A novel treatment modality based on nanosecond pulsed electric fields (nsPEF), also referred to as Nano-Pulse Stimulation (NPS) technology, could help combat antibiotic resistance in Cutibacterium acnes and allow better penetration of the pharmacological agents used to treat acne vulgaris, according to results of a recent study published in *Bioelectrochemistry*.\(^1\)

**Antibiotic Resistance continues on page 16**

---

**Treating Skin Conditions in Asian Patients**

**Lisette Hilton | Staff Correspondent**

Given the population growth among Asian Americans, dermatologists in the United States will likely be treating more patients from this diverse cultural community. Ensuring positive outcomes starts with understanding the differences in which skin conditions most commonly affect these patients and what that means for treatment regimens, according to an expert panel presentation at the American Academy of Dermatology Virtual Meeting Experience (AAD VMX) 2021, held in April.\(^1\)

Asian Americans were the fastest-growing sector among all racial and ethnic groups in the United States between 2000 and 2019. The US Asian

**Asian Skin continues on page 50**

---

**What’s New in Photoprotection?**

**Morgan Petronelli | Associate Editor**

With summer in full swing, dermatologists are counseling patients more frequently on sun and photoprotection. This year, they have even more options to discuss, according to Henry W. Lim, MD.

Lim, a dermatologist in the department of dermatology at the Henry Ford Health System in Detroit, Michigan, spoke about new developments in photoprotection in a presentation at the American Academy of Dermatology Virtual Meeting Experience 2021 (AAD VMX) held in April.\(^2\)

**Photoprotection continues on page 37**

---

**Clinical Insights Antiaging**

What’s New in Photoprotection?
INDICATIONS AND USAGE
ZILXI (minocycline) topical foam, 15% is a tetracycline-class drug indicated for the treatment of inflammatory lesions of rosacea in adults.

Limitations of Use: This formulation of minocycline has not been evaluated in the treatment of infections. To reduce the development of drug-resistant bacteria as well as to maintain the effectiveness of other antibacterial drugs, ZILXI should be used only as indicated.

IMPORTANT SAFETY INFORMATION

Contraindications
Persons who have shown hypersensitivity to any of the tetracyclines or any other ingredient in ZILXI.

Warnings and Precautions
Flammability: The propellant in ZILXI is flammable. Instruct the patient to avoid fire, flame, and smoking during and immediately following application.

ZILXI is a topical foam. While systemic absorption of ZILXI is low, and serious adverse reactions were not seen in clinical studies, the following adverse reactions associated with oral minocycline should be considered:

INDICATIONS AND USAGE
ZILXI (minocycline) topical foam, 15% is a tetracycline-class drug indicated for the treatment of inflammatory lesions of rosacea in adults.

Limitations of Use: This formulation of minocycline has not been evaluated in the treatment of infections. To reduce the development of drug-resistant bacteria as well as to maintain the effectiveness of other antibacterial drugs, ZILXI should be used only as indicated.

IMPORTANT SAFETY INFORMATION

Contraindications
Persons who have shown hypersensitivity to any of the tetracyclines or any other ingredient in ZILXI.

Warnings and Precautions
Flammability: The propellant in ZILXI is flammable. Instruct the patient to avoid fire, flame, and smoking during and immediately following application.

ZILXI is a topical foam. While systemic absorption of ZILXI is low, and serious adverse reactions were not seen in clinical studies, the following adverse reactions associated with oral minocycline should be considered:

IMPORTANT SAFETY INFORMATION, CONTINUED

- Teratogenic effects, inhibition of bone growth & permanent tooth discoloration: Use during the second and third trimesters of pregnancy, infancy and childhood up to the age of 8 years may cause permanent discoloration of the teeth (yellow-gray-brown) and reversible inhibition of bone growth.
- Clostridioides difficile associated diarrhea (CDAD): If CDAD occurs, discontinue ZILXI.
- Hepatotoxicity & metabolic effects: If renal impairment exists or if liver injury suspected, discontinue ZILXI.
- Central nervous system effects: Patients experiencing light-headedness, dizziness or vertigo should be cautioned about driving vehicles or operating heavy machinery.
- Intracranial hypertension: Clinical manifestations include headache, blurred vision, diplopia, and vision loss. Discontinue ZILXI immediately if symptoms occur.
- Autoimmune syndromes: Symptoms may be manifested by fever, rash, arthralgia, and malaise. Discontinue ZILXI immediately if symptoms occur.
**The first time minocycline has been approved for rosacea**

**Zilxi is the first and only topical minocycline proven effective in adult patients with inflammatory lesions of rosacea**

- Evaluated in 2 large, 12-week phase 3 trials (N=1522)
- Significantly reduced inflammatory lesion count by Week 12
- Demonstrated improvement in IGA treatment success by Week 12

**Proven safe and well-tolerated on already-sensitive skin**

- The most commonly reported adverse reaction was diarrhea (1%)
- Zilxi was well-tolerated throughout the treatment period

**Delivered in a gentle, proprietary foam vehicle**

- Leverages Molecule Stabilizing Technology (MST)™ for stable topical delivery
- Contains naturally moisturizing ingredients, is surfactant-free, and does not contain drying agents, such as ethyl alcohol

**IMPORTANT SAFETY INFORMATION, CONTINUED**

**Photosensitivity**: Patients should minimize or avoid exposure to natural or artificial sunlight while using ZILXI. Advise patients to discontinue treatment with ZILXI at the first evidence of sunburn.

**Hypersensitivity reactions**: Discontinue ZILXI immediately if symptoms of anaphylaxis, serious skin reactions, erythema multiforme, and drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome occur.

**Tissue hyperpigmentation**: Discoloration of organs, including nails, bone, skin, eyes, thyroid, visceral tissue, oral cavity (teeth, mucosa, alveolar bone), sclerae and heart valves.

**Superinfection**: Overgrowth of non-susceptible organisms, including fungi if superinfection occurs, discontinue ZILXI and institute appropriate therapy.

**Adverse Reactions**

The most common adverse reaction reported during clinical trials of ZILXI was diarrhea.

IGA=Investigator’s Global Assessment.

*Co-primary endpoints at Week 12 were absolute change from baseline in inflammatory lesion count and IGA treatment success. IGA treatment success was defined as an IGA score of 0 or 1 (clear or almost clear) and at least a 2-grade improvement (decrease) from baseline. Patients were included if they had 15-75 facial lesions (papules and pustules), no more than 2 facial nodules, and an IGA score of moderate or severe (grade 3 or 4) (N=1522).†

†Zilxi 15% topical foam contains the following inactive ingredients: soybean oil, coconut oil, light mineral oil, cyclomethicone, cetostearyl alcohol, stearic acid, myristyl alcohol, hydrogenated castor oil, white wax (beeswax), stearyl alcohol, docosanol, and propellants (butane + isobutane + propane).‡


Please see Brief Summary of Prescribing Information for ZILXI on the following pages.

Zilxi is a trademark of an affiliate of VYNE Therapeutics Inc. © 2020 VYNE Therapeutics Inc. All rights reserved. COM-ZIL-US-200041 09/2020
ZILXI™ (minocycline) topical foam, 1.5%  
BRIEF SUMMARY OF FULL PRESCRIBING INFORMATION.  
PLEASE SEE FULL PRESCRIBING INFORMATION.  

INDICATION  
ZILXI is indicated for the treatment of inflammatory lesions of rosacea in adults. Limitations of Use: This formulation of minocycline has not been evaluated in the treatment of infections. To reduce the development of drug-resistant bacteria as well as to maintain the effectiveness of other antibacterial drugs, ZILXI should be used only as indicated.  

CONTRAINdications  
This drug is contraindicated in persons who have shown hypersensitivity to any of the tetracyclines or any other ingredients within ZILXI.  

WARNINGS AND PRECAUTIONS  
• Flammability: The propellant in ZILXI is flammable. Instruct the patient to avoid fire, flame, and smoking during and immediately following application. Do not puncture or incinerate the containers. Do not expose containers to heat, flame, or storage at temperatures above 120°F (49°C).  
• Teratogenic Effects: Minocycline, like other tetracycline-class drugs, may inhibit bone growth when administered orally during pregnancy. Based on animal data, when administered orally, tetracyclines cross the placenta, are found in fetal tissues, and can cause skeletal malformation and retardation of skeletal development on the developing fetus. Evidence of embryotoxicity has been noted in animals treated orally early in pregnancy.  
• Inhibition of Bone Growth: All tetracyclines form a stable calcium complex in any bone-forming tissue. A decrease in fibula growth rate has been observed in fetuses at systemic exposures of 2,000 and 1,300 times, respectively, the exposure at the MRHD based on AUC comparison). However, oral administration of minocycline administered to pregnant rats and rabbits during organogenesis induced skeletal malformations and reduced size of extremities. No effects were observed on the physical development of the developing fetus.  
• Clostridioides difficile Associated Diarrhea: Clostridioides difficile associated diarrhea (CDAD) has been reported with nearly all antibacterial agents, including oral minocycline, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C. difficile. C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxic producing strains of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents. If CDAD is suspected or confirmed, antibiotic use not directed against C. difficile may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated.  
• Hepatotoxicity: Post-marketing cases of serious liver injury, including irreversible drug-induced hepatitis and fulminant hepatic failure (sometimes fatal) have been reported with oral minocycline use.  
• Metabolic Effects: The anti-anabolic action of the tetracyclines may cause an increase in blood urea nitrogen (BUN). In patients with significantly impaired function, higher serum levels of tetracycline-class drugs may lead to azotemia, hyperphosphatemia, and acidosis. If renal impairment exists, recommended oral or parenteral doses may lead to excessive systemic accumulations of the drug and possible liver toxicity. Under such conditions, adjust the dose downward, and if therapy is prolonged, serum level determinations of the drug may be advisable.  
• Central Nervous System Effects: Central nervous system side effects including light-headedness, dizziness or vertigo have been reported with oral minocycline therapy. Patients who experience these symptoms should be cautioned about driving vehicles or using hazardous machinery while on minocycline therapy. These symptoms may disappear during therapy and may disappear when the drug is discontinued.  

• Intracranial Hypertension: Intracranial hypertension has been associated with the use of tetracycline-class drugs. Clinical manifestations of intracranial hypertension include headache, blurred vision, diplopia and vision loss; papilledema can be found on fundoscopy. Women of childbearing age who are overweight or have a history of IH are at a greater risk for developing intracranial hypertension. Patients should be questioned for visual disturbances prior to initiation of treatment with tetracyclines. Concomitant use of isoretinoin and tetracycline should be avoided because isoretinoin, a systemic retinoid, is also known to cause intracranial hypertension. Although intracranial hypertension typically resolves after discontinuation of treatment, the possibility for permanent visual loss exists. If visual disturbance occurs during treatment, prompt ophthalmologic evaluation is warranted. Because intracranial pressure can remain elevated for weeks after drug cessation, patients should be monitored until they stabilize.  
• Autoimmune Syndromes: Tetracyclines have been associated with the development of autoimmune syndromes. The long-term use of oral minocycline has been associated with drug-induced lupus-like syndrome, autoimmune hepatitis and vasculitides. Sporadic cases of serum sickness have presented shortly after oral minocycline use. Symptoms may be manifested by fever, rash, arthralgia, and malaise. In symptomatic patients, immediately discontinue the use of all tetracycline-class drugs, including ZILXI.  
• Photosensitivity: Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking oral tetracyclines; this reaction has been reported less frequently with minocycline. Although ZILXI did not induce phototoxicity or photoallergic responses in human dermal safety studies, patients should minimize or avoid exposure to natural or artificial sunlight (tanning beds or UVA/B treatment) while using minocycline. If patients need to be outdoors while using ZILXI, they should wear loose-fitting clothes that protect skin from sun exposure and discuss other sun protection measures with their physician. Advise patients to discontinue treatment with ZILXI at the first evidence of sunburn.  
• Serious Skin/Hypersensitivity Reaction: Cases of anaphylaxis, serious skin reactions (e.g. Stevens Johnson syndrome, erythema multiforme, and drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome have been reported postmarketing with oral minocycline use. DRESS syndrome consists of cutaneous reaction (such as rash or exfoliative dermatitis), eosinophilia, and one or more of the following visceral complications such as: hepatitis, pneumonitis, nephritis, myocarditis, and pericarditis. Fever and lymphadenopathy may be present. In some cases, death has been reported with oral minocycline use. If this syndrome is recognized, discontinue ZILXI immediately.  
• Tissue Hyperpigmentation: Oral tetracyclines are known to cause hyperpigmentation. Tetracycline therapy may induce hyperpigmentation in many organs, including nails, bone, skin, eyes, thyroid, visceral tissue, oral cavity (teeth, mucosa, alveolar bone), sclerae and heart valves. Skin and oral pigmentation has been reported to occur independently of time or amount of drug administration, whereas other tissue pigmentation has been reported to occur upon prolonged administration. Skin pigmentation includes diffuse pigmentation as well as pigmentation over sites of scars or injury.  
• Development of Drug-Resistant Bacteria: ZILXI has not been evaluated in the treatment of infections. Bacterial resistance to the tetracyclines may develop in patients using ZILXI, therefore, the susceptibility of bacteria associated with infection should be considered in selecting antimicrobial therapy. Because of the potential for drug-resistant bacteria to develop during the use of ZILXI, it should be used only as indicated.  
• Superinfection/Potential for Microbial Overgrowth: Use of ZILXI may result in overgrowth of non-susceptible organisms, including fungi. If superinfection occurs, discontinue ZILXI and institute appropriate therapy.  

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 three (two Phase 3 and one Phase 2) multicenter, randomized, double-blind, vehicle-controlled trials, adult subjects applied ZILXI or vehicle once daily for 12 weeks. A total of 1,087 subjects were treated with ZILXI and 591 with vehicle. The majority of subjects were White (97%) and female (70%). Approximately 67% were non-Hispanic/ Latino. The mean age was 50.0 years and ages ranged from 18 to 86 years.  
• The most common adverse reaction reported by ≥1% of subjects treated with ZILXI and more frequently than in subjects treated with vehicle was diarrhea (1% vs. 0%), respectively.
WARNINGS AND PRECAUTIONS

As to maintain the effectiveness of other antibacterial drugs, ZILXI should be

INDICATION

PLEASE SEE FULL PRESCRIBING INFORMATION.

BRIEF SUMMARY OF FULL PRESCRIBING INFORMATION.

ZILXI™ (minocycline) topical foam, 1.5%

Clostridioides difficile

the placenta, are found in fetal tissues, and can cause retardation of skeletal
discontinued. Results of animal studies indicate that oral tetracyclines cross
every 6 hours. This reaction was shown to be reversible when the drug was
in premature human infants given oral tetracycline in doses of 25 mg/kg

All tetracyclines form a stable calcium complex in
tooth development.

repeated short-term courses. Enamel hypoplasia has also been reported with
long-term oral use of the tetracycline but has been observed following
the teeth (yellow-gray-brown). This adverse reaction is more common during

Minocycline, like other tetracycline-class drugs, may

metabolic effects:

fatal) have been reported with oral minocycline use.

Anticoagulants:

Because tetracyclines have been shown to depress plasma
prothrombin activity, patients who are on anticoagulant therapy may require
download adjustment of their anticoagulant dosage.

Penicillin: Since bacteriostatic drugs may interfere with the bactericidal
action of penicillin, it is advisable to avoid giving tetracycline-class drugs in
conjunction with penicillin.

Drug/Laboratory Test Interactions: False elevations of urinary catecholamine
levels may occur due to interference with the fluorescence test.

USE IN SPECIFIC POPULATIONS

Pregnancy: Risk Summary: Available data with ZILXI use in pregnant women are insufficient to evaluate for a drug-associated risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes. Systemic absorption of ZILXI in humans is low following once daily topical administration of ZILXI under maximal clinical use conditions. Because of low systemic exposure, it is not expected that maternal use of ZILXI will result in significant fetal exposure to the drug. Tetracycline-class drugs may cause permanent discoloration of teeth and reversible inhibition of bone growth when administered orally during pregnancy. Animal reproduction studies were not conducted with ZILXI. In animal reproduction studies, oral administration of minocycline administered to pregnant rats and rabbits during organogenesis induced skeletal malformations in fetuses at systemic exposures of 2,000 and 1,300 times, respectively, the maximum recommended human dose (MRHD based on AUC comparison) of ZILXI (see Data). The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data: Animal Data: Results of animal studies indicate that tetracyclines cross the placenta, are found in fetal tissues, and can cause retardation of skeletal development of the developing fetus. Minocycline induced skeletal malformations (bent limb bones) in fetuses when orally administered to pregnant rats and rabbits during the period of organogenesis at doses of 30 mg/kg/day and 100 mg/kg/day, respectively, (2,000 and 1,300 times, respectively, the systemic exposure at the MRHD based on AUC comparison). Reduced mean fetal body weight was observed when minocycline was orally administered to pregnant rats during the period of organogenesis at a dose of 10 mg/kg/day (680 times the systemic exposure at the MRHD based on AUC comparison).

Minocycline was assessed for effects on peri- and post-natal development of rats in a study that involved oral administration to pregnant rats during the period of organogenesis through lactation, at doses of 5, 10, or 50 mg/kg/day. In this study, body weight gain was significantly reduced in pregnant females that received 50 mg/kg/day (1,700 times the systemic exposure at the MRHD based on AUC comparison). No effects of treatment on the duration of the gestation period or the number of live pups born per litter were observed. Gross external anomalies observed in F1 pups (offspring of animals that received oral minocycline) included reduced body size, improperly rotated forelimbs, and reduced size of extremities. No effects were observed on the physical development, behavior, learning ability, or reproduction of F1 pups, and there was no effect on gross appearance of F2 pups (offspring of F1 animals).

Lactation: Risk Summary: Tetracycline-class drugs, including minocycline, are present in breast milk following oral administration. It is not known whether minocycline is present in human milk after topical administration to the nursing mother. There are no data on the effects of minocycline on milk production. Because of the potential for serious adverse reactions, advise patients that breastfeeding is not recommended during treatment with ZILXI.

Pediatric Use: The safety and effectiveness of ZILXI for the treatment of inflammatory lesions of rosacea have not been evaluated in pediatric patients.

Geriatric Use: There were 278 subjects aged 65 or older in the clinical trials of ZILXI (16.6% of 1,678 subjects). No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility: In a carcinogenicity study in which minocycline hydrochloride was orally administered to male and female rats once daily for up to 104 weeks at dosages up to 200 mg/kg/day, minocycline hydrochloride was associated in both sexes with follicular cell tumors of the thyroid gland, including increased incidences of adenomas, carcinomas and the combined incidence of adenomas and carcinomas in males, and adenomas and the combined incidence of adenomas and carcinomas in females. In a carcinogenicity study in which minocycline hydrochloride was orally administered to male and female mice once daily for up to 104 weeks at dosages up to 150 mg/kg/day, exposure to minocycline hydrochloride did not result in a significantly increased incidence of neoplasms in either males or females. Minocycline was not mutagenic in vitro in a bacterial reverse mutation assay (Ames test) or CHO/HGPRT mammalian cell assay in the presence or absence of metabolic activation. Minocycline was not clastogenic in vitro using human peripheral blood lymphocytes or in vivo in a mouse micronucleus test.

Male and female reproductive performance in rats was unaffected by oral doses of minocycline of up to 300 mg/kg/day (27,500 times the systemic exposure at the MRHD based on AUC comparison). However, oral administration of 100 or 300 mg/kg/day of minocycline to male rats (10,000 or 27,500 times, respectively, the systemic exposure at the MRHD based on AUC comparison), adversely affected spermatogenesis. Effects observed at 300 mg/kg/day of oral minocycline included a reduced number of sperm cells per gram of epididymis, an apparent reduction in the percentage of sperm that were motile, and (at 100 and 300 mg/kg/day) increased numbers of morphologically abnormal sperm cells. Morphological abnormalities observed in sperm samples included absent heads, misshapen heads, and abnormal flagella.

Handling: Allow the can to warm to room temperature before first use. Shake can well before use.

Warning: Flammable. Avoid fire, flame, or smoking during and immediately following application. Contents under pressure. Do not puncture or incinerate. Do not expose to heat or temperatures above 49°C (120°F).

For more information, including the FDA-approved Prescribing Information, go to www.ZILXI.com or call 1-844-375-3673.

ZILXI is a trademark of an affiliate of VYNE Therapeutics Inc. All other trademarks are the properties of their respective owners.

© 2020 VYNE Therapeutics Inc. All rights reserved.
Clinical Insights That Expand Expertise & Advance Practice.
From the latest updates in dermatology to exclusive interviews with leading industry experts and a glimpse at what goes on behind the scenes, the staff at Dermatology Times® brings you a podcast that will explore the impact of new data and support you in implementing innovative technologies that advance your patient care and practice.

Join us under the dermatoscope for The Cutaneous Connection.

Start Listening Now
Stay relevant, stay ahead with Dermatology Times®

Follow us on our social platforms to stay connected with the latest dermatology updates.

@DermTimesNow  @DermatologyTimes  Dermatology Times
ACNE: From New Science to Family Matters

by MIKE HENNESSY SR

In this issue, Dermatology Times® highlights June as Acne Awareness Month. Our continuing coverage of the American Academy of Dermatology (AAD) Virtual Meeting Experience 2021 and recent research offer an in-depth look at the breakthroughs and best practices dermatologists can implement to improve treatment outcomes for the most common skin condition in the United States.¹

As reported in this month’s special acne supplement, the ground rules for treatment options will change when AAD releases its updated acne guidelines in 2023 or 2024.¹ (page 1, supplement). Dermatologists can expect guidance on long-standing issues from dosing and monitoring established medications to exploring new antibiotics and addressing antibiotic stewardship.²,³

In the interim, William James, MD, the Paul R. Gross Professor of Dermatology at University of Pennsylvania Perelman School of Medicine in Philadelphia, breaks down some of the hottest controversies in acne treatment, including what he sees as the underutilization of spironolactone and the overmonitoring of patients on isotretinoin, into action steps (page 4). He also includes a valuable fact check on myths reality.

A novel therapy highlighted in this month’s lead cover story points to a discovery that may help address one of the biggest hurdles in advancing acne treatment: antibiotic resistance. Acne vulgaris is becoming increasingly challenging to treat due to the dramatic rise in antimicrobial-resistance. Biofilms play a central role in failed treatments. An experimental nanosecond pulsed electric field treatment may be a game-changer in acne therapy because it can adapt to the Cutibacterium acnes biofilm to allow for better penetration of therapies.

As dermatologists are all too aware, diagnosing and managing a treatment regimen is just one aspect of caring for patients with acne—especially young adults and adolescents. What may be just an embarrassing flare before a big event or hiding a face pimple in a video close-up among some of the 85% of individuals between the ages of 12 and 24 who will experience at least minor acne,¹ can be devastating for young people suffering with moderate to severe disease, according to Hillary Baldwin, MD.²

But, as a new survey by Sun Pharma, in collaboration with the American Academy of Rosacea Society (AARS) reveals (page 10), the impact of severe acne’s effect on teens involves their families as well. Results of this online survey showed 9 in 10 U.S. parents of teenagers with severe acne are “very worried” about their child’s physical, emotional, and social wellness, as well as what impact these factors will have on family dynamics. Their list of concerns range from permanent facial scarring to guilt stemming from not having consulted a dermatologist sooner.³,⁴

Baldwin, medical director of the Acne Treatment and Research Center in Brooklyn, New York, and past president of the AARS, and mother of twins who experienced severe acne, provides insights on how to map out optimal office visits, talk with teens and parents about compliance, how to address concerns about the psychological issues that can surface—and when to call in a mental health provider. As the parents who responded to the survey found out, acne is not just the occasional blistern. In moderate to severe cases among adolescents and increasing number of adults, it can be an ongoing disruptor to quality of life. Raising awareness of the true impact of a disease that affects up to 50 million Americans annually is vital to ending the stigma connected with less than perfect skin and creating a support network for people dealing with a challenging skin condition. ◆

MIKE HENNESSY SR is CHAIRMAN and FOUNDER of DERMATOLOGY TIMES®, PARENT COMPANY, MJH LIFE SCIENCES®.

References


 mMjhlifesciences.com
WE WILL
TRANSFORM
DERMATOLOGY

WE WILL CHALLENGE THE STATUS QUO.
WE WILL DELIVER ON OUR PROMISES.

dermavant®
DERMAVANT.COM
ACNE

NOVEL THERAPY FOR ANTIBIOTIC RESISTANCE

New therapy alters the *C. acnes* biofilm for better treatment penetration. CONTINUES ON PG. 16

CLINICAL INSIGHTS

Treating Skin Conditions in Asian Patients

Fast-growing patient population poses specific skin care challenges. CONTINUES ON PG. 50

ANTIAGING

What’s New in Photoprotection?

New regulations, absorption data, environmental and health impacts. CONTINUES ON PG. 37
columns

10 I OPERATED ON THE WRONG NEVUS
Wrong-site surgeries happen but they are preventable.

12 SKIN CARE PRODUCT ALLERGENS
In-office and at-home options help patients prevent allergic reactions.

16 NOVEL THERAPY FOR ANTIBIOTIC RESISTANCE
New therapy alters the *Propionibacterium acnes* biofilm for better treatment penetration.

22 CHOOSING INTEGRATIVE AD THERAPIES
Match the right topical, oral, and manual modalities for patients.

27 DEUCRavATINIB MEETS TRIAL END POINTS
First TYK2 inhibitor is on the horizon for plaque psoriasis.

29 FDA REVIEWS APREMILAST SNDA
Patients with mild to moderate plaque psoriasis may soon have an oral therapy.

30 MENTAL HEALTH AFFECTS PSA TREATMENT
Anxiety, depression reduce likelihood of MDA.

31 BIMEKIZUMAB RECEIVES POJUFA DATE
UCB could release the drug by second half of 2021.

32 TREATING BASAL, SQUAMOUS CELL CARCINOMAS
Refine established techniques with new approaches and technology.

36 REGENERATIVE SKIN CARE REALITIES
Maximize the efficacy, safety of products on the cutting edge of skin care.

37 WHAT’S NEW IN PHOTOPRETECTION?
New regulations, absorption data, environmental and health impacts.

45 TRICHOSCOPY ADVANCES DIAGNOSIS
Technique expands into severity grading and monitoring.

46 OTC SKIN CARE ENHANCES THERAPY
Moisturizers, cleansers improve the dysfunctional skin barrier.

50 TREATING SKIN CONDITIONS IN ASIAN PATIENTS
Fast-growing patient population poses specific skin care challenges.

53 VITAMIN D DEFICIENCIES IN SKIN OF COLOR
Low levels may be linked to higher COVID-19 burden among POC.

36 REGENERATIVE SKIN CARE REALITIES
Maximize the efficacy, safety of products on the cutting edge of skin care.

37 WHAT’S NEW IN PHOTOPRETECTION?
New regulations, absorption data, environmental and health impacts.

45 TRICHOSCOPY ADVANCES DIAGNOSIS
Technique expands into severity grading and monitoring.

46 OTC SKIN CARE ENHANCES THERAPY
Moisturizers, cleansers improve the dysfunctional skin barrier.

50 TREATING SKIN CONDITIONS IN ASIAN PATIENTS
Fast-growing patient population poses specific skin care challenges.

53 VITAMIN D DEFICIENCIES IN SKIN OF COLOR
Low levels may be linked to higher COVID-19 burden among POC.
Wrong-site surgery is considered a ‘never event.’ [It] is preventable.”

I Operated on The Wrong Nevus

by DAVID J. GOLDBERG, MD, JD

Goldberg is director of Skin Laser and Surgery Specialists of New York and New Jersey, past director of Mohs and Laser Research, Icahn School of Medicine at Mount Sinai; and adjunct professor of law at Fordham University School of Law, New York, New York.

Dr Mole is a well-respected dermatologist who sees countless patients for total body examinations. He is well-known for his expertise in dermoscopy and dermatologic surgery. He holds an academic title and lectures nationally on pigmented lesions.

Mole also sees many patients on a referral basis from other dermatologists. All patients referred to him are required to bring biopsy reports. Some even come with photographs of the biopsied area. Most patients have a pretty good idea of where on their body the biopsy was taken.

Two years ago, Mole saw a patient with a biopsy-proven dysplastic nevus with severe atypia. During the initial consultation, the patient also brought a photograph of the involved area.

The patient signed consent forms during the in-person consultation. Because the patient was so anxious about the upcoming surgery, Mole suggested taking antianxiety medication prior to surgery.

On the day of surgery, Mole’s patient took a double dosage of the antianxiety medication. The patient was sleepy and confused upon entering Mole’s office. Unfortunately, it was not a good day in this practice. Mole’s certified physician assistant provided local anesthesia to the wrong site. Mole then removed a significant segment of skin from that location.

As the staff began to teach the patient appropriate wound care, the patient’s family noticed that surgery was performed on the wrong site. Needless to say, they were appalled. They never returned to the office and filed a medical malpractice lawsuit and a claim with Mole’s state board of medical examiners. Now what?

Unfortunately, wrong-site surgeries do happen. More than 2 decades ago, a world-renowned New York neurosurgeon lost his medical license for operating on the wrong side of a patient’s brain. Hospitals also have been penalized for allowing wrong-site surgeries.

Wrong-site surgery is considered a “never event.” Medicare does not pay for repeat surgery if the first one is on the wrong body part. A number of private insurance companies have followed suit.

Wrong-site surgery is preventable.

One way to decrease the likelihood of such potentially mutilating and certainly unfortunate events from happening is to get the patient more involved. Prior to surgery, explain to the patient the importance of operating on the proper side of the body. Give the patient a marker to label the spot. Direct them to initial the appropriate location of the site on the body for consent. Double check the location on the day the patient arrives for surgery.

Other steps should also be taken. Schedule a “time out” before cutting. Have more than 1 team member identify the proper spot. Verify the site with any preop biopsy report, photos, and the consent form. Most patients will appreciate the extra attention paid to this process.

Patients are sometimes unclear as to the exact location of a biopsy. In some instances, biopsies are mislabeled. There are many times when there are no photographs. However, the hallmark of medicine is to do no harm. It is a clear-cut breach in the standard of care to operate on a site when, as in this case, the potentially malignant melanoma was present elsewhere.

Once the malpractice case is filed based on the above fact pattern, most attorneys would advise Mole to settle the case out of court. Similarly, Mole needs to try to settle with the state board of medical examiners.

LIKE WHAT YOU’RE READING? SIGN UP TO RECEIVE THE E-NEWSLETTER.
DermaLight KTP Laser System

Treatment of Choice for Vascular and Pigmented Lesions

- Color Touch Screen
- Wireless Foot Pedal
- Preset Protocols
- Portable / Affordable

INCLUDES:
- Mobile Cart
- Carry Case
- Two Year Warranty

“We use our DermaLight KTP Laser every day. It is very effective for treating vascular and pigmented lesions. We are very satisfied with the affordability, reliability and ease of use of this system.”

~ Dina N. Anderson, MD
Dermatologist, Clinical Instructor
Mount Sinai, New York City

For questions or to schedule a demo contact:

NewSurg
phone: (215) 570-4327
sales@newsurg.com | www.newsurg.com

MADE IN USA

FDA Approved
The Mystery of the Skin Care Product Allergy

by ZOE DIANA DRAELOS, MD

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

How do manufacturers test cosmetic products for irritant and allergic contact dermatitis?

Most products consumers buy will have been tested by the manufacturer for possible allergy and irritancy. The Human Repeat Insult Patch Test (HRIPT) is the industry standard for new product testing.

If testing is done, then how do problematic products enter the marketplace? The answer lies in understanding how HRIPT is conducted. A breathable patch with the product under review is placed on a study participant’s upper back and changed every Monday, Wednesday, and Friday for 3 weeks. The participant is then given a rest period and rechallenged. Usually, a negative control patch that contains nothing and a positive control patch that contains sodium lauryl sulfate also are placed on the participant’s upper back.

Unfortunately, this type of testing has limitations. For example, the upper back has some of the thickest and most resilient skin on the body. The skin on the back may not react, but the skin around the eyes can demonstrate irritancy. It is not possible to do patch testing around the eye, so the back serves as surrogate.

Another limitation of HRIPT is the panel selection. Over time, most contract research centers develop panels of participants with robust skin. As you might imagine, a participant who experienced a poor outcome probably would not volunteer again. Further, many of the HRIPT centers are located close to college campuses and use young individuals with healthy skin. All these factors limit the sensitivity of HRIPT and may not uncover issues that arise in the general population.

How should patients screen their new cosmetic purchases to prevent adverse reactions?

Simple, at-home testing can prevent overall facial irritation problems with new cosmetics. It is easy to teach patients with sensitive skin how to conduct the testing. Instruct the patient to apply a small amount of the cosmetic in the antecubital fossa for 7 nights in a row before going to bed. If no problems arise, the product then can be applied to the posterior ear for 7 nights in a row before going to bed. If there are still no problems, the patient may apply the product to their face, avoiding the eyes, for 7 nights. If no irritation or allergy occurs, the product can be applied to the entire face.

If problems arise, advise the patient to have more formal patch testing done under the dermatologist’s direction. This testing method only examines final formulations and will not detect specific ingredient allergies.

What ingredients in cosmetic products are most likely to produce irritant contact dermatitis?

Emulsifiers are the most irritating substances placed in cosmetic products. They are found in all formulations that contain hydrophilic (water loving) and hydrophobic (water hating) ingredients. Most cosmetic products are oil-in-water emulsions in which the oil is emulsified into the higher concentration dominant water phase. These emulsions tend to leave less residue on the skin and consequently dry more quickly as the water evaporates.

Emulsifiers are basically detergents that keep the oil and water from separating. All oil-in-water emulsion moisturizers contain small amounts of detergents that also emulsify the intercellular lipids and sebum. This is where the barrier breakdown occurs and the induction of irritation begins. Fortunately, the concentration of the emulsifier is usually small and carefully selected to avoid this problem. For people with extremely sensitive skin, it is best to recommend a moisturizer that is free of emulsifier. These would be ointment formulations that do not contain water. Although they are not as aesthetically pleasing as oil-in-water emulsion lotions, they will not incite irritant contact dermatitis.

The second most common problematic ingredient in moisturizers is the preservative. All water-containing moisturizers must contain a preservative because water supports microbial growth. Preservatives are not skin-friendly ingredients; their sole role is to kill bacteria. Ointments that do not contain water do not need to have high preservative concentrations and may need only antioxidants to prevent oxidation of the lipids resulting in rancidity. Here again, an ointment is the best choice to avoid problems in patients with extremely sensitive skin.
Five Financial Ratios to Watch to Track Your Practice’s Financial Health

BY DAVID NORRIS, MD | Staff Correspondent

As physicians we are quite familiar with methods in discovering the health of our patients. We use measures such as HDL:LDL ratio, waist-to-height ratio, waist-to-hip ratio and many other measurements to determine the health of our patients. In fact, we’re pretty good at it. We can even use this data to predict what problems the patients will face and even how long they might live.

Did you know there are similar ratios and methods that accountants and business leaders use to determine the financial health of a company? These ratios can tell you the financial health of your practice. I’ve listed the top 5 financial metrics that every physician should know and use every month.

These are just a few of the financial ratios physicians can perform using income statements and balance sheets provided to them by their accountants and office managers. These ratios will help you determine the level of financial stability of your practice and help you make better decisions for your future. Financial health is hard work. Just like we ask our patients to keep track of their diet and exercise activity, we should also closely monitor the financial health of our practices. We must be diligent to actively manage our business.

1 The Current Ratio
The current ratio is a solvency ratio called the current ratio. The current ratio is a simple calculation to perform but a few definitions are needed. When we say “current” in a financial report, we are indicating that we can either convert the asset into cash within a 1-year period or the liability is due within 1 year. Current assets are assets we can convert to cash within 1 year. Current assets are cash, cash equivalents, accounts receivable (A/R), bad debt allowance and any inventory we have on hand. Current liabilities are bills that must be paid within 1 year. Current liabilities are all notes and accounts payable due within 1 year, interest payable, wages payable and income taxes payable.

The current ratio is an indication of the firm’s ability to pay back its short-term liabilities. To obtain this ratio, we take all of the current assets and divide them by the current liabilities. If the current ratio is less than 1, this indicates the company has more debt due within 1 year than it has assets it can use to pay those debts. This is a critical ratio for any company, particularly in medical practice. If your current ratio is less than 1, you need to seriously consider how your practice will survive should something happen to your cash flow.

Another ratio similar to the current ratio is the quick ratio or acid test. This is the same as a current ratio except that inventories are not included in the numerator. It looks at the most liquid assets and compares them against the current liabilities. If your practice does not hold inventory, then your current ratio is a quick ratio or acid test.

2 Days in Accounts Receivable
Days in accounts receivable (A/R) measure a company’s ability to convert receivables into cash. A low days-in-A/R number indicates that the practice can quickly collect on its debts.

This ratio varies from industry to industry. The important thing to remember is that a low number is better. Unfortunately, if you have a low number of days in A/R, it may indicate patients are not paying their bills. This is a sign that the practice is not enforcing the rules of the practice. You must enforce the rules of the practice and the billing process. It’s important to make payments a priority and not an option. It’s also important to communicate to patients the importance of paying their bills on time. This ratio is a great indicator of how the practice is doing with its billing process.

“These ratios will help you determine the level of financial stability of your practice and help you make better decisions for your future.”

David Norris, MD, MBA

MEDICAL WORLD NEWS® CONTINUES ON PAGE 14
Operating Margin

Operating margin is a measure of what proportion of the company’s revenue is left over after paying the variable costs of production of the services or goods. These costs include wages, raw materials, etc. It is important to have a healthy operating margin so that the company has enough cash to pay its fixed costs. This is also known as an operating profit margin for the net profit margin. It is calculated by dividing the operating income by the net revenue.

Working Capital

Capital measures the practice’s abilities to pay its bills on time. It is another liquidity or solvency ratio. It is calculated by subtracting the current liabilities from the current assets. The larger the number, the larger the working capital and the larger the cushion the firm has should an unexpected downturn in revenue occur.

Days in Accounts Payable

Like days in A/R, days in accounts payable (A/P) measures how long it takes for the practice to pay its bills. This is an important ratio because it can be a lagging indicator of the financial health and solvency of the practice. Also, it can be a good indicator of how well the practice is using its cash. Paying bills too soon might put the practice in jeopardy of being short of funds, and paying bills too late puts the practice in jeopardy of having to pay a penalty. Days in A/P is another liquidity or solvency ratio. It is calculated by subtracting the number of days it takes to pay bills to the firm’s cash cycle and then multiplying by 365.

Days in Accounts Receivable

Like days in A/R, days in accounts receivable (A/R) measures how long it takes for the practice to collect on its receivables. This ratio is also important because it can be a leading indicator of the financial health and solvency of the practice. If the days in A/R ratio is increasing, it could mean that the practice is not collecting on its receivables as quickly as it should be. Days in A/R is another liquidity or solvency ratio. It is calculated by subtracting the number of days it takes to collect on a receivable from the revenue and then multiplying by 365.

Capital

Capital measures the practice’s abilities to pay its bills on time. It is another liquidity or solvency ratio. It is calculated by subtracting the current liabilities from the current assets. The larger the number, the larger the working capital and the larger the cushion the firm has should an unexpected downturn in revenue occur.

Months in Current Liabilities

Months in Current Liabilities is another liquidity or solvency ratio. It is calculated by dividing the current liabilities by the amount of cash on hand. The larger the number, the larger the working capital and the larger the cushion the firm has should an unexpected downturn in revenue occur.

Working Capital

Capital measures the practice’s abilities to pay its bills on time. It is another liquidity or solvency ratio. It is calculated by subtracting the current liabilities from the current assets. The larger the number, the larger the working capital and the larger the cushion the firm has should an unexpected downturn in revenue occur.
#1 Dermatology Specific Billing Service

TOP RATED SERVICE

- DERMATOLOGY-SPECIFIC ONLY
- US BASED - NO OUTSOURCING
- OVER 20 YEAR TRACK RECORD
- BILLING NATIONALLY
- LIVE PATIENT CALLS BY FRIENDLY VOICE
- COLLECTION RATIO BETWEEN 97-99%
- OVER 90 DAYS $ LESS THAN 10%

COMPETITORS

<table>
<thead>
<tr>
<th></th>
<th>COMPETITORS</th>
</tr>
</thead>
<tbody>
<tr>
<td>MOST AREN'T</td>
<td>MOST AREN'T</td>
</tr>
<tr>
<td>MOST OFFSHORE</td>
<td>MOST OFFSHORE</td>
</tr>
<tr>
<td>MOST AREN'T</td>
<td>MOST AREN'T</td>
</tr>
<tr>
<td>AUTOMATED</td>
<td>AUTOMATED</td>
</tr>
<tr>
<td>CAN'T MATCH</td>
<td>CAN'T MATCH</td>
</tr>
<tr>
<td>CAN'T MATCH</td>
<td>CAN'T MATCH</td>
</tr>
</tbody>
</table>

WE DO BILLING BETTER

We Are the Top Rated Dermatology Billing Revenue Cycle Management Company Owned and Operated by Inga Ellzey Since 1996

We have an unrivaled reputation in the industry for service, professionalism, knowledge, and unsurpassed outcomes assuring optimal income for providers for the services they render.  What more could you ask for?

www.dermatologybilling.com

1-800-318-3271
Quick Takes

Cutibacterium acnes and the biofilm it forms can cause standard treatment failure used for acne vulgaris. Novel technology can sensitize or kill off targeted bacteria, giving beneficial commensal bacteria on the skin a chance for regrowth. The nsPEF technique ablated some but not all C. acnes bacteria, making it immediately useful as an adjunctive rather than a stand-alone treatment modality.

Antibiotic Resistance from Page 1

This energy modality applies ultrafast, non-thermal energy pulses, with pulse durations from milliseconds up to a millisecond of a second. nsPEF energy pulses enter cells and are believed to alter the function of internal cellular organelles, including the mitochondria and endoplasmic reticulum, without disrupting the integrity of the outer cell membrane or extracellular tissue, like the dermal tissue.

This unique mechanism of action initiates a cascade of events within the affected cells, leading to regulated cell death (RCD). Histologic analysis demonstrates that NPS technology non-thermally stimulates a natural cell death that results in a less traumatic inflammatory response than thermal technologies like extreme heat or extreme cold.

C. acnes is an anaerobic bacteria that normally occupies the hair follicles and sebaceous glands. nsPEF has been shown to be highly effective and well tolerated in slowly eliminating targeted sebaceous glands. However, failure to kill 100% of the targeted bacteria may position the potential near-term use of this technique as an adjunctive therapy more than as a stand-alone one, concluded the study investigators.

The increasing prevalence of antimicrobial resistance has emerged as a major concern in dermatology and the medical community at large. Physicians and researchers point to a number of reasons for this development, including different antibiotic prescribing habits, concomitant use of topical agents (eg, retinoids, and benzoyl peroxide), varying methods of bacteria sampling, and different C. acnes populations.

The investigators also explored an additional challenge: the ability of C. acnes to adhere to surfaces, including human skin, in structured microbial communities known as biofilms. The cells in biofilms are more resilient to antimicrobial stresses than are free-living or planktonic cells.

As a result, acne therapeutic options such as topical or systemic antibacterial treatments often show incomplete responses, according to the investigators. In fact, they pointed to study results indicating that 94% of acne patients have C. acnes strains on their skin that are resistant to at least 1 antibiotic.

Current antimicrobial resistance reduction strategies include avoidance of antibiotic monotherapy, combination treatment with topical modalities, and limiting the duration of oral antibiotic use.

Destroying the biofilm is an interesting treatment approach and could represent a potential paradigm shift in acne treatment and management, study coauthor Erin B. Purcell, PhD, told Dermatology Times. Purcell is an assistant professor in the Department of Chemistry & Biochemistry at Old Dominion University in Norfolk, Virginia.

"Any treatment modality that could either, [1], sensitize cells and make them more vulnerable to existing antibiotics, or [2, subject them to] a physical killing method to which [they] can't develop genetic resistance, is really exciting," she said. "[nsPEF] is a different kind of therapeutic tool and helps us expand our treatment options beyond the antibiotics that we are practically running out of. An exciting aspect of this treatment modality is that it is a physical killing method that does not rely on antibiotics. As such, it cannot contribute to the growing problem of antibiotic resistance seen today."

In the study, researchers employed an investigatory prototype system (Pulse Biosciences) that utilizes the application of nsPEF, a new promising cell stimulation technology, to inactivate C. acnes. They cultured a series of C. acnes bacteria in a standard fashion, then treated them with the nsPEF device using a parameter range that included 250 to 2000 pulses, 280 nanosecond pulses, 28 kV/cm, 5 Hz; 0.5 to 4 kJ/ml.

Compared with conventional pulsed electric field technologies used to inactivate microorganisms, nsPEF utilizes much shorter pulses to cause a structural disorganization of the cell wall and partial destruction of the spore coat architecture, impacting bacterial cell viability, says Claudia Muratori, PhD, the corresponding author.

Results showed that all tested nsPEF doses failed to inactivate planktonic C. acnes. However, pretreatment with lysozyme (LY)—a naturally occurring cell-wall–weakening enzyme found in body secretions such as tears, saliva, and milk—increased C. acnes’ vulnerability to nsPEF treatment.

“Our results reveal for the first time the synergistic effect between LY and nsPEF at killing Gram-positive bacteria,” wrote investigators.

The researchers found that when C. acnes was growing in a biofilm, it appeared to become more sensitized to nsPEF-induced stress. The bacteria’s biofilm-derived cells demonstrated increased cell death after nsPEF treatments; the treatments did not affect planktonic cells. The biofilm inactivation by nsPEF was confirmed by treating intact biofilms grown on glass coverslips with an indium oxide conductive layer.

When bacteria contacts surfaces and forms biofilms, they are protected from sources of stress, including antibiotics, according to Purcell. Typically, the dose of antibiotics or other stress-causing agent that is needed to kill bacteria is higher if the bacteria are in biofilms than if they are in a free-moving individual form, she added.
“An exciting aspect of this treatment modality is that it is a physical killing method that does not rely on antibiotics. As such, it cannot contribute to the growing problem of antibiotic resistance seen today.”

Erin B. Purcell, PhD, assistant professor, Department of Chemistry & Biochemistry at Old Dominion University in Norfolk, Virginia

Disclosures
Pulse Biosciences funded the study. The authors reported no relevant or financial disclosures.

References
MINOCYCLINE IS AT YOUR PATIENT’S FINGERTIPS.

Visit AmzeeqHCP.com to learn more.

INDICATIONS AND USAGE
AMZEEQ is indicated for the treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris in adults and pediatric patients 9 years of age and older.

Limitations of Use: This formulation of minocycline has not been evaluated in the treatment of infections. To reduce the development of drug-resistant bacteria as well as to maintain the effectiveness of other antibacterial drugs, AMZEEQ should be used only as indicated.

IMPORTANT SAFETY INFORMATION
Contraindications: Persons who have shown hypersensitivity to any of the tetracyclines or any other ingredient in AMZEEQ.

Warnings and Precautions
Flammability: The propellant in AMZEEQ is flammable. Instruct the patient to avoid fire, flame, and smoking during and immediately following application.

AMZEEQ is a topical foam. While systemic absorption of AMZEEQ is low, and serious adverse reactions were not seen in clinical studies, the following adverse reactions associated with oral minocycline should be considered:

IMPORTANT SAFETY INFORMATION (cont.)
- Teratogenic effects, inhibition of bone growth & permanent tooth discoloration: Use during the second and third trimesters of pregnancy, infancy and childhood up to the age of 8 years may cause permanent discoloration of the teeth (yellow-gray-brown) and reversible inhibition of bone growth.
- Clostridium difficile associated diarrhea (CDAD): If CDAD occurs, discontinue AMZEEQ.
- Hepatotoxicity & metabolic effects: If renal impairment exists or if liver injury suspected, discontinue AMZEEQ.
- Central nervous system effects: Patients experiencing light-headedness, dizziness or vertigo should be cautioned about driving vehicles or operating heavy machinery.
- Intracranial hypertension: Clinical manifestations include headache, blurred vision, diplopia, and vision loss. Discontinue AMZEEQ immediately if symptoms occur.
- Autoimmune syndromes: Symptoms may be manifested by fever, rash, arthralgia, and malaise. Discontinue AMZEEQ immediately if symptoms occur.
THE FIRST AND ONLY TOPICAL MINOCYCLINE FOR ACNE

FOR YOUR PATIENTS WITH INFLAMMATORY LESIONS OF MODERATE TO SEVERE ACNE VULGARIS.

The minocycline you know and trust.¹
• In large, 12-week trials, Amzeeq demonstrated an improvement vs. vehicle foam in both inflammatory lesions and IGA scores.¹⁴
• The most commonly reported adverse reaction was headache (3%).¹²

The tolerability of a gentle foam.¹
• Proprietary oil-based foam vehicle contains naturally moisturizing ingredients without drying agents like ethyl alcohol.¹³†

The innovation you’ve been waiting for.
• Molecule Stabilizing Technology (MST™) enables minocycline to be placed into a lipophilic vehicle for stable topical delivery.⁴⁵

IMPORTANT SAFETY INFORMATION (cont.)
• Photosensitivity: Patients should minimize or avoid exposure to natural or artificial sunlight while using AMZEEQ. Advise patients to discontinue treatment with AMZEEQ at the first evidence of sunburn.
• Hypersensitivity reactions: Discontinue AMZEEQ immediately if symptoms of anaphylaxis, serious skin reactions, erythema multiforme, and drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome occur.
• Tissue hyperpigmentation: Discoloration of organs, including nails, bone, skin, eyes, thyroid, visceral tissue, oral cavity (teeth, mucosa, alveolar bone), sclerae and heart valves.
• Superinfection: Overgrowth of non-susceptible organisms, including fungi. If superinfection occurs, discontinue AMZEEQ and institute appropriate therapy.

Adverse Reactions: The most common adverse reaction reported during clinical trials of AMZEEQ was headache.

* Coprimary endpoints at Week 12 were: Absolute change from baseline in inflammatory lesion count and IGA endpoint success. IGA success was defined as an IGA score of 0 or 1 (clear or almost clear), and at least a 2-grade improvement (decrease). IGA = Investigator’s Global Assessment. 248 patients were included if they had 20–50 inflammatory lesions (papules, pustules, nodules) and 25–100 non-inflammatory lesions (open, closed comedones) and an IGA score on a 6-point scale of moderate or severe (grades 3 or 4).
† Amzeeq 4% topical foam contains the following inactive ingredients: soybean oil, coconut oil, light mineral oil, cyclomethicone, cetostearyl alcohol, stearyl, acid, myristyl alcohol, hydrogenated castor oil, white wax (beeswax), stearyl alcohol, docosanol, and propellants (butane + isobutane + propane).


See Brief Summary of Prescribing Information for AMZEEQ on following pages.

Amzeeq is a registered trademark of an affiliate of VYNE Therapeutics Inc.
© 2020 VYNE Therapeutics Inc. All rights reserved.
COM-AMZ-US-200216 11/2020
AMZEEQ® (minocycline) topical foam, 4%
BRIEF SUMMARY OF FULL PRESCRIBING INFORMATION. PLEASE SEE FULL PRESCRIBING INFORMATION.

INDICATION
AMZEEQ is indicated for the topical treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris in adults and pediatric patients 9 years of age and older.

Limitations of Use: This formulation of minocycline has not been evaluated in the treatment of infections. To reduce the development of drug-resistant bacteria as well as to maintain the effectiveness of other antibacterial drugs, AMZEEQ should be used only as indicated.

CONTRAINDICATIONS
This drug is contraindicated in persons who have shown hypersensitivity to any of the tetracyclines or any other ingredients within AMZEEQ.

WARNINGS AND PRECAUTIONS

• Flammability: The propellant in AMZEEQ is flammable. Instruct the patient to avoid fire, flame, and smoking during and immediately following application. Do not puncture and/or incinerate the containers. Do not expose containers to heat and/or store at temperatures above 120°F (49°C).

• Teratogenic Effects: Minocycline, like other tetracycline-class drugs, may inhibit bone growth when administered orally during pregnancy. Based on animal data, when administered orally, tetracyclines cross the placenta, are found in fetal tissues, and can cause skeletal malformation and retardation of skeletal development on the developing fetus.

• Tooth Discoloration: The use of tetracycline class drugs orally during tooth development (second and third trimesters of pregnancy, infancy, and childhood up to the age of 8 years) may cause permanent discoloration of the teeth (yellow-gray-brown). This adverse reaction is more common during long-term oral use of the tetracycline but has been observed following repeated short-term courses. Enamel hypoplasia has also been reported with oral tetracycline drugs. Use of tetracyclines is not recommended during tooth development. The safety and effectiveness of AMZEEQ have not been established in pediatric patients less than 9 years of age.

• Inhibition of Bone Growth: All tetracyclines form a stable calcium complex in any bone-forming tissue. A decrease in fibula growth rate has been observed in premature human infants given oral tetracycline in doses of 25 mg/kg every 6 hours. This reaction was shown to be reversible when the drug was discontinued. The safety and effectiveness of AMZEEQ have not been established in patients less than 9 years of age. Results of animal studies indicate that oral tetracyclines cross the placenta, are found in fetal tissues, and can cause retardation of skeletal development on the developing fetus. Evidence of embryotoxicity has been noted in animals treated orally early in pregnancy.

• Closstridium difficile associated Diarrhea: Closstridium difficile associated diarrhea (CDAD) has been reported with nearly all antibacterial agents, including oral minocycline, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the intestine. When antibacterial treatment is not absolutely necessary, consider discontinuing such treatment.

• Hepatotoxicity: Post-marketing cases of serious liver injury, including irreversible drug-induced hepatitis and fulminant hepatic failure (sometimes fatal) have been reported with oral minocycline use in the treatment of acne.

• Metabolic Effects: The anti-anabolic action of the tetracyclines may cause an increase in blood urea nitrogen (BUN). In patients with significantly impaired function, higher serum levels of tetracycline-class drugs may lead to azotemia, hyperphosphatemia, and acidosis. If renal impairment exists, recommended dosage should be administered. Consult the physician for further information.

• Central Nervous System Effects: Central nervous system side effects including light-headedness, dizziness or vertigo have been reported with oral minocycline therapy. Patients who experience these symptoms should be cautioned about driving vehicles or using hazardous machinery while on minocycline therapy. These symptoms may disappear during therapy and may disappear when the drug is discontinued.

• Intracranial Hypertension: Intracranial hypertension has been associated with the use of tetracycline-class drugs. Clinical manifestations of intracranial hypertension include headache, blurred vision, diplopia and vision loss; papilledema can be found on fundoscopy. Women of childbearing age who are overweight or have a history of HH are at a greater risk for developing intracranial hypertension. Patients should be questioned for visual disturbances prior to initiation of treatment with tetracyclines. Concurrent use of isotretinoin and tetracycline should be avoided because isotretinoin, a systemic retinoid, is also known to cause intracranial hypertension. Although intracranial hypertension typically resolves after discontinuation of treatment, the possibility for permanent visual loss exists. If intracranial hypertension occurs during treatment, prompt ophthalmologic evaluation is warranted. Because intracranial pressure can remain elevated for weeks after drug cessation, patients should be monitored until they stabilize.

• Autoimmune Syndromes: Tetracyclines have been associated with the development of autoimmune syndromes. The long-term use of oral minocycline in the treatment of acne has been associated with drug-induced lupus-like syndrome, autoimmune hepatitis and vasculitis. Sporadic cases of serum sickness have been presented shortly after oral minocycline use. Symptoms may be manifested by fever, rash, arthralgia, and malaise. In symptomatic patients, immediately discontinue the use of all tetracycline-class drugs, including AMZEEQ.

• Photosensitivity: Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking oral tetracyclines; this reaction has been reported less frequently with minocycline. Although AMZEEQ did not induce photosensitivity or phototoxic responses in human dermal safety studies, patients should minimize or avoid exposure to natural or artificial sunlight (tanning beds or UV/B treatment) while using minocycline. If patients need to be outdoors while using AMZEEQ, they should wear loose-fitting clothes that protect skin from sun exposure and discuss other sun protection measures with their physician. Advise patients to discontinue treatment with AMZEEQ at the first evidence of sunburn.

• Serious Skin/Hypersensitivity Reaction: Cases of anaphylaxis, serious skin reactions (e.g. Stevens Johnson syndrome), erythema multiforme, and drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome has been reported postmarketing with oral minocycline use in patients with acne. DRESS syndrome consists of cutaneous reaction (such as rash or exfoliative dermatitis), eosinophilia, and one or more of the following visceral complications: hepatosplenomegaly, nephritis, myocarditis, and pericarditis. Fever and lymphadenopathy may be present. In some cases, death has been reported with oral minocycline use. If this syndrome is recognized, discontinue AMZEEQ immediately.

• Tissue Hyperpigmentation: Oral tetracyclines are known to cause hyperpigmentation. Tetracycline therapy may induce hyperpigmentation in many organs, including nails, bone, skin, eyes, thyroid, visceral tissue, oral cavity (teeth, mucosa, alveolar bone), sclera and heart valves. Skin and oral pigmentation has been reported to occur independently of time or amount of drug administration, whereas other tissue pigmentation has been reported to occur upon prolonged administration. Skin pigmentation includes diffuse pigmentation as well as pigmentation over sites of scars or injury.

• Development of Drug-Resistant Bacteria: AMZEEQ has not been evaluated in the treatment of infections. Bacterial resistance to the tetracyclines may develop in patients using AMZEEQ; therefore, the susceptibility of bacteria associated with infection should be considered in selecting antimicrobial therapy. Because of the potential for drug-resistant bacteria to develop during the use of AMZEEQ, this drug should be used only as indicated.

• Superinfection/Potential for Microbial Overgrowth: Use of AMZEEQ may result in overgrowth of non-susceptible organisms, including fungi. If superinfection occurs, discontinue AMZEEQ and institute appropriate therapy.

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 3 randomized, double-blind, vehicle-controlled trials, subjects age 9 years and older applied AMZEEQ or vehicle once daily for 12 weeks. A total of 1,356 subjects were treated with AMZEEQ and 1,059 with vehicle. The majority of subjects were White (74%) and female (60%). Approximately 34% were Hispanic/Latino and 49% were younger than 18 years of age.

• The most common adverse reaction reported by ≥1% of subjects treated with AMZEEQ and more frequently than in subjects treated with vehicle was
headache, which was reported in 3% of subjects treated with AMZEEQ and 2% of subjects treated with vehicle. Local tolerability evaluations were conducted at each study visit in the clinical trial by assessment of erythema, dryness, hyperpigmentation, skin peeling and itching. The active assessment of the signs and symptoms of local facial tolerability at Week 12 in subjects treated with AMZEEQ were as follows (mild, moderate, severe): erythema (14.2%, 1.5%, 0%), dryness (6.8%, 0.6%, 0%), hyperpigmentation (12.4%, 2.6%, 0.1%), skin peeling (3.2%, 0.2%, 0%), and itching (5.1%, 0.8%, 0.1%). Hyperpigmentation was most frequently assessed as characteristic of inflammatory and post-inflammatory changes associated with acne. Local tolerability signs and symptoms occurred in similar frequency and severity as subjects treated with the vehicle component of AMZEEQ. In a 40-week open-label extension safety study (for a total of up to 52 weeks of treatment), frequency of several local tolerability signs and symptoms at Week 52 were comparable to those reported at Week 12.

DRUG INTERACTIONS
- **Anticoagulants:** Because tetracyclines have been shown to depress plasma prothrombin activity, patients who are on anticoagulant therapy may require downward adjustment of their anticoagulant dosage.
- **Penicillin:** Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, it is advisable to avoid giving tetracycline-class drugs in conjunction with penicillin.
- **Drug/Laboratory Test Interactions:** False elevations of urinary catecholamine levels may occur due to interference with the fluorescence test.

USE IN SPECIFIC POPULATIONS
- **Pregnancy:** Risk Summary: Available data with AMZEEQ use in pregnant women are insufficient to evaluate for a drug-associated risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes. Systemic absorption of AMZEEQ in humans is low following once daily topical administration of AMZEEQ for 21 days. Because of low systemic exposure, it is not expected that the maternal use of AMZEEQ will result in significant fetal exposure to the drug. Tetracycline-class drugs may cause permanent discoloration of teeth and reversible inhibition of bone growth when administered orally during pregnancy. Animal reproduction studies were not conducted with AMZEEQ. In animal reproduction studies, oral administration of minocycline does not cause adverse effects to pregnant rats and rabbits during the period of organogenesis induced skeletal malformations in fetuses at systemic exposures of 750 and 500 times, respectively, the maximum recommended human dose (MRHD, based on AUC comparison) of AMZEEQ (see Data). The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2.4% and 15-20%, respectively.
- **Data (Animal Data):** Results of animal studies indicate that tetracyclines cross the placenta, are found in fetal tissues, and can cause retardation of skeletal development of the developing fetus. Minocycline induced skeletal malformations (bent limb bones) in fetuses when orally administered to pregnant rats and rabbits during the period of organogenesis at doses of 30 mg/kg/day and 100 mg/kg/day, respectively, (750 and 500 times, respectively, the systemic exposure at the MRHD based on AUC comparison). Reduced mean fetal body weight was observed when minocycline was orally administered to pregnant rats during the period of organogenesis at a dose of 10 mg/kg/day (250 times the systemic exposure at the MRHD based on AUC comparison).
- **Minocycline was assessed for effects on peri- and post-natal development of rats in a study that involved oral administration to pregnant rats during the period of organogenesis through lactation, at doses of 5, 10, or 50 mg/kg/day. In this study, body weight gain was significantly reduced in pregnant females that received 50 mg/kg/day (650 times the systemic exposure at the MRHD based on AUC comparison). No effects of treatment on the duration of the gestation period or the number of live pups born per litter were observed. Gross external anomalies observed in F1 pups (offspring of animals that received oral minocycline) included reduced body size, improperly rotated forelimbs, and reduced size of extremities. No effects were observed on the physical development, behavior, learning ability, or reproduction of F1 pups, and there was no effect on gross appearance of F2 pups (offspring of F1 animals).
- **Lactation:** Risk Summary: Tetracycline-class drugs, including minocycline, are present in breast milk following oral administration. It is not known whether minocycline is present in human milk after topical administration to the nursing mother. There are no data on the effects of minocycline on milk production. Because of the potential for serious adverse reactions, advise patients that breastfeeding is not recommended during treatment with AMZEEQ.
- **Pediatric Use:** The safety and effectiveness of AMZEEQ have been established in pediatric patients 9 years of age and older for the treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris. Use of AMZEEQ for this indication is supported by three adequate and well controlled 12-week trials in patients 9 years of age and older; two of the trials included a 40-week open-label extension. Additional data was obtained from a 10-week open-label safety and pharmacokinetics study conducted in 20 patients 10 years to less than 17 years of age with acne vulgaris. A total of 686 subjects 9 years of age and older received AMZEEQ in these clinical trials. Safety and effectiveness for this indication have not been established in pediatric patients less than 9 years of age. The use of oral tetracycline drugs during tooth development below the age of 8 years may cause permanent discoloration of the teeth (yellow-gray-brown) and inhibition of bone growth.
- **Geriatric Use:** Clinical studies of AMZEEQ did not include sufficient numbers of subjects aged 65 years and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

NONCLINICAL TOXICOLOGY
- **Carcinogenesis, Mutagenesis, Impairment of Fertility:** In a carcinogenicity study in which minocycline hydrochloride was orally administered to male and female rats once daily for up to 104 weeks at dosages up to 200 mg/kg/day, minocycline hydrochloride was associated in both sexes with follicular cell tumors of the thyroid gland, including increased incidences of adenomas, carcinomas and the combined incidence of adenomas and carcinomas in males, and adenomas and the combined incidence of adenomas and carcinomas in females. In a carcinogenicity study in which minocycline hydrochloride was orally administered to male and female mice once daily for up to 104 weeks at dosages up to 150 mg/kg/day, exposure to minocycline hydrochloride did not result in a significantly increased incidence of neoplasms in either males or females. Minocycline was not mutagenic in vitro in a bacterial reverse mutation assay (Ames test) or CHO/HGPR mammalian cell assay in the presence or absence of metabolic activation. Minocycline was not clastogenic in vitro using human peripheral blood lymphocytes or in vivo in a mouse micronucleus test.
- **Male and female reproductive performance in rats was unaffected by oral doses of minocycline of up to 300 mg/kg/day (10,000 times the systemic exposure at the MRHD based on AUC comparison). However, oral administration of 100 or 300 mg/kg/day of minocycline to male rats (3,800 or 10,000 times, respectively, the systemic exposure at the MRHD based on AUC comparison), adversely affected spermatogenesis. Effects observed at 300 mg/kg/day of oral minocycline included a reduced number of sperm cells per gram of epididymis, an apparent reduction in the percentage of sperm that were motile, and (at 100 and 300 mg/kg/day) increased numbers of morphologically abnormal sperm cells. Morphological abnormalities observed in sperm samples included absent heads, misshapen heads, and abnormal flagella.
- **HANDLING:** Allow the can to warm to room temperature before first use. Shake well before use.
- **WARNING:** Flammable. Avoid fire, flame, or smoking during and immediately following application. Contents under pressure. Do not puncture or incinerate. Do not expose to heat or temperatures above 49°C (120°F).

For more information, including the FDA-approved Prescribing Information, go to www.amzeeq.com or call 1-844-375-3673.

AMZEEQ is a registered trademark of an affiliate of VYNE Therapeutics Inc. All other trademarks are the properties of their respective owners.

©2020 VYNE Therapeutics Inc. All rights reserved.
Nasal Papules Linked to Acne

Lesions are most common in Hispanic males.

MARY SCOVIAK | Managing Editor

Acne is a common disease that affects nearly 50 million Americans each year.1 What’s not as well known is that nasal papules may be 1 of its sequelae. According to the authors of a recent single site case series,2 flesh-colored nasal papules are likely to be a sequela of acne, however the authors found them mentioned only twice in the literature.3,4

The authors performed a retrospective review of electronic medical records of patients who had nasal papules in connection with acne vulgaris and had been seen between April 2018 and April 2019. The authors recorded clinical and histologic findings. They reported that 20 patients presented with the unique clinical phenotype of nasal papules in the setting of acne. Patients ranged in age from 12 to 37 years, with an average age of 14 at the onset of acne and 16 at presentation.

“The majority of patients were Hispanic (17/20); the remaining were African American (2/20), and Asian (1/20). Seventeen of the patients were male, and 18 patients had concurrent acne at initial presentation, rated as moderate to severe,” the authors wrote.

The 2 patients without concomitant acne were adults with a history of acne whose papules had appeared along with the acne during adolescence. Patients had been previously treated with a variety of topical preparations, antibiotics, and isotretinoin. None had keloidal or hypertrophic scarring, however, 8 had atrophic scarring on the face. Some also had papules on the chin.

“There was a clinical spectrum that ranged from a few, small skin-colored papules to large, dome-shaped papulonodules to more extensive rhinophymatous-like change,” the authors wrote.

The lesions were biopsied and showed dome-shaped proliferation of spindle and stellate-shaped cells with thickened collagen bundles and dilated thin-walled blood vessels that were clinically indistinguishable from angiofibroma (AF). However, this does not mean that they are AFs.

AF, PAPULES, AND OTHER CONDITIONS OR DISORDERS
AFs can be features of a variety of other disorders, including tuberous sclerosis complex (TSC), multiple endocrine neoplasia syndrome type 1, and Birt-Hogg-Dubé syndrome. However, the health history and clinical presentation of the papules seen in the case series led the authors to believe that none of these were present, although they caution that without further testing or screening it’s impossible to rule out TSC. With the data collected, they have no reason to suspect TSC in the patients studied.

CAUSES AND RISK FACTORS
Because this is an underresearched acne sequela, little is known about precise risk factors. Further research is needed to determine why these papules have a predilection for the nose or why they seem to disproportionately affect Hispanic males. The authors noted that it is possible that the mechanistic target of rapamycin (mTOR) is involved. Problems in mTOR signaling may play a role in acne vulgaris in general, they wrote.

TREATMENT
These lesions do not respond to conventional acne treatments, according to the authors. Topical mTOR inhibitors, used in the treatment of AFs caused by TSC, have not been tried for acne-related papules. Cryotherapy was not attempted due to the risk of hypopigmentation. One patient underwent treatment with an Erbium YAG laser with good results, and surgical excision and dermabrasion have been used on angiofibromas.

There are limitations to a retrospective study and a prospective study would be helpful in understanding this disorder, according to study authors.

References

Differences between acne-related papules and tuberous sclerosis complex (TSC) angiofibromas:

ACNE: predilection for the nose; possibly some papules on the chin. Onset is often in adolescence.

TSC: angiofibromas equally distributed across cheeks, nasolabial folds, nose, and chin. Because this condition normally has other systemic manifestations, it would be likely that a patient with only angiofibromas would have forme fruste TSC. This is very uncommon in pediatric patients with only 2 cases reported.
Let’s talk money
Curated content to achieve personal financial success

Physician’s MONEY DIGEST

Find more financial content at: www.medicaleconomics.com/physicians-money-digest
A focused look at procedures, trends and new products in the aesthetics industry.

Subscribe today to receive our eNewsletter featuring the latest in aesthetic practice management and treatment insights.

aestheticauthority.com/subscribetoday
Access trusted content from *Dermatology Times*® every day

**Digital Edition**
Explore our archive of digital content for information at your fingertips.

**Subscribe to eNews**
Receive quick and easy access to our new content every week.

[dermatologytimes.com/enews](http://dermatologytimes.com/enews)
atopic dermatitis

**Quick TAKES**

- Sunflower, coconut, oat, and borage seed oils have been shown to benefit patients with AD. Olive oil may worsen AD.
- Multiple forms of supplementation may be helpful for patients with AD.
- Acupuncture may be more effective as a treatment rather than prevention for itching.

How to choose integrative AD therapies

From oat oil to acupuncture to prebiotics, there are many topical, oral, and manual options.

MARY SCOVIAK | Managing Editor

Patients with atopic dermatitis (AD) can benefit from a wide range of integrative therapies that help treat or prevent multiple symptoms. “Many patients turn to integrative management for atopic dermatitis due to the lack of efficacious prescription medication in the past,” said Vivian Shi, MD, FAAD, an associate professor in the Department of Dermatology at the University of Arkansas for Medical Sciences College of Medicine in Little Rock.

Shi discussed multiple types of treatment at the American Academy of Dermatology 2021 Virtual Meeting Experience in April. She noted that integrative approaches are a popular topic in her eczema clinics.

Some types of cold-pressed, natural oils can help combat the defective skin barrier in patients with AD, Shi noted. Sunflower seed oil, which has up to 60% linoleic acid content; coconut oil, which has antibacterial effects; oat oil (also called oatmeal oil), which helps reduce inflammation; and borage seed oil, which has a high concentration of beneficial fatty acids, can reduce inflammation and repair the skin barrier (Table 1).

Olive oil, however, despite being a healthy choice to consume, contains oleic acid and can be irritating to the skin of patients with AD. In children with AD, virgin coconut oil produced greater improvements in stratum corneum hydration, SCORing Atopic Dermatitis, and transepidermal water loss than mineral oil, Shi said.

Another topical treatment to consider is cream containing palmitoylethanolamide. Studies of both adult and pediatric patients with AD have demonstrated that it was more effective combined with a topical corticosteroid than a traditional moisturizer and topical corticosteroid combination, Shi said.

A meta-analysis of existing studies also considered oral prebiotics and probiotics (together known as synbiotics) (Table 2). According to research, they help treat but not prevent AD in patients older than 1 year, said Shi.

Synbiotics appear to be more effective than probiotics alone; however, prebiotics alone can lower AD severity. Mixed-strain synbiotics are more effective than single strain. However, head-to-head studies comparing synbiotics with probiotics are lacking.

According to Shi, many kinds of supplementation are effective in patients with AD. Vitamin E 400 mg taken for 4 to 8 months can improve AD, and higher dietary vitamin E consumption can improve AD in children. Low blood vitamin C levels have been linked to more severe AD. Higher vitamin C content in breast milk lowers the risk of atopy in infants, but it is not known if vitamin C consumption during pregnancy affects the disease in infants. Low blood levels of vitamin D are linked with more asthma food allergies, eczema, and higher amounts of *Staphylococcus aureus*.

**TABLE 1**

<table>
<thead>
<tr>
<th>Oil</th>
<th>Properties</th>
<th>Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sunflower seed</td>
<td>High linoleic acid content, high in vitamin E</td>
<td>Helps speed skin barrier repair, decreases skin inflammation</td>
</tr>
<tr>
<td>Coconut oil</td>
<td>Contains monolaurin</td>
<td>An antimicrobial against <em>Staphylococcus aureus</em>, some yeasts and viruses</td>
</tr>
<tr>
<td>Oat oil (oatmeal oil)</td>
<td>Contains avenanthramides</td>
<td>Decreases inflammation, increases ceramides in the skin barrier</td>
</tr>
<tr>
<td>Borage seed oil</td>
<td>High in gamma linolenic acid</td>
<td>Has high content of beneficial fatty acids for the skin</td>
</tr>
<tr>
<td>Olive oil</td>
<td>Contains oleic acid</td>
<td>Can irritate skin and worsen AD (topical use)</td>
</tr>
</tbody>
</table>

INTEGRATIVE AD THERAPIES CONTINUES ON PAGE 24
REIMAGINING SOLUTIONS IN DERMATOLOGY

At Incyte, we’re committed to improving patients’ lives through meaningful science. That’s why we’re researching and developing innovative solutions for a number of dermatologic conditions, including atopic dermatitis and vitiligo.

Learn more at Incyte.com/derm.
**JUNE 2021**

**ABROCITINIB EFFECTIVE AS FLEXIBLE DOSE FOR ATOPIC DERMATITIS**

*By LINDA STOCUM, Assistant Editor*

**ABROCITINIB** (PF-04965842; Pfizer), a Janus kinase 1 (JAK1) inhibitor, is an oral, once-daily oral treatment for moderate to severe atopic dermatitis (AD) in patients 12 years or older. Andrew Blauvelt, MD, MBA, president of Oregon Medical Research Center in Portland, presented the results of the JADE REGIMEN trial (NCT03627767) at the American Academy of Dermatology Virtual Meeting Experience 2021 (AAD VMX) held in April. The purpose of this study was to measure flaring in patients when taking abrocitinib.

Of the 1733 patients screened, 1233 were enrolled and 798 then were randomized. Based on the patients’ IGA scores, approximately 60% had moderate AD and 40% had severe AD. The average EASI score was 30. After the first 12 weeks, 65.2% of patients achieved IGA 0/1 and EASI 75. Patients who had flare-ups and were not in the high-dose group were treated with 200 mg of abrocitinib. Those who were in the high-dose group were then treated with an additional topical corticosteroid. More than 90% of placebo recovered EASI 75 vs 74.5% of the low-dose abrocitinib patients and 55% of high-dose abrocitinib patients.

"As far as [adverse] effects, there are a number of things listed," Blauvelt said. "We saw a little more nausea, a little more CPE [creatine kinase], and a little bit more acne in the 200-mg group compared with the 100-mg group [and placebo]. All adverse events affected fewer than 10% of patients. Also, there was approximately a 35% decrease in platelet levels during the first 12 weeks of the abrocitinib study. However, these returned to baseline after continued treatment, said Blauvelt.

“We now have data on dose flexibility [with abrocitinib] for your patients with moderate to severe atopic dermatitis,” Blauvelt said.

**Disclosure**

Blauvelt has served as a scientific adviser and/or clinical study investigator for Pfizer, AbbVie, Accutana, Alphan Therapeutics, Almirall, Amgen, Arista Biotherapeutics, Arena, Altheon, Boehringer-Ingelheim, Bristol-Meyers Squibb, Dermot, Eli Lilly and Company, Evoluent, Forte Pharma Laboratories, Galderma, Inotera, Janssen, Lendor, Blyphaire, LEO Pharma, Novartis, Rapt Therapeutics, Regeneron, Sanofi Genzyme, Sun Pharmaceuticals, and UCB.

**Reference**


**PROBIOTICS**

- Fructo-oligosaccharides
- Lactobacillus acidophilus
- Lactobacillus rhamnosus
- Lactobacillus paracasei
- Bifidobacterium lactis
- Bifidobacterium breve
- Bifidobacterium longum

**PREBIOTICS**

- Inulin
- Fructo-oligosaccharides
- Galactooligosaccharides

**Table 2**

**EXAMPLES OF PREBIOTICS AND PROBIOTICS FOR AD**

**Topical Management of Atopic Dermatitis**

**Integrative AD Therapies FROM PAGE 22**

> Many patients turn to integrative management for atopic dermatitis due to a lack of efficacious prescription medication in the past.”

Vivian Shi, MD, FAAD, associate professor in the Department of Dermatology at the University of Arkansas for Medical Sciences College of Medicine in Little Rock
A formulation that absorbs quickly into the skin

Altreno is the first ever tretinoin to treat acne in a hydrating and moisturizing lotion formulation.

The unique polymeric honeycomb mesh helps to uniformly distribute the active tretinoin and hydrating ingredients (sodium hyaluronate, soluble collagen and glycerin) into the skin.1,2

INDICATIONS AND USAGE
Altreno® (tretinoin) Lotion, 0.05% is indicated for the topical treatment of acne vulgaris in patients 9 years of age and older.

IMPORTANT SAFETY INFORMATION
Altreno is for topical use only. Not for ophthalmic, oral, or intravaginal use.

Skin Irritation: Patients using Altreno may experience application site dryness, pain, erythema, irritation, and exfoliation. Depending upon the severity of these adverse reactions, instruct patients to use a moisturizer, reduce the frequency of the application of Altreno, or discontinue use. Avoid application of Altreno to vesicular or sunburned skin.

Ultraviolet Light and Environmental Exposure: Minimize unprotected exposure to ultraviolet light, including sunlight and sunlamps. Warn patients with frequent sun exposure and those with inherent sensitivity to sunlight to exercise caution. Use sunscreen and protective clothing over treated areas when exposure cannot be avoided.

Fish Allergies: Altreno contains soluble fish proteins. Use with caution in patients with known sensitivity or allergy to fish. Advise patients to contact their healthcare provider if they develop pruritus or urticaria.

Adverse Reactions: The most common adverse reactions in clinical trials were application site dryness (4%), pain (3%), erythema (2%), irritation (1%), and exfoliation (1%).

Nursing Women: It is not known whether topical administration of tretinoin could result in sufficient systemic absorption to produce detectable concentrations in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for Altreno and any potential adverse effects on the breastfed child from Altreno.

To report suspected adverse reactions, contact Customer Service at 1-800-321-4076 or the FDA at 1-800-FDA-1088 or fda.gov/medwatch.

Please see Brief Summary of full Prescribing Information on adjacent page.

References:

Ortho Dermatologics™
Altreno is a trademark of Ortho Dermatologics’ affiliated entities. © 2021 Ortho Dermatologics affiliated entities. ALT0046USA2V10
BRIEF SUMMARY OF PRESCRIBING INFORMATION

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

ALTRENO® (tretinoin) Lotion, for topical use
Initial U.S. Approval: 1973

INDICATIONS AND USAGE
ALTRENO® (tretinoin) Lotion, 0.05% is indicated for the topical treatment of acne vulgaris in patients 9 years of age and older.

CONTRAINDICATIONS
None.

WARNINGS AND PRECAUTIONS

Skin Irritation
Patients using ALTRENO may experience application site dryness, pain, erythema, irritation, and exfoliation. Depending upon the severity of these adverse reactions, instruct patients to use a moisturizer, reduce the frequency of the application of ALTRENO, or discontinue use. Avoid application of ALTRENO to excoriated or sunburned skin.

Ultraviolet Light and Environmental Exposure
Minimize unprotected exposure to ultraviolet light including sunlight and sunlamps during the use of ALTRENO. Warn patients who normally experience high levels of sun exposure and those with inherent sensitivity to sunlight to exercise caution. Use sunscreen products and protective clothing over treated areas when sun exposure cannot be avoided.

Fish Allergies
ALTRENO contains soluble fish proteins. Use with caution in patients with known sensitivity or allergy to fish. Advise patients to contact their healthcare provider if they develop pruritus or urticaria.

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 clinical practice.

In 2 randomized, double-blind, vehicle-controlled trials, subjects age 9 years and older applied ALTRENO or vehicle once daily for 12 weeks. The majority of subjects were White (74%) and female (55%). Approximately 47% were Hispanic/Latino and 45% were younger than 18 years of age. Adverse reactions reported by ≥1% of subjects treated with ALTRENO and more frequently than vehicle are summarized in Table 1.

Table 1: Adverse Reactions Reported by ≥1% of Subjects Treated with ALTRENO and More Frequently Than Vehicle

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>ALTRENO N=767</th>
<th>Vehicle N=763</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application site dryness</td>
<td>29% (10)</td>
<td>1% (1)</td>
</tr>
<tr>
<td>Application site pain</td>
<td>25% (9)</td>
<td>3% (2)</td>
</tr>
<tr>
<td>Application site irritatio</td>
<td>12% (4)</td>
<td>1% (1)</td>
</tr>
<tr>
<td>Application site exfoliation</td>
<td>10% (3)</td>
<td>3% (2)</td>
</tr>
</tbody>
</table>

Skin irritation was evaluated by active assessment of erythema, scaling, hyperpigmentation, itching, burning and stinging. The percentage of subjects who were assessed to have these signs and symptoms at any post baseline visit are summarized in Table 2.

Table 2: Application Site Tolerability Reactions at Any Post Baseline Visit

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>ALTRENO N=760</th>
<th>Vehicle N=762</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enzymia</td>
<td>65% Mild/Mod/Severe</td>
<td>44% Mild/Mod/Severe</td>
</tr>
<tr>
<td>Scaling</td>
<td>49%</td>
<td>30%</td>
</tr>
<tr>
<td>Hyperpigmentation</td>
<td>12%</td>
<td>10%</td>
</tr>
<tr>
<td>Hyperpigmentation</td>
<td>35%</td>
<td>35%</td>
</tr>
<tr>
<td>Itching</td>
<td>35%</td>
<td>28%</td>
</tr>
<tr>
<td>Burning</td>
<td>30%</td>
<td>14%</td>
</tr>
<tr>
<td>Stinging</td>
<td>21%</td>
<td>8%</td>
</tr>
</tbody>
</table>

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary
Available data from published observational studies of topical tretinoin in pregnant women have not established a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. There are no data on ALTRENO use in pregnant women. The systemic levels following topical administration are lower than with oral administration of tretinoin; however, absorption of this product may result in fetal exposure. There are reports of major birth defects similar to those seen in infants exposed to oral retinoids, but these case reports do not establish a pattern or association with tretinoin-related embryopathy (see Data).

Animal reproduction studies have not been conducted with ALTRENO. Topical administration of tretinoin in a different formulation to pregnant rats during organogenesis was associated with malformations (craniofacial abnormalities [hydrocephaly], asymmetrical thyroids, variations in ossification, and increased supernumerary ribs) at doses up to 0.5 mg tretinoin/kg/day, approximately 2 times the maximum recommended human dose (MRHD) based on body surface area (BSA) comparison and assuming 100% absorption. Oral administration of tretinoin to pregnant cynomolgus monkeys during organogenesis was associated with malformations at 10 mg/kg/day (approximately 100 times the MRHD based on BSA comparison and assuming 100% absorption) (see Data).

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies, even those exposed to a retinoid, have a background risk of major birth defects, loss, and other adverse outcomes. The background risk in the U.S. general population of major birth defects is 2 to 4%. In cases of maternal smoking, 15% to 20% of clinically recognized pregnancies have been associated with topical tretinoin and major birth defects or miscarriage.

The available studies have methodologic limitations, including small sample size and in some cases, lack of physical exam by an expert in birth defects.

Fish Allergies
ALTRENO contains soluble fish proteins. Use with caution in patients with known sensitivity or allergy to fish. Advise patients to contact their healthcare provider if they develop pruritus or urticaria.

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 clinical practice.

In 2 randomized, double-blind, vehicle-controlled trials, subjects age 9 years and older applied ALTRENO or vehicle once daily for 12 weeks. The majority of subjects were White (74%) and female (55%). Approximately 47% were Hispanic/Latino and 45% were younger than 18 years of age. Adverse reactions reported by ≥1% of subjects treated with ALTRENO and more frequently than vehicle are summarized in Table 1.

Table 1: Adverse Reactions Reported by ≥1% of Subjects Treated with ALTRENO and More Frequently Than Vehicle

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>ALTRENO N=767</th>
<th>Vehicle N=763</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application site dryness</td>
<td>29% (10)</td>
<td>1% (1)</td>
</tr>
<tr>
<td>Application site pain</td>
<td>25% (9)</td>
<td>3% (2)</td>
</tr>
<tr>
<td>Application site irritatio</td>
<td>12% (4)</td>
<td>1% (1)</td>
</tr>
<tr>
<td>Application site exfoliation</td>
<td>10% (3)</td>
<td>3% (2)</td>
</tr>
</tbody>
</table>

Skin irritation was evaluated by active assessment of erythema, scaling, hyperpigmentation, itching, burning and stinging. The percentage of subjects who were assessed to have these signs and symptoms at any post baseline visit are summarized in Table 2.

Table 2: Application Site Tolerability Reactions at Any Post Baseline Visit

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>ALTRENO N=760</th>
<th>Vehicle N=762</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enzymia</td>
<td>65% Mild/Mod/Severe</td>
<td>44% Mild/Mod/Severe</td>
</tr>
<tr>
<td>Scaling</td>
<td>49%</td>
<td>30%</td>
</tr>
<tr>
<td>Hyperpigmentation</td>
<td>12%</td>
<td>10%</td>
</tr>
<tr>
<td>Hyperpigmentation</td>
<td>35%</td>
<td>35%</td>
</tr>
<tr>
<td>Itching</td>
<td>35%</td>
<td>28%</td>
</tr>
<tr>
<td>Burning</td>
<td>30%</td>
<td>14%</td>
</tr>
<tr>
<td>Stinging</td>
<td>21%</td>
<td>8%</td>
</tr>
</tbody>
</table>

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary
Available data from published observational studies of topical tretinoin in pregnant women have not established a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. There are no data on ALTRENO use in pregnant women. The systemic levels following topical administration are lower than with oral administration of tretinoin; however, absorption of this product may result in fetal exposure. There are reports of major birth defects similar to those seen in infants exposed to oral retinoids, but these case reports do not establish a pattern or association with tretinoin-related embryopathy (see Data).

Animal reproduction studies have not been conducted with ALTRENO. Topical administration of tretinoin in a different formulation to pregnant rats during organogenesis was associated with malformations (craniofacial abnormalities [hydrocephaly], asymmetrical thyroids, variations in ossification, and increased supernumerary ribs) at doses up to 0.5 mg tretinoin/kg/day, approximately 2 times the maximum recommended human dose (MRHD) based on body surface area (BSA) comparison and assuming 100% absorption. Oral administration of tretinoin to pregnant cynomolgus monkeys during organogenesis was associated with malformations at 10 mg/kg/day (approximately 2 times the MRHD based on BSA comparison and assuming 100% absorption) (see Data).

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies, even those exposed to a retinoid, have a background risk of major birth defects, loss, and other adverse outcomes. The background risk in the U.S. general population of major birth defects is 2 to 4%. In cases of maternal smoking, 15% to 20% of clinically recognized pregnancies have been associated with topical tretinoin and major birth defects or miscarriage.
TYK2 Inhibitor Is on the Horizon for Plaque Psoriasis

Deucravacitinib meets primary end points for treating moderate to severe psoriasis.

LINDA STOCUM | Assistant Editor

In 2 recent phase 3 trials, deucravacitinib (BMS-986165, Bristol Myers Squibb [BMS]), demonstrated progress toward becoming a new treatment for moderate to severe plaque psoriasis.1,2

Deucravacitinib is the first and only tyrosine kinase 2 (TYK2) inhibitor in clinical studies across multiple immune-mediated diseases, according to Mary Beth Harler, MD, senior vice president and head of immunology and fibrosis development, global drug development, at Bristol Myers Squibb in Princeton, New Jersey.

“The impetus for our research came from genetic analysis in human populations that revealed the small subset of individuals with impaired TYK2 function were actually protected from certain immune-mediated diseases, such as psoriasis, without an increased risk of significant complications,” she told Dermatology Times®.

BMS scientists designed deucravacitinib to target TYK2, thereby inhibiting signaling of key cytokines IL-12, IL-23, and Type 1 IFN, involved in psoriasis pathogenesis, Harler said.

“Deucravacitinib achieves a high degree of selectivity for TYK2 by uniquely binding to its regulatory domain, locking it in an inactive state,” she said. “This is called allosteric inhibition, which is different from how JAK [Janus kinase] inhibitors work. At therapeutic doses, deucravacitinib is intended to block TYK2 without inhibiting JAK1, JAK2, or JAK3, thus potentially avoiding adverse events [AEs] associated with these inhibitors.”

This novel oral medication, which earned BMS the 2019 Thomas A. Edison Patent Award for the science underpinning of its clinical development, met its primary and secondary end points in 2 phase 3 studies investigating the safety and efficacy of the drug as a treatment for moderate to severe psoriasis. POETYK PSO-1 (NCT03624127) and POETYK PSO-2 (NCT03611751) compared deucravacitinib with both placebo and apremilast (Otezla; Amgen).1,2

April Armstrong, MD, MPH, professor of dermatology and associate dean of clinical research at Keck School of Medicine at the University of Southern California in Los Angeles, presented the results from these studies at the American Academy of Dermatology Virtual Meeting Experience 2021 in April.1

“PSO-1 and PSO-2 were global, double-blinded, 52-week studies that were identical in design up to week 24,” Armstrong said. PSO-1 enrolled 666 patients and PSO-2 enrolled 1020.

Study patients who met the Psoriasis Area and Severity Index (PASI), static Physician Global Assessment (sPGA), and body surface area standards for moderate to severe plaque psoriasis were randomized using a 2:1:1 ratio into 3 possible treatment groups taking 6 mg of deucravacitinib once daily, placebo, or 30 mg of apremilast twice daily. Placebo patients were switched to deucravacitinib at week 16 in both studies. Patients taking apremilast who failed to reach PASI 50 in the PSO-1 study or PASI 75 in the PSO-2 study were switched to deucravacitinib at week 24. (Table)

“PSO-2 also included a randomized withdrawal phase at week 24,” Armstrong said. “The results will be presented at a future date. Mean patient weight was slightly higher in PSO-2 compared [with] PSO-1, likely reflecting the difference between geographic distribution of patients.”

The study’s coprimary endpoints were the proportion of patients achieving PASI 75 or sPGA 0/1, defined as clear or almost clear responses, at week 16 for deucravacitinib vs placebo. The baseline demographics were similar between the 2 studies and typical for trials in moderate to severe plaque psoriasis, Armstrong said. PSO-1 included sites in Asia whereas PSO-2 did not.
Results showed that by 16 weeks, 58.7% of patients who received deucravacitinib achieved a PASI 75 response compared with 35.1% of apremilast and 12.7% placebo. This trend continued through week 24. Importantly, 82.5% of patients in POETYK PSO-1 and 81.4% in POETYK PSO-2 who achieved PASI 75 at week 16 and continued treatment, maintained their response through week 52.

For sPGA, 53.6% of patients receiving deucravacitinib in PSO-1 achieved a 0/1 response at week 16 vs 32.1% of those on apremilast and 7.2% placebo. These results were consistent through week 24 and comparable with the PSO-2 trial.

More than 60% of patients had moderate to severe plaque psoriasis affecting the scalp at baseline. The breakdown of patients who met scalp-specific sPGA 0/1 responses by week 16 in PSO-1 was as follows: 70.8% of patients receiving deucravacitinib vs 39.1% with apremilast and 17.4% with placebo. These outcomes were similar to those observed in PSO-2, Armstrong said.

“Improvements were seen in base in PSSD [Psoriasis Symptoms and Signs Diary] symptoms, which include itching, pain, stinging, and skin tightness,” Armstrong said.

Approximately 95% of patients also had Dermatology Life Quality Index (DLQI) scores of greater than or equal to 2 at baseline. More than 40% of patients taking deucravacitinib compared with 28.6% of patients taking apremilast and 10.6% of patients taking placebo achieved DLQI 0/1 response at week 16 in PSO-1. Deucravacitinib’s effectiveness was also greater than apremilast’s effectiveness through week 24.

Deucravacitinib, apremilast, and placebo had a similar total number of AEs and serious adverse events (SAEs). These numbers include both the POETYK PSO-1 and the POETYK PSO-2 trials. Deucravacitinib had 2.4% of AEs that led to study discontinuation, which was less than 3.8% with placebo and 5.2% with apremilast.

The most common AEs across treatment groups were nasopharyngitis, upper respiratory tract infection, headache, diarrhea, and nausea. One death occurred in each of the treatment groups, but none was attributed to the study.

“Due to the randomizations at week 16 and week 24 from apremilast, the total exposure to deucravacitinib is nearly 1000 patient years, with less than 250 patient years for placebo and apremilast,” Armstrong said. “The safety profile for weeks 0 to 52 is similar to those observed from week 0 to 16 with no new safety findings.”

Deucravacitinib had a low incidence rate of approximately 2% for patients who experienced folliculitis and acne and led 1 patient to discontinue use. The exposure-adjusted incidence rate (EARI) for AEs of interest showed malignancies and serious infections had similar rates across treatment groups in both studies. None of the patients who had a serious infection on deucravacitinib discontinued the study.

There were 4 arterial thrombotic events reported in the deucravacitinib group, 1 of which was considered serious. There was 1 SAE adjudicated as a venous thromboembolism at week 48. This patient was hospitalized, underwent an aortic repair, recovered, and restarted treatment with deucravacitinib for the long-term study.

The study also looked at 4 laboratory parameters that can be affected within the first 4 months of treatment with JAK inhibitors. “Importantly, no clinically meaningful changes were observed in total cholesterol, creatine phosphokinase, neutrophils, or platelets with deucravacitinib at 16 weeks,” she said. “Similar results were observed in 52 weeks in these and other parameters.”

In both studies, deucravacitinib demonstrated superiority compared with placebo and apremilast in PASI 75 and sPGA 0/1 at week 16; therapeutic effect was maintained through week 52. Also, deucravacitinib had a consistent safety profile between both studies and was well tolerated, according to Armstrong.

“Based on these findings, deucravacitinib has the potential to become an efficacious, well-tolerated treatment of choice for patients with moderate to severe plaque psoriasis,” Armstrong said. “It also has significant potential to be broadly applicable to a range of immune-mediated diseases such as psoriatic arthritis, ulcerative colitis, Crohn disease, and lupus.”

### TABLE

#### RESULTS OF DEUCRAVACITINIB CLINICAL TRIALS

<table>
<thead>
<tr>
<th>End Point</th>
<th>POETYK PSO-1 (n = 666)</th>
<th>POETYK PSO-2 (n = 1020)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Deucravacitinib 6 mg (n = 332)</td>
<td>Otse 30 mg (n = 168)</td>
</tr>
<tr>
<td><strong>PASI 75</strong></td>
<td><strong>Week 16</strong></td>
<td>58.7% *†</td>
</tr>
<tr>
<td></td>
<td><strong>Week 24</strong></td>
<td>69.0% *†</td>
</tr>
<tr>
<td><strong>sPGA 0/1</strong></td>
<td><strong>Week 16</strong></td>
<td>53.6% *†</td>
</tr>
<tr>
<td></td>
<td><strong>Week 24</strong></td>
<td>56.4% *†</td>
</tr>
<tr>
<td><strong>(Scalp) ss-PGA 0/1</strong></td>
<td><strong>Week 16</strong></td>
<td>70.8% *†</td>
</tr>
<tr>
<td></td>
<td><strong>Week 24</strong></td>
<td>71.8% *†</td>
</tr>
<tr>
<td><strong>PSSD-Symptoms CFB</strong></td>
<td><strong>Week 16</strong></td>
<td>-26.7% *†</td>
</tr>
<tr>
<td></td>
<td><strong>Week 24</strong></td>
<td>-31.9</td>
</tr>
<tr>
<td><strong>DLQI 0/1</strong></td>
<td><strong>Week 16</strong></td>
<td>40.7% *†</td>
</tr>
<tr>
<td></td>
<td><strong>Week 24</strong></td>
<td>47.8% *†</td>
</tr>
</tbody>
</table>

**DLQI:** Dermatology Life Quality Index; **PASI:** Psoriasis Area and Severity Index; **ss-PGA:** static Physician Global Assessment; **sPGA:** static-specific Physician Global Assessment; **PSSD:** Psoriasis Symptoms and Signs Diary.
FDA to Review sNDA, Set Action Date for Apremilast

Phase 3 clinical trial results show improvement regardless of body surface area affected.

LINDA STOCUM | Assistant Editor

Oral therapy may be on the horizon for adults with mild to moderate plaque psoriasis who are candidates for phototherapy or systemic therapy. Following a phase 3 trial that met primary and secondary end points, the FDA has accepted for review the supplemental New Drug Application (sNDA) for apremilast (Otezla; Amgen).1

This opens potential for the phosphodiesterase4 (PDE4) inhibitor to be the first approved oral therapy for adults with mild to moderate disease. The FDA has set a Prescription Drug User Fee Act (PDUFA) action date of December 19, 2021, for its decision.

“Otezla has been prescribed to hundreds of thousands of patients with moderate to severe plaque psoriasis,” said David M. Reese, MD, executive vice president of research and development at Amgen, Thousand Oaks, California. “Based on the positive phase 3 ADVANCE data, we believe it could play an important role in addressing the unmet need for adults affected by mild to moderate plaque psoriasis who have had challenges managing their disease with existing topical therapies alone. The FDA’s acceptance of this sNDA for Otezla is a significant milestone toward achieving our goal of potentially providing the first and only oral treatment option for the underserved... patient population.”

If approved, it would be the fourth indication for Otezla. The therapy is FDA approved for adults with active psoriatic arthritis and adults with oral ulcers associated with Behçet disease.

Investigators examined the efficacy and safety indication for apremilast as a novel oral treatment for patients with mild to moderate psoriasis who are candidates for phototherapy or systemic therapy.

“Approximately three-quarters of the 8 million [individuals] in the United States living with psoriasis have disease that is considered mild, yet they are undertreated,” Sven Richter, MD, global medical affairs lead at Amgen, told Dermatology Times®. “Many of these patients report substantial disease burden despite having limited body surface area [BSA] affected because of the location of plaques and other symptoms that interfere with daily living activities. They typically rely on topical treatments that may not address hard-to-treat manifestations of this disease.”

As previously reported by Dermatology Times®, the sNDA acceptance is supported by data from the phase 3 ADVANCE study (NCT03721172). ADVANCE was a double-blind, multicenter, placebo-controlled trial that examined apremilast in 595 adult participants with mild to moderate plaque psoriasis. Patients were given 30 mg of apremilast or placebo twice daily for 16 weeks, followed by an open-label extension study that continued until week 32. Results of the extension study were presented via poster at the American Academy of Dermatology Virtual Meeting Experience 2021 in April.2

Study data demonstrated positive outcomes with apremilast, achieving its primary end point of a statistically significant improvement in static Physicians Global Assessment (sPGA) response at week 16 vs placebo. The secondary end points were met with a minimum of 75% improvement from baseline in BSA percent affected, an alteration in Psoriasis Area and Severity Index (PASI) score from baseline, and a change in BSA score from baseline.3

Safety was evaluated in the study with the safety profile mimicking those in previous studies. The most common treatment-related adverse events (≥5%) include nausea, headache, nasopharyngitis, upper respiratory tract infection, and diarrhea. The is consistent with previously repotted data from clinical trial programs.

“Findings from the Phase 3 ADVANCE trial demonstrated the potential role Otezla can play as an oral systemic treatment for [individuals] with mild to moderate plaque psoriasis, who are commonly undertreated,” according to the study. “In ADVANCE, oral Otezla 30 mg twice daily achieved a statistically significant improvement of the primary end point of static Physician’s Global Assessment response at week 16 compared with placebo [21.6% vs 4.1%, P < .0001]. These clinical improvements were maintained through week 32. Time to relapse was not measured in ADVANCE.”

FDA sets December 19, 2021, PDUFA action date.

References
4. FDA’s acceptance of this sNDA for Otezla is a significant milestone toward achieving our goal of potentially providing the first and only oral treatment option for the underserved... patient population.”

Disclosures
This study was sponsored by Amgen Inc. Writing support was funded by Amgen and provided by Kristin Carlin, RPh, of OPEN Health.
Mental Health Affects PsA Treatment

Anxiety, depression reduce likelihood of MDA.

ROBERT KRONEMYER | Staff Correspondent

Symptoms of anxiety and depression significantly reduce the likelihood of achieving sustained minimal disease activity (MDA) in patients with psoriatic arthritis (PsA), according to a prospective study in *Arthritis Care & Research.*

“We always struggle getting patients into remission with treatment for PsA,” said principal investigator Vinod Chandran, MD, PhD, DM, MBBS, an associate professor at the University of Toronto in Ontario, Canada, a scientist with the Krembil Research Institute, a staff physician at the University Health Network and Mount Sinai Hospitals, and a member of the graduate faculty at the Institute of Medical Science and the Department of Laboratory Medicine and Pathobiology at the University of Toronto. He co-directs the Psoriatic Arthritis Program at the University Health Network in Toronto.

“Although we have many immunomodulatory treatments for PsA, there are other factors that also influence treatment response and the ability to achieve remission,” he said.

The current study was designed to evaluate whether mental health—mainly depression and anxiety—affects treatment response for PsA, specifically remission or MDA.

“Mental health is less investigated than physical health among the comorbidities associated with PsA, even though it is an issue that many patients mention during clinic visits,” Chandran told *Dermatology Times.*

The study comprised of 743 adult patients with PsA who were treated for the condition at the University of Toronto Psoriatic Arthritis Clinic between 2008 and 2017.

Because the investigators did not personally diagnose patients for depression or anxiety, the presence of depression/anxiety fell under 1 of 3 definitions: (1) a score of less than or equal to 38 on the mental component summary of the 36-Item Short Form Health Survey (SF-36); (2) a score of less than or equal to 56 on the mental health subscale of the SF-36; and (3) a rheumatologist’s report of the diagnosis of depression/anxiety made by the patient’s family physician or psychiatrist, or pharmacotherapy for depression/anxiety, as recorded in the PsA clinic protocol.

The percentage of patients identified as having depression/anxiety at their first visit was 44.54%, 48.99%, and 28.4%, respectively.

Overall, 45.36% of the entire cohort failed to achieve sustained MDA. Specifically, the presence of depression/anxiety reduced the probability of achieving sustained MDA by 70% with the first definition, 66% with...
the second definition, and 53% with the third definition.

Two other variables independently associated with a reduced probability of achieving sustained MDA were the Charlson Comorbidity Index and the presence of fibromyalgia. Interestingly, daily alcohol consumption was linked to a higher probability of achieving sustained MDA.

The study, however, did not evaluate whether more severe symptoms of PsA were associated with higher rates of depression/anxiety. But the effect of depression/anxiety was independent of other comorbidities and disease severity as measured by the number of damaged joints or medications taken.

“In general, the results were expected,” Chandran said. “One of the outcomes we look at for PsA remission is pain, which correlates strongly with mental health. Similar findings have been reported in Europe.”

Chandran said patients with other inflammatory diseases are also more prone to anxiety/depression. “Some studies have looked at treating depression with biologic agents, although the results have been mixed,” he said.

“But mental health also needs to be managed in a multidisciplinary fashion,” Chandran said. “This may be less of a challenge earlier in the disease state; however, when the disease is present for some time, mental health becomes problematic because of persistent inflammation and chronic pain. The inflammation and the pain are probably driving depression/anxiety. Early control of pain might reduce the burden of mental health issues.”

Conversely, by treating the depression/anxiety, pain is better managed, according to Chandran.

The presence of depression/anxiety may lead not only to increased pain sensitivity, but also to avoidance, inactivity, deconditioning, and social isolation, thus contributing to a reduced likelihood of achieving remission.

Because of the high prevalence of mental health challenges among patients with PsA, Chandran firmly believes that a comprehensive evaluation needs to include a proper assessment of mental health. He conceded, however, that evaluating for mental health is difficult to integrate into clinical practice.

One alternative solution is online mindfulness-based interventions. “Also, in addition to a rheumatologist evaluating a patient, the patient might be seen by another clinician like a psychologist or even a nurse with expertise in mental health,” Chandran said.

Disclosure
Chandran reports relevant financial disclosures.

Reference
Trifillio A, Wu J, Cook GJ, Stolman GD, Chandran V. Depression and anxiety reduce the probability of achieving a state of sustained minimal disease activity in patients with psoriatic arthritis. Arthritis Care & Research. Published online March 4, 2021. doi:10.1002/acr.24993

FDA SETS PDUFA DATE FOR BIMEKIZUMAB

UCB could release the drug for the treatment of psoriasis by the second half of 2021.

By LINDA STOCUM, Assistant Editor

The FDA has set the Prescription Drug User Fee Act (PDUFA) date for bimekizumab’s Biologics License Application, according to UCB, the drug’s developer. Bimekizumab is used for the treatment of adults with moderate to severe plaque psoriasis. The FDA plans to make an approval decision for the drug on October 15, 2021, according to a news release from the company.

Bimekizumab is an investigational humanized monoclonal immunoglobulin (Ig)G1 antibody that selectively inhibits IL-17A and IL-17F, both of which are considered key cytokines driving inflammatory processes. The drug is supported by data from multiple phase 3 studies (BE READY NCT03410992, BE SUITE NCT03412747, BE VIVID NCT03370133) investigating the safety and efficacy of the biologic in adult moderate to severe chronic plaque psoriasis patients. Primary end points were met across the studies, with patients treated with bimekizumab demonstrating superior skin clearance at week 16 vs patients treated with adalimumab (Humira; AbbVie) and placebo as measured by the Psoriasis Severity Index (PASI 90 or higher) and by an Investigator Global Assessment response of clear (0) or almost clear (1).

Additionally, all phase 3 studies met their secondary end points. In 2 of the studies, patients treated with bimekizumab demonstrated total skin clearance at week 16 (PASI 100), verifying superior over ustekinumab (Stelara; Janssen) and adalimumab. Bimekizumab was superior to ustekinumab, adalimumab, and placebo in achieving rapid response (PASI 75 at week 4), and clinical responses were sustained up to 1 year across all studies. The studies’ safety profiles were consistent with previous clinical studies. If approved, UCB will release bimekizumab starting in the second half of 2021.

References

SUBSCRIBE TO OUR E-NEWSLETTER TO GET OUR LATEST ARTICLES.
Advances in preventing, diagnosing, and treating basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) come from increased knowledge and debate around how best to use proven techniques and new technologies and medications. But current innovations in treating BCC are not necessarily bold-faced change, said Suzanne Olbricht, MD, FAAD, dermatologist-in-chief at Beth Israel Deaconess Medical Center and associate professor of dermatology at Harvard Medical School in Boston, Massachusetts, in a presentation at the Skin Cancer Symposium 2021. Instead, margin debates for excision and the ability to use a large armamentarium of treatment options allow dermatologists and dermatological surgeons to offer increasingly personalized care.

**BASAL CELL CARCINOMA**

The list of known risk factors for BCC has grown, Olbricht said. Tanning bed use is a well-known risk factor. But antihypertensive use has also been linked to BCC in numerous studies, and citrus consumption and chronic stress also are risk factors. Occupational risks include being a pilot, arc welder, or interventional cardiologist, however, Olbricht didn’t detail the reasons for the increased risk, she did point out that both patients and dermatologists need to be more aware of occupational sun exposure, not just leisure sun exposure. Conversely, vitamin D3 in skin and caffeine consumption are associated with decreased risk of BCC.

Moving from prevention to treatment, Olbricht discussed the debate around margins in treating BCC with Mohs surgery or similar techniques. She favors 4-mm margins, citing a much lower risk of recurrence when compared with results from excisions with 2-mm margins, as shown in results of a 2020 study. She added that in her practice most patients prefer a slightly longer scar to the risk of a second procedure.

In her second presentation, Olbricht gave an overview of the nonsurgical options available to treat BCC. “For each cancer and each patient, all options are worth considering,” she said. “Basically, what I think is that if you have a small, well-demarcated lesion on the trunk…almost anything is going to treat it well, so you have an opportunity to explore a number of treatment options with the patient.”

With such a large toolkit to choose from, patient health, lifestyle, and preferences can vary widely. Olbricht cited examples from her practice where 3 patients with small BCCs chose 3 different options for treatment: electrodessication and curettage, topical imiquimod, and Mohs surgery. All were satisfied with their treatment.

Olbricht stressed the importance of extending this kind of individualized treatment in consultation to all patient populations. For older patients, in particular, it is vital for the medical team to consider the individual and not simply the demographic they occupy. Olbricht chooses observation or minimal treatment more often for this patient population, but once she decides to treat the toolkit is the same as for younger patients.
A special thank-you to our distinguished editorial board for all they do.

Zoe Diana Draelos, MD
Chief Medical Editor

For more information about our distinguished board, go to dermatologytimes.com/editorial-info
NEW OFFICERS, BOARD MEMBERS ELECTED TO AAD
The American Academy of Dermatology Announced the results from its annual election, with 2 officers and 4 board members assuming their new positions in March 2022. The newly elected officers and board members will represent over 20,000 physicians specializing in the diagnosis and medical, surgical, and cosmetic treatment of skin, hair, and nail conditions.

Terrence A. Cronin, Jr., MD, FAAD, Melbourne, Florida, will be appointed as president-elect in March 2022 and hold the office of president for 1 year beginning in March 2023. Cronin is currently an assistant voluntary professor at the University of Miami and an advisor to the AAD’s Council on Education.

Robert S. Kirsner, MD, PhD, FAAD, Miami, Florida, will be appointed as vice president-elect in March 2022 and hold the office of vice president for 1 year beginning in March 2023. Kirsner is also the chair and Harvey Blank endowed professor at the Dr. Phillip Frost Department of Dermatology and Cutaneous Surgery at the University of Miami Miller School of Medicine. He most recently served on the Academy’s Board of Directors and previously chaired the Academy’s Council on Education.

The newly elected board members include the following: Tammie Ferringer, MD, FAAD; Brad P. Glick, DO, MPH, FAAD; Adrian O. Rodriguez, MD, FAAD; Ruth Ann Vleugels, MD, MPH, MBA, FAAD.

AAD FINDS ONE THIRD OF AMERICANS’ FAIL QUIZ ON SKIN CANCER
A survey from the American Academy of Dermatology found that younger generations lack skin cancer knowledge.

REVANCE PRESENTS STUDY DATA ON DAXI AND HA FILLER AT AAD VMX
Revance presents 4 AAD VMX ePoster abstracts examining phase 3 study data for DAXI, and the impact of HA filler manufacturing technologies on HA chain degradation.

STEP UP SURVEILLANCE STRATEGIES FOR SKIN CANCER
More detailed tumor classifications, patient data advance surveillance strategies for the high-risk patient population.

TIPS TO IMPROVE HIGH-RISK SKIN CANCER MANAGEMENT
In part 2 of this skin cancer report from the American Academy of Dermatology Virtual Meeting Experience 2021 (AAD VMX), an expert shares pearls on regular medication reviews.

‘ZOOM DYSMORPHIA’ BECOMING RISING ISSUE AMONG PATIENTS
A survey found a large proportion of dermatologists surveyed said their patients referenced video conferencing as the reason for seeking cosmetic consultation since the start of the pandemic.

PHASE 2 STUDY OF RUXOLITINIB CREAM FOR VITILIGO ANNOUNCES NEW FINDINGS
Incyte’s Phase 2 study evaluating ruxolitinib cream for vitiligo meets primary endpoint, shows improvement in body and facial repigmentation compared to placebo.

GAME CHANGERS IN DERMATOLOGY
Experts in core dermatological specialties share their insights on the game-changing research and innovation that advancing skin disease management and patient care.

TREMFYA PHASE 3 DATA SHOW CONTINUED CLEARANCE AFTER 5 YEARS
Tremfya phase 3 data shows skin clearance rates were maintained at 5 years.

CLEARING THE CONFUSION AROUND SPECIFIC DERMATOSES OF PREGNANCY
In a presentation at the American Academy of Dermatology Virtual Meeting, Marcia S. Driscoll, MD, PharmD, gave guidelines for diagnosing and treating four dermatoses of pregnancy.

MEDICAL, SURGICAL TACTICS HELP MANAGE HS
Thanks to new drug approvals, medical management is replacing surgery as the first-line treatment for inflammation caused by hidradenitis suppurativa. However, surgery is often necessary to relieve pain related to tunnels.

AESTHETIC DEVICE CONSIDERATIONS FOR SKIN OF COLOR
Patients of color make up a growing market for aesthetic dermatology. Physicians must learn how to tailor treatments and assess skin of color risk to best serve this emerging patient population. Doing so will deliver positive outcomes and drive patient satisfaction.

CAN TELEMEDICINE SURVIVE BEYOND COVID-19?
Telemedicine flourished among dermatology practices in the wake of COVID-19. But as the world tentatively reopens, questions about connectivity, regulations, and payment will have to be addressed before physicians decide what role virtual visits will play in their practices.

HAIR RESTORATION GOES HIGH-TECH
Futuristic tools including robotics and new types of lasers are just some of the therapeutic innovations aimed at slowing hair loss and increasing hair growth.

PEDIATRIC ATOPIC DERMATITIS LINKED TO LEARNING DISABILITIES
According to objective and subjective measures, children with more severe atopic dermatitis were more likely to report a learning disability.
AAD VMX 2021
Conference Recap

This year’s virtual meeting experience was a success — and Dermatology Times® was “there!”

Get current with our recap of discoveries and developments in skin cancer, psoriasis, atopic dermatitis, aesthetics and more.

Explore now: dermatologytimes.com/aad-2021
Regenerative Skin Care

LISETTE HILTON | Staff Correspondent

Skin care companies are marketing regenerative topicalcs featuring stem cells, exosomes, and platelet-rich plasma (PRP).

But do they work? And is it safe to use stem cells, exosomes, and PRP in skin care? Dermatology Times® and its sister publication, Aesthetic Authority®, asked experts in the regenerative skin care space for answers.

“There are no products that contain stem cells in over-the-counter skin care,” said Amy Forman Taub, MD, FAAD, founder and medical director of Advanced Dermatology in Lincolnshire, Illinois. “There are companies that have cultured media [extracted growth factors] from these cells, but these products have not been proven to be more effective than what we currently have from cultured media, ie, growth factor products from prenatal or perinatal tissue.”

The use of stem cells in skin care has taken a decade to evolve after early issues with stem cell sources, such as embryonic vs adult stem cells, and the requisite clinical studies to demonstrate consistent efficacy, according to Lawrence A. Rheins, PhD, chief scientific officer at Aesthetics Biomedical in Phoenix, Arizona, creator of SoME skin care.

“A few years ago, there was interest in using botanical stem cells for skin care products. Frankly, I do not understand how that would work,” Rheins said. “Those stem cells are not going to get into the skin. [Plus], how physiologically relevant are botanical stem cells to human skin? Adipose adult stem cells are finding a significant growing role in aesthetic medicine including facial rejuvenation.”

According to Taub, exosomes are noncellular and may be able to lyophilize, but research is in the early phases. In other research, Mayo Clinic investigators reported in Science Daily that puriﬁed exosomal product, known as PEP, an off-the-shelf, room-temperature-stable exosome, can heal wounds that do not have adequate blood supply in single exosome application.

Safety concerns are a hurdle for stem cells and exosomes in skin care. The FDA regulates products containing stem cells and exosomes. Although exosome-containing products are available in the marketplace, some companies that make them have received FDA warning letters, according to Rheins. These FDA safety concerns could limit the commercial potential of exosome-containing skin care topicals for the near term, he said.

PRP OPENS THE REGENERATIVE DOOR

The use of a patient’s own PRP growth factors in personalized skin care has gained rapid momentum in recent years as clinical science has shown its safety and efficacy, according to Rheins.

SoME, which features patients’ autologous PRP in a serum mixture for topical application, is proven to be stable and able to keep growth factors alive.

Autologous PRP is safe, according to Taub. “SoME is stable for 3 months, if refrigerated,” Taub said. “PRP is great for healing, so this could afford some correction of damage, but this does require drawing your patient’s blood and spinning it down to extract the PRP.”

According to Rheins, SoME took a different approach in product development.

“We are not taking stem cells. We are not taking synthetic exosomes. We are using the body’s own autologous physiological growth factors,” he said. “Consumers want personalized and more individualized skin care products. There is nothing more individualized or personalized than your own growth factors.”

Aesthetics Biomedical has patented a way of preserving platelet function for more than 90 days in SoME products, Rheins said.

After centrifuging a patient’s blood, the physician drops 3 mL of the patient’s PRP into the prepared SoME serum bottles. The patient takes the 3 bottles home in a supplied mini refrigerator and uses the product twice daily for the next 90 days.

“It’s the unique physiological electrolyte base formula of 23 ingredients that provides us with the opportunity to keep the platelets stable,” Rheins said. “The change in temperature, going from the small refrigerator to air temperature to skin temperature, causes platelet activation, and the granules inside the platelets begin to degranulate to release hundreds of the growth factors including exosomes… which are small enough to get into the skin. The patient puts the bottle back in the fridge and the platelets basically go back into a senescent state.”

Scientific journals published 2 studies on SoME in recent years. Investigators of the first study, published in 2019 in Journal of Cosmetic Dermatology, studied 20 female and male participants aged 30 to 60 years in a single-site, investigator-blinded, vehicle-controlled, split-face study to look at the effect of serum containing PRP vs the serum alone on facial photosaging. Study results showed the serum contained stable PRP for 90 days, and PRP-treated facial skin biopsies showed improvement in skin architecture and upregulation for collagen type I with concomitant upregulation of mRNA for collagen after 8 weeks of topical use.
Quick TAKES
A study found UV filters stayed on the skin for more than 1 day.
Several studies have investigated the impact of UV filters on the environment and human health.
Patients are advised to wear sun protection and apply broad spectrum sunscreen with sun protection factor 30 or higher.

In his presentation, Lim began by discussing the skin absorption of UV filters, mentioning a study published in 2020 that examined 48 healthy individuals with Fitzpatrick skin types II to IV. Study participants were instructed to apply a single application of sunscreen on day 1 and then 4 applications per day at 2-hour intervals on days 2 through 4. Participants used 2 mg/cm² of sunscreen on 75% of their body surface area.

Investigators tested 4 sunscreen products—lotion, aerosol spray, non-aerosol spray, and pump spray—that contained the active ingredients oxybenzone, octocrylene, octisalate, octinoxate, and homosalate. Blood samples were collected on days 1 through 21 and stratum corneum was evaluated for UV concentration via tape stripping on days 7 and 14.

Lim also noted that 0.5 ng/mL plasma level is a threshold used by the FDA when waiving safety studies.

Results of the study showed that levels greater than 0.5 ng/mL were detected after a single application on day 1 for all the active ingredients. The findings also revealed that the geometric mean for maximal plasma concentrations was greater than 0.5 ng/mL, levels of the same concentration were detected up to day 7 and up to day 21 for oxybenzone, and all active ingredients were detected in the skin on days 7 and 14.

“All UV filters were detected in the skin on day 7 and day 14 by tape stripping method, which is not surprising because when we apply sunscreen we want a UV filter to stay on the surface of the skin,” Lim said.

The results do not indicate that individuals should refrain from using sunscreen, and there is a need for further studies to help determine the clinical significance of the findings, according to the study authors.

REGULATIONS
During his presentation, Lim also provided an up-to-date walkthrough of current photoprotection regulations.

An FDA proposed rule released February 26, 2019, suggested that of the 16 UV filters listed in the 1999 Final Monograph, 2 filters were Category I—zinc oxide and titanium dioxide, which were considered to be generally recognized as safe and effective (GRASE). Furthermore, 2 filters fell under Category II but were not considered GRASE—para-aminobenzoic acid (PABA) and trolamine salicylate. And 12 filters fell under Category III with insufficient safety data to make a positive GRASE decision.

“The rule also proposed an SPF [sun protection factor] cap at 60 plus and strengthening of broad-spectrum coverage by adding UVA1 over UVA plus UBV to a ratio of 0.7,” Lim said. “That would make sunscreen have a more potent UV protection, which I believe is good for all of us.” A final rule was scheduled for September 2020, but no such guidance has yet been released, he noted.

Lim also delved into the impact of the Coronavirus Aid, Relief, and Economic Security (CARES) Act, which was signed into law in March 2020.

Under the CARES Act, the FDA is moving away from a “laborious rulemaking process” to an administrative order process, meaning that it should take less time to implement a monograph. Therefore, there will not be a final rule.

Also, under the provisions of the act, the FDA is required to issue a proposed administrative order by September 27, 2021. Once issued, the industry would have 1 year to have the products they offer in the United States comply with the order.

“Currently, Lim said, Hawaii has banned oxybenzone and octinoxate as of January 2021 and the U.S. Virgin Islands has banned octocrylene. In the same month, 3 bills (HB102, SB366, and SB132) were introduced that proposed a ban on sunscreens containing avobenzone and octocrylene.

HOW TO ADVISE PATIENTS
With more areas of the world considering the ban of some UV filters for health and environmental reasons, patients may be reluctant or confused when choosing a sunscreen or other form of protectant, Lim said.

He suggested physicians advise their patients to seek shade, wear protective clothing—such as sunglasses and wide-brimmed hats—and apply broad spectrum, tinted sunscreen of SPF 30 or more to exposed areas.

For patients concerned about the environmental effect of oxybenzone and octinoxate, Lim recommended using mineral sunscreen and practicing rigorous photoprotection by taking 600 to 800 IU of vitamin D daily.

“We know that adverse effects of sun exposure are well established, so the practice of photoprotection is essential,” Lim said.

For full list of references, see dermatologytimes.com

They identified 14 various organic UV filters found in seawater near coral reefs in the nanograms per liter range. Also, the review found 9 papers that reported toxicological findings in the micrograms per liter to milligrams per liter range.

When compared with concentrations in seawater, toxic effects of UV filters were found at 1000 to 1 million-fold higher concentrations.

The review concluded that there is currently limited evidence suggesting coral reefs are adversely affected by exposure to UV filters, however, the authors noted major data gaps that should be immediately addressed with high-quality monitoring, fate, and toxicity studies.

In his presentation, Lim also mentioned the effects of photoprotection on human health.

A study published in September 2020 investigated the effects of UV filters on human health. Results found that current evidence was not sufficient to support the causal relationship between the elevated systemic level of oxybenzone or octinoxate and adverse health outcomes.

Despite these findings, on February 9, 2021, the National Academies of Sciences, Engineering, and Medicine formed a committee dedicated to studying the relationship between UV filters and environment and human health, which is sponsored by the Environmental Protection Agency, according to Lim. AAD has also advocated for the study and selected 2 members for the committee.

They know that adverse effects of sun exposure are well established, so the practice of photoprotection is essential.”

Henry W. Lim, MD, dermatologist, department of dermatology, Henry Ford Health System, Detroit, Michigan.

“The CARES Act also incentivizes innovation by providing for an 18-month exclusivity period for new filters to the requesting manufacturer,” Lim said. “Looking at this timeline and assuming everything runs smoothly, we will see products on the shelves in compliance with these particular guidelines around 2023.”

ENVIRONMENTAL AND HEALTH IMPACTS
Lim also mentioned the environmental and health impacts associated with photoprotection. In a critical review highlighted in his presentation, investigators reviewed all of the published photoprotection studies up to June 2020, 32 in total.
PRX-T$_{33}$: a versatile tool to combat ageing in high-phototype skin

Rejuvenation and skin quality improvement without peeling.
Ethnic skin, or “skin of colour”, is being recognized as an area of aesthetics that has in the past been neglected. Often, the aesthetic clinical trials, training and teaching are based on Caucasian skin; so the requirements of patients with ethnic skin of colour is often overlooked. Specific training may be required to treat these patients and some of the clinical conditions that they face. In recent years more research, scientific papers and expertise on high-phototype patients (IV-V) has been developed, and we are building a much-required database of knowledge in this area.

Additionally, the correct products are also required; in this respect, PRX-T33, is becoming the go-to treatment for many clinics focussing on treating skin of patients with higher phototypes. PRX-T33, is relatively safe, effective, well tolerated and responds to one of the most frequent demands of aesthetic patients that of skin quality improvement.

What are the specific characteristics?

Patients with higher phototype skin present with issues common to all patients as well as those specific to the skin type. In general, the skin is prone to being reactive, particularly to inflammation and may be subject to dedicated conditions, such as dermatitis papulosa nigra.

The main concern from the practitioner and patient is of post-inflammatory hyperpigmentation (PIH). This is also quoted as one of the main reasons both for patients and for practitioners to refrain to undertake all but the most basic of aesthetic procedures; the lack of dedicated protocols further complicates this situation.

What are the concerns?

Due to this heightened risk of PIH from treatments such as peels or Energy-Based Devices (EBDs), and the presence of PIH from acne scars or past lesions, many patients are reluctant to request aesthetic treatments. However, market analysis shows that there is a growing interest in improving the appearance, and that this is a fast-growing sector of the aesthetic market. Patients also require their practitioners to understand and be empathetic to their specific concerns.

Compared with other racial/ethnic groups, African American women report the slowest onset and least severe signs of facial aging. They tend to report moderate-to-severe signs of facial aging later, being delayed until 50-79 years of age. Between the ages 70-79, over 70% are still without moderate-to-severe perioral lines, loss of lip fullness, or mid-face volume loss. African Americans tend to be most concerned by their tear trough and submental areas, which are also among the most likely to be prioritized in a future treatment, however, they express the lowest consideration rate for injectable treatment options and EBDs. A primary reason for considering injectables is to seek a natural appearance for their age, but cost, safety, and possible side effects are often cited as the main barriers.

Why PRX-T33?

PRX-T33, may be comparatively new on the US market, but it has a long history; originating from Italy and patented in 2006. It has been on the market since 2012. PRX-T33, is available in many international aesthetic markets as far and diverse as Japan, Europe, Russia and the Middle East. Its unique formulation comprises Trichloroacetic acid (TCA @ 33%), Hydrogen peroxide and Kojic acid. TCA is normally contraindicated in patients with higher phototype skins, but if you read on, you’ll discover why in this formulation it works in a completely different way and is well tolerated in these skin types.

PRX-T33, is best regarded as a “dermal rejuvenator” that works by activating the skin’s own regenerative system leading to a natural and quick improvement. It is applied topically in the office, with a manual technique taught during specialised training sessions. The procedure is quick, painless, and many patients find the gentle pressure used to encourage the product to penetrate the skin, very relaxing.

The application leads to an immediate glow and pore tightening, that allows you to send your clients on their way with a noticeable yet subtle result – as opposed to other therapies, that will make you look worse before you look better! By repeating the sessions at weekly intervals as needed, and with the right recommended home care products, the result will stabilise; the skin will regain tone and a natural complexion is achieved.

Many “newcomers” to aesthetic medicine choose PRX-T33 because it is non-invasive yet highly effective, while more established clinics choose to add it to their arsenal to complement other therapies, such as microneedling, EBDs, threading and so on. PRX-T33, can be integrated relatively easily with many other services, and you can use it throughout the year, because it does not peel or cause photosensitivity.

But why do so many practitioners use PRX-T33 to treat patients with skin of colour? PRX-T33 – far from being a simple peel — causes a controlled degree of inflammation in the skin due to its balanced formulation. This will rejuvenate the skin but avoids causing PIH. Additionally, PRX-T33 contains Kojic acid; a well-known skin brightening agent, which will act as a “safety belt” to reduce the risk of hyperpigmentation even in predisposed patients. Moreover, another one of the key ingredients in PRXT-33 is Hydrogen peroxide (H₂O₂), another skin lightener; at a concentration which does not “bleach” the skin. The H₂O₂ in this formulation and concentration works in conjunction with the TCA, making it non-aggressive in terms of skin peeling by coagulation and enables the TCA to penetrate into the dermis and stimulate the regenerative process. This allows all patients with a range of skin photo-types to enjoy its skin lightening properties without the risks normally associated with TCA. This may sound counter-intuitive, however, once you see how PRX-T33 works on the skin, this concept is understood.

Combining PRX-T33 with microneedling or EBDs, will provide the extra stimulation allowing you to avoid using the full depth of the needles, or the full power of the device, which usually carries a high risk of side effects. This is considerably of even greater importance when performing laser treatments on higher phototypes.

Even in today’s era of high-tech devices, lasers, light and energy sources, the key to success is still the ability of the practitioner to tune or adapt the basic protocols for maximum safety and results. Our patients do not settle for one-size-fits-all therapies, they require holistic beauty plans, personalised consultations with specific protocols, and this is particularly true with skin of colour. PRX-T33 can be the best ally both in a practice focussing on high-phototype patients, and a more generally oriented practice that wants to become more inclusive and offer their services safely and effective to people of all photo-types.

Mr M D Humzah
BSc(Hons), MBBS(Hons), AKC, FRCS(Glas), FRCS(Plast), MBA
Consultant Plastic, Reconstructive & Aesthetic Surgeon

ABOUT
PRX-T33 “effortless transformation” is an innovative skin care product that will revolutionize American approach to aesthetic medicine. It is the only product that will have long lasting immediate results after a painless procedure with little or no downtime.

CONTACT
contact@wiqo.us
www.wiqo.us

WiQO
IN PARTNERSHIP WITH WIQO
Dr. Humzah is a leading plastic surgeon in plastic surgery, cosmetic surgery, breast surgery, liposuction, botulinum and rhinoplasty.
HUMIRA is the only FDA-approved treatment for your HS patients¹-³

Results Your HS Patients Can See

MODERATE/STAGE II
Actual HUMIRA-treated patient achieving HiSCR

Before

After

HiSCR is at least a 50% reduction in total abscess and inflammatory nodule count, with no increase in abscesses and draining fistulas relative to baseline¹

Indication¹
Hidradenitis Suppurativa: HUMIRA is indicated for the treatment of moderate to severe hidradenitis suppurativa in patients 12 years of age and older.

Safety Considerations¹
Serious Infections: Patients treated with HUMIRA are at increased risk for developing serious infections that may lead to hospitalization or death. These infections include active tuberculosis (TB), reactivation of latent TB, invasive fungal infections, and bacterial, viral, and other infections due to opportunistic pathogens. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.

Malignancies: Lymphoma, including a rare type of T-cell lymphoma, and other malignancies, some fatal, have been reported in patients treated with TNF blockers, including HUMIRA.
Clinically Meaningful Improvement (HiSCR) at Week 12

- In the PIONEER clinical trials, 42% (PIONEER I) and 59% (PIONEER II) of HUMIRA-treated adult patients achieved HiSCR at Week 12 (primary endpoint) vs 26% and 28% on placebo, respectively.

HUMIRA also has flare data available for HS

**OCCURRENCE OF FLARE THROUGH 3 MONTHS**
Pre-specified Other Secondary Endpoint in Period A

- **88%** of patients on HUMIRA experienced no flares.
- **65%** control

HUMIRA-treated patients: n=316 for HUMIRA EW
Control patients: n=317 for control

PIONEER I (N=307) and II (N=326) were 36-week, randomized, double-blind, placebo-controlled clinical trials in adult patients with moderate to severe HS on HUMIRA 40-mg weekly (after initial doses).

- 22% (of 100) patients who were withdrawn from HUMIRA after 12 weeks experienced flare.

**DATA LIMITATIONS**
- Since PIONEER I did not reach statistical significance at the first key secondary endpoint, all endpoints in this integrated analysis cannot be regarded as statistically significant.

**Safety Considerations**
- **Other Serious Adverse Reactions**: Patients treated with HUMIRA also may be at risk for other serious adverse reactions, including anaphylaxis, hepatitis B virus reactivation, demyelinating disease, cytopenias, pancytopenia, heart failure, and a lupus-like syndrome.
- Please see additional Important Safety Information, including BOXED WARNING on Serious Infections and Malignancy, on the third page of this advertisement.
- Please see Brief Summary of full Prescribing Information on the pages following this advertisement.

To learn more, please go to ResultsforHS.com
IMPORTANT SAFETY INFORMATION FOR HUMIRA® (adalimumab)

SERIOUS INFECTIONS
Patients treated with HUMIRA are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids. Discontinue HUMIRA if a patient develops a serious infection or sepsis. Reported infections include:

- Active tuberculosis (TB), including reactivation of latent TB. Patients with TB have frequently presented with disseminated or extrapolumonary disease. Test patients for latent TB before HUMIRA use and during therapy. Initiate treatment for latent TB prior to HUMIRA use.
- Invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis. Patients with histoplasmosis or other invasive fungal infections may present with disseminated, rather than localized, disease. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. Consider empiric anti-fungal therapy in patients at risk for invasive fungal infections who develop severe systemic illness.
- Bacterial, viral, and other infections due to opportunistic pathogens, including Legionella and Listeria.

Carefully consider the risks and benefits of treatment with HUMIRA prior to initiating therapy in patients: 1. with chronic or recurrent infection, 2. who have been exposed to TB, 3. with a history of opportunistic infection, 4. who resided in or traveled in regions where mycoses are endemic, 5. with underlying conditions that may predispose them to infection. Monitor patients closely for the development of signs and symptoms of infection during and after treatment with HUMIRA, including the possible development of TB in patients who tested negative for latent TB infection prior to initiating therapy.

- Do not start HUMIRA during an active infection, including localized infections.
- Patients older than 65 years, patients with co-morbid conditions, and/or patients taking concomitant immunosuppressants may be at greater risk of infection.
- If an infection develops, monitor carefully and initiate appropriate therapy.
- Drug interactions with biologic products: A higher rate of serious infections has been observed in RA patients treated with rituximab who received subsequent treatment with a TNF blocker. An increased risk of serious infections has been seen in the combination of TNF blockers with anakinra or abatacept, with no demonstrated added benefit in patients with RA. Concomitant administration of HUMIRA with other biologic DMARDs (e.g., anakinra or abatacept) or other TNF blockers is not recommended based on the possible increased risk for infections and other potential pharmacological interactions.

MALIGNANCY
Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, including HUMIRA. Postmarketing cases of hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma, have been reported in patients treated with TNF blockers, including HUMIRA. These cases have had a very aggressive disease course and have been fatal. The majority of reported TNF blocker cases have occurred in patients with Crohn’s disease or ulcerative colitis and the majority were in adolescent and young adult males. Almost all of these patients had received treatment with azathioprine or 6-mercaptopurine concomitantly with a TNF blocker at or prior to diagnosis. It is uncertain whether the occurrence of HSTCL is related to use of a TNF blocker or a TNF blocker in combination with these other immunosuppressants.

- Consider the risks and benefits of HUMIRA treatment prior to initiating or continuing therapy in a patient with known malignancy.
- In clinical trials, more cases of malignancies were observed among HUMIRA-treated patients compared to control patients.
- Non-melanoma skin cancer (NMSC) was reported during clinical trials for HUMIRA-treated patients. Examine all patients, particularly those with a history of prolonged immunosuppressant or PUVA therapy, for the presence of NMSC prior to and during treatment with HUMIRA.

- In HUMIRA clinical trials, there was an approximate 3-fold higher rate of lymphoma than expected in the general U.S. population. Patients with chronic inflammatory diseases, particularly those with highly active disease and/or concurrent exposure to immunosuppressant therapies, may be at higher risk of lymphoma than the general population, even in the absence of TNF blockers.

- Postmarketing cases of acute and chronic leukemia were reported with TNF blocker use. Approximately half of the postmarketing cases of malignancies in children, adolescents, and young adults receiving TNF blockers were lymphomas; other cases included rare malignancies associated with immunosuppression and malignancies not usually observed in children and adolescents.

HYPERSENSITIVITY
Anaphylaxis and angioneurotic edema have been reported following HUMIRA administration. If a serious allergic reaction occurs, stop HUMIRA and institute appropriate therapy.

HEPATITIS B VIRUS REACTIVATION
Use of TNF blockers, including HUMIRA, may increase the risk of reactivation of hepatitis B virus (HBV) in patients who are chronic carriers. Some cases have been fatal.

- Evaluate patients at risk for HBV infection for prior evidence of HBV infection before initiating TNF blocker therapy.
- Exercise caution in patients who are carriers of HBV and monitor them during and after HUMIRA treatment.
- Discontinue HUMIRA and begin antiviral therapy in patients who develop HBV reactivation. Exercise caution when resuming HUMIRA after HBV treatment.

NEUROLOGIC REACTIONS
- TNF blockers, including HUMIRA, have been associated with rare cases of new onset or exacerbation of central nervous system and peripheral demyelinating diseases, including multiple sclerosis, optic neuritis, and Guillain-Barre syndrome.
- Exercise caution when considering HUMIRA for patients with these disorders; discontinuation of HUMIRA should be considered if any of these disorders develop.
- There is a known association between intermediate uveitis and central demyelinating disorders.

HEMATOLOGIC REACTIONS
- Rare reports of pancytopenia, including aplastic anemia, have been reported with TNF blockers. Medically significant cytopenia has been infrequently reported with HUMIRA.
- Consider stopping HUMIRA if significant hemolytic abnormalities occur.

CONGESTIVE HEART FAILURE
- Worsening and new onset congestive heart failure (CHF) has been reported with TNF blockers. Cases of worsening CHF have been observed with HUMIRA; exercise caution and monitor carefully.

AUTOIMMUNITY
- Treatment with HUMIRA may result in the formation of autoantibodies and, rarely, in development of a lupus-like syndrome. Discontinue treatment if symptoms of a lupus-like syndrome develop.

IMMUNIZATIONS
- Patients on HUMIRA should not receive live vaccines.
- Pediatric patients, if possible, should be brought up to date with all immunizations before initiating HUMIRA therapy.
- Adalimumab is actively transferred across the placenta during the third trimester of pregnancy and may affect immune response in the in utero exposed infant. The safety of administering live or live-attenuated vaccines in infants exposed to HUMIRA in utero is unknown. Risks and benefits should be considered prior to vaccinating (live or live-attenuated) exposed infants.

ADVERSE REACTIONS
- The most common adverse reactions in HUMIRA clinical trials (>10%) were: infections (e.g., upper respiratory, sinusitis), injection site reactions, headache, and rash.


Please see Brief Summary of full Prescribing Information on the following pages.
**WARNING: SERIOUS INFECTIONS AND MALIGNNANCY**

**ADVERSE INFECTIONS**

Patients treated with HUMIRA are at increased risk for developing serious infections. Patients with moderate to severe rheumatoid arthritis have a higher infection risk than patients with less active disease.

Infection serious adverse reactions included in the labeling: Serious infections, including listeriosis, sepsis, and tuberculosis (TB) have been observed in patients treated with HUMIRA. Patients who had a history of TB infection prior to starting HUMIRA are at increased risk for reactivation of latent TB infection.

**Reported Infections include:**

- Acute infections
- Infections with chronic or moderate duration
- Infections requiring hospitalization
- Infections requiring intravenous antibiotic therapy
- Infections with severe adverse reactions including sepsis, septic shock, or severe hypotension

**Infections and Malignancies**

- Infections have been reported in patients treated with HUMIRA including bacterial, viral, fungal, and other infections.
- Malignancies have been reported in patients treated with HUMIRA including lymphoma and other malignancies, some fatal.
- Patients who have had a history of malignancy or who are at increased risk for malignancy should be monitored closely.

**Serious Infections**

- Drug interactions with biologic products: A higher rate of serious infections has been observed in patients taking concomitant immunosuppressants, including TNF blockers, compared to patients taking HUMIRA alone. The concomitant use of a TNF blocker and abatacept or anakinra was associated with a higher risk of serious infections.

**Tuberculosis**

- Consider stopping HUMIRA if significant hematologic abnormalities occur.
- Consider immunization with an inactivated vaccine for patients who had latent TB infection and who are at high risk for TB disease.
- Consider empiric TB treatment in patients with a past history of latent or active TB, with a history of latent or active TB in a household contact or close contact, who have been exposed to TB, or who are at high risk for TB disease.

**Hematologic Reactions**

- There have been reports of severe hepatic reactions including acute liver failure in patients receiving HUMIRA. Use of TNF blockers, including HUMIRA, may increase the risk of reactivation of hepatitis B virus (HBV) in patients who are chronic carriers of this virus. In some instances, HBV reactivation occurring in conjunction with increased alanine aminotransferase (ALT) levels and clinical deterioration including hepatic failure or death has been reported in patients who were carriers of HBV with and without underlying chronic liver disease.

**Infections**

- Clinically significant exacerbation of infection in patients who have received biologic products is not recommended in the treatment of patients with RA.

**IMMUNIZATIONS**

- Patients should have current immunization status prior to starting HUMIRA.
- In the controlled portions of 39 global HUMIRA clinical trials in adult patients with RA, Ps, AS, CD, UC, and PsA, 2.4% of patients had a history of TB infection.

**Influenza**

- Patients who have undergone recent influenza vaccination have been reported to have post-vaccination anti-influenza antibodies at a rate similar to controls. HUMIRA has not been formally studied in patients with active or recent influenza.

**Varicella Zoster Infection**

- Patients treated with HUMIRA are at increased risk for developing varicella-zoster virus (VZV) infections. Patients who have been vaccinated or are presumed to be immune should be considered prior to vaccinating (live or live-attenuated) exposed infants.

**Cytomegalovirus**

- Patients receiving anti-TNF therapy for the treatment of inflammatory arthritis or inflammatory bowel disease are at increased risk of severe infections due to reactivation of cytomegalovirus.

**Malignancies**

- Malignancies, including lymphoma and other malignancies, some fatal, have been reported in patients treated with HUMIRA.

**INVESTIGATIONS**

**Drug Interactions**

- There have been reports of increased risk of infections and malignancies with the concomitant use of antineoplastic agents and biologic products.

**Adverse Reactions**

- The most common adverse reaction with HUMIRA was injection site reactions.

**Clinical Trials Experience**

- In clinical trials, patients were treated under various testing conditions. Adverse reactions observed in the clinical trials of a single drug cannot be directly compared to clinical trials of another drug and may not reflect the experience of patients treated with the combination of HUMIRA with TNF blockers in clinical trials.

**SEROLOGIC RESPONSES**

- Patients who have undergone recent influenza vaccination have been reported to have post-vaccination anti-influenza antibodies at a rate similar to controls. HUMIRA has not been formally studied in patients with active or recent influenza.

**Malignancies**

- Malignancies, including lymphoma and other malignancies, some fatal, have been reported in patients treated with HUMIRA.

**ADVERSE REACTIONS**

- The most common adverse reaction with HUMIRA was injection site reactions.
Body As A Whole:

Warnings and Precautions, Adverse Reactions

HUMIRA has been studied in 464 adult patients with uveitis (UV) in placebo-controlled and open-label extension studies. Uveitis Clinical Studies

- In placebo-controlled portions of the clinical trials in Ps, approx. 2% of patients in the placebo group and 5% of patients in the HUMIRA group developed positive anti-drug antibodies by 12 weeks of treatment. The mean time to development of anti-drug antibodies was approx. 6 weeks in patients who included previously incidental adrenal insufficiency or adrenal insufficiency. In approximately 60% of patients included previously incidences of upper respiratory tract infection and nasopharyngitis.

- In Study JIA-II, HUMIRA was studied in 32 patients who were 2 to <4 years of age or 4 years of age and older. Ten patients were younger than 4 years of age and 22 patients were age 4 years and older. In the 4 years of age and older inclusion group, 14 patients had treated with HUMIRA and 8 patients with placebo.

- In Study JIA-II, HUMIRA was studied in 32 patients who were 2 to <4 years of age or 4 years of age and older. Ten patients were younger than 4 years of age and 22 patients were age 4 years of age and older. In the 4 years of age and older inclusion group, 14 patients had treated with HUMIRA and 8 patients with placebo.

Sepsis

- In all patients

- In patients receiving concomitant MTX, the incidence of anti-drug antibody was 1% compared to 29% in patients not receiving MTX.

- In placebo-controlled portions of the clinical trials in Ps, the incidence of anti-drug antibody was 1% compared to 29% in patients not receiving MTX.

- In placebo-controlled portions of the clinical trials in Ps, the incidence of anti-drug antibody was 1% compared to 29% in patients not receiving MTX.

- In placebo-controlled portions of the clinical trials in Ps, the incidence of anti-drug antibody was 1% compared to 29% in patients not receiving MTX.

- In placebo-controlled portions of the clinical trials in Ps, the incidence of anti-drug antibody was 1% compared to 29% in patients not receiving MTX.

- In placebo-controlled portions of the clinical trials in Ps, the incidence of anti-drug antibody was 1% compared to 29% in patients not receiving MTX.

- In placebo-controlled portions of the clinical trials in Ps, the incidence of anti-drug antibody was 1% compared to 29% in patients not receiving MTX.
Trichoscopy Advances Hair, Scalp Disease Diagnoses

KATIE HOBBS | Editor

In a presentation at the American Academy of Dermatology Virtual Meeting Experience 2021 in April, Lidia Rudnicka, MD, PhD; Anna Waśkiew-Burnat, MD, PhD; Sergio Vañó-Galván, MD, PhD; and Bianca Marie Piraccini, MD, discussed best-practice recommendations for using trichoscopy as an aid in hair and scalp diagnosis and treatment.1 Rudnicka, a professor and chairman of the department of dermatology at Warsaw Medical University in Poland, discussed the 7 distinct ways to spot trichotillomania in patients with hair loss.2

Trichotillomania, a mental disorder classified under the obsessive-compulsive umbrella, involves “the recurrent and irresistible urge to pull hair from the scalp, eyebrows, eyelashes, and other body areas,” she said. She listed tips for diagnosing the disorder:

1. Look for evidence of hook hairs—hairs with a distal end shaped like a hook—due to its high link to the mental disorder. “If we see a field of view with multiple hook hairs, we can be almost sure this is trichotillomania because the hook hairs have a 100% positive predictive score,” she said.

2. Check for the presence of coiled hairs, seen to be irregular in shape with a jagged end. This is not to be confused with circle/pigtail hairs seen in alopecia areata (AA), which are regular in shape with a sharp distal end.

3. Watch for V-sign hairs from a patient pulling 2 or more hairs from 1 follicle unit. An indication of the disorder, they are formed from creating breakage in similar areas of the strands.

4. Monitor for trichoptilosis, which are young short hairs with split ends.

5. Look for flame hairs—hair residue that is semi-transparent, wavy, and thinning toward the distal end.

6. Watch for hair powder, which is even more dispersed particles of hair residue.

7. Identify any sign of tulip hair—diagonal hair breakage—which has the shape of a tulip head.

Rudnicka also highlighted the lesser-known trichotillomania incognita. “This is a case of a person who has almost normal-looking hair but complains of a tendency of hair that has stopped growing,” she said. “With trichoscopy, you will see very discreet features of trichotillomania.” Highlighting the main trichoscopic features of lichen planopilaris (LPP), Vañó-Galván, head of the trichology unit at Ramón y Cajal Hospital in Madrid, Spain, discussed the difference between active and inactive lesions. He included other features such as pili torti, blue gray dots in a target pattern, and broken hairs.3

Active lesions can be distinguished by peri-follicular scaling and peripilar casts. According to Vañó-Galván, these scales migrate along the hair shaft and form a tubular structure that covers the proximal portion of the emerging hair shaft. This is believed to occur due to changes in the outer hair follicle root sheath, he said.

Elongated linear blood vessels are another indicator of active LPP lesions. These vessels form a V with the corresponding emerging hair shaft. Violaceous follicular erythema is additional evidence of this, according to Vañó-Galván.

Inactive lesions have irregular, large white dots, white or milky red areas, and tufted hairs. Piraccini, an associate professor in the department of specialized experimental and diagnostic medicine in the Alma Mater Studiorum at the University of Bologna, Italy, uses trichoscopy not only as a diagnostic tool but also to grade severity, diagnose associated diseases, and monitor treatment outcomes for androgenetic alopecia.4

She uses the tool in mostly the anterior/vertex/temples where there are androgen-sensitive hair follicles and the occipital area where hair follicles are not as sensitive to androgens. Androgenetic alopecia trichoscopy signs include reduced hair thickness with an increased number of hairs with the diameter of less than 3 mm, empty follicles, reduced number of hairs per pilosebaceous unit, and peripilar halos, according to Piraccini. Thinning is especially evident in the frontal area because of hair follicle miniaturization, she said.

She monitors treatment outcomes through trichoscopy as a clear and easy way for patients to understand the indicators of increased hair density and health.

“After the first 6 months trichoscopy shows improvement,” Piraccini said. “I show the patient the positive outcomes in the number of hairs and the thickness.”

Trichoscopy, as presented by the 4 experts, plays an essential role for diagnosing hair or scalp disease, and showcases the ease of treatment monitoring.
Quick TAKES

- Moisturizers and cleansers play a key role in improving the dysfunctional skin barrier.
- Prescription medication and OTC skin care products improve symptoms.
- Physicians need to reinforce the importance of using OTC skin care products to their patients.

OTCs Enhance Therapy

ILYA PETROU, MD | Staff Correspondent

A s the list of oral and topical medications to treat rosacea grows, OTC skin care products remain instrumental in rosacea therapy. The products address skin barrier dysfunction and should be integrated in patients’ treatment regimens, according to results of a recent study in Journal of Drugs in Dermatology. The 4 subtypes of rosacea, according to the presentation of symptoms, are erythematotelangiectatic rosacea (erythema, flushing, telangiectasias), papulopustular rosacea (erythema, edema, acne-like lesions), phymatous rosacea (rhinophyma, papillomatosis), and lichenoid rosacea, which can cause significant inflammation leading to eye dryness, redness, and irritation.

Breaking the cycle of inflammation that causes barrier dysfunction appears to be key in improving rosacea symptoms. “Repeated episodes of flushing can lead to progressive damage of the endothelium, angiogenesis, as well as inflammatory changes in the dermis, leading to barrier dysfunction and exacerbation of rosacea disease,” said Hilary Baldwin, MD, medical director of The Acne Treatment and Research Center in Brooklyn, New York, and past president of the American Acne and Rosacea Society; and head author of the study.

For the study, 9 dermatologists from the United States and Canada convened for a webinar to discuss the evidence of barrier dysfunction in rosacea, the role of OTC skincare products for treatment, and optimal therapeutic regimens to treat the disease.

Prior to the meeting, the physicians completed a survey on OTC skincare products recommended for patients with rosacea in their practice including monotherapy, adjuncts to prescription medications, and maintenance therapy. Clinical guidelines, algorithms, and evidence-based recommendations were culled from the literature through August 2020.

Data that indicate barrier deficiency in rosacea include evidence of increased transepidermal water loss (TEWL); decreased skin hydration; increased stratum corneum pH; increased lactate acid stinger reaction; symptoms of itching, burning, and stinging; and an increased incidence of irritant and allergic contact dermatitis. According to Baldwin, it is believed that the impaired epidermal barrier facilitates the entry of irritants and allergens. This causes hypersensitivity to exogenous stimuli, vasodilation, and inflammation, promoting a cycle of disease and episodic exacerbations.

“The disturbed barrier often translates into a situation where patients’ skin is too irritated to permit the use of the medications and products that would otherwise result in clinical improvement,” Baldwin said. “As such, addressing barrier repair early in the treatment phase with the integration of OTC skincare products [and] continuing such care throughout acute treatment and the maintenance phase [are] paramount.”

The panel considered moisturizers, cleansers, and ultraviolet protection. In addition to prescription medications, consensus revealed that the OTC products recommended for monotherapy included ceramide-containing cleansers and moisturizers, mineral sunscreens, redness creams, niacinamide-containing lotions, and azelaic acid 10%.

For adjunctive therapy, ceramide-containing skin care products and corrective gel were recommended by 37.5% of physicians. A cleanser and antiredness cream were used by 37.5%. A gentle cleanser, moisturizer with sun protection factor (SPF), or various types of serum were recommended by 25%. Although the advantages of concomitant skincare in rosacea therapy in achieving quicker and longer lasting treatment outcomes are clear, Baldwin said that some physicians may not discuss adjuvant skincare in their patients’ rosacea treatment regimen.

“No visit for rosacea is finished until you have discussed skin care with the patient,” Baldwin said. “Physicians need to make sure that they get their patients on good quality skincare that will help to repair the barrier and improve rosacea independent of pharmacologic therapy.”

Inflammation is recognized as a common denominator in many inflammatory skin diseases, so taking measures to minimize it will likely lead to an improvement of rosacea symptoms, she added.

“In the past, OTC skincare in rosacea has not been given the attention it deserved,” Baldwin said. “Now we are recognizing that it is at least half the battle.”

Disclosure

Baldwin and coauthors received an unrestricted educational grant from CeraVe USA for support with research as well as consultancy fees for the study.

Reference

66% of users surveyed on RealSelf said they would choose Vivace® over seven different leading traditional and RF microneedling treatments.

The Vivace® is the FDA-cleared, industry leading, top trending, radiofrequency microneedling device designed for an incomparable patient experience.

The most comfortable experience with minimal downtime
31 multilevel precise robotic depth adjustments
0.5mm-3.5mm depth
Robotic soothe glide hand piece for gentle insertion
36 golden perfectly-sized insulated needles
Protect epidermis for the most comfortable patient experience
Patterned RF emissions by chevron circuit
1MHz radio frequency
AVC (Automatic Visualization Confirmation)

"An evaluation of electrocoagulation and thermal diffusion following radiofrequency microneedling using an in vivo porcine skin model"

Shaun Woroten BSE
Zosia E. Zawacki VMD
Lawrence A. Khan A, PhD
Carlos Machado DVM, PhD, DACVP
Zoe Diana Drkose MD

Learn how Vivace® can strengthen your practice at VivaceExperience.com
Dangers, Benefits of Biologics Must Be Carefully Weighed

Caution is warranted when contemplating immunosuppression therapy in patients with chronic infectious diseases.

ILYA PETROU, MD  |  Staff Correspondent

Biologic therapy in dermatology has transformed the treatment of various systemic and cutaneous diseases. However, immunosuppression and immunomodulatory therapies can be challenging in patients with chronic infectious diseases, and clinicians must practice caution when contemplating treatment in this patient population, said Kieron Leslie, MD, in a presentation at the American Academy of Dermatology 2021 Virtual Meeting Experience (AAD VMX) in April.¹

"Particularly in patients with chronic infectious diseases such as viral hepatitis, tuberculosis (TB), HIV, and now COVID-19 infections, finding the appropriate treatment can be difficult," said Leslie, dermatologist in the dermatology clinic at Mount Zion and professor of dermatology at the University of California, San Francisco School of Medicine, both located in San Francisco, California.

"As systemic immunosuppressive therapies are precluded in this patient population, physicians need to be clear on what they can prescribe and what to avoid."

"The AAD guidelines regarding the restart of medications, however, are not clearly defined, as they could mean restart 7 to 14 days after symptoms subside or after polymerase chain reaction [PCR] testing becomes negative," Leslie said. "As such, the decision has been left up to the clinician's discretion and judgment."

Clinicians have several immunosuppressive therapies to choose from in the dermatologic armamentarium. Options include high-dose corticosteroids, etanercept, guselkumab (Tremfya; Janssen Biotech) and methotrexate (MTX). Leslie advised avoiding high-dose corticosteroids when possible. No other agents have been implicated yet in an increased risk of COVID-19 infection.

The AAD has not issued guidelines regarding how to vaccinate patients on immunosuppression, however, the American College of Rheumatology (ACR) has. It shares many of the same medications used in dermatology.² Based on the ACR guidelines, Leslie noted that there are no modifications to therapy or vaccination timing with regard to immunosuppressives, apart from MTX and JAK inhibitors such as tofacitinib.

Patients taking certain JAK inhibitors should be placed on a drug holiday 1 week after each vaccination dose. For rituximab, the vaccine series should be initiated approximately 4 weeks prior to the next scheduled rituximab cycle. The administration of infliximab does not require modifications to the timing of COVID-19 vaccination.

"Particularly in patients with chronic infectious diseases...finding the appropriate treatment can be difficult. As systemic immunosuppressive therapies are precluded in this patient population, physicians need to be clear on what they can prescribe and what to avoid."

Kieron Leslie, MD, dermatologist in the dermatology clinic at Mount Zion and professor of dermatology at the University of California, San Francisco School of Medicine, San Francisco, California.
Individuals with HIV are more susceptible to a whole host of inflammatory skin diseases, particularly psoriasis and eczema, and often have extremely severe disease, especially when their HIV is not controlled well. According to Leslie, antiretroviral therapy is effective for these patients and can quickly improve their psoriasis symptoms.

“Psoriasis is very common in [individuals] living with HIV, almost double the incidence of patients without HIV, and is particularly severe when the CD4+ count is low,” Leslie said. “The first line therapy here is antiretrovirals together with concomitant skin-directed therapies including topical corticosteroids, phototherapy, and retinoids.”

There is no evidence on whether immunosuppressive agents can be used safely in HIV-positive patients who fail these treatment measures because all patients with HIV are typically excluded from these clinical studies, Leslie said. National Psoriasis Foundation guidelines issued in 2010 suggest optimizing antiretroviral therapy, using topical medications, and, as a second line, using systemic acitretin.

“This approach does not work for everyone and...there have been many case reports of various agents being used in [HIV-positive] patients with psoriasis, including cyclosporine, MTX, apremilast, and IL-17 blockers such as secukinumab and guselkumab, essentially most of the agents that are FDA approved,” Leslie said.

The greatest body of evidence from case series and case reports are tumor necrosis factor α blockers, which, according to Leslie, likely reflect the clinicians’ familiarity with these agents, followed by the IL-12 and IL-23 blockers, such as ustekinumab, and the IL-17 blockers.

“It’s fair to say that the biologics are preferred to conventional disease modifying drugs such as cyclosporine or MTX, as these do seem to [lead to] a higher rate of infection,” Leslie said.

Various types of eczema and prurigo are also very common in individuals with HIV infection. Recently, there have been a number of case series using dupilumab in patients with HIV without any reported adverse events. Leslie noted that the safety profile reported thus far with dupilumab is encouraging.

According to the National Psoriasis Foundation, Leslie said, acitretin is the only medication that can be safely used in HIV-positive patients, as the retinoids are considered a second-line agent in this patient population.

Leslie also sees broader issues evolving. Chronic infectious diseases such as viral hepatitis, TB, HIV, and COVID-19 disproportionately affect minority populations and individuals immigrating to the United States who may not have health coverage. Bringing appropriate therapy to these patient subsets can be challenging and should be addressed, Leslie said.

Disclosure
Leslie reported no relevant financial disclosures.

References
Prurigo pigmentosa is easy to treat with doxycycline or minocycline. But topical steroids and antihistamines do not work.”

Hye Jin Chung, MD, MMSc, assistant professor at Harvard Medical School and director of the Asian Skin Clinic at Beth Israel Deaconess Medical Center in Boston, Massachusetts.

Asian Americans are a fast-growing population in the United States and a major emerging market for dermatological services. Dermatologists need to become more knowledgeable about the most common skin conditions in Asian patients. Certain skin disease signs and symptoms may differ for Asian patients, as will optimal approaches and treatment regimens.

The “keto rash” has been reported in those on the ketogenic (keto) diet, which includes consuming high fats and low carbohydrates. The new entity known as keto rash is actually prurigo pigmentosa, according to Chung, and now dermatologists are seeing patients with prurigo pigmentosa from other racial backgrounds.

Prurigo pigmentosa is linked to the ketogenic diet may resolve without medical intervention if patients increase their carbohydrate intake.

Prurigo pigmentosa presents as recurrent, pruritic, erythematous papules with reticular pigmentation. “The main differential diagnosis for pruritic papules on the trunk of young people would be pityrosporum folliculitis,” she said. “But in pityrosporum folliculitis, the papules are all follicular centric and you do not see reticular postinflammatory hyperpigmentation.”

The early stage of prurigo pigmentosa is characterized by a superficial perivascular infiltrate of neutrophils, whereas spongiosis and necrotic keratinocytes often appear in later stages. “A definitive mechanism of pathogenesis has yet to be determined,” Chung said. “But its relationship with ketosis has been well documented. Prurigo pigmentosa is associated with anorexia nervosa, diabetes mellitus, strict ketogenic diet, and bariatric surgery.”

The population grew 81% during that time, from approximately 10.5 million to a record 18.9 million. By 2060, the number of Asian Americans in the US is projected to surpass 46 million, according to the Pew Research Center.

Learning to differentiate common and uncommon conditions is key to serving this expanding patient population, said AAD VMX session speaker Hye Jin Chung, MD, MMSc, assistant professor at Harvard Medical School and director of the Asian Skin Clinic at Beth Israel Deaconess Medical Center in Boston, Massachusetts.

She outlined the 4 inflammatory disorders predominately found in Asian patients—prurigo pigmentosa, cutaneous plasmacytosis, Kikuchi-Fujimoto disease (also known as histiocytic necrotizing lymphadenitis), and lipodystrophia centrifugalis abdominalis infantilis—and offered strategies on how to optimize treatments for these patients.

PRURIGO PIGMENTOSA

Chung presented a case of a 68-year-old Vietnamese man with a rash on his trunk for more than 30 years. It began as pruritic but became asymptomatic. A punch biopsy on his back revealed dense perivasucular and interstitial inflammation in the upper and middle dermis.

He received a diagnosis of cutaneous plasmacytosis, a benign proliferation of mature plasma cells. The pathogenesis is unknown, and it is common in middle-aged Asian individuals, Chung said.

Cutaneous plasmacytosis presents as skin lesions on the trunk, face, nape of the neck, and axilla as brown, red, and purple-colored non-scaly patches, according to Chung. There have been recent case reports of partial improvement with PUV A, a combination treatment consisting of prescribing the parent compound psoralen (P) and then exposing the skin to long-wave ultraviolet light (UVA) or excimer laser.

Steroid injections, oral doxycycline, thalidomide, and retinoids have been tried with minimal success. The mainstay of treatment is UVB phototherapy.

CUTANEOUS PLASMACYTOSIS

Chung presented a case of a 68-year-old Vietnamese man with a rash on his trunk for more than 30 years. It began as pruritic but became asymptomatic. A punch biopsy on his back revealed dense perivasucular and interstitial inflammation in the upper and middle dermis.

He received a diagnosis of cutaneous plasmacytosis, a benign proliferation of mature plasma cells. The pathogenesis is unknown, and it is common in middle-aged Asian individuals, Chung said.

Cutaneous plasmacytosis presents as skin lesions on the trunk, face, nape of the neck, and axilla as brown, red, and purple-colored non-scaly patches, according to Chung. There have been recent case reports of partial improvement with PUV A, a combination treatment consisting of prescribing the parent compound psoralen (P) and then exposing the skin to long-wave ultraviolet light (UVA) or excimer laser.

Steroid injections, oral doxycycline, thalidomide, and retinoids have been tried with minimal success. The mainstay of treatment is UVB phototherapy.
Bangkok, Thailand.

Woraphong Manuskiatti, MD, professor of dermatology at Siriraj Skin Laser Center at Mahidol University in Bangkok.

KIKUCHI-FUJIMOTO DISEASE

Kikuchi-Fujimoto disease presents with lymphadenopathy, fever, and erythematous macules with small central crusting on the head and neck. It is a rare benign condition that mimics tuberculosis lymphadenitis or lymphoma.

“Patients are generally younger than 40 years of age with female predominance,” Chung said. “It is mainly described in Asia but also reported in America, Africa, and Europe.”

Skin manifestation, or skin rash, has been reported in 10% to 40% of patients with Kikuchi-Fujimoto disease, she said. Signs and symptoms usually resolve within 1 to 4 months. Chung said dermatologists can treat these patients with more supportive measures, including analgesics, antipyretics, and rest. In more severe cases, she recommended considering short-course oral corticosteroids and/or hydroxychloroquine.

Although it is usually a self-remedying disease, it may recur in 3% to 4% of cases. Patients with Kikuchi-Fujimoto disease should be carefully monitored for development of systemic lupus erythematosus, which has been associated with Kikuchi-Fujimoto, Chung advised.

LIPODYSTROPHIA CENTRIFUGALIS ABDOMINALIS INFANTILIS

Authors of a statistical analysis of 168 cases of lipodystrophy centrifugalis abdominalis infantilis found that 160 were from Japan, South Korea, and China. The male-to-female ratio of cases was 1:1.6, and 80% of cases were on the abdomen, lumbar area, buttocks, or thighs. More than 90% of patients present by age 5, and mechanical irritation is the cause in only 10% of cases, according to Chung.

Although the lesions progress slowly over several years, Chung said spontaneous resolution has been observed in more than 50% of patients by the time they reach their teens.

“Topical tacrolimus and pimecrolimus have been reported to prevent enlargement of lesions,” she said, adding that chloroquine, penicillin, vitamin E, and ibuprofen, as well as topical therapies such as corticosteroids or vitamin A, can help treat the condition.

DIFFERENTIATING MELANONYCHIA FROM NAIL UNIT MELANOMA

Treating Asian patients also requires in-depth knowledge of the differences in how skin disorders present. Mi Ryung Roh, MD, PhD, associate professor of dermatology at Yonsei University College of Medicine and head of dermatologic surgery at Gangnam Severance Hospital in Seoul, South Korea, detailed how to differentiate melanonychia, a common disorder in the Asian population, from nail unit melanoma (Table 2).

“Longitudinal melanonychia is a longitudinally oriented brown-black band that extends from the matrix to the distal portion of the nail plate. It accounts for nearly half of the cases of chromonychia,” she said. “The most common cause of melanonychia in all morphologies is subungual hemorrhage, followed by nail matrix nevus and trauma.”

Nail unit melanoma, or subungual melanoma, is rare in Western countries, with a prevalence of 0.7% to 3.5% of all melanoma cases. In South Korea, Japan, and China, the prevalence is 10% to 25% of all melanoma cases. Peak incidence is in the fifth to seventh decade of age but can be diagnosed younger. Thumb and great toe are common sites. Longitudinal melanonychia is the first manifestation in 38% to 76% of cases.

Nail matrix biopsy is the recognized standard for diagnosing nail unit melanoma, but clinicians should consider biopsy-caused nail scarring and deformity, according to Roh.

Dermoscopic features favoring nail unit melanoma in longitudinal melanonychia include a bandwidth percentage higher than 40% to 65%, multicolor features, granular pigmentation, subungual hyperkeratosis, and micro-Hutchinson sign.

Longitudinal melanonychia caused by melanocytic activation commonly occurs in skin phototypes IV, V, and VI. Inflammatory disorders, including psoriasis, can activate longitudinal melanonychia, as can systemic disorders such as Addison disease. Trauma is also a common cause of melanocytic activation that causes longitudinal melanonychia, Roh said.

Iatrogenic factors, such as chemotherapeutic and other drugs, can cause melanonychia. Other causes include nutritional deficiency such as vitamin D deficiency, Roh said.

“Melanonychia is a challenging symptom for clinicians irrespective of the patient’s age,” she said. “With careful history, clinical examination, and dermoscopy it is possible to determine whether it is benign or malignant. In suspected cases, nail matrix biopsy must be performed [because] tissue diagnosis remains the gold standard for diagnosis.”

DIAGNOSING AND TREATING COMMON FACIAL PIGMENTARY DISORDERS

The 5 most common pigmentary concerns among Asian patients are solar lentigines, melasma, acquired bilateral nevus of Ota-like macules, nevus of Ota, and postinflammatory hyperpigmentation, according to Woraphong Manuskiatti, MD, professor of dermatology at Siriraj Skin Laser Center at Mahidol University in Bangkok, Thailand.

“Hydroquinone remains the most effective topical treatment for melasma, but no matter how effective it is, a topical treatment alone does not produce impressive results in treating melasma.”

Woraphong Manuskiatti, MD, professor of dermatology at Siriraj Skin Laser Center at Mahidol University in Bangkok, Thailand.

TABLE 2

<table>
<thead>
<tr>
<th>THE ABCS OF DIAGNOSING MELANOMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, peak incidence in fifth to seventh decade for Asian Americans, African Americans, and Native Americans</td>
</tr>
<tr>
<td>Any changes over months or years</td>
</tr>
<tr>
<td>Lesion breadth of 3 mm or more, brown to black coloration and variegated borders</td>
</tr>
<tr>
<td>Extension of pigmentation onto the proximal or lateral nail fold</td>
</tr>
<tr>
<td>Digits most commonly involved, typically thumb, hallux, or index finger: single digits more common than multiples</td>
</tr>
<tr>
<td>Family history includes melanoma or dysplastic nevi. Other concerning signs are nonhomogeneous pigmentation or triangular shape of the band, nail plate splitting, or blunted lateral borders</td>
</tr>
</tbody>
</table>

SOURCE: MI RYUNG ROH, MD

"Melanonychia is a challenging symptom for clinicians irrespective of the patient’s age," she said. “With careful history, clinical examination, and dermoscopy it is possible to determine whether it is benign or malignant. In suspected cases, nail matrix biopsy must be performed [because] tissue diagnosis remains the gold standard for diagnosis.”

DIAGNOSING AND TREATING COMMON FACIAL PIGMENTARY DISORDERS

The 5 most common pigmentary concerns among Asian patients are solar lentigines, melasma, acquired bilateral nevus of Ota-like macules, nevus of Ota, and postinflammatory hyperpigmentation, according to Woraphong Manuskiatti, MD, professor of dermatology at Siriraj Skin Laser Center at Mahidol University in Bangkok, Thailand.

“Hydroquinone remains the most effective topical treatment for melasma, but no matter how effective it is, a topical treatment alone does not produce impressive results in treating melasma.”

Woraphong Manuskiatti, MD, professor of dermatology at Siriraj Skin Laser Center at Mahidol University in Bangkok, Thailand.

"Hydroquinone remains the most effective topical treatment for melasma, but no matter how effective it is, a topical treatment alone does not produce impressive results in treating melasma.”

Woraphong Manuskiatti, MD, professor of dermatology at Siriraj Skin Laser Center at Mahidol University in Bangkok, Thailand.
Manuskiatti, MD, professor of dermatology at Siriraj Skin Laser Center at Mahidol University in Bangkok, Thailand.

Manuskiatti, who presented on common facial pigmentary disorders in Asian people and their treatment at the virtual AAD meeting, said making the right diagnosis is the most important first step.9

“Solar lentigines present with multiple brown macules, mostly scattered all over the face,” Manuskiatti said.

Although acquired bilateral nevus of Ota-like macules, or Horii nevus, is a similar condition to nevus of Ota, there are important differences. Average age of onset is 30, or between 6 and 54 years, for Horii nevus, whereas nevus of Ota is congenital. Horii’s nevus has a bilateral distribution vs a predominately unilateral distribution in nevus of Ota. There is no mucosal involvement in Horii nevus but there is in nevus of Ota.

Hori nevus histology features melanocytes in papillary and middle dermis vs melanocytes in papillary and reticular dermis for nevus of Ota. Hori nevus is less likely than nevus of Ota to respond to laser treatment, and the incidence of postinflammatory pigmentation is from 50% to 75% with Horii nevus compared with 10% in nevus of Ota, Manuskiatti said. (Table 3)

Melasma, another common pigmentary disorder in Asia, presents as brown pigment distributed symmetrically around the face, usually on the forehead, bilateral cheeks, upper lid, chin, or nasal bridge.

Treatments vary according to the condition. For example, solar lentigines, acquired bilateral nevus of Ota-like macules (ABNOM or Horii’s nevus), and nevus of Ota can be treated with lasers. Melasma treatment usually begins with topicals, then chemical peeling, and oral treatment, with lasers as an adjunct when needed. Postinflammatory hyperpigmentation is treated topically with oral therapy and laser as needed, according to Manuskiatti.

Manuskiatti presented a case of solar lentigines treated singularly with the Q-switched 532 nm Nd:YAG laser. Within 1 month, the patient was close to 100% improved. He also presented on a patient with acquired bilateral nevus of Ota-like macules that were successfully treated 10 times with the Q-switched 1064 nm Nd:YAG laser, as well as a case of nevus of Ota 3 months after the eighth treatment with the 755 nm picosecond laser.

However, “melasma is still a headache for us,” he said.

First-line treatment for melasma includes tyrosinase inhibitors, hydroquinone, azelaic acid, kojic acid, arbutin, and licorice extracts. “Hydroquinone remains the most effective topical treatment for melasma, but no matter how effective it is a topical treatment alone does not produce impressive results in treating melasma,” Manuskiatti said.

Studies have found that lasers should not be used as a first-line treatment for melasma but can be used as an adjunct in resistant cases.10

He explained that when he does use a laser to treat melasma, it is a low-fluence Er:YAG laser or 755-nm picosecond laser.

Authors of a retrospective study of 561 Asian patients with melasma treated for 4 months with oral tranexamic acid found nearly 90% improved, 10% did not improve, and 0.4% worsened. But, the melasma often recurs after stopping the medication. In this study, 27.2% relapsed in a median 7 months.11

“Tranexamic acid may the game changer for treating melasma,” he said. When treating postinflammatory hyperpigmentation, he starts with topical treatment.

“We also found the use of oral tranexamic acid is quite effective for treating postinflammatory hyperpigmentation,” Manuskiatti said. “Pico toning [with the 755-nm picosecond laser] can be useful for treating laser-induced postinflammatory hyperpigmentation.”

Disclosures
Chung, Manuskiatti, and Roh reported no relevant financial disclosures.

References

TABLE 3
CHARACTERISTICS OF ABNOMS (HORI NEVUS) VS NEVUS OF OTA

<table>
<thead>
<tr>
<th>ABNOM* (Hori Nevus)</th>
<th>Nevus of Ota</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average age of onset</td>
<td>30 years (6-54)</td>
</tr>
<tr>
<td>Distribution</td>
<td>Bilateral</td>
</tr>
<tr>
<td>Mucosal involvement</td>
<td>No</td>
</tr>
<tr>
<td>Histology</td>
<td>Melanocyte in papillary and middle dermis</td>
</tr>
<tr>
<td>Response to laser treatment</td>
<td>Less likely</td>
</tr>
<tr>
<td>Incidence of PIH**</td>
<td>50-75%</td>
</tr>
</tbody>
</table>

* ABNOMs, Acquired bilateral nevus of Ota-like macules; ** PIH, Postinflammatory hyperpigmentation.

---

Tranexamic acid may the game changer for treating melasma.

Mi Ryung Roh, MD, PhD, associate professor of dermatology at Yonsei University College of Medicine and head of dermatologic surgery at Gangnam Severance Hospital in Seoul, South Korea.
COVID-19 Increases Urgency of Addressing Vitamin D Deficiencies in Patients With Skin of Color

CHERYL GUTTMAN KRADER, BSPHARM | Staff Correspondent

Dermatologists are well aware that skin pigmentation affects cutaneous vitamin D synthesis, making vitamin D deficiency more common among people with skin of color. Now the COVID-19 pandemic increases the need to give due consideration to that connection, according to Pearl E. Grimes, MD.

Soon after COVID-19 case numbers started to rapidly rise worldwide, investigators began to hypothesize and investigate risk factors for infection and worsened outcomes. Results showing an association with vitamin D deficiency appeared early and continued to grow.

In an article published in July 2020, Grimes and colleagues were the first to suggest that low vitamin D status could be among the variables explaining the higher burden of COVID-19 among people of color.1 Noting the need for further research to corroborate their hypothesis, the authors called on physicians to be aware of the higher prevalence of vitamin D deficiency in patients with skin of color and address the issue as a possible way to resolve the disparities in COVID-19 risks affecting minority populations.

Nine months later, information in an accumulating body of literature strengthens this call to action, said Grimes, director of The Grimes Center for Medical and Aesthetic Dermatology and founder and director of Vitiligo and Pigmentation Institute of Southern California in Los Angeles. “As we move this agenda forward, we need a cohesive effort where all physicians are talking to their patients about the importance of having a healthy level of vitamin D,” she told Dermatology Times.2 “Physicians must continue to emphasize the importance of vaccination, frequent handwashing, wearing masks, and social distancing as strategies for protecting against COVID-19 infection. However, the available evidence indicates that having a healthy level of vitamin D is also important for decreasing the risk. Furthermore, data also support the idea that for individuals who develop COVID-19, having a healthy vitamin D level will increase the likelihood of having a better outcome.”

PUBLISHED EVIDENCE
Reviewing the evidence on the associations between vitamin D status and COVID-19 infection and outcomes, Grimes cited a meta-analysis published online in March 2021. Aggregating literature published through November 26, 2020, the authors identified 39 studies meeting the criteria for inclusion in their systematic review.3 Results of the meta-analysis showed linked vitamin D deficiency with increased risks of COVID-19, as well as higher composite severity and increased mortality from the disease. The findings were replicated in another meta-analysis published later in the month that reviewed 43 published studies using a literature search cutoff date of January 31, 2021.4

The relationship between vitamin D status and COVID-19 infection as it specifically applies to race and ethnicity was the topic of another study conducted at the University of Chicago, with results published online in March 2020.5 The findings further corroborate research showing an association between vitamin D deficiency (<20 ng/mL) and COVID-19 infection.

However, the study was primarily designed to investigate potential racial differences in COVID-19 risk among persons with vitamin D levels of 30 to less than 40 ng/mL, which some experts consider sufficient. The investigators found that among Black people, the risk of testing positive for COVID-19 rose significantly, by 2.64-fold, among those with a vitamin D level of 30 to less than 40 ng/mL compared with those who had a level of at least 40 ng/mL. COVID-19 positivity rates among White people did not differ significantly when comparing the subgroup with a vitamin D level of 30 to less than 40 ng/mL and their counterparts with a higher level. The authors concluded that their findings support the idea that vitamin D supplementation could lead to COVID-19 infection rates.

ACCOUNTING FOR THE RISK
As reviewed in the numerous published papers, including the article by Grimes, an association between vitamin D status and COVID-19 risk and outcomes has substantiated plausibility. First, vitamin D signaling...
plays a key role in maintaining healthy innate and adaptive immune responses. In addition, and of particular relevance, vitamin D has been shown to mediate the induction of key antimicrobial peptides in the respiratory epithelium and inhibit production of proinflammatory cytokines that are upregulated in the COVID-19 cytokine storm.

“Two other recent meta-analyses published in the years preceding the COVID-19 pandemic linked vitamin D with risk of respiratory tract infections,” she said. “One found an increased risk of community-acquired pneumonia in persons with vitamin D levels less than 20 ng/mL. Another reported vitamin D supplementation protected against acute respiratory tract infection.”

COMMUNITY OUTREACH

As she aims to raise health care providers’ awareness that vitamin D status may be an important modifiable risk factor for COVID-19, especially in patients with skin of color, Grimes is also taking the message directly to the public, encouraging patients to have a dialogue with their physicians about vitamin D. To accomplish this, Grimes collaborated with producer and director Felicia D. Henderson to produce an informational YouTube video, “The Colors of COVID: Saving Lives and the Benefits of D-Z-C.”

The 13-minute film features Henry W. Lim, MD, chairman and C.S. Livingood chair of the department of dermatology at Henry Ford Health System in Detroit, Michigan, alongside other medical and nutrition experts (Jonathan Sackier, MB; R. Swamy Venuturupalli, MD; and Lee Bell, BCHN) and Black celebrity activists (Tyler Perry, Angela Bassett, Nicole Ari Parker, and Jennifer Lewis). It concludes with this appeal: “Please consult your health care professional to ascertain what supplementation is right for you.”

THE BIGGER PICTURE

Hopefully, concern about contracting COVID-19 will lessen in the future. However, the need to recognize and address low vitamin D status in patients with skin of color will continue to be a priority, according to Grimes. “Clinicians need to be aware of evidence showing that vitamin D insufficiency is a risk factor for many serious diseases, including diabetes, hypertension, cardiovascular disease, autoimmune diseases, and various cancers that occur at disproportionately high rates in skin of color populations,” she said.

Grimes acknowledged that there are conflicting data about the benefit of vitamin D supplementation for reducing disease risks and improving health outcomes. In particular, skeptics cite results from the Vitamin D and Omega-3 Trial (VITAL; NCT01169259), a nationwide, randomized, placebo-controlled trial of healthy adults that found supplementation with vitamin D₃ 2000 IU per day did not lower the risk of invasive cancers or major cardiovascular events. “However, when you dive into the details of the published article, you see that the study [results] found a possible benefit for decreasing the incidence of cancer among Black participants,” she said.

While awaiting results from prospective studies that may help define the benefits of different dosing strategies, physicians should encourage patients with skin of color to take a daily vitamin D supplement, Grimes said. “The Institute of Medicine–recommended dietary allowance for vitamin D is 600 to 800 IU per day for adults, and the recommendation is based on bone health. Given the very high incidence of vitamin D deficiency in African Americans who do not take supplements, higher doses are needed to achieve healthy levels. “I think physicians can feel comfortable recommending to their adult patients that they take 1000 to 2000 IU of a vitamin D₃ supplement each day,” she continued. “According to the National Academy of Medicine, most people can safely take up to 4000 IU per day without significant risk of hypercalcemia. I encourage health care providers to read the literature to develop their own knowledge base on this topic.”

References

“Clinicians need to be aware of evidence showing that vitamin D insufficiency is a risk factor for many serious diseases... that occur at disproportionately high rates in skin of color populations.”

Pearl E. Grimes, MD, director, The Grimes Center of Medical and Aesthetic Dermatology, and founder and director, Vitiligo and Pigmentation Institute of Southern California, Los Angeles, California
“Some [patients] clear 6-plus months, some clear 2-plus years, so don’t ‘refer and forget’ about patients receiving immunotherapy.”

Brent Moody, MD, FACP, FAAD, physician-dermatology, Skin Cancer Surgery Center, Nashville, Tennessee

Skin Cancer Update FROM PAGE 32

Mohs does not constitute a quality-of-life concern for elderly patients.

For those patients who choose observation or minimal treatment, there were 2 markers: neurocognitive impairment and impairment in everyday activities. Patients who have someone caring for them or helping to care for them must involve that person in treatment decisions. Olbricht noted that in some cultures adult children are the decision-makers for their parents’ health care, even if the parents are fully capable of handling their medical decisions. The medical team needs to be sensitive to those differences, she said.

She also stressed that, because of the range of therapies, medical professionals need to consider their core competencies. Patients’ needs and desires are the primary driver for care, but medical providers also need to play to their strengths, she said.

“Some people do excellent electrodessication and curettage, some do excellent cryotherapy, and some excel at other techniques,” she said. “You have to be using the technique enough to be comfortable.” She prefers a blunt tip for electrodessication. “You’re not cutting and not destroying more than you want. To me, it’s hands down the best, but if you’re used to using a sharp tip you can do a good job that way.”

The same goes for the choice of field destruction technique. Olbricht used cryotherapy early in her career but switched to electrodessication and curettage after treating a patient and seeing that cryotherapy left that patient with weeping sores. The effectiveness of electrodessication and curettage were similar to cryotherapy, but the scarring was more subtle and the patient was happier with wound care.

For topical therapies, the challenge is in ensuring patient adherence, such as a 4-6 week course of twice-daily application of 5-fluorouracil cream.

Olbricht predicted that targeted biologics would become more prevalent over the next 15 years.

SQUAMOUS CELL CARCINOMA

Despite SCC being a fairly common disease, dermatologists need to think outside the box when traditional diagnostics and treatments aren’t an exact match for the case. The 2 most widely accepted staging systems, those from the American Joint Committee on Cancer (AJCC) and Brigham and Women’s Hospital, provide excellent negative predictive value, said Brent Moody, MD, FACP, FAAD, a dermatologist at Skin Cancer Surgery Center in Nashville, Tennessee, during a presentation at the symposium.1 Dermatologists can offer patients at low risk excellent reassurance. The positive predictive value, on the other hand, is more problematic in both staging systems. Moody prefers the Brigham and Women’s system because it provides 4 distinct categories. In the AJCC system, he said, risk factors between cancers staged as T2 and T3 behave so similarly that they effectively represent only 1 stage. The issue, according to Moody, is that both systems struggle to predict which patients at high risk will develop a recurrence or nodal metastases. He has started to use genetic expression profiling to stage these high-risk patients more accurately. A lower-level staging in this new test would allow for deesca- lation of treatment—a higher one alerts dermatologists that more frequent radiographic scans and clinical follow-ups are necessary.

When it comes to imaging, Moody prefers to use CT scans to check for bone or lymph node involvement. “MRIs have the advantage of not having ionizing radiation and [are] better to check for soft tissue and perineural involvement,” he said. He also sees a role for ultrasound as another inexpensive, radiation-free option, but noted that it was more operator-dependent than MRI or CT scans.

Surgery remains the first-line treatment for SCC. “If you can fix it with a knife, you should,” he said. If that’s not possible, such as for medical reasons or patient preference, it’s critical to have a network of interdisciplinary collaborators ready to help the patient in their field of expertise, he said. Moody also cautioned that there will be cases where it’s not clear if surgery is the best option. In those cases, don’t be afraid to reach out. The patient can be sent for a second opinion or brought in front of a tumor board or multidisciplinary team for their call.

Moody detailed steps dermatologists and dermatological surgeons can take to better treat patients. Make sure the pathology lab can be trusted to provide not only accurate, but highly detailed reports, he said. For practices not in a university or large health system setting, Moody encourages dermatologists to reach out to medical and radiation oncology professionals in the area to find one with an interest in skin cancers to whom the dermatologist can send patients.

He noted that proton therapy has a role to play in SCC as it is more targeted than traditional options and can be used on tumors that recur after traditional radiation. Whereas immunotherapy is more effective in treating SCC than any other type of skin cancer, according to Moody, there is no clear guidance as to when to stop, so dermatologists must monitor those patients.

“One [patients] clear 6-plus months, some clear 2-plus years, so don’t ‘refer and forget’ about patients receiving immunotherapy,” Moody said. He’s also seen new lesions form in patients on immunotherapy but explained that those are usually lower grade and can be treated with Mohs.
REDUCE YOUR CREDIT CARD PROCESSING FEES

Rates as low as .05%*

Access to Care Credit® (Apple Pay, etc.) | EMV® | Chip & Pin
Next Day Funding with weekend settlement

OPTIONAL PROGRAMS:
- Cash Discount: Make the same profit margin with cash and non-cash payments!
- Curbside Ordering: Point of Sale Systems, Recommendations, Solutions & Integrations

GROW YOUR BUSINESS. PARTNER WITH NAB TODAY!
866.481.4604


<table>
<thead>
<tr>
<th>PRACTICE SALES &amp; APPRAISAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expert Services for:</td>
</tr>
<tr>
<td>✔ Buying or Selling a Practice</td>
</tr>
<tr>
<td>✔ Practice Appraisal</td>
</tr>
<tr>
<td>✔ Practice Financing</td>
</tr>
<tr>
<td>✔ Partner Buy-in or Buy-out</td>
</tr>
</tbody>
</table>

Call for a Free Consultation
(800) 416-2055
www.TransitionConsultants.com

CAREERS
NORTH CAROLINA

Well established aesthetic surgery practice seeking a BC/BE Dermatologist to practice in major metropolitan area in NC. Ideal candidate would be 100% cosmetic focused. Practice has fully accredited on site surgical suites. Candidate will receive a competitive compensation package, bonuses, benefits, and vacation.

Please submit resume and communication to: cosmesurgeryhrdept@gmail.com

Joanna Shippoli
(440) 891-2615
shippoli@mhrlawservices.com

Reach your target audience.

Our audience.

Contact me today to place your ad.

Joanna Shippoli
(440) 891-2615
shippoli@mhrlawservices.com

DermatologyTimes

AD INDEX

<table>
<thead>
<tr>
<th>ADVERTISER</th>
<th>PRODUCT</th>
<th>WEBSITE</th>
<th>PAGES</th>
</tr>
</thead>
<tbody>
<tr>
<td>AAD</td>
<td>dermatologymark.com/aad-2021</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>Abbvie</td>
<td>Humira</td>
<td>humira.com</td>
<td>40–44</td>
</tr>
<tr>
<td>Aesthetics Biomedical</td>
<td>visacareexperience.com</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>Almirall</td>
<td>Sefsara</td>
<td>kilsyri.com</td>
<td></td>
</tr>
<tr>
<td>Allergan</td>
<td>Zilix</td>
<td>zilxhpc.com</td>
<td>CV2–3</td>
</tr>
<tr>
<td>Galderma</td>
<td>galderma.com/us</td>
<td>CV4</td>
<td></td>
</tr>
<tr>
<td>Incyte</td>
<td>incyte.com/dermatology</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Inga Ellzey</td>
<td>dermatologybilling.com</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Janssen</td>
<td>Tremfya</td>
<td>tremfya.com</td>
<td>insert, 33</td>
</tr>
<tr>
<td>NewSurg</td>
<td>newsurg.com</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Ortho Derm</td>
<td>Allreno</td>
<td>allreno.com</td>
<td>25–26</td>
</tr>
<tr>
<td>Sun Pharma</td>
<td>Ilumya</td>
<td>ilumyapro.com</td>
<td>7–8</td>
</tr>
<tr>
<td>Wipro</td>
<td>wiqo.us</td>
<td>38–39</td>
<td></td>
</tr>
</tbody>
</table>

This index is provided as an additional service. The publisher does not assume any liability for errors or omissions.
The Department of Dermatology at Penn State Health Milton S. Hershey Medical Center is seeking a full-time Dermatologist to join our practice in State College, PA.

Position Highlights:
- Appointment will be at the Assistant or Associate Professor level
- Join a growing and busy academic practice
- Large primary care referral base
- Highly collaborative culture
- Faculty rank commensurate with experience
- Competitive salary and generous benefits

Position Requirements:
- M.D., M.D./Ph.D. or equivalent degree
- BE/BC Dermatology
- A strong commitment to patient care and education. Research interests not required

Community:
- State College, PA is home to Pennsylvania State University & University Park, which is the largest campus in the Penn State system.
- State College is more than just a quintessential college town. It is vibrant with exciting nightlife, great shopping, many options for arts & culture, and a diverse array of restaurants.
- State College Area School District ranks in the top 100 school districts in the State of Pennsylvania.
- Nestled at the base of Mount Nittany, State College is a unique and wonderful combination of small town charm and college town action that makes it no surprise that this area of central Pennsylvania is known as “Happy Valley.”

Penn State Health:
- Penn State Health is a multi-hospital health system serving patients and communities across central Pennsylvania.
- More than 1,300 physicians and direct care providers at 78 medical office locations.

For more information please contact:
Jeffrey J. Miller, MD, MBA
Professor and Chair, Department of Dermatology
Penn State Health Milton S. Hershey Medical Center
nhabt Henderson | Physician Recruiter
nhenderson1@pennstatehealth.psu.edu

Penn State Holy Spirit Medical Group is seeking Dermatologists with clinical expertise in general dermatology to join our growing community practice at our Camp Hill office.

What we’re seeking:
- Medical degree - MD, DO, or foreign equivalent
- Completion of an accredited residency program
- Excellent patient care abilities and interest in teaching

As a member of The Department of Dermatology you will be associated with:
- An outstanding program with a national reputation
- A highly collaborative culture
- Cutting-edge basic and clinical dermatology research and top-notch facilities at both the Hershey and the University Park campuses
- Interaction with dynamic clinicians across all dermatology-related departments and participation in innovative educational approaches

About Penn State Health:
Penn State Health is a multi-hospital health system serving patients and communities across 29 counties in central Pennsylvania. It employs more than 14,000 people systemwide. The system includes Penn State Health Milton S. Hershey Medical Center, Penn State Children’s Hospital, and Penn State Cancer Institute based in Hershey, PA; Penn State Health St. Joseph Medical Center in Reading, PA; and more than 2,800 physicians and direct care providers at more than 100 medical office locations. Additionally, the system jointly operates various health care providers, including Penn State Health Rehabilitation Hospital, Hershey Outpatient Surgery Center, Hershey Endoscopy Center, Horizon Home Healthcare and Pennsylvania Psychiatric Institute. In December 2017, Penn State Health partnered with Highmark Health to facilitate creation of a value-based, community care network in the region. Penn State Health shares an integrated strategic plan and operations with Penn State College of Medicine, the university’s medical school. With campuses in State College and Hershey, PA, the College of Medicine boasts a portfolio of more than $90 million in funded research and more than 1,700 students and trainees in medicine, nursing, other health professions and biomedical research.

For immediate consideration, please contact:
Nabat Henderson
Physician Recruiter, Penn State Health
Email: nhenderson1@pennstatehealth.psu.edu