage. In such a practice, coverage for surgical procedures might be best undertaken by those with expertise in those areas.

Published August 2022
**Focusing on Feet**

**By Zoe Diana Draelos, MD**

Draelos is an adjunct assistant professor of dermatology at Duke University School of Medicine in Durham, North Carolina, and chief medical editor of Dermatology Times®.

**Q: How can you heal cracked heels?**

Cracked heels are a common debilitating problem in mature adults. Due to the trauma of walking, which can increase with advancing age and orthopedic issues, the skin on the heels can thicken. In addition, skin desquamation does not proceed with its youthful fervor in maturity. Although seemingly innocuous, cracked heels can become a major medical issue in patients with diabetes as the crack can extend into viable skin and provide an entry for infection. The pain of cracked heels can also interfere with ambulation. I have an instruction sheet I give my patients to assist with cracked heels because I get asked so frequently about this problem. I thought I would share my time-saving instructions with you.

**HEALING CRACKED HEELS**

This procedure is best done in the evening just before going to bed.

1. Fill a plastic dishpan with about 2 inches of lukewarm water to completely submerge your heels.
2. Add 2 drops of dish soap and swirl the solution a few times with your hand.
3. Put a towel close by for drying your feet.
4. Place the dishpan on the floor and put your feet in for 15 minutes.
5. After 15 minutes, take your right foot out and set it on your left leg. Leave your left foot in for continued soaking.
6. Use your fingernails to scrape away the dead skin on your right foot. Do not use scissors, sharp files, or grinders. Only scrape away what can be easily removed. Put your right foot back in the dishpan.
7. Take your left foot out of the dishpan and set it on your right leg. Leave your right foot in for continued soaking.
8. Use your fingernails to scrape away the dead skin on your left foot. Again, do not use scissors, sharp files, or grinders. Only scrape away what can be easily removed. Put your left foot back in the dishpan.
9. Repeat scraping the dead skin from both feet until no more can be easily removed. Usually 2 to 3 repetitions are sufficient, depending on the amount of dead skin.
10. Apply petroleum jelly to your feet and put on thin socks. Retire for the evening and sleep in the socks.
11. Remove the socks in the morning and go about your regular daily grooming.
12. Repeat the soaking procedure nightly until the cracked calloused skin has been removed.
13. Repeat the procedure as often as necessary to prevent calloused skin from returning.

**Q: What is the best way to cut and groom thickened toenails?**

Thickened toenails can be very challenging to cut. The same procedure described above can also be used to soften thickened toenails by hydrating the keratin. Hydrated keratin is more ductile and softer, making it much easier to cut with scissors or toenail clippers. The same instructions as above can be used, except after step 9 add the following: Use a scissors or toenail clipper to trim your softened nails on both feet. Then resume with step 10, instructing the patient to apply petroleum jelly and wear thin socks to bed. The lukewarm water penetrates the nail plate better when the dishwashing detergent is added. The surfactant aids in water penetration by removing any oily debris from the surface and slightly denaturing the keratin protein, thus opening up water-binding sites. This allows extra hydration to occur, which softens the keratin and decreases the cutting force. This is important so the nail does not crack.

**Q: What is unique about products designed for diabetic feet?**

A number of companies have launched products specifically for diabetic skin, including foot products. This segmentation of the moisturizer market has led to products for eczema, itchy skin, rough skin, bumpy skin (keratosis pilaris), and diabetic skin. This is a way of creating more sales through expanded product offerings with descriptions that encourage sales by speaking to certain populations that may not be traditional users of moisturizer. An individual may purchase the moisturizer because “it is just for me and my unique skin condition.” The question remains whether these segmented moisturizers contain different ingredients from those in nonsegmented moisturizers. The answer is “maybe.” Diabetic foot products tend to have a higher viscosity and more moisturizing ingredients that occlude the skin surface to encourage hydration, such as petrolatum, shea butter, and dimethicone. Although these ingredients are indicative of the extra dry skin found in diabetic feet, they are not unique to diabetic foot products.
Part I
Protecting a Physician’s Most Valuable Asset:
Insurance Basics for Young Dermatologists

BY JASON M. O’DELL, MS, CWM & MICHAEL LEWELLEN, CFP®

The most valuable asset for nearly every dermatologist is their ability to practice their profession, as the future income stream from this asset is significant and quantifiable. To protect this asset for themselves and for others dependent on them, dermatologists rely on disability and life insurance as fundamental “asset protectors.” Young dermatologists should secure these tools early in their careers, and established physicians should regularly review existing insurance policies to ensure they are maintaining necessary levels of protection.

In part 1 of this 2-part article, we will focus on the basics physicians need to know about disability insurance, and we will cover life insurance in part 2.

THE NEED FOR DISABILITY INSURANCE

The disability of the family breadwinner can be more financially devastating to a family than premature death. With many disability cases, the medical care alone can cost hundreds of dollars per day, increasing expenses significantly while income is reduced or eliminated.

EMPLOYER-PROVIDED COVERAGE OFTEN INADEQUATE

If you are an employee of a university, hospital, or large dermatology practice, your employer may provide long-term disability coverage. Group disability, however, often limits either the term of the coverage or the amount of benefits paid. For instance, benefits may last only a few years or benefit payments may represent only a small part of your annual compensation. Since this is most commonly an employer-paid benefit, the money received during your disability will be income taxable to you. Additionally, employer or group disability coverage can be terminated at any time and for any reason, leaving you without coverage.

GETTING THE BEST INSURANCE COVERAGE FOR THE MONEY:
INDIVIDUAL DISABILITY

Because many physicians do not have access to group disability insurance and group coverage can prove lacking if the need arises, all dermatologists should consider individual disability insurance to protect the value of their future incomes. When evaluating options for an individual disability insurance policy, it is important to work with a reputable and experienced insurance adviser, who can help you with answers to the following questions:

1. WHAT IS THE BENEFIT AMOUNT?
   Most policies are capped at a benefit amount that equals 60 percent of income. You must ask yourself how much money your family would need if you became disabled.

2. WHAT IS THE WAITING PERIOD (ELIMINATION PERIOD)?
   This is the period of time that you must be disabled before the insurance company will pay disability benefits. The longer the waiting period before benefits begin, the lower your premium will be. Essentially, the waiting period serves as a deductible relative to time—you cover your expenses for the waiting period, then the insurance company steps in from that point forward.

3. HOW LONG WILL COVERAGE LAST?
   It’s a good idea to get a benefit period of coverage that lasts until Social Security benefit payments begin, sometime between aged 62 and 70 years. Unless you are still too young to qualify for Social Security, a policy that provides lifetime benefits, at costly premiums, is generally not worth the added expense.

4. WHAT IS THE DEFINITION OF DISABILITY?
   Definitions vary from insurance company to insurance company, and even from policy to policy within the same company. The definition of disability used for a policy is of the utmost importance. The main categories are own-occupation, any-occupation, and loss of income. The own-occupation policies, which pay a benefit if you can’t continue your own occupation (even if you can and do work in another occupation after the disability), are the most comprehensive.

5. DOES THE POLICY OFFER PARTIAL BENEFITS?
   If you can work only part time instead of your previous full-time hours, will you receive benefits? Unless your policy states that you are entitled to partial benefits, you won’t receive anything unless you are totally unable to work. Also, are extended partial benefits paid if you go back to work and suffer a reduction in income because you cannot keep up the same rigorous schedule you had before you became disabled?

6. IS BUSINESS OVERHEAD EXPENSE COVERED?
   If you are a practice owner, whether you have $10,000 or $20,000 of monthly disability benefit, you likely don’t have enough to cover your lost income plus the costs of running the practice.

7. IS IT NONCANCELLABLE OR GUARANTEED RENEWABLE?
   The difference between these terms is very important. If a policy is noncancellable, you will pay a fixed premium throughout the contract term and your premium will not go up for the term of the contract. If it is guaranteed renewable, the policy cannot be canceled but your premiums could go up. Idle-
ally you want a policy that is both noncancelable and guaranteed renewable.

8 HOW FINANCIALLY STABLE IS THE INSURANCE COMPANY?
Before buying a policy, check the financial soundness of your insurer.

CONCLUSION
The value of a dermatologist’s future income is a valuable asset that needs protection, both for the physician and for dependents who rely on that income. Dermatologists rely on disability and life insurance as fundamental protectors of this asset and should purchase these policies early in their careers. Here, in part 1 of this 2-part article, we focused on what doctors need to know about disability insurance. We will cover life insurance in part 2.

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Inside the Practice: Inside a Physician Assistant’s Online Brand
In an interview during the Society of Dermatology Physicians Associates (SDPA) 2022 Annual Meeting in June, Savanna Perry, PA-C, creator of The PA Platform and a physician assistant at Evans Dermatology, discusses her session on building social presence as a health care professional.

Deep Dive into Psoriatic Arthritis
Terence Rooney, MD, explains the innovative research methods Janssen utilizes and the benefits of precision medicine in the treatment of psoriatic arthritis and discusses the recent findings indicating that guselkumab provided patients with psoriatic arthritis sustained improvements in health-related quality of life through 2 years.

Second Opinion: CGRP for Migraine
Lauren Nabrany, MD, and Deena Kuruvilla, MD, join Second Opinion to talk about real-world experiences with the CGRP class of medications for migraine.

Well-being Checkup: Managing Chronic Stress
Jennifer Bourgeois, PharmD, a clinical pharmacist and founder of Well & Free, LLC, shares her tips for managing chronic stress, prioritizing rest, and practicing self-care as a pharmacist.
INDICATION

ADBRY™ (tralokinumab-ldrm) is indicated for the treatment of moderate-to-severe atopic dermatitis in adult patients whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. ADBRY can be used with or without topical corticosteroids.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATION

• ADBRY is contraindicated in patients who have known hypersensitivity to tralokinumab-ldrm or any excipients in ADBRY.

WARNINGS AND PRECAUTIONS

• **Hypersensitivity**: Hypersensitivity reactions, including anaphylaxis and angioedema have occurred after administration of ADBRY. If a serious hypersensitivity reaction occurs, discontinue ADBRY immediately and initiate appropriate therapy.

• **Conjunctivitis and Keratitis**: Conjunctivitis and keratitis occurred more frequently in atopic dermatitis subjects who received ADBRY. Conjunctivitis was the most frequently reported eye disorder. Advise patients to report new onset or worsening eye symptoms to their healthcare provider.

• **Parasitic (Helminth) Infections**: Treat patients with pre-existing helminth infections before initiating treatment with ADBRY. If patients become infected while receiving ADBRY and do not respond to antihelminth treatment, discontinue treatment with ADBRY until the infection resolves.

• **Risk of Infection with Live Vaccines**: ADBRY may alter a patient’s immunity and increase the risk of infection following administration of live vaccines. Prior to initiating therapy with ADBRY, complete all age appropriate vaccinations according to current immunization guidelines. Avoid use of live vaccines in patients treated with ADBRY. Limited data are available regarding coadministration of ADBRY with non-live vaccines.

ADVERSE REACTIONS

• The most common adverse reactions (incidence ≥1%) are upper respiratory infections, conjunctivitis, injection site reactions, and eosinophilia.

Please see additional Important Safety Information and Brief Summary of Prescribing Information on following pages.
**Adbry—for lasting control and itch relief**

**PATIENTS EXPERIENCED LASTING IMPROVEMENT FOR UP TO 52 WEEKS WITH ADBRY**

<table>
<thead>
<tr>
<th>Visible Skin Clearance and Itch Relief With Adbry at Week 16</th>
<th>ADBRY MONOTHERAPY</th>
<th>COMBINATION THERAPY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ECZTRA 1</td>
<td>ECZTRA 2</td>
</tr>
<tr>
<td></td>
<td>Adbry 300 mg Q2W</td>
<td>placebo</td>
</tr>
<tr>
<td>No. of patients randomized and dosed (FAS)*</td>
<td>601</td>
<td>197</td>
</tr>
<tr>
<td>IGA†‡</td>
<td>16% vs 7% (P=0.002)</td>
<td>21% vs 9% (P=0.001)</td>
</tr>
<tr>
<td>EASI-75†‡</td>
<td>25% vs 13% (P=0.001)</td>
<td>33% vs 10% (P=0.001)</td>
</tr>
<tr>
<td>No. of patients with baseline Worst Daily Pruritus NRS (weekly average) score ≤4</td>
<td>594</td>
<td>194</td>
</tr>
<tr>
<td>Worst Daily Pruritus NRS (24 point reduction)†§</td>
<td>20% vs 10% (P=0.002)</td>
<td>25% vs 9% (P=0.001)</td>
</tr>
</tbody>
</table>

*Full Analysis Set (FAS) includes all subjects randomized and dosed.
†Subjects were defined as subjects with an IGA 0 or 1 (“clear” or “almost clear”).
‡Subjects who received rescue treatment or with missing data at 16 weeks were considered as nonresponders.
§Percentage of patients who achieved response.
EASI=Eczema Area and Severity Index; IGA=Investigator’s Global Assessment; NRS=Numeric Rating Scale; TCS=topical corticosteroids.

**NEARLY 9 OUT OF 10 RESPONDERS AT WEEK 16 EXPERIENCED LASTING DISEASE CONTROL AT WEEK 32 WITH ADBRY 300 MG Q2W+TCS AS NEEDED**

<table>
<thead>
<tr>
<th>Percentage of patients who maintained response at Week 32</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECZTRA 3</td>
</tr>
<tr>
<td>Adbry Q2W+TCS as needed</td>
</tr>
<tr>
<td>92% (60/65)</td>
</tr>
<tr>
<td>89% (40/45)</td>
</tr>
</tbody>
</table>

More than half of responders at Week 16 maintained response at Week 52 with Adbry Q2W monotherapy, without any TCS use†‡:

- **ECZTRA 1**: IGA 0/1 and EASI-75 response was maintained by 51% (20/39) and 60% (28/47) of patients on Adbry Q2W, respectively; 47% (9/19) and 33% (10/30) of patients on placebo maintained response.
- **ECZTRA 2**: IGA 0/1 and EASI-75 response was maintained by 60% (32/53) and 57% (43/76) of patients on Adbry Q2W, respectively; 23% (6/26) and 20% (8/40) of patients on placebo maintained response.

*Responders were defined as subjects with an IGA 0 or 1 (“clear” or “almost clear”) or EASI-75 at Week 16. At Week 16, responders (defined as subjects with an IGA 0 or 1 or EASI-75 at Week 16) were randomized to Adbry 300 mg Q2W with TCS or Adbry Q4W with TCS for another 16 weeks.
†Subjects who received rescue treatment or with missing data at 16 weeks were considered as nonresponders.
‡Subjects who achieved response.

**Study designs**

The efficacy and safety of Adbry were assessed in 3 randomized, double-blind, placebo-controlled trials with a total of 1934 patients 18 years of age and older, with moderate-to-severe atopic dermatitis not adequately controlled by topical medications. In ECZTRA 1, 2, and 3, subjects received subcutaneous injections of Adbry 600 mg or placebo on Day 0, followed by Adbry 300 mg or placebo Q2W for 16 weeks. In ECZTRA 3, patients received concomitant TCS as needed (mometasone furoate 0.1% cream was dispensed at each dosing visit). ECZTRA 1, 2, and 3 assessed the primary endpoints of the proportion of subjects with an IGA 0 or 1 at Week 16 and the proportion of subjects with EASI-75 at Week 16. Secondary endpoints included the reduction of Worst Daily Pruritus NRS (weekly average) of at least 4 points on the 11-point itch NRS from baseline to Week 16. At Week 16, patients with an IGA 0/1 or EASI-75 response were re-randomized to Adbry Q2W, Q4W, or placebo for another 36 weeks (ECZTRA 1, 2) and Q2W or Q4W for another 16 weeks (ECZTRA 3).

**IMPORTANT SAFETY INFORMATION (cont’d)**

**USE IN SPECIFIC POPULATIONS**

- **Pregnancy**: There are limited data from the use of ADBRY in pregnant women to inform a drug-associated risk of adverse developmental outcomes. Human IgG antibodies are known to cross the placental barrier; therefore, ADBRY may be transmitted from the mother to the developing fetus.
- **Lactation**: There are no data on the presence of tralokinumab-ldrm in human milk, the effects on the breastfed infant, or the effects on milk production. Maternal IgG is present in breast milk. The effects of local gastrointestinal exposure and limited systemic exposure to ADBRY on the breastfed infant are unknown.
- **Pediatric Use**: The safety and effectiveness of ADBRY have not been established in pediatric patients.
When topical Rx therapies only go so far
Start with Adbry and see progress continue

Adbry is the first and only biologic to specifically target and neutralize IL-13.

Adbry demonstrated significant skin clearance, improvements in lesion extent and severity, and itch relief at Week 16, and was studied for long-term control at Weeks 32 and 52.

Demonstrated long-term safety through 52 weeks:
- Most common adverse reactions (AR) (incidence ≥1%) for Adbry vs placebo (ECZTRA 1 and ECZTRA 2 pooled) and Adbry + TCS vs placebo + TCS (ECZTRA 3), respectively, at Week 36 are upper respiratory tract infections (23.8% vs 20.4%, 30% vs 15.4%), conjunctivitis (7.5% vs 3.1%, 13.6% vs 4.9%), injection site reactions (7.4% vs 4.1%, 11.1% vs 0.8%), and eosinophilia (1.4% vs 0.5%, 1.2% vs 0%).
- The safety profile of Adbry during maintenance treatment was consistent with that in the initial 16-week treatment period. In addition, the frequency of adverse reactions with Adbry Q2W and Q4W in ECZTRA 1 and ECZTRA 2 was 44% and 34%, respectively, and 43% and 26% with Adbry + TCS Q2W and Q4W in ECZTRA 3, respectively.

The flexibility to treat with Q2W or Q4W dosing:
- An initial dose of 600 mg (four 150 mg injections), followed by 300 mg (two 150 mg injections).
- Maintenance dose of 300 mg (2 prefilled syringes) Q2W.
- Q2W or Q4W dosing may be considered in patients <100 kg (220 lb) who achieve “clear” or “almost clear” skin after 16 weeks of treatment.

Adbry has no boxed warning, and no requirement for initial lab testing or ongoing lab monitoring in the Prescribing Information.
Adbry is a targeted biologic therapy and is not an immunosuppressant or a steroid.

IMPORTANT SAFETY INFORMATION (cont’d)
You are encouraged to report side effects of prescription drugs to the FDA.
Visit www.fda.gov/medwatch or call 1-800-FDA-1088.
You may also report side effects to LEO Pharma Inc. at 1-877-494-4536, option 1, or email to usdrugsafety@leo-pharma.com
Please see Brief Summary of Prescribing Information on next page.

FIND OUT MORE ABOUT ADBRY: Visit AdbryHCP.com

References:

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The only biologic to exclusively target IL-13
ADBY™ (tralokinumab-lidrm) injection, for subcutaneous use

**Initial U.S. Approval 2021**

**Brief Summary of Prescribing Information**

This Brief Summary does not include all the information needed to use ADBY™ safely and effectively. Please see Full Prescribing Information.

**For Only**

- **INDICATIONS AND USAGE**
  - ADBY™ is indicated for the treatment of moderate-to-severe atopic dermatitis in adults with disease that is not adequately controlled with topical prescription therapy, or when use of these therapies are not advisable. ADBY™ can be used with or without topical corticosteroids.

**CONTRAINDICATIONS**

- ADBY™ is contraindicated in patients who have known hypersensitivity to tralokinumab-lidrm or any excipients in ADBY™.

**WARNINGS AND PRECAUTIONS**

- Hypersensitivity
  - Hypersensitivity reactions including anaphylaxis and angioedema, have been reported with use of ADBY™. If a serious hypersensitivity reaction occurs, discontinue ADBY™ immediately and initiate appropriate therapy.
  - Joint and Keratitis
  - Concomitant use of non-steroidal anti-inflammatory drugs (NSAIDs) or aspirin may increase the risk of serious GI adverse reactions including, but not limited to, ulceration, bleeding, and perforation with the use of ADBY™.

**Parasitic (Helminth) Infections**

Treat patients with pre-existing helminth infections before initiating treatment with ADBY™. If a patient become infected while receiving ADBY™ and does not respond to antimicrobial treatment, discontinue treatment with ADBY™ until the infection resolves.

**Risk of Infection with Live Vaccines**

ADBY™ may alter a patient’s immunity and increase the risk of infection following administration of live vaccines. Prior to initiating therapy with ADBY™, consult the appropriate health authority regarding use of live vaccines in patients treated with ADBY™. Limited data are available regarding coadministration of ADBY™ with non-live vaccines.

**ADVERSE REACTIONS**

The following adverse reactions are discussed in greater detail elsewhere in the prescribing information.

- **Hyper敏sity**
  - **Concomitant and Keratitis**

Clinical Trials Experience

Although clinical trials are conducted under well-controlled 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 safety of ADBY™ was evaluated in a pool of 5 randomized, double-blind, placebo-controlled trials: ECZTRA 1, ECZTRA 2, ECZTRA 3 (a dose-finding trial), and a vaccine response trial.

The safety of ADBY™ was evaluated in a pool of 5 randomized, double-blind, placebo-controlled trials: ECZTRA 1, ECZTRA 2, and ECZTRA 3, a dose-finding trial, and a vaccine response trial.

The safety profile of ADBY™ injection was evaluated in a pool of 5 randomized, double-blind, placebo-controlled trials: ECZTRA 1, ECZTRA 2, and ECZTRA 3 (a dose-finding trial), and a vaccine response trial.

**Patient Counseling Information**

- **ADBY™ for the treatment of moderate-to-severe atopic dermatitis in adults with disease that is not adequately controlled with topical prescription therapy, or when use of these therapies are not advisable. ADBY™ can be used with or without topical corticosteroids.

ADBY™ injection site reactions include pain, erythema, swelling, and discomfort. Eosinophilia cluster includes eosinophilia and eosinophil count increased.

In the monotherapy trials (ECZTRA 1 and ECZTRA 2), through Week 16, the proportion of subjects who experienced adverse reactions due to adverse reactions was 0.7% on the ADBY™ monotherapy every other week group and 1% of the placebo group in the conjunctivitis TCS if ECZTRA 1 through Week 16, the proportion of subjects with conjunctivitis and/or dermatitis due to adverse reactions was 0.8% in the ADBY™ monotherapy every other week group and 3% in the placebo group + TCS group. The most common adverse reactions leading to discontinuation in the ADBY™ group compared to the placebo group were injection site reaction (1.0% vs 3.0%) and eosinophilia (0.3% vs 0%) in ECZTRA 1 and ECZTRA 2, and injection site reaction (8.4% vs 0%) and conjunctivitis (0.4% vs 0%) in ECZTRA 3.


The safety profile of ADBY™ monotherapy every other week with or without TCS during maintenance treatment was consistent with that in the initial 16-week treatment period. In addition, the frequency of adverse reactions with ADBY™ monotherapy every other week and every 4 weeks in ECZTRA 1 and ECZTRA 2 was consistent (44% vs 43%, respectively) and 43% and 26% with ADBY™ monotherapy + TCS every other week and every 4 weeks in ECZTRA 3, respectively.

**Specific Adverse Reactions**

- **Conjunctivitis and Keratitis**
  - **Joint and Keratitis**

**Clinical Trials Experience**

- **Conjunctivitis and Keratitis**
  - **Joint and Keratitis**

**ADVERSE REACTIONS**

The following adverse reactions are discussed in greater detail elsewhere in the prescribing information.

- **Hyper敏sity**
  - **Concomitant and Keratitis**

Clinical Trials Experience

- **Parasitic (Helminth) Infections**
  - **Risk of Infection with Live Vaccines**
  - **ADVERSE REACTIONS**
  - **Hyper敏sity**
  - **Concomitant and Keratitis**

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Clinical Trials Experience

- **Parasitic (Helminth) Infections**
  - **Risk of Infection with Live Vaccines**
  - **ADVERSE REACTIONS**
  - **Hyper敏sity**
  - **Concomitant and Keratitis**
Atopic dermatitis (AD) is one of the most common inflammatory skin diseases. It is characterized as a chronic, type II inflammatory skin disease that exhibits the following prominent features: xerosis, pruritis and, ill-defined erythematous plaques. There were limited treatment options until recently, with an increased understanding of the immunological nature of this disease. There is now a rich pipeline of new therapies for AD, especially systemic therapies. Eric Simpson, MD, MCR, and professor of dermatology at Oregon Health & Science University, delivered a broad presentation at Maui Derm NP+PA Summer 2022 on systemic therapies of AD, focusing on appropriate use criteria. “This is an exciting time for offering safe and effective novel therapies to patients with moderate-to-severe AD who are inadequately controlled with topical therapy,” Simpson said.

The presentation began with an overview of the current treatment armamentarium for AD, which includes topical medications for mild to moderate disease and systemic treatments for moderate-to-severe disease. As disease severity increases, clinicians should consider moving from topical to systemic medications. However, this decision is sometimes complicated and may differ from one clinician to another. Guidelines were presented by the International Eczema Council, which suggested that systemic therapy should be employed if aggressive topical therapy is not achieving control of the disease. How-ever, before moving straight to systemic therapy, clinicians must ensure that adequate education is delivered and any infectious comorbidities (which could make mild AD seem more like a moderate-to-severe presentation) are addressed. Also, phototherapy should be considered before oral or injectable therapy and systemic therapy should be considered early in the patient’s treatment course if their disease is having a large impact on their quality of life.

While the International Eczema Guidelines provide some guidance on the appropriate use of systemic AD treatments, some clinicians feel they are vague, and one clinician’s definition of “aggressive topical therapy” may differ from another’s definition. The Atopic Dermatitis Control Tool (ADCT) mitigates this issue by using an extensively validated, 6-item questionnaire to assess the severity of a patient’s AD. “This instrument boasts multiple domains, including sleep, intense itching, emotions, and daily activities. The ADCT is free to download and use and is great for serially tracking a patient’s response in one’s practice. Validation studies performed on this measure concluded that this holistic tool displays good-to-excellent content validity, construct validity, internal consistency, reliability, and discriminant ability.” I encourage all dermatology providers to recognize a patient with inadequate disease control prompting a discussion of new options and to not just refill topical or oral steroids,” said Simpson.

Before moving on to systemic treatments for AD, Simpson reminded the audience that this disease could have many comorbidities, including dyspigmentation, infection, and hand/facial involvement. These issues are especially prevalent in skin-of-color patients and should be considered when selecting an appropriate AD therapy. He warned that overuse of steroids should be considered a topical therapy failure and that clinicians must remember that treating with topical steroids is not without adverse effects. These include perioral dermatitis, atrophy, acne, and steroid withdrawal. Some inexperienced clinicians may aggressively use high-potency topical steroids in severe cases of AD, which could lead to further complications. “This is another reason why tools such as the ADCT are useful in clinical practice.

Systemic treatments were reviewed in depth during the next part of the presentation. “There are now 2 biologics targeting type 2 inflammation and 2 oral JAK inhibitors that provide your patients with AD hope for a life free of itch and eczema,” Simpson said. He reminded the audience that traditional immunosuppressants (such as methotrexate or cyclosporine) and Narrowband Ultraviolet B Phototherapy are also options for systemic treatment of AD, in addition to biologics and JAK inhibitors. “Traditional immunosuppressants (ie, cyclosporine, methotrexate, mycophenolate, azathioprine) still have utility in today’s therapeutic landscape. The biggest factor is cost, as traditional therapies are much cheaper and easier to access than the newer JAK inhibitors and biologics. Cyclosporine at high doses remains 1 of the most efficacious systemic AD therapies. One of the biggest disadvantages is that these therapies are used off label. Also, rigorous lab monitoring requirements and solid organ toxicities make these agents difficult to use on a regular basis. Specifically, cyclosporine can cause renal toxicity, and methotrexate can cause liver and blood toxicity. Strict monitoring of creatinine is necessary while using cyclosporine and sometimes a test dose of methotrexate is given to patients to ensure there is no precipitous drop in blood cell counts.

There are numerous factors to consider when prescribing a systemic therapy for AD. While severity of disease and associated comorbidities...
“This is an exciting time for offering safe and effective novel therapy to patients with moderate-to-severe AD who are inadequately controlled with topical therapy.”

Eric Simpson, MD

are important, clinicians need to also consider issues such as access, coverage, age, risk aversion, and previous therapeutic history. Simpson stressed the importance of shared decision-making when discussing systemic therapy. This is critical, as some systemic therapies for AD carry black box warnings that patients may ask about. In short, shared decision-making comprises 3 domains—team talk, option talk, decision talk—and encourages active listening with careful deliberation. An example of option talk is the following statement: “Let’s compare the possible options for you on systemic therapies of AD.” Simpson used cyclosporine, methotrexate, and dupilumab as examples of option talk highlighting unique adverse events such as hypertransaminase, liver toxicity, and conjunctivitis, respectively.

While biologic agents such as dupilumab and tralokinumab do not have some of these more serious adverse events, they are not good options for needle-phobic patients or for patients who want a short-term solution. These therapies are very versatile and can be used for any patient without adequate control on topical therapy. Simpson reviewed the clinical trial data for dupilumab, an interleukin-4 receptor-α antagonist, and specifically highlighted its recent FDA approval for AD treatment. In the Phase III clinical trials, dupilumab achieved an EASI 75 of about 90% at week 32. Drug survival studies indicate that this high response rate is maintained over a 2-year period. Data were presented showing that treatment with tralokinumab leads to a shift towards a non-lesional skin phenotype over a 2-year period.

Simpson ended his presentation16 by discussing JAK inhibitors, the newest class of systemic medications for the treatment of AD. The JAK/STAT signaling pathway was reviewed along with the advantages that JAK inhibitors offer for AD treatment. Not only do JAK inhibitors offer flexible dosing regimens with an oral route of administration, but they can also provide relief of symptoms as early as 1 to 2 weeks after treatment initiation. Simpson reviewed the 2 FDA approved therapies, abrocitinib and upaclacitinib. These are both JAK 1 inhibitors but upaclacitinib is approved down at age 12 years. Unfortunately, these agents have black box warnings so they should not be used in patients with a history of malignancy, severe infections, thrombotic events, severe renal/hepatic disease, or significant cardiovascular disease. He ended the presentation by offering a few practical considerations for JAK inhibitor use in the clinical setting. Drug-to-drug interactions should be checked before prescribing, patients should be up to date on vaccinations, and labs should be drawn at baseline and every 1 to 3 months thereafter.

While more research is needed, it is not advised to use these medications during pregnancy or breastfeeding. For any provider who treats even just a few AD patients per week, this talk was certainly not to be missed given the excellent and practical tips that were presented.

Disclosures:

Simpson is a consultant for Arenis Pharmaceuticals, Bionveris, Brillic Ltd, Biotherapix, Boehringer Ingelheim, Collaborative Medicines, DaVita, Dermaceuticals, Eosin, Forte Biosciences, Inc., Janssen Pharmaceuticals, Ortho Dermatologics, Pfizer, and Takeda, and has received grants from Abbvie, Amgen, Daraprim, Fampridine, Galderma, Incyte, Kymriah, Kyowa, Leo Pharma, Merck & Co., Novartis, Pfizer Inc., and Regeneron Pharmaceuticals, Inc.

References:

To end an informative first day of dermatology sessions, Sanofi and Regeneron Pharmaceuticals’ representative, Cynthia J. Trickett, physician assistant (PA) in North Dallas, Texas, adjunct faculty member at the University of Texas Southwestern and University of North Texas, and vice chair of the Dermatology PA Foundation, presented treatment results for adult and pediatric patients with moderate-to-severe atopic dermatitis (AD).

Most recently, dupilumab (Dupixent; Sanofi and Regeneron Pharmaceuticals, Inc) was approved by the US Food and Drug Administration (FDA) to treat AD patients 6 months and older.1

The FDA approved dupilumab for children aged 6 months to 5 years with uncontrolled moderate-to-severe AD on June 7, 2022.2 Trickett began her presentation by discussing the importance of considering each patient’s quality of life in the event that topical steroids are ineffective and the patient’s itch is out of control.1

“They may come on a day where it’s not flared, and 2 months ago they were just in the worst flare of their life, so please make sure you get the full picture of what their disease is doing in the past 12 months to 24 months,” said Trickett.

The FDA approval of dupilumab to treat AD patients down to 6 months is groundbreaking for dermatologists and patients because1,2:

- Dupixent is the first and only biologic approved to treat uncontrolled moderate-to-severe AD from infancy (aged 6 months) to adulthood.
- Patients experienced rapid itch relief at week 2.
- Adult patients sustained skin clearance at 1 year.
- Dupixent is not an immunosuppressant or steroid.
- There is no requirement for initial lab testing or monitoring.

Trickett explained that this approval is reassuring for adult patients with AD who have not been prescribed dupilumab yet. It is safe for an infant as young as 6 months to receive treatment, then older pediatric patients or adults can also feel a sense of comfort in the safety and efficacy of the biologic. An estimated 253,000 patients with uncontrolled moderate-to-severe AD have filled at least 1 dupilumab prescription to date as the drug continues to change the way dermatologists treat their patients with AD.

AD is recognized as a chronic, systemic, immune-mediated, type 2 inflammatory disease characterized by skin lesions and pruritus. The lesions can present differently on the body depending on the patient’s age. For infants, lesions typically appear on their face, scalp, neck, trunk, and extensor surfaces. Lesions can appear on children as polymorphous manifestations, particularly in flexural folds. Lesions on adults also appear as polymorphous manifestations in flexural folds, but also on the hands.1 Patients describe lesions as chronically recurring, itchy, and a persistent burden.2

Continuing with the theme of quality of life, Trickett said 2.6 million patients (aged > 6 months) have uncontrolled moderate-to-severe AD, despite treatment.3 In a survey asking over 2000 participants about their disease, patients with moderate-to-severe AD 2 years and older living with flares reported experiencing flares 136 days per year. Even in remission, 50% of the survey participants said they worry about their next flare-up. Trickett explained that there is guilt associated with AD and the patient’s caregivers. Many caregivers worry, for example, if they made the bath water just a little too hot for the AD patient, or if they should not have had a specific food.

To date, 6 pivotal clinical trials have been conducted with more than 2,800 patients with AD.4 Many of the patients in the clinical study had a history of comorbidities, with 68% of pediatric patients (aged 6 months to 5 years) reporting having food allergies. Results from the clinical studies include:

- 39% of adult patients reached clear or almost clear at week 16 compared with 12% of the placebo group;
- 28% of pediatric patients (aged 6 months to 5 years) reached clear or almost clear at week 16 compared with 4% of the placebo group;
- 24% of pediatric patients (aged 12 to 17 years) reached clear or almost clear at week 16 compared with 2% of the placebo group;
- there was a 68% improvement in itch from baseline for adults and adolescents treated with Dupixent at 18 months.

Dupilumab has no boxed warning, it is not metabolized through the liver or excreted through the kidneys, there are no known drug-to-drug interactions, and live vaccines should be avoided immediately prior to and while receiving dupilumab, said Trickett. She ended her presentation by urging dermatologists to use Dupixent’s support programs to assist their patients through the insurance process.

References

How Dupilumab Improves Moderate-to-Severe AD

Cynthia J. Trickett, PA-C, MPAS, discusses the personal and clinical effects of atopic dermatitis in adult and pediatric patients at the Maui Derm NP+PA 2022 Summer Conference in Colorado Springs, Colorado.

KAITLYN BADER | Associate Editor
Joshua Zeichner, MD, an associate professor of dermatology and director of cosmetic and clinical research in the Department of Dermatology at Mount Sinai Hospital in New York, New York; and Mona Gohara, MD, a dermatologist at Dermatology Physicians of Connecticut in Hamden, Connecticut, and president of the Women’s Dermatologic Society discussed their experiences and preferences in treating acne with non-prescription drugs.

To determine the efficacy of over the counter (OTC) acne drugs, Zeichner and Gohara first discussed a 2019 study1 that analyzed adherence issues of topical treatments for acne vulgaris. Patients from the study used retinoids, antibacterial treatments, benzoyl peroxide, retinoid antibacterial treatments, and formulas containing resorcinol salicylic acid. Nearly half of the patients discontinued topical therapy before their scheduled time, citing unresponsiveness and adverse effects as primary reasons. Gohara began the discussion by saying she is not surprised by the number of patients who discontinue topical therapies, noting that many of her patients have told her their topical therapies did not work.

Gohara stressed that retinoids and benzoyl peroxide are the gold standards for acne treatment in dermatology, but only when used correctly. While these OTC drugs are not prescription strength, they can still be irritating to the skin when used in large quantities or mixed with other irritating agents. Gohara began the discussion by saying she is not surprised by the number of patients who discontinue topical therapies, noting that many of her patients have told her their topical therapies did not work.

Gohara stressed that retinoids and benzoyl peroxide are the gold standards for acne treatment in dermatology, but only when used correctly. While these OTC drugs are not prescription strength, they can still be irritating to the skin when used in large quantities or mixed with other irritating agents. Gohara explained that she gives her patients a handout that shows how to use OTC drugs, such as retinoids, correctly. She said dermatologists should take time to talk with their patients about how to use the product, as well as realistic expectations.

Zeichner echoed these experiences, saying he gives his patients specific guidance on how much product to use, how often, and what other OTC products to combine with topical therapies for the best results. He noted that a pea-sized amount of product is typically all you need; a cherry tomato-sized amount is too much. Overall, Zeichner sees that many patients want results too quickly; most patients will not see results until approximately week 12. Another way Zeichner tries to understand his patients’ expectations is by asking them to walk him through their skin care regimen. This helps Zeichner know what they already use and what kind of results they desire.

“I always say to patients when they come back, ‘First of all, how do you feel about your skin?’ I like to hear what they have to say before I make a comment and I’ll say to them, ‘Take me through your regimen.’ I always ask open-ended questions. We have to be nonjudgmental, educate our patients, and set realistic expectations,” said Zeichner.

Most importantly, both experts stressed that it’s crucial not to be judgmental. Asking patients questions will benefit both the dermatologist and the patient to come up with an agreed-upon acne treatment plan. Gohara also mentioned a few tricks, such as mixing a light moisturizing cream with a retinoid or benzoyl peroxide to cut the irritation and not using retinoids as a spot treatment.

Zeichner and Gohara discussed non-prescription cleansers and moisturizers for acne-prone skin. In a 2020 study4, 4 name-brand, lipid-free cleansers were studied and compared. Gohara began by pointing out the beneficial ingredients of each product. She stressed that hydrating ingredients are always beneficial, no matter
the type of skin. Both Zeichner and Gohara mentioned the importance of a healthy skin barrier. A strong skin barrier is not always the first thought in acne management, but it’s the skin’s line of defense. Ceramides in cleansers help the outermost layer of skin by keeping irritants out and keeping water locked in. Skin barrier dysfunction is related to blockages in the pores that contribute to acne.

“Lipid-free cleansers are primarily composed of water and glycerin; those are the 2 primary ingredients, which are obviously very highly rated,” said Gohara. “We can see that primarily, these cleansers will have very low rates of irritation on the skin and can help the skin barrier, which is what we were talking about before. Lipid-free cleansers can mitigate the irritation that patients may be getting from retinoids and benzoyl peroxides.”

The main goal of moisturizers is to repair significant defects in the skin barrier and assist with acne treatment. Gohara said dermatologists and patients must be deliberate when selecting a moisturizer. She considers structural components of the skin and whether the moisturizer is depositing ceramides into the epidermal barrier. Additionally, moisturizers can have other ingredients such as sunscreen that are also beneficial to the skin.

Both Zeichner and Gohara noted 3 top ingredients for hydrating skin in moisturizers:

- **occlusives**: create a blanket to prevent transepidermal water loss (TEWL)
- **humectants**: suck water up from the dermis and epidermis
- **emollient**: a layer between epidermal cells to stop TEWL

Moisturizers should have more ingredients than just a humectant, as humectants are great at grabbing water, not trapping it. Hyaluronic acid is an example of one that should not be used alone and should be layered with a moisturizer.

To end another informative webinar series, Zeichner and Gohara concluded that OTC skin care products such as cleansers and moisturizers should never compromise the integrity of the skin barrier. Products should include ingredients that will protect, soften, and hydrate the skin, not irritate it. Discussing OTC products and individualized treatment plans with acne-prone patients will result in better adherence rates as well as achievable expectations.

Reference:
In a study of patients with acne, almost 40% of treatment non-adherence was due to side effects.1

Strategic use of OTC skincare, including gentle cleansers and moisturizers, can promote adherence by improving tolerability.2,3

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Prescription of isotretinoin is a challenging endeavor, requiring collaboration among providers, office administrative staff, pharmacists, insurance companies, and laboratory facilities. As the administrative burden is not well elucidated, a group of researchers conducted a study aiming to quantify the workload required to manage patients on isotretinoin compared to non-isotretinoin medications for acne treatment.

“We wanted to explore this topic because often in the clinic we encountered issues with processing isotretinoin prescriptions and many patients faced difficulty with the process,” said Anna Kirkorian, MD, chief of dermatology at Children’s National Hospital in Washington, DC. “For example, our nurses would have to spend hours on the phone explaining the iPLEDGE process and how to complete the online questionnaires to patients, as well as speak with insurance companies regarding medication prior authorizations.”

In the article, “The administrative burden of prescribing and treating with isotretinoin,” Kirkorian and the research team explored the effectiveness of the iPLEDGE program and found it decreased patient access and increased administrative burden. The study included all patients under 21 years who received both isotretinoin and non-isotretinoin medications for acne treatment at Children’s National between 2012 and 2019.

“We performed a retrospective chart review of all patients who received isotretinoin for the treatment of acne,” said Nidhi Shah, MD, George Washington University School of Medicine and Health Sciences, who served as lead author. “Patients generally have to fail other medications such as topical and oral antibiotics prior to receiving isotretinoin, hence, we compared the administrative burden associated with prescribing these other acne medications (pre-isotretinoin) and for prescribing isotretinoin in the same patient cohort.”

From the chart review, the researchers extracted information such as patient demographics and treatment information, as well as the number and type of communications made by the nursing staff. “We explored the nursing communications, which provided insight on the number of calls that the staff had to make to different stakeholders, including patient, pharmacy, insurance company, physician, and iPLEDGE,” Shah said. “Additionally, we explored the reasons behind the communications, which allowed us to understand the biggest hurdles to isotretinoin prescription.”

The data showed a total of 1,609 communications occurred during isotretinoin treatment; 40 percent were calls with patients, 24 percent were calls with pharmacies, 13 percent were calls with insurance, and 19 percent were messages with providers. The majority of the calls involved prior authorization processing and patient education about iPLEDGE.

“By comparing the number of communications required for non-isotretinoin medication and isotretinoin within the same patient population, we were able to control for variables and appreciate the vast difference in workload required for isotretinoin vs other medications.” Shah said.

One notable takeaway of the data is that despite having similar lengths of treatment of non-isotretinoin and isotretinoin, prescription of isotretinoin resulted in significant more workload for the administrative staff (10.70 ± 8.54 communications/patient occurred during isotretinoin treatment vs 1.72 ± 2.66 communications/patient during non-isotretinoin treatment [P < .01]).

Another was that significantly more communications/patient occurred for patients with public insurance (2.24 ± 1.72) than for those with private insurance (1.58 ± 1.28) (P < .003) and when a prior authorization (PA) was required (2.38 ± 1.34) than when no PA was required (1.64 ± 0.97) (P < .001). “Although we were not surprised to learn that isotretinoin prescriptions required a greater workload than non-isotretinoin acne medications, we were definitely surprised by the significant difference in the amount of workload,” Kirkorian said. “Additionally, when translating the call lengths to the cost on the health care system, we were surprised that the cost to process 1 isotretinoin prescription could range from $6.15 to $147.80 in non-reimbursable staff hours.”

One of the biggest challenges for the administrative staff that was gleaned during the study was the coordination of prior authorization process between the pharmacy and the insurance company, especially within the 7-day prescription window, which added a time urgency.

The administrative staff served as an intermediary among stakeholders, investigating, for example, why the physician sign-off was not displaying on the pharmacy’s iPLEDGE portal or coordinating PAs between the pharmacy and insurance company. “The iPLEDGE program was originally implemented in early 2005 by the FDA to prevent fetal exposure to isotretinoin and to inform prescribers, pharmacists, and patients about isotretinoin’s serious risks and safe-use conditions, and was approved as the iPLEDGE REMS in 2010.” iPLEDGE requires each stakeholder to complete their own set of required tasks (eg, physician must sign off in iPLEDGE, patient must take an online questionnaire, pharmacy must verify patient’s iPLEDGE status),” Shah said. “The multiple steps required, especially for childbearing patients, poses a lot of obstacles for patients and the nursing staff is in the center to coordinate all of the items. The administrative staff is racing against time to ensure successful prescription of isotretinoin and this orchestration is burdensome and costly and takes away time from other duties.”

Since the implementation of iPLEDGE, there has been a shift in isotretinoin prescription pattern from low-volume general providers to high-volume specialist providers, which may be secondary to the administrative burden associated with isotretinoin prescription.

“Given that many of the patient barriers to
acne & rosacea

accessing isotretinoin—for example, patient delays in insurance prior authorization or inability to find an iPLEDGE-participating pharmacy—align with the reasons for the significant administrative burden,” Kirkorian said. “Our study sheds light on the implications of iPLEDGE from a physician/administrative perspective, with hopes that future changes in the program both work toward decreasing the burden on both patients and providers to increase access and treatment adherence.”

While the study was limited to a single site and pediatric population, Shah noted that by comparing the workload for isotretinoin and non-isotretinoin in the same cohort, the research team could control for patient variables, contributing to workload differences.

Therefore, the findings underestimate the actual administrative burden as non-phone communications and time spent on documentation, iPLEDGE portal activities, and electronic PA submissions were not included.

“The administrative staff is racing against time to ensure successful prescription of isotretinoin, and this orchestration is burdensome, costly, and takes away time from other duties,” she said. While iPLEDGE serves an important role in preventing fetal exposure to isotretinoin, streamlining the process of prescription could decrease both the administrative and patient workload, thereby reducing potential treatment barriers.”

References


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Before discussing treatments, Harper took time to highlight the goals of acne treatment and she shared her CLEAR acronym for effective treatment. The 3 most important goals of acne treatment are achieving meaningful improvements in lesion count, preventing sequelae, and improving quality of life. The CLEAR acronym can help accomplish this by reminding providers how to best counsel patients on effective treatment—C: communicate expectations, L: listen to customize treatment, E: treat early, A: treat aggressively, R: don’t resist isotretinoin. This was followed by a brief discussion on the role of topical therapy in acne treatment. Topical therapy is considered first-line treatment in most mild to moderate patients and it can be used as monotherapy or as combination therapy. However, topical antibiotics should rarely be used as monotherapy. There is also some utility for topical therapy in the treatment of acne sequelae.

Harper began her focused update on treatments with topical retinoids, which work by binding to the retinoid acid receptor, which modulates genes associated with acne etiology. Specifically, topical retinoids normalize follicular epithelial hyperkeratinization and are anti-inflammatory in nature. There have been 4 generations of FDA-approved topical retinoids, with the most recent approval for trifarotene 0.005% cream in 2019. This novel topical therapy is the first new retinoid molecule the FDA has approved in over 20 years and was studied on facial and truncal acne. In phase 3 clinical trials, trifarotene achieved a 42% IGA/PGA success rate at week 12 and a 65% absolute reduction in inflammatory lesions for both face and trunk. Topical retinoids remain a cornerstone of acne treatment. I am grateful that we have seen innovation in this space. We have a whole new retinoid molecule, trifarotene, created to specifically and precisely target the retinoic acid receptors (RAR) receptor,” Harper said.

Harper followed her discussion of trifarotene with another retinoid, tazarotene lotion 0.1%. In a phase 2 study, tazarotene lotion performed better than tazarotene 0.1% cream in percent change in mean inflammatory and non-inflammatory lesions at week 12. The novel vehicle, polymeric emulsion technology, allows for a lower percentage of active ingredients, which improves the tolerability of tazarotene, traditionally an irritating agent. Before moving on to oral agents, Harper mentioned 2 other important topical therapies. First was E-tretinoin 0.1%/E-BPO 3% cream, which can be stabilized together through microencapsulation technology. This technology also allows for improved tolerability of the medication. Next, clascoterone was highlighted and the unique mechanism of action was displayed. Clascoterone is a topical anti-androgen that binds to the androgen receptor and has limited systemic activity. In 1 clinical trial, IGA treatment success for clascoterone was 16.1% vs 7% for the vehicle. This medication is the first topical antiandrogen for acne and is appropriate for use in both male and female patients. “We all have a tendency to think of our oral antibiotics in the management of acne as being the heavy hitter once they are added to a treatment regimen, but in fact the topicals are the unsung heroes,” Harper said.

“While there are no head-to-head studies, clinical trials consistently show more acne patients achieve clear or almost clear with topical agents than with oral antibiotics.”

Harper also discussed oral therapy, which she said is equally as important as topical therapy. Oral therapy is recommended for moderate-to-severe acne that does not respond to other treatments or for inflammatory acne that is unresponsive to topical antibiotics. Sarecycline, the newest oral antibiotic therapy, offers a narrow spectrum of therapy because it has a minimal effect against gram-negative bacilli. The advantage of this narrow spectrum may be a reduced tendency to disrupt normal gut flora. Sarecycline is taken once a day with or without food, and adverse events, while uncommon, include nausea and vaginal yeast infections. Its activity against C. acnes is equivalent to that of doxycycline and minocycline.

Harper highlighted spironolactone oral therapy, which is not FDA approved for acne treatment but remains a popular option. She reviewed some high-yield pearls when using spironolactone. There is no need to check potassium in healthy women (between aged 18 and 45 years). There is no evidence of an increased risk of breast cancer, despite its FDA black box warning stating that “spironolactone has been shown to be a tumorigen in chronic toxicity study in rats.” Spironolactone takes 2 to 3 months to achieve optimal efficacy. An ideal way to use this medication is in combination with other acne treatments (topical therapies or oral antibiotics) and it even can be used in combination with oral contraceptives. Practically, dosage should be between 25 and 200 mg, but Harper prefers a maximum dose of 100 mg. A higher dose of spironolactone will lead to a high rate of side effects.

Harper ended her talk with isotretinoin, one of the most commonly used medications for the treatment of acne. She noted that the goal of isotretinoin therapy is complete clearance with 1 course of treatment while minimizing adverse effects and risks. An appropriate end point often varies by provider but a study by Tan et al found that the traditional end point dose of 120 to 150 mg/kg appears to vary with severity. Optimal end point dosing of isotretinoin has the goal of preventing relapse. Relapse can be defined in different ways, such as deterioration in acne requiring systemic therapy and those who require retreatment with oral isotretinoin. Relapses still occur in 20% to 30% of cases and less than 120 mg/kg is considered a cumulative dose that is too low. Patient characteristics that make relapse more common include younger age, male gender, severe presentation, females with polycystic ovary syndrome, and patients who present with a large number of comedones.

Harper reviewed laboratory monitoring with isotretinoin therapy. A study by Zane et al found that the greatest perturbation in laboratory abnormalities on isotretinoin were in triglycerides and total cholesterol. As such, the FDA package insert states that “blood lipid determination should be performed before isotretinoin is given and then at intervals until lipid response is established, which is usually about 4 weeks.” A meta-analysis on laboratory evaluation of isotretinoin found that while lab values demonstrated a change from baseline, none of them were considered high risk changes.

The authors recommended performing lipid and hepatic panels at baseline and 2 months after therapy, with repeat labs dictated by medical history. Harper wrapped up her presentation with a discussion on the risk of depression and suicide in patients on isotretinoin therapy, a traditionally contentious topic. A systematic review on the topic conducted by Huang et al in The Journal of The American Academy of Dermatology analyzed the 3 most important goals of acne treatment are achieving meaningful improvements in lesion count, preventing sequelae, and improving quality of life. ”

Julie Harper, MD
IT’S TIME YOU KNOW ABOUT TYK2

Pathbreaking research is shedding light on the role of TYK2 in psoriasis

At BMS, we are committed to helping patients prevail over serious immune-related diseases such as psoriasis. We’re excited about our innovative research on the TYK2 pathway and the role it may play in dermatology.

References:
Acne May Impair Sleep Quality for Adult Patients

ORIANA LERNER  | Staff Correspondent

Quick TAKES

There are limited resources available on the impact of acne on sleep. Many patients with acne report waking up during sleep or being unable to sleep because of their acne. Research suggests there may be an influence of acne severity on subjective sleep quality and vice versa, confirming prior findings of the impact acne has on quality of life and mental health. The authors wrote. 1

All 3 studies relied on self-reported sleep habits.

References:

Almost one-third of adults in the United States get less than the recommended amount of sleep. While that carries risks for several health conditions, the body of literature on the impact of sleep on acne risk or the effect of acne on sleep quality in adults is more limited.

Three studies over the last 3 years have looked at the relationship between acne and sleep. Each of the study populations was predominantly female, while the average age varied. Chaudhary et al included adolescents in their research, while Schrom and Halioua et al did not.

Schrom and Halioua et al found a relationship between acne and sleep issues. We have demonstrated that adult acne is associated with sleep issues. Patients did not report different levels of sleep issues depending on severity levels but, when asked specifically about the effect of their skin on sleep, more than 30% of severe patients reported being woken or prevented from sleeping because of their skin disease, thereby demonstrating a difference between severity levels. Our results confirm a recently published study, which reported significantly more (P < .001) individuals with acne (54.6%) than without (47.6%) who reported lacking sleep and significantly more (P < .001) individuals without acne (52.4%) than those with acne (50.3%) who reported restless sleep,” wrote Halioua et al.2 Neither they nor Chaudhary et al found a significant relationship between sleep quality and acne severity.

Schrom et al uncovered a relationship between acne severity and sleep. Although fatigue can be a symptom of depression and patients whose quality of life has been more severely impacted by acne are more stressed, research demonstrates that, when controlling for depressive symptoms and quality of life impact, subjectively worse sleep quality is associated with objectively worse acne. 3

This suggests that there may be an influence of acne severity on subjective sleep quality and vice versa, confirming prior findings of the impact acne has on quality of life and mental health.”

>30% of patients with severe acne reported being woken or prevented from sleeping because of their skin disease.

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Watch the series!
Study Measures Health-Related Quality of Life in Patients with Acne

KEITH LORIA | Staff Correspondent

There are several patient-reported outcome measures (PROMs) for health-related quality of life (HRQoL) for patients with acne. Still, not much is known about the content validity and other measurement properties of these PROMs.

That led a group of researchers to learn more, systematically reviewing PROMs for HRQoL in adults or adolescents with acne, and presenting their findings online in *JAMA Dermatology* in June.

John Barbieri, MD, department of dermatology for Brigham and Women’s Hospital, Boston, Massachusetts, served as the lead study author and noted that incorporating patient-reported outcomes into everyday practice can help dermatologists ensure they are capturing the patient’s voice.

“Although one might think taking a good history should be enough on its own, studies support that patient-reported outcomes help invite patients to discuss their lived experience, which can improve shared decision-making and individualize treatment suggestions,” said Barbieri.

“In addition, as patient-reported outcomes can be completed asynchronously before the visit, they can save time as well in a busy clinical setting.”

The authors theorized that patient-reported outcomes would enable robust and objective outcome tracking over time, which could facilitate research using real-world clinical data.

“Patient-reported outcomes provide complementary information to clinical outcomes and are a valuable tool to ensure we are capturing the patient’s perspective in both routine clinical care and clinical trials,” said Barbieri. “Understanding the patient’s perspective is critical to individualize treatment recommendations to each patient’s unique lived experience.”

Furthermore, patient-reported outcomes are preferred by patients in clinical trials, he added.

While many patient-reported outcomes are available to assess health-related quality of life in patients with acne, little is known about which ones perform best.

To find out, the study team collected full-text articles published in both English and Spanish on development, pilot, or validation studies for acne-specific, dermatology-specific, or generic HRQoL PROMs from PubMed and Embase.

“We conducted a systematic review of patient-reported outcomes for use among patients with acne, following the COmmittee-based Standards for the Selection of Health Measurement Instruments (COSMIN) criteria,” said Barbieri.

The development studies consisted of original development studies, even those not studied in acne patients per COSMIN recommendations. Barbieri explained that if a study included several diagnoses, the majority of patients had acne, or acne-specific subgroup analyses must have been available.

From there, 2 independent reviewers performed abstract and full-text screening, applying the COSMIN checklist and extracting and analyzing the data.

PROM properties (target population, domains, recall period, development language), PROM development and pilot studies, content validity (relevance, comprehensiveness, comprehensibility), and remaining measurement properties (structural validity, internal consistency, cross-cultural validity, reliability, measurement error, criterion validity, construct validity, and responsiveness) were all considered.

“For each distinctive PROM, quality of evidence was graded by measurement property,” said Barbieri. “An overall recommendation level was assigned based on content validity and quality of the evidence of measurement properties.”

In the findings, the research team identified 54 acne PROM development or validation studies for 10 acne-specific PROMs, 6 dermatology-specific PROMs, and 5 generic PROMs. Few PROMs had studies for responsiveness.

Only 2 acne-specific PROMs showed sufficient evidence for content validity.

“We found that while some evidence on content validity and measurement properties were lacking for all the patient-reported outcomes that were evaluated, 2 can currently be recommended for use in acne clinical trials and clinical practice: the Acne-Q and CompAQ,” Barbieri said. “We found that the Acne-Q and Acne Symptom and Impact Scale could also be recommended according to the COSMIN framework if additional evaluation of content validity is performed.”

Nevertheless, the study participants agree there is still a need for further research to better define content validity as well as other measurement properties such as responsiveness and interpretability.

“Patient-reported outcome measures used for research or in clinical settings should have sufficient content validity and other measurement properties; these results suggest that while 2 measures can be currently recommended, further understanding of these and other measures will be critical for patient-reported outcome measure use among patients with acne,” said Barbieri. “Therefore, further research investigating the quality of remaining acne-specific, dermatology-specific, and generic HRQoL PROMs is required to recommend their use.”

Disclosure

Barbieri is a member of the Acne Core Outcomes Research Network, which holds the copyright for the CompAQ.

References:

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NMFs=natural moisturizing factors.
Find the Rosacea and Acne Treatments That Best Fit Your Patients

In part 2 of her presentation at the 2022 SDPA Annual Summer Meeting, Shanna M. Miranti, MPAS, PA-C, discusses the best treatment regimen for your rosacea patients.

Miranti began by talking about how clinicians treat rosacea today. “We no longer categorize patients into 4 subtypes,” she said. Addressing the inflammation, redness, and textural changes should be the priority of the clinician treating their patient’s disease as well as treating the flushing and bumps. Miranti also stressed the importance of recognizing rosacea symptoms in all skin types and advising patients about the chronicity of treatment.

GUIDELINES
The current guidelines classify patients into 3 phenotypes: diagnostic, major, and secondary. Diagnostic is characterized as fixed centrofacial erythema in a distinguishing pattern that may periodically intensify or display phymatous changes. Major is described as flushing, the presence of papules and pustules, telangiectasia, and ocular manifestations. Secondary is defined as a burning and/or stinging sensation, edema, dryness, and ocular manifestations.

Miranti also pointed out that redness does not always appear “red,” especially in patients with skin of color (SOC). “It is very important to recognize the inflammation of rosacea in our skin-of-color patients,” she said.

WHAT’S APPROVED?
Miranti provided a list of current FDA-approved treatments for rosacea, including a group of topical therapies, as follows:

- Metronidazole (0.75%, 0.1%)
- Azelaic acid (Finacea Gel, Foam)
- Sodium sulfacetamide/sulfur
- Brimonidine (Mirvaso)*
- Ivermectin (Soolantra)*
- Oxymetazoline HCl (Rhofade)*
- Minocycline 1.5% foam (Zilxi)*
- 8-Benzoyl peroxide (Epsolay)*

*FDA-approved within the last 10 years.

However, there is only 1 systemic therapy FDA-approved for rosacea: Oracea 40mg (doxycycline).

Miranti said there are multiple-therapeutic approaches to treating rosacea. This includes the topical treatment of papules and pustules, the use of topical vasoconstrictors, oral sub-antimicrobial dosed antibiotics, lasers and intense pulsed light devices (PDL), and cleansers/cosmeceuticals for rosacea-prone skin.

With PDL, Miranti suggested advising patients that it will take multiple treatment sessions to see a significant improvement in disease. This treatment modality may require touch-up treatments, but patients can continue their current rosacea medications. She added that clinicians may wish to engage these patients and start a prescription if they are not already on a rosacea regimen.

Overall, in developing a treatment regimen for rosacea, Miranti said patients will be more adherent if they are involved in medical decision-making. Additionally, specialty pharmacies often get patients better pricing on medications and offer free home delivery.

In the second part of her presentation at the 2022 SDPA Annual Summer Meeting, Miranti detailed how to determine what will work for your patients with acne. With so many medications and cosmeceuticals on the market, it can be difficult to determine what will work for your patients with acne. With so many medications and cosmeceuticals on the market, it can be difficult to determine the best approach, but Miranti shared how to optimize an acne treatment regimen for different patients.

She discussed current treatment guidelines, new therapies on the market, how various treatment options differ for specific acne subcategories, why every patient should not be given tretinoin, and why clinicians should continue to prescribe Accutane.

ACNE CATEGORIES
Miranti said patients are divided into 3 cate-
Addressing the inflammation, redness, and textural changes should be the priority of the clinician treating their patient’s disease as well as treating the flushing and bumps

TREATING DIFFERENT ACNE SUBTYPES

With all of these new medications in clinicians’ toolbox, Miranti dived into how these therapies can be used on different acne subtypes such as preteens, patients with comedonal acne, oily and inflammatory teens, patients with female hormonal acne, SOC patients who are prone to postinflammatory hyperpigmentation (PIH), and patients with inflammatory/cystic/scarring acne.

Preteens (aged 9 to 12 years), Miranti suggested keeping the regimen simple and selecting a tolerable vehicle for this patient population’s tender skin. She noted that generic tretinoin cannot be prescribed for this age group as it is approved only for patients 12 years and older. Miranti also noted that acne at aged 9 years is no longer considered precocious puberty; however, workup for precocious puberty needs to be done if acne starts prior to aged 7 years.

In comedonal acne, Miranti emphasized the importance of befriending a good aesthetician who can perform extractions and teen facials. Miranti also recommended AHA or BHA washes, pads, or scrubs to aid in breaking up pilosebaceous congestions and using tolerable retinoid vehicles to prevent microcomedone formation. Regarding treatment, Amzeeq, Aklief, Twyneo, Fabior, and Arazlo have all shown efficacy and treating this acne subtype.

For oily and inflammatory acne in teens, Miranti recommended BPO if the patient can tolerate it and looking for products with good data on inflammatory and noninflammatory lesion reduction. A simple regimen is suggested for this age group to promote better treatment adherence. She also noted that both sebum production and inflammation can be driven by androgens. Winlevi and Aklief are recommended as treatments for this subtype.

In female hormonal acne, Miranti recommended focusing on the androgens. She said adult females are more motivated to perform more complex regimes, adding recommended serums, antioxidants, and washes to their skin care routine. Regarding treatments, Miranti suggested prescriing spironolactone for patients 18 years and older, starting at 50 mg. Also, Winlevi has been shown to be effective as a twice-daily treatment, retinoids have both acne and antiaging benefits, and Aczone has displayed specific female hormonal data.

The SOC patient population is often bothered by PIH more than active acne, so this symptom should be addressed early, according to Miranti, and patients should be urged to use sunblock. Hydroquinone, especially in combination treatment like Tri-luma (fluocinolone/hydroquinone/tretinoin; Galderma), can be very effective in SOC patients, but Miranti warned clinicians to be aware of overwhitening/halo and ochronosis in high-percentage compounds. Cyspera (cysteamine) is also now available without a prescription and helps regulate melanin synthesis. Other available treatments include Aklief, Arazlo, Finacea (azelaic acid), and antioxidants such as Heliocare and Skin-Ceuticals Phloretin Discoloration Defense.

Finally, in patients with inflammatory, cystic, and scarring acne, Miranti said Accutane (isotretinoin) is still the gold standard for nodulocystic/scarring acne. Oral antibiotics/oral nonantimicrobial dose antibiotics can be effective in reducing inflammation. However, she emphasized that clinicians should never prescribe antibiotics as monotherapy. Instead, they should always add a BPO wash, topical, or combination therapy to reduce the risk of bacterial resistance. Other treatments that have shown efficacy for the acne subtype include retinoids, lasers, radio frequency devices, microneedling, and platelet-rich plasma.

Disclosure

Miranti is a speaker for EPI Health, Galderma, Incyte, Ortho Dermatologics, Venus Pharmaeuticals, and Saoa. Also, she is consultant for Venus and Saoa, and an advisory board member for Galderma and Incyte.

Reference


<table>
<thead>
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<th>NEW TREATMENTS</th>
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<td><strong>Aklief (trifarotene; Galderma)</strong></td>
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<tr>
<td>fourth-generation retinoid</td>
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<td>Amzeeq (minocycline; Journey Medical)</td>
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<tr>
<td>Topical foam</td>
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<tr>
<td><strong>Arazlo (tazarotene 0.045%; Ortho Dermatologics)</strong></td>
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<td>third-generation retinoid</td>
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<tr>
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<tr>
<td><strong>Seysara (sarecycline; Almirall)</strong></td>
<td>FDA-approved in 2019</td>
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<tr>
<td>oral antibiotic</td>
<td>part of a weight-based tetracycline class</td>
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<td>approved for patients 9 years and older</td>
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<tr>
<td><strong>Winlevi (clascoterone; Sun Dermatology)</strong></td>
<td>FDA-approved in 2020</td>
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<tr>
<td>first in class</td>
<td>topical anti-androgen</td>
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<td><strong>Twyneo (tretinoin 1% and BPO 3%; Galderma)</strong></td>
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<tr>
<td>microencapsulation of ingredients</td>
<td>approved for patients 9 years and older</td>
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Quick Takes

The FDA recently approved roflumilast cream for patients 12 years and older for plaque psoriasis.

Some 9 million people in the United States suffer from plaque psoriasis.

Roflumilast was proven to be both safe and effective treatment for this condition.

FDA Approves Roflumilast Cream 0.3% for Plaque Psoriasis

Arcutis Biotherapeutics’ roflumilast cream provides relief to patients 12 years or older with plaque psoriasis.

KAITLYN BADER | Associate Editor

The US Food and Drug Administration (FDA) has approved roflumilast cream 0.3% (Zoryve; Arcutis Biotherapeutics) for the treatment of plaque psoriasis in adolescents and adults. This novel drug is the first and only topical phosphodiesterase-4 (PDE4) inhibitor approved for the treatment of plaque psoriasis. Roflumilast cream provides fast clearance of psoriasis plaques while also reducing itch across affected parts of the body.

The cream is approved to treat varying degrees of plaque psoriasis, including mild, moderate, and severe, with no limitations on the duration of use. The steroid-free cream should be applied once daily to the affected areas for both treatment and relief. Arcutis Biotherapeutics reported that the cream is a safe and well-tolerated formulation that is uniquely formulated to simplify disease management for patients with plaque psoriasis.

“We are very excited to have a new nonsteroidal topical agent to help us manage our psoriasis patients with the recent approval of roflumilast cream 0.3%. It is incredible to see the evolution in therapies for psoriasis, and the expansion of therapies for topical treatment is especially important to help manage the large set of patients who might not need systemic therapies,” said Lawrence Eichenfield, MD, chief of pediatric and adolescent dermatology at Rady Children’s Hospital-San Diego and professor of dermatology and pediatrics and vice-chair of the Department of Dermatology at UC San Diego School of Medicine. “My psoriasis teens and young adults are diverse in many ways and in their disease manifestations; I look forward to using roflumilast to help minimize their disease and its impact on their lives.”

Approximately 9 million people in the US have plaque psoriasis, including adolescents and adults. Topical therapies have typically been the primary treatment option for plaque psoriasis, but determining a treatment plan has not always been easy. Plaque psoriasis affects different parts of the body, including the face, elbows, knees, genitalia, and other areas of skin-to-skin contact. With varying degrees of skin sensitivities in each area, some cases require multiple topical medication prescriptions which can become complicated and frustrating.

Roflumilast cream was proven to be safe and effective in all hard-to-treat areas, making it a promising steroid-free option. The approval is based on data from the pivotal DERMIS-1 and DERMIS-2 phase 3 studies. According to the release, roflumilast cream improved the severity and impact of itch as early as week 2. Two-thirds of patients with a Worst Itch-Numerical Rating Score (WI-NRS) of 4 or higher at baseline achieved a greater than 4-point reduction in itch at week 8. Roflumilast is the only topical treatment for which efficacy has been specifically demonstrated in the treatment of intertriginous psoriasis, as measured by intertriginous IGA success (72% vs 14% in DERMIS-1 and 68% vs 17% in DERMIS-2 at week 8 [P<0.0001]).

Common adverse events include diarrhea, headache, insomnia, nausea, application site pain, upper respiratory tract infection, and urinary tract infection.

Reference

Generalized Pustular Psoriasis Poses Challenges

LINDA STOCUM | Associate Editor

There are many kinds of psoriasis, and each has unique risk factors and prevalence in the patient population. Kelly Gordon, PharmD, senior associate director of immunology, clinical development, and medical affairs at Boehringer Ingelheim, dove into why generalized pustular psoriasis (GPP) can be especially challenging when considering the lack of consensus on how to diagnose the disease.

Although GPP has been defined as a disease since 1910, the clinical aspects of the disease are not as well understood as they could be. According to Gordon, women are more often affected by this disease than men and the onset of symptoms usually occurs between ages 40 and 60 years. “If there is a genetic predisposition,” she said, “patients can present much earlier in life and sometimes as early as 1 month of age, although this is quite rare.”

The prevalence of GPP—a rare neutrophilic skin disease characterized by widespread erection of sterile cholesterol—is between 0.004% and 0.046% and this condition has a mortality range of 2% to 10%, Gordon said it may affect as many as 12% of those who have plaque psoriasis; moreover, 70% of patients who have GPP also have plaque psoriasis. “The clinical course [of GPP] is heterogeneous, and it can be characterized as a relapsing disease, with recurrent flares or persistent disease with intermittent flares,” she said.

Knowing these facts, how can physicians better diagnose GPP? Gordon pointed out that GPP is characterized by its rapid onset of sterile pustules, erythema, and scaling. “The clinical course of GPP is characterized by its rapid onset of sterile pustules that are sterile and typically localized to the trunk.”

Laboratory tests can be helpful in diagnosis, but Gordon cautioned that there is no one test to determine whether a patient has GPP. “So, it’s important to look at the whole patient and the whole picture,” she advised. What lab tests such as an immunoglobulin (IgG) or IgA test can do, according to Gordon, is determine the severity of the disease because patients often have raised IgG or IgA levels.

The vague process and lack of consensus in international guidelines are not the only issues with this disease. It also affects patient quality of life (QoL). Patients have reported that GPP affects their social relationships, mental health, work environment, sexual activity, and daily life activities, Gordon explained. These patients’ life quality burden from GPP is comparable to that of major medical or psychiatric illness.

“A patient said that they feel like their whole body is on fire,” Gordon said. “And one patient also mentioned that they had had fevers and aches—big, huge waves of searing pain—and they wanted to die because it hurt so badly.”

The flares and systemic symptoms associated with GPP significantly impact the patient’s QoL, Gordon explained, and further research is needed to better understand not only the burden of disease but also the health-related QoL outcomes in patients with GPP. There is a pressing need for the development of treatments to reduce the overall burden of GPP not only for patients but also for their family and caregivers, Gordon said.

References
THE ONE-OF-A-KIND
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For uncontrolled, mild to moderate atopic dermatitis in non-immunocompromised patients aged ≥12 years

> **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.\(^1\)

\(^\dagger\)In TRuE-AD1 and TRuE-AD2, respectively.\(^1\),\(^2\)

\(^\ddagger\)≥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
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.
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.

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
Lymphomas 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 other 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 Cancer: 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, 22% were Black, and 4% were Asian. The serious 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%), Esophagitis counted 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 weight 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, at all 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 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].

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A mouse model under development one day may unlock the role of adenomatous polyposis coli (APC) mutations in melanoma brain metastases. A $100,000 pilot award from the Melanoma Research Alliance (MRA) in Washington, DC, will allow University of Minnesota researchers to lay groundwork for additional funding.2

“What this means is we can afford to do the initial development of the tools, model, and resources so that we can apply for multimillion-dollar federal research funds. Without this award, we wouldn’t be able to do that,” said lead investigator James Robinson, PhD. He is assistant professor at The Hornell Institute, University of Minnesota in Austin.

Immune checkpoint inhibitors have revolutionized melanoma treatment, but few patients experience complete responses. Patients with mutations in the APC and beta-catenin genes suffer from a higher incidence of brain metastases than do patients without these mutations, which can alter cell growth, identity, movement, and death. However, Robinson said, it is unclear whether these mutations drive metastatic development, particularly to the brain, which remains a common point of checkpoint inhibitor failure.

If one could identify patients with APC mutations sooner, he said, such patients may benefit from more aggressive treatment or mutation-specific treatment. Because APC mutations reside in the relatively well-understood Wnt signaling pathway, Robinson added, many drugs already in clinical trials or under investigation for other diseases could merit melanoma trials, depending on which mutations investigators choose to target.

The team has developed a unique mouse model for use in this research.3 In transgenic mouse models, tumors arise over time from multiple cells. Conversely, Robinson and colleagues use a single gene to produce melanoma from melanocytes. “We can put in different genetic alterations, such as these mutations we’re studying, or the typical mutations found in melanoma—for instance, BRAFV600E or deletion of PTEN—and study the whole melanoma from the point of initiation,” Robinson said. Once investigators have preliminary data from this project, they plan to screen melanoma samples nationally for the presence of these mutations and to ascertain whether and why these mutations are causing metastases.

“In human samples,” Robinson said, “you can look to see what actually happens in the patients with mutations. But it’s hard to do a direct, controlled experiment because there are obviously thousands of different changes that occur in tumors, and melanomas are the single most mutated human tumor. So it’s sometimes hard to see the woods for the trees.”

The mouse model allows researchers to ask direct questions such as how changing 1 base pair in a single gene impacts a melanoma tumor. “We’re going to look at all the immune components of the brain metastases in the primary tumors using state-of-the-art genomic techniques that allow you to interrogate different populations of tumor cells and normal cells within the tumor,” Robinson said. For example, antibody assays will allow investigators to differentiate the CD45 immune-cell component from the melanoma-cell component of the tumors.

“Many centers as possible and having the funding to advance studies in brain metastases. ‘Are the cancer cells growing? Are they more motile, more invasive? Or do they survive in circulation to become metastatic cancer cells, as opposed to primary tumor cells?’ None of this is known,” notes Robinson.

Working from a single paraffin block that may contain pieces of tumors sampled decades ago, the MIBI process will allow researchers to take a much closer look at brain metastases. Using mouse models allow researchers to take a much closer look at brain metastases.

References:
Understanding Damage from Sunlight and Advances in Sun Protection

Tune in to an expert interview series with dermatologist Susan Taylor, MD, FAAD, on helping your patients have safe fun in the sun!

Dr. Taylor provides an overview of skin damage caused by sunlight, exploring differences between UVA, UVA1 and UVB light; and compares sunlight damage differences in individuals with light skin versus individuals with dark skin.

She also discusses advancements in sunscreen research, and offers guidance on recommending proper sunscreen for your patients.

Watch Now!
Theodore Rosen, MD, professor of dermatology at Baylor College of Medicine in Houston, Texas, discussed multiple interventions for tackling hair loss last week at the Society for Dermatology Physician Assistants (SDPA) Annual Summer Dermatology Conference in Austin, Texas.¹

Rosen, who also spoke at Maui Derm NP+PA Summer 2022,² drilled down on 2022’s biggest news in hair loss treatment in a session at this conference on new drugs and new therapies co-presented with George Martin, MD, program chair of Maui Derm NP+PA Summer 2022 and a dermatologist at Dr. George Martin Dermatology Associates in Kihei, Hawaii.

The FDA’s June 13, 2022, approval of baricitinib (Olumiant; Eli Lilly and Company and Incyte) made this oral Janus kinase (JAK) inhibitor the first-in-disease systemic treatment specifically approved to treat adult patients with severe hair loss.³

“Baricitinib represents a major breakthrough that could deliver 80% scalp coverage for 1 out of 3 patients on a 4-mg daily dose or 1 out of 5 on a 2-mg dose at 36 weeks, Rosen noted.⁴ This much-anticipated approval addresses a long-standing, unmet need for a drug targeted to the complexities of this widespread condition, he added.

“We have had a variety of medications [FDA approved for other indications] that worked as treatments for hair loss in certain areas, but there was no single drug that improved outcomes for the whole head,” Rosen said in his session at Maui Derm NP+PA Summer 2022. “Baricitinib is a game changer for severe AA—and it may be just of the first of several.”⁵

At the SDPA conference, Rosen covered a variety of scarring alopecias, including central centrifugal cicatricial alopecia (CCCA), and frontal fibrosing alopecia (FFA).

Rosen says CCCA is more commonly found among Black patients.

For FFA, Rosen said, both men and women have shown to do well on finasteride, but this medication has not helped most people with CCCA. He recommends 5 mg per day for both men and women. Hydroxychloroquine has also shown to be successful for FFA, but Rosen cautioned that systemic lupus can start with frontal hair loss, so the medication could be treating lupus and not the hair loss.

For CCCA, Rosen suggested using minoxidil (not the women’s version) for both men and women but to avoid letting it drip down the face as it can cause hair growth in unwanted areas. Additionally, medications like finasteride, minoxidil, and hydroxychloroquine can be started when symptoms have been almost eliminated by steroids.

Low-level light therapy (LLLT) can also be beneficial for hair loss, Rosen said. LLLT can be performed in either the physician’s office or the patient’s home. Rosen suggested that Capillus is the best at-home treatment, but it is pricey. Rosen suggested that providers communicate with their patients that they will need to do the 6-minute treatment every day and the most expensive one is the best.

Rosen concluded that patients should see less hair shedding by 6 months, hair growth by 1 year, and cosmetic improvement by 2 years. ▶

For references, visit, dermatologytimes.com

MORGAN PETRONELLI | Managing Editor

Top Treatment Interventions for Scarring Alopecias

Maui Derm NP+PA Summer 2022

“Used to be said that CCCA was caused by hair hygiene such as hot oils and hair straightening,” Rosen said. “Those thoughts have really taken a back seat now to the likelihood that most of these cases of CCCA are actually genetic.”⁶

Rosen said the cause of FFA can more than likely be linked to genetics rather than hair hygiene and is predominantly reported in Caucasians.

“Let’s talk reality here. These are scarring alopecias. When the hair has been scarred over and the hair follicle doesn’t exist, then you are not likely to regrow a whole lot of hair. And you must tell patients that from the very beginning,” Rosen said.

Both of these scarring alopecias can be asymptomatic or highly symptomatic. If patients have symptoms, Rosen urged clinicians to make relieving those symptoms their first priority. The second priority is to stop the hair loss process from expanding, and the third is to potentially regrow their patient’s hair. However, Rosen warned providers not to promise the ability to regrow hair because they might not be able to do much. Realistically, most patients won’t grow more than 20% to 30% of their hair back, according to Rosen.

For both CCCA and FFA, some therapies overlap including intralesionale injections of corticosteroids every 6 to 8 weeks starting at 4 mg, topical steroids to relieve symptoms and potentially stop regression, and systemic steroids.
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Pigmentary disorders of the skin can be the cause of significant psychological distress in affected patients.

The bottom line is that it is important to keep an open mind regarding a multi-therapy approach, possibly involving office-based procedures and/or newer more literature-based treatment modalities,” said Seemal R. Desai, MD, FAAD, clinical assistant professor, Department of Dermatology, University of Texas Southwestern Medical Center, Dallas, Texas, who recently spoke at the Maui Derm NP+PA Summer 2022 conference.

Typically, my personal workhorse compound therapy for melasma has been a hydroquinone-based triple combination lightening therapy consisting of hydroquinone ranging from 4% to 6%, tretinoin 0.025%, and dexamethasone 0.01%. Although used off label, in my experience this combination therapy has worked very well to help lighten the targeted skin in my melasma patients,” Desai said.

After taking standardized baseline photographic images, Desai will often use hydroquinone-based triple combination therapy for about 12 weeks in his melasma patients and, importantly, will always avoid prescribing unlimited refills for treatment. When patients follow up after the treatment course and appear to be doing better, Desai will switch them to a non-hydroquinone-based product to maintain the improvements achieved.

Although there have been multiple studies on the safety of hydroquinone, Desai does not consider the medication to be carcinogenic because of the paucity of substantial evidence in randomized, double-blinded, placebo-controlled trials.
Once some therapeutic success is achieved, we try to keep patients off hydroquinone for as long as we can and only go back to the medication when it is absolutely necessary. According to Desai, many patients are very excited to try new treatments and combination therapies simply because of the significant frustration and psychological burden associated with their disease. Many patients see their physician and can get easily frustrated after failing any number of therapi- es. Nevertheless, they need to be educated and well informed that there are evolving treatments that are proving to be effective, and it is the clinical path that patients and their physicians must travel together in search of the right treatment plan that works for their individual case,” Desai said.

Unfortunately, relapses are not uncommon and Desai said tacrolimus 0.1% cream can help stabilize the disease. According to Desai, many times one can reduce the risk of relapse to about 10% of repigmentation by applying tacrolimus ointment twice weekly as a pulse monotherapy, as was recently shown in a study by Cavalié et al.2

“Relapses are not a doomed failure of treatment, but instead should be simply viewed as a setback, a common occurrence in inflammatory diseases such as vitiligo. Should a relapse occur, the key is not to panic because they can be managed, as we have many different treatment options to quell symptoms. The ‘right’ therapeutic regimen just needs to be found for the individual patient,” Desai said.  

References

Disclosures:
Desai is a consultant to Goldman Laboratories, Almirall, Venables Laboratories, Verrica Pharmaceuticals, UC Irvine and UC Irvine Health; is a speaker for Pfizer; is a board member or executive for the Foundation for Research and Education of Dermatology, Dermavant Sciences, and the American Dermatologic Society; does contract research for AbbVie, Incyte Corporation, Dermavant Sciences, and AOBiome; has ownership interests in Gore Range Capital; and has no other financial relationships with the entities/organizations listed above.

LIKE WHAT YOU’RE READING? SUBSCRIBE TODAY!
Dermatologists regularly see a broad range of skin diseases and conditions, not all of which may have a textbook presentation. This can lead to confusion and diagnostic ambiguity and can often require extensive differential diagnoses as well as meticulous diagnostic workup to help elucidate the case. Matthew J. Zirwas, MD, recently presented on a number of these skill-stretching cases at Maui Derm NP+PA Summer 2022.

Zirwas is an associate professor at Ohio University Heritage College of Medicine in Athens, Ohio. He has published over 160 peer-reviewed articles, and is a co-author of the 7th edition of Fisher’s Contact Dermatitis. He offered these examples of cases that challenge even the most experienced dermatologists and shared how he solved them.

**THE PATIENT WITH THE HANDS AND FEET**

A few years ago, Zirwas followed the clinical journey of a 66-year-old female patient who presented in his clinic with a 1-year history of a pruritic rash on the arms, hands, and chest. Biopsy revealed a spongiotic dermatitis and patch testing showed a strong allergy to budesonide, a marker for steroid allergy. The patient was subsequently switched to low-allergenicity topical desoximetasone and systemic dexamethasone steroid treatment.

After an initial slight improvement of symptoms, the patient presented with a severely swollen and tender left arm. Culture revealed a MRSA infection, and negative for clot. After failing trimethoprim sulfamethoxazole, minocycline, and cephalaxin treatment regimens, the patient responded to a 10-day course of linezolid and improved for 6 months. The patient relapsed again but this time responded to trimethoprim sulfamethoxazole and dexamethasone therapy, improving for another 6 months.

The patient’s clinical journey continued with a diagnosis of lung cancer, which was treated with surgery without the need for chemotherapy, with the exanthem resolving about 1 year after the diagnosis. However, the patient then presented with the rash on the face, central chest, arms, and scalp, with another biopsy revealing dermatitis.

Symptoms improved with prednisone but flared again 2 months later. The patient received a diagnosis of breast cancer and was subsequently treated with surgery, radiation, and chemotherapy. The rash cleared for about 1 year and then recurred on the neck, chest, and hands, with prominent involvement of the fingernails and periungual areas causing extreme pain and itch. Unfortunately, not much improvement was achieved with systemic steroids and antibiotics, and the rash spread to the soles of the feet with vesicle formation causing severe pain and immobility.

As the patient met the American Academy of Dermatology (AAD) criteria for atopic dermatitis, a course of dupilumab (Dupixent; Sanofi and Regeneron Pharmaceuticals) was started for 3 months, after which the symptoms worsened. Dupilumab was discontinued and cyclosporine 300 mg/day was started with some success. Unfortunately, because of tremors, cyclosporine was also discontinued, and the patient then received ixekizumab for presumed psoriasis, which was also discontinued because of tremor relapse.

“Approved for the classic Th2 disease atopic dermatitis, and Th1 diseases rheumatoid arthritis and psoriatic arthritis, Janus kinase (JAK) inhibitors have a wide spectrum of activity and are a reasonable go-to when you have somebody you cannot get off of systemic steroids” — Matthew J. Zirwas, MD.
Zirwas then started the patient on medium-dose (2.25 mg/day) dexamethasone and apremilast (Otezla; Amgen). After a worsening of symptoms, apremilast was discontinued and the dexamethasone dose was increased to 4.5 mg/day. Continuing with dexamethasone, Zirwas also administered methotrexate (MTX) 10 mg/week to the patient, upon which symptoms worsened.

Oral tacrolimus 2 mg/bid was then started, which proved to be moderately helpful but the tremors recurred. After discontinuing tacrolimus, the patient received upadacitinib 15 mg/day and valacyclovir 500 mg/qid. Finally, the patient’s symptoms dramatically improved with upadacitinib (Rinvoq; AbbVie) therapy and laboratory results have stabilized.

Zirwas believes the patient had a chronic, pruritic, spongiotic, non-contact dermatitis, sparing the groin and axilla. Although it is very difficult to know exactly what the patient really has, Zirwas said the patient meets the criteria for atopic dermatitis (AD).

“Approved for the classic Th2 disease atopic dermatitis, and Th1 diseases rheumatoid arthritis and psoriatic arthritis, Janus kinase (JAK) inhibitors have a wide spectrum of activity and are a reasonable go-to when you decide to believe her, which would mean she has atopic dermatitis and not contact dermatitis, so I initiated dupilumab, which cleared her symptoms,” Zirwas said.

THE PATIENT WITH SKIN CANCER

A 72-year-old female patient presented with a history of multiple eruptive keratoacanthomas on the lower legs and a widespread rash on the body. Patch testing showed positive for formaldehyde and betaine-related lathering ingredients, which correlated well with the distribution of the dermatitis. Unfortunately, avoidance proved ineffective, but according to Zirwas, the symptoms and clinical picture met the AAD criteria for AD.

“We initiated dupilumab therapy and the dermatitis cleared. The hope is that it will decrease the rate of keratoacanthomas since recent reports have shown resolution of warts and molluscum contagiosum,” Zirwas said.

Unfortunately, however, the patient continued to develop keratoacanthomas on the lower legs in the rhythm of about 1 per month, with significant dermatitis present in the area of the lesions. Dupilumab was discontinued and methotrexate (MTX) was initiated. After an initial flare of the dermatitis, the patient improved following 8 weeks of MTX treatment.

Zirwas is a speaker for Genentech, Novartis, Sanofi, and Regeneron Pharmaceuticals, Inc. He is a consultant for Sanofi/Regeneron Pharmaceuticals, Rigel, Janssen, LEO Pharma, Pfizer, Inc., Eli Lilly and Company, Arcutis Biotherapeutics, Ortho-Dermatologics, Sol-Gel Technologies, Bausch Health, and EPI Health Inc. He is an investigator for Sanofi/Regeneron Pharmaceuticals, LEO Pharma, Janssen Pharmaceuticals Companies of Johnson & Johnson, Incyte, Vyera Pharmaceuticals Inc., UCB, Pfizer, Inc., Lilly and Company, Aclaris Biogenetics LLC, Avanos, LEO Pharma, Estee Lauder, Goldema, Dermovant Sciences, Amgen, Biogen, Janssen, and EPI Health Inc. and Concert Pharmaceuticals Inc. He is a partner of AsepticMD.

Reference

“\ The patient did not have childhood dermatitis and had no significant personal history of atopy, no flexural predominance, and patch testing that fit perfectly with the distribution of the dermatitis.”
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DermatologyTimes

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BRIEF SUMMARY
This summary contains important information about VTAMA cream. It is not meant to take the place of your doctor’s instructions. Read this information carefully before you start using VTAMA cream. Ask your doctor or pharmacist if you do not understand any of this information or if you want to know more about VTAMA cream. For full Prescribing Information and Patient Information, please see the package insert.

WHAT IS VTAMA cream?
VTAMA cream is a prescription medicine used on the skin (topical) to treat plaque psoriasis in adults. It is not known if VTAMA cream is safe and effective in children under 18 years of age.

Do not use VTAMA cream for a condition for which it was not prescribed. Do not give VTAMA cream to other people, even if they have the same symptoms you have. It may harm them.

Important: VTAMA cream is for use on the skin (topical use) only. Do not use VTAMA cream in your eyes, mouth, or vagina.

WHAT SHOULD I TELL MY DOCTOR BEFORE USING VTAMA cream?
Before you use VTAMA cream tell your doctor about all of your medical conditions, including if you:

• Are pregnant or plan to become pregnant. It is not known if VTAMA cream will harm your unborn baby; and/or
• Are breastfeeding or plan to breastfeed. It is not known if VTAMA cream passes into your breast milk. Talk to your doctor about the best way to feed your baby during treatment with VTAMA cream.

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

HOW SHOULD I USE VTAMA cream?
• Use VTAMA cream exactly as your doctor tells you to use it.

• Apply a thin layer of VTAMA cream only to your psoriasis skin lesions one (1) time a day. Avoid applying VTAMA cream to unaffected areas of your skin.

• Wash your hands after application, unless VTAMA cream is for treatment of your hands.

• If someone else applies VTAMA cream for you, they should wash their hands after application.

WHAT ARE THE POSSIBLE SIDE EFFECTS OF VTAMA cream?
The most common side effects include: folliculitis (red raised bumps around the hair pores), nasopharyngitis (pain or swelling in the nose and throat), contact dermatitis (skin rash or irritation, including itching and redness, peeling, burning, or stinging), headache, pruritus (itching), and influenza (flu).

These are not all the possible side effects of VTAMA cream. Call your doctor for medical advice about side effects.

You are encouraged to report negative side effects of prescription drugs to the FDA at www.fda.gov/medwatch or call 1-800-FDA-1088.

HOW SHOULD I STORE VTAMA cream?
• Store VTAMA cream at room temperature, between 68°F to 77°F (20°C to 25°C).

• Do not freeze VTAMA cream.

• Protect VTAMA cream from exposure to excessive heat.

• Keep VTAMA cream and all medicines out of the reach of children.

WHAT ARE THE INGREDIENTS IN VTAMA cream?
Active ingredient: tapinarof

Inactive ingredients: benzoic acid, butylated hydroxytoluene, citric acid monohydrate, diethylene glycol monoethyl ether, edetate disodium, emulsifying wax, medium-chain triglycerides, polyoxyl 2 stearyl ether, polyoxyl 20 stearyl ether, polysorbate 80, propylene glycol, purified water, and sodium citrate dihydrate.

VTAMA is a trademark of Dermavant Sciences, GmbH or its affiliates.

Dermavant Sciences Inc., Long Beach, CA 90806 USA
Now FDA Approved

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References:
2. VTAMA (tapinarof) cream, 1%. Prescribing Information. Dermavant; 2022.
3. Strober B, Stein Gold L, Bissonnette R, et al. Tapinarof cream 1% once daily for plaque psoriasis: long-term, open-label extension study of patients (n=73)

Important Safety Information:
Indication: VTAMA® (tapinarof) cream, 1% is an aryl hydrocarbon receptor agonist indicated for the topical treatment of plaque psoriasis in adults.
Adverse Events: The most common adverse reactions (incidence ≥1%) in subjects treated with VTAMA cream were folliculitis (red raised bumps around the hair pores), nasopharyngitis (pain or swelling in the nose and throat), contact dermatitis (skin rash or irritation, including itching and redness, peeling, burning, or stinging), headache, pruritus (itching), and influenza (flu).

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See the data: VTAMA.com

VTAMA cream can give plaque psoriasis patients significantly clearer skin. So they’re free to think about...literally anything. VTAMA cream is a once-daily, non-steroidal topical for adults with plaque psoriasis.

Safe and well-tolerated even on the face, neck, intertriginous areas, inframammary areas, axillae, genitalia, and anal crux.

36% and 40% Physician Global Assessment (PGA) success rate* in two 12-week pivotal studies vs 6% and 6% for vehicle^2

A median ~4 month off-treatment effect seen in long-term, open-label extension study of patients (n=73)^2

*PGA success rate defined as PGA=0 or 1 and ≥2-grade improvement from baseline at week 12.

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