Three Experts Chart Game-Changing Innovations That Will Shift the Boundaries of Dermatology.

Guidelines Address COVID-19 Vaccine Concerns Related to Dermal Fillers

GLA Offers Promise as Add-on Therapy to Minocycline

ANTIAging

GLA Offers Promise as Add-on Therapy to Minocycline

GLA THERAPY CONTINUES ON PAGE 23 ▶
INDICATIONS AND USAGE
ZILXI (minocycline) topical foam, 1.5% 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 1.5% 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.

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COM-ZIL-US-200041 09/2020
**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 and/or incinerate the container. 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 tetracycline drugs is not recommended during tooth development.

- **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. 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.

- **Clostridoides difficile Associated Diarrhea:** Clostridoides 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. Hypertoxin 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 HI 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 isotretinoin and tetracyclines 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 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 vasculitis. 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 UV-A/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.

**INDICATION**

ZILXI™ (minocycline) topical foam, 1.5% BRIEF SUMMARY OF FULL PRESCRIBING INFORMATION.

Please see full prescribing information.
• During the two Phase 3 trials, local tolerability evaluations were conducted at each study visit by assessment of erythema, telangiectasia, burning/stinging, flushing/blushing, dryness, itching, peeling and hyper-pigmentation. Subjects treated with ZILXI had improved local tolerability signs and symptoms at Week 12 when compared with corresponding baseline values. These occurred at a similar frequency and severity as subjects treated with the vehicle component of ZILXI. The local tolerance assessments in ZILXI patients (N = 1,008, of which 897 had local tolerability assessments at week 12) by incidence rate (%) and severity grade were as follows (mild, moderate, severe): erythema (36.2%, 18.3%, 0.7%), Telangiectasia (61.0%, 18.8%, 0%), burning/stinging (13.3%, 2.8%, 0%), flushing/blushing (39.0%, 9.6%, 0.9%), dryness (23.9%, 4.0%, 0.1%), itching (20.0%, 3.3%, 0%), skin peeling (16.1%, 1.9%, 0.1%), and hyperpigmentation (22.5%, 2.8%, 0%). Hyperpigmentation was most frequently assessed as characteristic of inflammatory and post-inflammatory changes associated with inflammatory lesions of rosacea. In a 40-week open-label extension safety study (for a total of up to 52 weeks of treatment) [NCT03276936], frequency and severity of 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 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.

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How pharmaceutical innovation is saving the world

by MIKE HENNESSY, SR

In nine months, the United States and the world must appreciate the role of the pharmaceutical industry—the investigators, physicians and business leaders—who are rescuing the world from COVID-19. It’s the medical breakthrough of our lifetime.

Instead of dwelling on why many in the media are ignoring this, let’s review some facts.

Since the discovery of COVID-19, here is what scientists have accomplished: They identified a novel virus; unlocked and sequenced its genetic code; created new therapies to save lives; and developed multiple safe and effective vaccines using messenger RNA technology, a technology hopefully applicable to future vaccine development. Margaret Liu, MD, a biomedical scientist and member of the MJH Life Sciences COVID Coalition, called it a breakthrough for mRNA vaccines. The United States has 2 vaccines approved for emergency use, 1 from Pfizer/BioNTech and another from Moderna. The Astrazeneca/Oxford vaccine has been approved for emergency use in the UK. In addition, there are 64 vaccines undergoing clinical trial at the moment, including 20 in phase 3 trials. In the United States and throughout the world, the pharmaceutical industry has answered the call and invested heavily in this effort.

This was the fastest vaccine development program in history, and it’s not even close. David Pride, MD, PhD, a microbiologist at the University of California, San Diego, estimates that vaccines typically take 10 to 15 years to develop. Until the COVID-19 pandemic, the fastest development timeline was 4 years, for the mumps vaccine.

Many government systems moved quickly to lessen the burden of onerous regulations and provide funding so that vaccines could be developed quickly but with rigorous standards. Perhaps it should be a lesson to all of us that regulation and innovation can be calibrated more effectively during “normal” times as industry races to develop new therapies for other epidemics—cancer, diabetes, heart disease, and more.

The next step of the process—distribution of the vaccine—will be as challenging as the development phase, if not more so. But again, the pharmaceutical industry is rising to the occasion. Factories worldwide are working overtime to produce hundreds of millions of vaccine doses.

Less than a month after the Pfizer vaccine was approved, more than 15.4 million doses of vaccine have been distributed throughout the country, and more than 4.6 million individuals have received their first dose, according to CDC data. Many patients are already receiving their second dose.

Although 15.4 million doses are impressive, some expected 20 million doses. But that is moving the goal line, as 6 months ago many observers didn’t think a vaccine would be available until 2021.

Members of our COVID Coalition told us that the holidays slowed the rollout considerably. Nancy Messonnier, MD, a physician with the National Center for Immunization and Respiratory Diseases at the CDC, expects a rapid increase in administered vaccines during the first few days of 2021.

Every day, more people will be vaccinated. After healthcare workers and our most vulnerable citizens, other frontline workers will be next. Teachers will be vaccinated so our children can return to school. And soon, all Americans will be able to receive the vaccine at their doctor’s office or at a CVS or Walgreens.

Remember, we accomplished this in 9 months, with the help, dedication, and expertise of our pharmaceutical industry heroes. Next time you turn on the TV and see negativity, turn it off and imagine instead where we will be in 9 months.

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

DermatologyTimes is guided by a core group of trusted physician experts who review meetings, suggest topics and sources, and conduct interviews.

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Dermatologist, Clinical Instructor
Mount Sinai, New York City

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Physicians consider a momentous year for Health Information Technology

BY MEDICAL ECONOMICS® STAFF

Have you used telehealth to see patients this year?

Yes: 93%
No: 7%
What percentage of your patient visits were via telehealth before COVID-19?

- None: 70%
- Up to 25%: 23%
- 26% to 50%: 4%
- 51% to 75%: 1%
- 76% to 100%: 2%

Who provides your telehealth technology?

- Free software (Skype, Facetime, etc): 28%
- Contracted third-party vendor: 24%
- Electronic health record (EHR): 22%
- Hospital system: 12%
- Don’t know: 5%
- Other: 9%

Is your telehealth program integrated with your EHR?

- Yes: 40%
- No: 60%

Did the coronavirus disease 2019 (COVID-19) pandemic cause you to use telehealth for the first time?

- Yes: 77%
- No: 23%

What percentage of your patient visits are via telehealth now?

- None: 6%
- Up to 25%: 51%
- 26% to 50%: 17%
- 51% to 75%: 11%
- 76% to 100%: 15%

Once the COVID-19 crisis is over, what do you expect will happen with the frequency of your telehealth visits?

- Telehealth visits will decrease: 43%
- Telehealth visits will remain about the same: 26%
- Telehealth visits will increase: 13%
- I’ll stop doing telehealth visits: 10%
- Not sure: 8%
Telehealth satisfaction

How satisfied are you with the quality of care you are able to provide your patients using telehealth?

Not at all satisfied 0

5.9

How satisfied are you with the telehealth technology and how well it functions?

Extremely satisfied 10

5

6

6.8

How satisfied would you say your patients are with a telehealth visit?

What are the biggest challenges you’ve faced using telehealth?

Explaining to patients how to use telehealth: 60%
Internet connection/bandwidth issues: 53%
Problems with scheduling/staff efficiency: 33%
Patient getting distracted while on call: 25%
Figuring out the interface: 22%
Integrating it with existing software: 22%
Upgrading technology so telehealth can be used: 19%
Training office staff: 17%
Cost: 13%

Do you use a prescreening process to determine whether a patient can be seen virtually or requires an office visit?

Yes 64%
No 36%

Do you think the investment in telehealth is worth it?

Yes 75%
No 25%
Don’t know 33%

Have you been getting reimbursed at the same rates for virtual visits as you have for in-office visits since the beginning of the COVID-19 pandemic?
No court has yet determined whether the long-term impacts of COVID-19 are a disability.”

So, I Really Can Terminate an Employee Who Has COVID-19?

by DAVID J. GOLDBERG, MD, JD

Dr 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.

Jane Doe, a nurse in the busy dermatologic practice of Dr Skin, plays an active assistant role in all aspects of the practice. Skin recently sold his practice to a private equity group, Drs Best Group, agreeing to stay on for 2 years as an employee physician to introduce his patients to the Drs Best Group providers. Six months after the sale, Doe undergoes testing for coronavirus disease 2019 (COVID-19). The results are positive. The laboratory director, a physician who has known Skin for 20 years, calls Skin with the results, which Skin subsequently passes on to the CEO of Drs Best Group. Doe becomes quite sick but fully recovers; however, she has multiple post-COVID-19 maladies. The word gets out about her illness, and patients are frightened to return to the office, which leads to substantial financial losses for the practice.

The CEO, who is not a doctor, wants to terminate Doe because of her negative impact on the practice. He has read past Dermatology Times® Legal Eagle columns and knows that he is unable to terminate her simply because of the consequences to his practice after word got out that she brought COVID-19 into the office. He places Doe on paid leave until he determines his course of action.

Ultimately, the practice offers Doe a clerical job in a hidden back office, with no direct patient interaction, at 75% of her previous salary. She declines and files a lawsuit against Drs Best Group under the Americans With Disabilities Act (ADA). What will happen?

The ADA, which became law in 1990, was drafted to protect the rights of disabled citizens in a constantly changing society. The act prohibits discrimination “against a qualified individual with a disability.” A disabled individual is defined as any person who has a physical or mental impairment that substantially limits at least 1 major life activity.

Unlike previous antidiscrimination laws, the ADA applies to the professional office of a health care provider. There is no violation if the terminated employee poses a direct threat, which is defined as “a significant risk to the health or safety of others that cannot be eliminated by a modification of policies, practices or procedures, or by the provision of auxiliary aids or services.”

To file a claim of discrimination under the ADA, a plaintiff must prove that they are disabled. Next, a plaintiff must prove that they are a qualified individual, defined as one who is able to “with or without reasonable accommodation…perform the essential functions of the employment position that such individual holds or desires.” Next, the plaintiff must show that discrimination occurred and was based on the disability. Court decisions have found that accommodation is reasonable as long as it does not impose undue hardship. If the accommodation requires what the ADA describes as “a fundamental alteration in the nature of the program,” it would be unreasonable.

Proof of disability is not as straightforward as it seems. No court has yet determined whether the long-term impacts of COVID-19 are a disability. Only with time and the evolution of COVID-19-related court cases will we have an answer. ◀
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Cosmetics and the COVID-19 Face Mask

by ZOE DIANA DRAELOS, MD

Dr. Draelos is a consulting professor of dermatology at Duke University School of Medicine in Durham, North Carolina.

Q. Do cosmetics compromise face mask protection from severe acute respiratory syndrome coronavirus 2?

The current shortage of personal protective equipment (PPE) has left many dermatologists and their patients wearing single-use face masks multiple times. This means that facial oils, moisturizers, sunscreens, foundation, and so on are present on the internal surface of the mask. These substances can get into the woven materials and decrease the mask’s ability to filter viral particles. So, after cleaning the face, it is probably best not to apply products in the area covered by the mask.

Q. How can you wear cosmetics under a mask?

It is very difficult to wear cosmetics under a mask, and they do shorten the mask’s wear life. During the coronavirus disease 2019 (COVID-19) pandemic, it is probably best to wear only upper-face cosmetics, because the rest of the face should be covered at all times when in public. Facial foundation, moisturizers, and sunscreen can be applied from the lateral canthus on the right and left face over the forehead. Apply eyeliner and mascara only to the upper eyelid; lower eyelid cosmetics will smear onto the mask. Upper-eyelid shadow can be worn without a problem. Consider applying a bold line and glittery eye shadow to diminish the COVID-19 doldrums.

Q. Can you wear lipstick under a face mask?

Yes, you actually can wear lipstick without it smearing all over your face if use a new 16-hour lip color (Provocalips; Rimmel) that does not rub off under a mask. The product creates a waterproof film over the lip surface, adding color without a waxy film that stains the inside of mask. Using the sponge-tipped applicator in the tube, first apply the color, coating the lips to the vermilion border and then inside, just to the mucous membrane. Smooth the colorcoat with the brush to deposit a thin, even layer. Then immediately use a second brush, also included, which contains a clear setting gel. Allow the products to dry thoroughly before a mask is worn.

Because the lip product is waterproof and rubproof, it can be difficult to remove. This is another job for micellar water. Saturate a round cotton facial pad with micellar water and rub it vigorously over the lips until the film loosens and can wiped away. Divide the lips into quadrants and work on 1 quadrant at a time until the color is removed. The lip product can cause dryness, so make sure to wear lip balm overnight to minimize peeling.

“Keep the face clean under the mask as oils can decrease its ability to filter viral particles.”
Racial Differences for Preferred Acne Care

CHERYL GUTTMAN KRADER, BS PHARM | Staff Correspondent

F actoring in a patient’s genetic heritage when choosing an acne care regimen could improve adherence, according to survey results that identify race-related differences in preferred sources of information and treatments for acne.

The findings also have implications for increasing satisfaction with treatments and physician care, said Rosapal V. Kundu, MD, senior author of the study and a professor of dermatology and medical education at Northwestern University Feinberg School of Medicine in Chicago, Illinois.

“Dermatologists are well trained and knowledgeable in making deep and meaningful connections with our patients to treat not only the cutaneous aspects of dermatological diseases but also the psychosocial implications,” Kundu said. “Our study shows that patients’ cultural and social constructs may influence their management preferences for acne. Understanding these preferences will allow us to improve the care delivered to all of our patients.”

The cross-sectional study of adults, conducted by Kundu in collaboration with Monica Mehta, MD, a research intern at Feinberg, noticed that subpopulations of patients presenting at different stages of acne voiced different preferences in prioritizing topical or oral medications, and often had tried various OTC and homeopathic remedies.

“Although there are many studies in the literature describing how perceptions of health and skin disease burden vary across races and cultures, there appears to be less research exploring differences in preferred treatment attributes,” Kundu said.

Kundu and Mehta designed a 31-item online survey to collect data on demographics, acne severity, treatment preferences and adherence, perceptions of causes of acne, and treatment valuation. Approximately 1200 18 to 73 year old individuals with self-identified acne were sent the survey, and 214 returned a completed questionnaire.

White individuals made up the majority of the study population (67%), followed by South Asian (13.8%), East Asian (12.4%), and Black (8.7%) individuals. The remainder were of mixed or other race. Women accounted for 85% of the population.

Responses regarding treatment varied. White respondents were significantly more likely than East Asians and South Asians to see a health care professional for treatment (88% [n = 126] vs 44% [n = 12]; P < 0.001 and (53% [n = 16]; P = 0.002, respectively.

White individuals (27%, n=39) preferred using prescription face washes/creams/gels, while East Asian (41%, n=11), South Asian (60%, n=18), and Black (37%, n=7) respondents preferred OTC washes/creams/gels.

White respondents were less likely to prefer OTC products for acne (20% vs 36%-60%) and more likely to use a variety of prescription treatments, including topical agents, oral antibiotics, oral contraceptives, and isotretinoin, Kundu said.

East Asians (63% [n = 17]) were less likely to get information from health care professionals (P = .03). This group was more likely (93% [n = 25]) to get information about acne causes and treatments from the internet compared with all other races (P = .002, respectively.

White individuals (27%, n=39) preferred using prescription face washes/creams/gels, while East Asian (41%, n=11), South Asian (60%, n=18), and Black (37%, n=7) respondents preferred OTC washes/creams/gels.

White respondents were less likely to prefer OTC products for acne (20% vs 36%-60%) and more likely to use a variety of prescription treatments, including topical agents, oral antibiotics, oral contraceptives, and isotretinoin, Kundu said.

East Asians (63% [n = 17]) were less likely to get information from health care professionals (P = .03). This group was more likely (93% [n = 25]) to get information about acne causes and treatments from the internet compared with all other races (P = .04), and 56% sought recommendations from family and friends.

White respondents turned to health care professionals more frequently than the internet (87% vs 74%), as did South Asians (77% vs 60%). Approximately three-fourths of the Black participants said they preferred both health care professionals and the internet as sources.

Studies are under way or planned to look more deeply at preferred treatments and resources for patients with acne and explore racial and cultural preferences for treating skin aging, vitiligo, and keloids, according to Kundu.

“Differences exist in perception and treatment preferences for acne between races, and exploring them may enhance providers’ understanding of their patients’ preferences,” Kundu said. “Health care organizations and professionals may need to utilize the internet and social media to access non-White populations.”

Disclosures Kundu and Mehta report no relevant disclosures or financial interests.

Reference

BY THE NUMBERS

PROPORTION OF WHITE RESPONDENTS
who sought acne treatment information from a health care professional vs the internet

PROPORTION OF EAST ASIAN
RESPONDENTS who used the internet rather than consult health care professionals for treatment information

87%
93%
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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:

- Photosensitivity: Patients should minimize or avoid sun exposure. Advise patients to discontinue AMZEEQ if symptoms occur.
- Hypersensitivity reactions: Discontinue AMZEEQ immediately if symptoms of anaphylaxis, serious skin reactions, erythema multiforme, and drug reaction with eosinophilia and systemic symptoms occur.
- Overgrowth of non-susceptible organisms: If superinfection occurs, discontinue AMZEEQ.
- 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.

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.
- Tissue hyperpigmentation: Patients who have shown hyperpigmentation should be warned not to use AMZEEQ on face, neck, or other prominent sites. For elderly patients or others at greater risk of hyperpigmentation, discontinue treatment at the first sign of hyperpigmentation.
- Photosensitivity: Patients should avoid sun exposure. Advise patients to discontinue AMZEEQ if symptoms occur.

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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.

† Amzeeq 4% 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).


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

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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 dentition. Tetracycline antibiotics administered to children up to 8 years of age and to pregnant women may affect tooth and skeletal development. Tetracycline antibiotics should not be used orally 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 an extracellular 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.
- **Clostridium difficile Associated Diarrhea:** Clostridium 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. Hypertoxin producing strains of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colpectomy. 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 hepatocellular 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 oral or parenteral dosages 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 examination. Women of childbearing age who are overweight or have a history of III 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 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 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 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 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 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 have 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 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 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), sclerae and heart valves. Skin and oral pigmentation has been reported to occur independently of the 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, it should be used only as indicated.

**Superinfection/Potential for Microbical 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 trials, 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 1,058 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%, 2.8%, 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 and severity of 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 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 administered 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 corporally 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 7-day 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.

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- Ability to Ask Doctors Questions in Advance Via Text Message: 25%
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A national online survey of 1,002 U.S. consumers, ages 18+, was conducted by Propeller Insights on behalf of DrFirst between June 16 and June 19, 2020, with a maximum margin of sampling error of ±3 percentage points at a 95 percent level of confidence.

**TELEHEALTH DISTRACTIONS**

Source: DrFirst

73% of respondents report multitasking during telehealth visits.

- 24.5% Surfing Web, Checking Email, Texts
- 21% Scrolling Through Social Media
- 18% Exercising
- 10% Driving
- 9.4% Having a “Quarantini” Cocktail or Other Alcoholic Beverage
- 24% Watching the News, TV, or Movie
- 18% Exercising

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New topicals, narrow-spectrum antibiotics, and research on the skin microbiome are paving the way for the future of acne treatment, according to Jenna Lester, MD.

In a presentation at the ODAC Conference Pre-Conference Sneak Peek | Inflammatory Diseases Symposium held virtually in December 2020, Lester provided an overview of promising treatments and therapies for patients with acne vulgaris. She is an assistant professor in the Department of Dermatology at University of California, San Francisco (UCSF), Health and founder and director of UCSF Skin of Color Clinic.

The US Food and Drug Administration (FDA) approved trifarotene (Aklief, Galderma), a topical retinoid for treatment of facial and truncal acne, in May 2020. Retinoids such as trifarotene, which bind to the retinoic acid receptor (RAR), have 3 isoforms: RARα, RARβ, and RARγ. Trifarotene is unique; it is the only topical retinoid that selectively targets RARγ, the most common RAR found in the skin. The drug is also the first topical treatment studied and proven to treat both facial (forehead, cheeks, nose, and chin) and truncal (chest, shoulders, and back) acne, according a press release from Galderma.

In a 52-week open-label comparative study, 435 patients were given trifarotene. Data showed the agent was well tolerated among participants, with the most common adverse effects being pruritus, irritation, and sunburn, all of which occurred most frequently within the first 3 months of treatment. Results showed that at 52 weeks, more than half (57.9%) of patients achieved treatment success. Results showed that at 52 weeks, more than half (57.9%) of patients achieved treatment success. In 2 randomized, vehicle-controlled, double-blind studies investigating the cream in 1440 males and nonpregnant females (all White), results showed a reduction in inflammatory and noninflammatory lesions and was well tolerated, according to Lester.

Minocycline (Amzéeq; Vyne Therapeutics) was FDA-approved in October 2019 for the treatment of nonnodular inflammatory moderate-to-severe acne in patients 9 years and older. A 4% minocycline foam falls under the tetracycline class of antibiotics, Lester said.

Results of a randomized, double-blind, vehicle-controlled study investigating 4% minocycline foam in 1488 patients showed an improvement in inflammatory lesions and revealed that 30.8% of patients achieved treatment success (Investigator Global Assessment of 0 or 1 and an improvement of 2 grades by week 12).

“Of the tetracyclines, minocycline has the least potential for significant [adverse] effects profile when comparing with doxycycline or tetracycline,” she said. “However, we know that there is potential for significant [adverse] effects, particularly discoloration and acne scarring, when taken systemically.”

The US Food and Drug Administration (FDA) approved sarecycline (Seysara; Almirall), a novel narrow-spectrum tetracycline class antibiotic FDA approved in 2018 to treat acne in patients 9 years and older.

The drug possesses a stable C-7 moiety and works by targeting Cutibacterium acnes while having little activity against gram-negative organisms and intestinal microflora, Lester said. Protecting the microflora decreases short-chain fatty acids, which can be anti-inflammatory, and prevents gastrointestinal distress, which, when disrupted, could make patients less likely to stay on the medication, she added.

“If you’re not already recommending [sarecycline] for your patients, this is an excellent option,” she said.

THE MICROBIOME CONNECTION

Lester emphasizes the importance of protecting the skin and gut microbiome, adding that certain phylotypes of Cutibacterium are associated with acne. Others are associated with healthy skin, and some attack unhealthy types of acne. In addition, gut organisms can influence glycemic control, tissue lipid content, and inflammation, which can have a direct impact on skin disease.

The results of one study found that consuming Lactobacillus acidophilus, Lactobacillus delbrueckii bulgaricus, and Bifidobacterium bifidum was just as effective as taking minocycline, whereas other study findings showed a decrease in inflammatory lesions. More research must be done on the skin and gut microbiome and how they influence inflammatory skin diseases, according to Lester.

Disclosures:
Lester reports no relevant disclosures or financial interests.

References:
GLA supplementation as an add-on to minocycline has the additional benefit of improving TEWL [transepidermal water loss] and stratum corneum hydration by restoring skin barrier function, which results in [higher] patient satisfaction.”

Ji Hyun Kim, MD, Department of Dermatology, Ulsan University Hospital, University of Ulsan College of Medicine in Korea, et al

GLA therapy
FROM PAGE 1

Quick TAKES

- Tetracycline and antibiotics such as doxycycline and minocycline are effective, but associated adverse effects may limit their use and impede outcomes.
- The inflammatory effect of γ-linolenic acid (GLA) has been shown to regenerate a defective skin barrier.
- Nearly 70% of study participants receiving minocycline supplemented with GLA achieved treatment success (investigator’s global assessment ≤ 1) at week 8 versus 33.33% of those receiving minocycline alone.

“...This chronic inflammation leads to increased transepidermal water loss (TEWL) and decreased stratum corneum hydration, thus initiating a vicious cycle.”

The result: a functionally impaired stratum corneum permeability barrier, which can lead to dryness, stinging, burning, and skin irritation. Known for its anti-inflammatory effect, GLA, an essential omega-6 fatty acid, has been shown to regenerate a defective skin barrier, according to the authors. GLA can be used both topically and systemically.

The prospective, double-blind, placebo-controlled trial included 31 adults with rosacea who were randomized to receive 320 mg/day GLA (Evolv; Biochemix; n = 16) or placebo (n = 15) in addition to 100 mg/day of minocycline for 8 weeks. The study included both erythematotelangiectatic and papulopustular rosacea subtypes. The investigators assessed clinical severity and improvements from treatment at weeks 0, 4, 8, and 12 using investigator global assessment (IGA) and patient global assessment (PGA) scores. They also measured and assessed changes post-treatment of several biophysical parameters, including melanin index, erythema index, TEWL, lipid concentration, and stratum corneum hydration.

Results showed that a higher proportion of patients who received GLA compared with the placebo group achieved treatment success (IGA ≤ 1) at week 8 (68.75% vs 33.33%) and patient satisfaction (PGA ≥ 3) at weeks 8 (75.0% vs 40.0%) and 12 (81.3% vs 46.6%). Data revealed a trend toward improvement in erythema index, melanin index, TEWL, and stratum corneum hydration in both groups over the 12-week study period. Results also demonstrated a significant difference in TEWL and stratum corneum hydration over time between the 2 groups. The investigators found GLA to be generally well tolerated, and no serious AEs were recorded in either treatment group.

“GLA supplementation as an add-on to minocycline has the additional benefit of improving TEWL and stratum corneum hydration by restoring skin barrier function, which results in [higher] patient satisfaction,” the authors wrote.

According to the investigators, the results demonstrate statistically significant and clinically meaningful improvements with GLA in rosacea symptoms of both erythematotelangiectatic and papulopustular rosacea subtypes, as well as skin barrier restoration. They suggest that future studies include larger patient cohorts and subgroup analysis between rosacea subtypes, which could help reveal differences in the additive effect of GLA among subtypes.

Disclosures

The authors report no relevant disclosures.

References

Managing AD Pain, Long-Term Therapy Effectively

MORGAN PETRONELLI | Associate Editor

Although generally considered a childhood disease, atopic dermatitis (AD) affects nearly 11% of adults, 10% of whom first experience the skin condition as an adult, Adam Friedman, MD, FAAD, said during a presentation at the ODAC Preconference Sneak Peek Inflammatory Diseases Symposium held virtually in December 2020. Friedman is interim chair of the Department of Dermatology, residency program director, and director of the Supportive Oncodermatology Clinic at the George Washington University School of Medicine and Health Sciences in Washington, DC.

“Just because there’s no past history [of disease] at childhood or adolescence doesn’t mean it can’t be atopic dermatitis [in an adult], and a very large subset, roughly a third, have moderate-to-severe disease,” Friedman said.

For many patients, AD’s effects go beyond red, weepy blisters or patches on the skin. In results of an Atopic Dermatitis in America survey, 61% of adults with AD reported pain from their disease. Moreover, 33% said they experience pain at least once a week, and 5% reported having pain daily. The findings also showed a correlation between disease severity and pain frequency.

Additionally, the survey found that among 7 disorders examined, AD was associated with an overall higher total impact on quality of life compared with heart disease, food allergies, diabetes, and autoimmune disorders in both men and women.2

“One thing we don’t think or talk about when it comes to atopic dermatitis is pain, and... this is also a very painful condition,” Friedman said. “It’s important to be aware of that and to ask our patients about pain, both from a management standpoint and in terms of the DIY approach that they’re taking at home to not just manage itch but maybe pain, as well.”

In 2014, the American Academy of Dermatology came out with guidelines to facilitate diagnosis of AD, which recommended assessing severity by asking patients about itch, sleep, persistence of disease, and the impact on daily activities.3 Although no biomarkers currently exist, Friedman suggested that clinicians use diagnostic criteria for AD; remember the many expressions of erythema, especially when presented on darker skin types, and, when in doubt, biopsy an area that has not been treated for at least two to three weeks.

Friedman also advised employing the AD yardstick to determine treatment and management based on disease severity.4 This method is categorized by nonlesional, mild, moderate, and severe disease. Best practices include reassessing AD control every four to eight weeks for the first three months to determine whether the therapy is working and giving patients a written action plan to promote proper medication use and adherence.

“But no matter where you are, from nonlesional to severe, certain rules always apply, such as basic management and trigger avoidance,” Friedman said. “We need both an active and a long-term management arm.”

SIMPLE STEPS TO MANAGE AD
Physicians can follow Friedman’s five rules to ensure an effective AD management plan, which he calls “Easy E’s.”

Education: Educate patients, using resources from the National Eczema Association and the American Academy of Dermatology.

Expectation: Give realistic expectations, for example, when to expect results from treatments or the chronicity and recurrence of disease.

Encouragement: Encourage patients to maintain treatment through early follow-up visits.

Enough: Give enough of an effective medication.

End: End misdiagnoses.

Friedman also gave tips on encouraging trigger avoidance among patients, creating an active and long-term management plan, and using appropriate soaps. He suggested avoiding “true” soaps and paying attention to pH to protect the acid mantle, recommending that patients with AD use moisturizing, soap-free and modified surfactant cleansers.

Bathing education is also vital for AD management, according to Friedman. He prefers that patients take baths rather than showers, especially during flare-ups. There is no standard for the frequency, type, or duration of bathing for patients with AD.

Friedman also recommended generous use of moisturizers with these three ingredients categories: emollients, occlusives, and humectants.

TOPICAL AND SYSTEMIC THERAPIES
An AD management plan might include the following:

- Topical steroids are effective when first used strongly and then reduced for maintenance.
- Frequent moisturizing and minimizing even mild soaps help patients manage the disease.

Atopic dermatitis

Quick TAKES
 Clinicians should factor in a patient’s pain when considering a treatment plan for atopic dermatitis.

Topical steroids are effective when first used strongly and then reduced for maintenance.

Frequent moisturizing and minimizing even mild soaps help patients manage the disease.

Morgan Petronelli | Associate Editor

February 2021 DermatologyTimes®

CONTINUES ON PAGE 26
Investigators Take Global Look at Best-Practice AD Care

JOHN JESITUS | Staff Correspondent

Several universal gaps in diagnosis and treatment of atopic dermatitis (AD) as well as real-world interventions for improvement are the focus of a ground-breaking report.1

“I’ve never seen this done anywhere else in dermatology,” said Eric L. Simpson, MD, professor of dermatology at Oregon Health & Science University (OHSU) in Portland and a member of the report’s steering committee. “It was a very ambitious goal—how to improve quality of care for patients with atopic dermatitis on a global scale.”

Assembled by KPMG, “Improving Quality of Care in Atopic Dermatitis” identifies gaps in areas ranging from patient awareness to physicians’ monitoring of long-term treatment (See Figure 1). Based on literature reviews, input from AD experts, and visits to 32 care centers worldwide, the 734-slide report offers targeted interventions supported by hundreds of clickable case studies.

“They sent a team out for days to each center to interview everyone involved with care—not just the physicians but also the nurses and support staff—to find out their shared challenges and the approaches to care that make them leaders,” Simpson said.

The report highlights 10 good-practice interventions along the patient-care pathway and

**FIGURE 1**

Best practice interventions for AD

<table>
<thead>
<tr>
<th>What is offered as part of the intervention and how has it been implemented in different centers?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EASY</strong></td>
</tr>
<tr>
<td>Supporting coordination of patient consultations (especially for complex patients)</td>
</tr>
<tr>
<td>Locating a patient’s electronic medical record or referral notes ahead of first physician consultation</td>
</tr>
<tr>
<td>Collecting patient information and family history before physician consultation (and presenting information to physician)</td>
</tr>
<tr>
<td>Providing brief education following physician consultations (e.g., disease education, demonstration of treatment application, reviewing treatment plan; about 15 mins)</td>
</tr>
<tr>
<td>Performing AD scoring indices or patient reported outcomes (PROs) before/after or during consultations</td>
</tr>
<tr>
<td>Traging patient questions received from patients (via telephone, email or online portal) to relevant HCP</td>
</tr>
<tr>
<td>Sharing information about additional support options (e.g., community HCPs, patient groups) within or outside consultations</td>
</tr>
<tr>
<td>Attending team meetings (i.e., being integrated into the team for discussion of patients)</td>
</tr>
<tr>
<td><strong>MEDIUM</strong></td>
</tr>
<tr>
<td>Providing telephone consultations for patients</td>
</tr>
<tr>
<td>Providing in-depth education following physician consultations (e.g., disease education, demonstration of treatment application, reviewing treatment plan; about 30–45 mins)</td>
</tr>
<tr>
<td>Performing 1:1 or joint consultation (with physician) with patients, as main HCP contact (about 30–45 mins)</td>
</tr>
<tr>
<td>Running specialist AD clinics (e.g., drug-monitoring clinic)</td>
</tr>
<tr>
<td>Collating patient information from cross-specialty consultations (and presenting information to physician and/or team meetings)</td>
</tr>
<tr>
<td>Performing allergy testing and education (patch test or prick test)</td>
</tr>
<tr>
<td>Developing patient education materials (online or paper based)</td>
</tr>
<tr>
<td><strong>ADVANCED</strong></td>
</tr>
<tr>
<td>Developing a mobile phone application for education of patients</td>
</tr>
<tr>
<td>Designing and running patient group education panels</td>
</tr>
<tr>
<td>Involvement in the setup of patient groups and member of advisory boards</td>
</tr>
<tr>
<td>Managing prior authorization process of treatment for dermatology patients</td>
</tr>
<tr>
<td>Organizing and delivering HCP education (for nurses and PCPs)</td>
</tr>
<tr>
<td>Prescribing treatment and/or creating treatment plans (where allowed)</td>
</tr>
</tbody>
</table>

KEY: AD, atopic dermatitis; HCP, health care providers

**Note:** With input from the steering committee, KPMG categorized these activities by level of resource required to implement, however this may vary across center settings (e.g., depending on existing resources)

**SOURCE:** IMPROVING QUALITY OF CARE IN AD
Managing AD FROM PAGE 24

Topical steroids used to suppress inflammation and pruritus, which continues to be the mainstay of treatment, according to Friedman. He recommended that clinicians “hit hard” with strong steroids and then scale down to a maintenance regimen. Starting with a lower-potency steroid that ultimately needs to be used for longer can lead to the expected problems of abuse, not proper use, creates problems.

If patients hesitate to use topical steroids because of possible adverse effects, Friedman urged discussing those concerns and pointing out that abuse, not proper use, creates problems.

“If excessive amount of greater than 50 g per week is avoided, and treatment vacations are implemented as per the product indications, it appears that superpotent topical steroids may be safe to use over the long haul, without causing systemic effects,” wrote the authors of a 2017 study.3

Topical AD treatments also include calcineurin inhibitors and phosphodiesterase 4 inhibitors.

The systemic therapies azathioprine, cyclosporine, methotrexate, and mycophenolate are currently used off-label for AD. Meanwhile, JAK1 and JAK 1/2 inhibitors such as baricitinib, abrocitinib, and upadacitinib are being investigated to treat moderate-to-severe AD and appear to be effective.

“It’s all about picking the right regimen for the right patient, not taking a one-size-fits-all [approach],” Friedman said.4

It’s all about picking the right regimen for the right patient, not taking a one-size-fits-all [approach].

Adam Friedman, MD, FAAD

References:

Disclosures:
Friedman has been a consultant and investigator for Sanofi and Regeneron Pharmaceuticals.

References:

Previously, Simpson’s approach, which included having his own allergist and contact allergy specialist, involved easy and medium interventions. “The more challenging intervention that can potentially promote even better care is having a multidisciplinary clinic where patients see more than 1 specialist that’s important to their care,” he said.

Now his department is incorporating adult and pediatric allergists, plus a contact dermatitis specialist to provide patch testing. “It’s going to provide convenience for the participant and improve communication among all of us in 1 sitting,” he said.

The report spotlights OHSU’s close ties to the National Eczema Association (NEA), a relationship that gives patients a trusted source of education and updates on emerging therapies, as well as a way to connect with other patients, Simpson said. “The NEA has funded important research projects in our department. I would recommend that everyone not only use them but volunteer. It’s a win-win for providers and patients.”

Disclosures
Simpson has been a consultant and investigator for Soroj and Regeneron Pharmaceuticals.

It’s all about picking the right regimen for the right patient, not taking a one-size-fits-all [approach].

It’s all about picking the right regimen for the right patient, not taking a one-size-fits-all [approach].

Adam Friedman, MD, FAAD
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Personalization key to optimal use of biologics

ILYA PETROU, MD | Staff Correspondent

L-17 and IL-23 inhibitors may outperform older biologics and oral therapies. Biologics represent a huge step forward in psoriasis treatment, but their proliferation over the past few years makes it critical for clinicians to become familiar with each drug’s properties. Making the right decision for each patient means looking at more than 1 measure of efficacy or safety.

Beyond its cutaneous manifestations, psoriasis is recognized as a systemic disease that is associated with comorbidities including psoriatic arthritis, Crohn disease, uveitis, obesity, type 2 diabetes mellitus, dyslipidemia, hypertension, and depression. Finding an effective regimen that can achieve and maintain a high clearance of psoriatic lesions, as well as address the potential mosaic of comorbidities with minimal adverse effects, is the ideal treatment goal.

For patients with mild psoriasis, topical agents form the mainstay of treatment and include corticosteroids, vitamin D analogues, calcineurin inhibitors, and keratolytics. Patients experiencing moderate-to-severe psoriasis and psoriatic arthritis might receive systemic therapies including cyclosporine, methotrexate, apremilast (Otezla, Amgen), and retinoids, traditionally used to suppress the immune system and keratinocyte proliferation. However, the dermatologist’s growing armamentarium has generated much interest among clinicians and their patients with psoriasis; among the new tools: biologic agents, including inhibitors to tumor necrosis factor α (TNF-α) such as etanercept, infliximab, and adalimumab; IL-12 and IL-23 inhibitor ustekinumab (Stelara, Janssen Pharmaceuticals); IL-17 inhibitors secukinumab (Cosentyx, Novartis) and ixekizumab (Taltz, Eli Lilly and Company); IL-17RA inhibitor brodalumab; and IL-23 inhibitors guselkumab (Tremfya, Janssen Pharmaceuticals), risankizumab (Skyrizi, Boehringer Ingelheim/AbbVie Inc), and tildrakizumab. Two agents in the pipeline, mirikizumab (Eli Lilly and Company) and bimekizumab (UCB), show strong results in phase 3 clinical trials.

PINPOINTING A PATHWAY

Investigators in the immunopathogenesis of psoriasis have identified IL-23 and IL-17 as fundamental contributors in the disease’s immune pathways. The discovery of the IL-23/T17 signaling pathway and significant therapeutic advances, including novel biologic therapy, have led to better treatment and management of psoriatic disease, according to a recent review paper.

“The discovery of the roles for [IL-17] and IL-23 on the development of psoriatic disease has led to substantial advances in our understanding of the pathogenic immune events in psoriasis and has led to a paradigm shift in the treatment of this condition,” wrote Jim G. Krueger, MD, PhD, professor, senior attending physician, and head of the Laboratory of Investigative Der-
The unprecedented success of selective IL-17 and IL-23 antagonists for the treatment of psoriasis underscores the essential nature of these cytokines in the pathogenesis of this chronic inflammatory condition.

Jim G. Krueger, MD, PhD, professor, senior attending physician, and head of Laboratory of Investigative Dermatology, The Rockefeller University, New York, New York
New Treatments Aim to Increase Survival Rate

Improvements in diagnostics and new therapies

LISETTE HILTON | Staff Correspondent

Cutaneous squamous cell carcinoma (cSCC) appears to be far surpassing melanoma as a cause of skin cancer–related death. Each year, more than 15,000 individuals in the United States die of cSCC, which is more than twice the number of deaths related to melanoma.

This concerning statistic has captured the attention of the industry and investigators, who are developing new ways to assess squamous cell carcinoma risk and better treat the disease.

INDIVIDUALIZED RISK ASSESSMENT BY GENE EXPRESSION PROFILING

Cancer staging systems for squamous cell carcinoma, including those of the American Joint Committee on Cancer and Brigham and Women's Hospital, have helped improve dermatologists’ ability to accurately stage the cancer, according to Sherrif F. Ibrahim, MD, PhD, an associate professor of dermatology at University of Rochester Medical Center in New York and a Skin Cancer Foundation spokesperson. “When we stage cancers, however, it doesn’t really help the individual. It tells us that if you take everybody with a given stage of squamous cell carcinoma, they have a certain chance of having a poor outcome,” Ibrahim said.

A new type of testing might be more useful to individual patients, according to Ibrahim. In September 2020, the (FDA) approved a novel personalized gene expression profile test indicated for use in squamous cell carcinoma, DecisionDx-SCC (Castle Biosciences).

“Using this test, we can actually study individual genes in a given patient’s squamous cell carcinoma and determine their risk for metastasis,” Ibrahim said. “What we are hoping for is…to approach staging on an individualized level, not just in an individual patient, but even for an individual cancer on a patient who has multiple cancers. And we can determine which of these patients might need closer monitoring, closer follow-up, more imaging, and perhaps additional treatment down the road.”

Castle Biosciences has a similar approved test for melanoma. “Individualized risk assessment by gene expression profiling is an exciting development, but of course more work needs to be done to determine how these tests will become incorporated in our day-to-day management of these diseases,” Ibrahim said.

Skin cancer care is moving in the direction of more accurate risk assessment coupled with more personalized treatment. This will be especially valuable in the setting of cSCC, Ibrahim said: “We do not have good guidelines on how often to image patients, what type of imaging to use, and what type of adjuvant treatment would most benefit high-risk squamous cell carcinoma patients. But with this individualized genetic testing, we might be able to really start probing those questions to develop more structured guidelines for the management of more advanced cases, of which we are seeing a lot more.”

“It is an exciting and rapidly changing time in the field of skin cancer. With many new advances in understanding the genetic underpinnings of disease and better nonsurgical options to treat all severities of tumors, we hope to bring better outcomes to our patients.”

Sherrif F. Ibrahim, MD, PhD, associate professor of dermatology, University of Rochester Medical Center in New York, and a Skin Cancer Foundation spokesperson
NEW AND EMERGING THERAPIES FOR CSCC AND BASAL CELL CANCER

The FDA has approved 2 checkpoint inhibitors, cemiplimab (Libtayo; Regeneron Pharmaceuticals) and pembrolizumab (Keytruda; Merck), for locally advanced or metastatic squamous cell carcinoma. Pembrolizumab received the OK for treatment of recurrent or metastatic cSCC in June 2020.1 The FDA approved cemiplimab in September 2018 for patients with metastatic or locally advanced cSCC who are not candidates for curative surgery or curative radiation.2

“A lot of people do not realize that there are these new and other emerging therapies,” Ibrahim said. “We have seen great advances for locally advanced nonmelanoma skin cancer, including the Hedgehog inhibitors vismodegib and sonidegib for basal cell carcinoma.”

Treatment of small sporadic nonmelanoma skin cancers also is advancing, including many injectable and topical agents, according to Ibrahim. “For instance, we have a trial under way with Regeneron that is looking at intralesional immune checkpoint inhibitor treatment. It includes injectable therapy for small, 1- to 2-cm squamous cell carcinomas. The hope is that we will have excellent results without the [adverse] effect profile of delivering these drugs systemically,” he said.

Ibrahim is among the researchers studying an investigational virally mediated interferon. Interferon works well for basal cell cancers when injected, but the required 4 or 5 painful shots a week for several weeks is prohibitive. Stamford Pharmaceuticals’ new agent, an injectable slow-release interferon, calls for just 1 injection per week for 3 weeks. “We expect to achieve over 90% clearance for sporadic basal cell cancers using this therapy,” Ibrahim said.

A topical Hedgehog inhibitor, patidegib, has moved further through the pipeline and is in phase 2 trials. When given systemically, Hedgehog inhibitors have a high adverse effect (AE) profile. The hope is that this topical agent from PellePharm may help patients with or at risk for basal cell carcinoma with fewer AEs.

Intralesional treatments for run-of-the-mill small skin cancers will provide a much-needed nonsurgical treatment option, Ibrahim said. “It is an exciting and rapidly changing time in the field of skin cancer,” he said. “With many new advances in understanding the genetic underpinnings of disease and better nonsurgical options to treat all severities of tumors, we hope to bring better outcomes to our patients.”

Disclosures

Ibrahim is a speaker and investigator for Castle Biosciences, Genentech, and Regeneron; an adviser and a speaker for Stamford Pharmaceuticals and an advisor and investigator for Stamford Pharmaceuticals.

References


NEW AND EMERGING THERAPIES

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<th>Treatment</th>
<th>Manufacturer</th>
<th>Purpose</th>
<th>FDA Approval Status</th>
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<tr>
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<td>Regeneron Pharmaceuticals</td>
<td>Checkpoint inhibitor</td>
<td>Approved</td>
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<td>Regeneron Pharmaceuticals</td>
<td>Injectable checkpoint therapy for small cSCCs</td>
<td>In trials</td>
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<td>Slow-release interferon</td>
<td>Stamford Pharmaceuticals</td>
<td>Therapy for sporadic basal cell cancers</td>
<td>In trials</td>
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<tr>
<td>patidegib</td>
<td>PellePharm</td>
<td>Topical Hedgehog inhibitor</td>
<td>In phase 2 trials</td>
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<td>pembrolizumab (Keytruda)</td>
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TABLE
DAXI Impresses; Approaches FDA Approval

LISEtte hILTon | Staff Correspondent

The long-awaited, longer-lasting neuromodulator drug candidate DaxibotulinumtoxinA for Injection (DAXI), a botulinum toxin type A formulated with a novel peptide excipient, may be nearing FDA approval.

In mid-December 2020, Revance Therapeutics shared results from its phase 2 upper facial lines study (NCT04259086),1 in which investigators looked at DAXI for combined treatment of glabellar, dynamic forehead, and lateral canthal lines.

The authors reported on a multicenter study of 48 patients enrolled to receive 40, 32, and 48 U of DAXI for injection in the glabellar complex, forehead, and lateral canthal areas, respectively. At week 4, nearly 92% of patients achieved an Investigator Global Assessment (IGA) score indicating no or mild wrinkle severity with maximum contraction on their lateral canthal lines. Nearly 96% achieved similar results on their forehead and glabellar lines at week 4.

Wrinkle severity returned to baseline at a median of 7.6 months post treatment, according to the phase 2 study findings.

The treatment was well tolerated in all upper facial regions. The most common adverse event (AE) was injection site erythema, which occurred in 6.3% of patients. The authors reported no eyelid or brow ptosis.

This was Revance’s first DAXI study on not just glabellar lines but also on forehead and periorbicular lines, or crow’s-feet, according to Jeffrey S. Dover, MD, FRCPC, a phase 2 study investigator and a dermatologist at SkinCare Physicians in Chestnut Hill, Massachusetts. “I think this is yet more evidence that the Revance neuromodulator produces an impressive effect on lines of negative facial expression and lasts longer than any of the other neuromodulators approved by the FDA thus far,” said Dover.

Dermatologic Surgery published 2 papers on the investigational neuromodulator in January 2021. In one study,2 investigators evaluated the use of up to 3 DAXI treatments for moderate or severe glabellar lines. They focused on data from SAKURA 1 and 2 (NCT03014622 and NCT03014635), two identical phase 3, open label, multicenter studies in which investigators evaluated single and repeat treatment of the glabellar lines with 40 U of DAXI.

The authors reported on safety results for nearly 2700 patients, including 882 who received a second treatment and 568 who got DAXI a third time. Treatment-related AEs, which were generally mild and resolved, occurred in 17.8% of patients. Eyelid ptosis occurred in 0.9% of treatments.

Investigators of 2 other studies3,4 focused on DAXI efficacy among nearly 2700 subjects enrolled in Revance’s preceding pivotal trials. Participants received repeat treatments when they returned to baseline on the IGA–Frown Wrinkle Severity (FWS) and IGA–Patient Frown Wrinkle Severity (PFWS) scales at 12 weeks and up to 36 weeks after treatment.

More than 96% of patients achieved no or mild severity in glabellar wrinkles on the IGA-FWS scale after each of the 3 treatments, with peak responses between weeks 2 to 4, and about one-third or more saw no or mild severity at week 24. Response rates reached highs of 92% or more at weeks 2 to 4 on the IGA-PFWS scale.

“The median duration for return to moderate or severe severity was 24 weeks,” the authors said.

“If approved, I believe daxibotulinumtoxinA will change the landscape of neuromodulators significantly. The approved ones all last 3 months. They all give nice results and have few adverse effects,” Dover said.

He and other investigators have seen no rise in AEs, and those that did occur lasted no longer than those of Botox, he said.

Revance appears to be preparing for approval. The company announced on December 22, 2020, that it has a strategic commercial manufacturing agreement with Ajinomoto BioPharma Services for the supply of DAXI.5

As of November 24, 2020, the FDA had deferred a decision on the neuromodulator because the required factory inspection could not be conducted due to travel restrictions related to coronavirus disease 2019.6 The FDA did not indicate any other issues.

Disclosures
Dover reports no relevant disclosures or financial interests.

References
For a full list of references, see DermatologyTimes.com.
Clinical Study Points to OT's Antiaging Benefits

Neuropeptide hormone’s anti-inflammatory effect could promote younger-looking skin.

CHERYL GUTTMAN KRADERM BS PHARM | Staff Correspondent

The so-called feel-good hormone may also have benefits for the skin. In results of a pilot study, high oxytocin (OT) levels correlated with more youthful-looking skin, as measured by skin age score (SAS).1

“This research links previous findings on the neuropeptide hormone’s role in preventing the release of certain proinflammatory cytokines, which may lead to skin aging, with clinical evidence of OT levels’ effect on skin’s appearance. Together, the clinical and preclinical evidence identify the OT signaling pathway as a potential target for strategies to protect against photodamage and, possibly, intrinsic aging of the skin,” according to Nicole Hayre, MD.

Hayre, graduate of Massachusetts Institute of Technology, and founder of Cosmetic Dermatology Center in McLean, Virginia, undertook the pilot study based on clinical observations of skin appearance. “I have been impressed that people who are in love generally look fantastic and seem to have a glow to their skin that is absent in people who are going through divorce or suffered the death of a spouse,” she told Dermatology Times.1

“Granted, a person’s mood and whether they are caring for themselves are important contributors to appearance, but I was curious about whether there was some biochemical explanation.”

The observation that factors such as social bonding, mental state, and enjoyment of intimacy in personal relationships differentiate the 2 cohorts turned Hayre’s attention to OT—also called the “love hormone.”

“Searching the literature, I found several basic science studies on oxytocin and the skin.2-4 The research showed that both oxytocin and its carrier protein are synthesized in keratinocytes,” she said. “In addition, there was evidence that fibroblasts express an OT receptor and that binding of OT to this receptor suppresses a senescence-associated secretory phenotype composed of an array of proinflammatory cytokines, chemokines, extracellular matrix-remodeling proteases, and growth factors.”

Although this study was small and oxytocin [OT] levels are likely to vary over time…results show [that] the higher the OT levels, the greater the reduction in skin age score compared with expectations based on chronological age.”

Nicole Hayre, MD, founder, Cosmetic Dermatology Center, McLean, Virginia

CONNECTING THE DOTS

To explore the relationship between OT levels and skin aging, Hayre designed a clinical pilot study. Participants included 6 women aged 48 to 61 years with Fitzpatrick skin types II to IV. Individuals were excluded if they had undergone cosmetic procedures/treatments in the previous 6 months, were using topical antiaging products, or were on hormone supplements. All participants had an average body mass index and were nonsmokers.

Each woman provided a 24-hour urine sample for OT measurement and completed a questionnaire on sunscreen use and ultraviolet light (sun/tanning) exposure. Hayre used data from each participant’s history to calculate sun exposure score (possible range, 1 [least] to 7 [greatest]). Using photographs taken with a medical imaging camera and software system (Canfield Scientific, Parsippany, NJ), she used the images to grade facial skin aging for each subject and calculate their SAS. From that value and the expected SAS score, which correlates with chronological age, she calculated an estimated percent change of SAS, she said. (Table)

Sun exposure scores for the 6 participants ranged from 1 to 7, OT levels ranged from 86 to 306 pmol/L per 24 hours, and actual SAS scores ranged from 23 to 53. The results for estimated percent change of SAS showed that the actual score for all participants was lower (more youthful) than expected. A plot of each woman’s OT level against the percent change showed an inverse, almost linear relationship between the 2 variables—the higher the OT level, the greater the percent change in SAS (Figure).

“It was interesting to find that several patients with high OT levels had SAS that correlated with more youthful skin in spite of high sun exposure scores, whereas others with lower OT levels and minimal sun exposure had higher SAS scores,” Hayre says. “This evidence connects clinical findings with previously published benchwork research showing that OT binding to receptors in fibroblasts can halt skin degradation by inhibiting SASP.”

Patients with high oxytocin levels had significantly lower (more youthful-looking) skin age scores than expected, even with strong histories of lifetime sun exposure.

This neuropeptide hormone may protect against photoaging, intrinsic aging, or both.
Hayre would like to expand the pilot study and further explore the OT’s potential importance in the skin. She is now working with a pharmaceutical company to evaluate a safe, nonhormonal, botanical that appears to have an OT-like effect on the skin.

In the meantime, it may be possible to take advantage of OT’s potential benefits by encouraging certain behaviors, she said. “For skin health, dermatologists tell patients to wear sunscreen, use appropriate skin care products, and avoid smoking,” Hayre said. “Perhaps our counseling should also include advice about making time for love and affection. Research shows that aside from intimacy and hugging partners, family, and friends, snuggling a pet and even caressing the skin can release OT.”

“Higher OT levels protecting the skin and making subjects appear healthier and more youthful likely promotes further social interaction. This OT Social Exchange System appears to work as a positive feedback loop which I speculated likely affects more than just the skin.” Hayre adds that this theory intrigued her to search the literature for information on other biological effects of OT. “I found preliminary research involving every system in the body and how it is affected by OT,” she says. “We have always known that love and affection improve mental and emotional well-being, but I am amazed that after centuries of medicine, we are just learning about the importance of our social interactions on physical health.”

Intrigued by her research, Hayre searched the literature for information on other biological effects of OT. “I found preliminary research involving every system in the body and how it is affected by OT,” she says. “We have always known that love and affection improve mental and emotional well-being, but I am amazed that after centuries of medicine, we are just learning about the importance of our social interactions on physical health.”

Patient with the highest oxytocin levels in Hayre’s study.

Photo courtesy of Nicole Hayre.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (y)</th>
<th>Fitzpatrick type</th>
<th>OT pmol/L/24hr</th>
<th>Skin age score (SAS)</th>
<th>Estimated change in SAS based on age</th>
<th>Sun exposure score</th>
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<td>42</td>
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</tbody>
</table>

The pilot study’s subject participant with the highest oxytocin level in the pilot study (306 pmol/L/24 hr) was a 57-year-old woman. She had a history of using only basic skin care and a strong lifetime sun exposure history (score, of 5 out of a possible 7). Her SAS skin age score was 23, which is a 60% reduction from the expected score for her age and consistent with her relatively youthful looking skin.

Disclosure

The author reports no relevant disclosures or financial interests.

References

COVID guidelines FROM PAGE 1

diately upon treatment developed heart racing and tingling and swelling of her face, exactly where the filler had been placed in the lips and cheeks. This lasted throughout the rest of the day [and] that evening, and subsided on its own the next day, totally with no treatment,” Dover said.

According to Dover, Moderna trial investigators reported that the AE was not serious but was medically significant. “This is very uncommon. Reactions are mild and might be related to preex-pediting filler. It has not happened as far as we know with the Pfizer vaccine yet,” Dover said.

Based on what Moderna reported to the FDA, on December 29, 2020, the American Society for Dermatologic Surgery (ASDS) released its COVID-19 vaccine guidance.1 Sue Ellen Cox, MD, coauthor of the guidance and ASDS president-elect, said she has not yet encountered a filler patient having a similar reaction post vaccine. Cox does about 3000 filler injections annually at her aesthetic and research-based practice in Chapel Hill, North Carolina, and is adjunct faculty at Duke University and the University of North Carolina.

“Basically, what the FDA data showed was that there were 3 participants out of 15,184 patients who received 1 dose of the mRNA-1273 vaccine. Those 3 patients developed either facial swelling or lip swelling, which was presumed to be related to the filler placement,” Cox said.

All 3 patients were women aged 29 to 51 years. One patient experienced lip angioedema 2 days after receiving the Moderna vaccine and reported having the same reaction after getting the influenza vaccine.

What is not known is what type of filler each patient had. “We don’t know whether the swelling was diffuse, which I think would be important information,” Cox said. “We know that each case resolved. We do not know what treatment was used to make it resolve.”

THE IMPORTANCE OF COMMUNICATION

Dermatologists and their teams should be on the same page when talking with patients about how the Moderna vaccine might affect them. Dover and his staff work from this script: “The media have reported on a few cases of inflammation at the site of filler injections after patients received the Moderna COVID-19 vaccine. The inflammation seems to be similar to what is infrequently reported after other vaccines, like flu vaccines.

This has not been reported with the Pfizer vaccine, although it may simply be because it is so uncommon. Based on early reports, it appears that filler inflammation that may be related to the COVID-19 vaccine can be successfully treated in the unlikely event [it occurs]. Several reliable treatment options are available to our physicians. As always, if you have any concerns about a reaction at a filler injection site, we encourage you to contact your physician.”

The ASDS states that currently available data suggest that patients already treated with dermal fillers should not be discouraged or precluded from receiving vaccines of any kind. “Similarly, patients who have had vaccines should not be precluded from receiving dermal fillers in the future,” according to ASDS.

People should get the vaccine as soon as it is available,” he said. “They should watch out for potential swelling in the area where they have had filler before, and they can notify us if they have any problems whatsoever.”

Until more is known, Dover said, he intends to recommend that patients who are slated to receive the Moderna vaccine consider getting their filler injections after receiving 2 doses of the vaccine.

Evidence suggests that delayed dermal filler inflammatory reactions with hyaluronic acid and non-hyaluronic acid fillers can be immunologically triggered by viral and bacterial illness, vaccinations, and dental procedures, according to ASDS. Dermatologists might first treat the filler-related AE of the vaccine with an antihistamine or prednisone, Cox said, and prescribe oral antibiotics if the area might be infectious.

Cox would not try to dissolve the filler with hyaluronidase at the onset: “First of all, you have to know what the filler was, because if it is not a hyaluronic acid filler, it is not going to dissolve with hyaluronidase. The second thing is that these typically are so easily treated with a little bit of steroid or your antihistamine of choice, and they resolve quite easily with that. You wouldn’t want to dissolve somebody’s filler that they paid a lot of money for and are happy with if you can just calm it down with a little steroid and antihistamine,” she said.

If the patient’s inflammatory reaction continues beyond initial treatment with an antihistamine or prednisone, dissolving the filler might be appropriate. For a patient who has a filler of silicone or polymethyl-methacrylate microspheres or one of the permanent types, treatment might include prednisone and intralesional triamcinolone with 5-fluouracil, Cox said.

The possible association between dermal fillers and this COVID-19 vaccine AE is an evolving issue that should become clearer with more data, according to Cox. Until then, dermatologists should avoid making legal statements or claims about how patients should or should not be treated. “And every patient should be seen by a board-certified dermatologist if they have an issue like this to get proper treatment,” Cox said.

Disclosures: Cox and Dover report no relevant disclosures or financial interests.

Reference

Quick takes

In the Moderna coronavirus disease 2019 (COVID-19) vaccine trials, 3 participants reported facial or lip swelling after receiving the vaccine. The symptoms in all cases were mild. ASDS guidelines state that patients with a history of dermal filler injections should not avoid vaccinations.

People should get the vaccine as soon as it is available. They should watch out for potential swelling in the area where they have had filler before, and they can notify us if they have any problems whatsoever.” Jeffrey S. Dover, MD, FRCP, SkinCarePhysicians, Chestnut Hill, Massachusetts

FEBRUARY 2021 DermatologyTimes®
Trichoscopy aids diagnosis, prognosis

JOHN JESITUS | Staff Correspondent

Trichoscopy (a dermoscopy-based diagnostic method) not only helps diagnose hair disorders and monitors treatment but also predicts treatment efficacy, Anna Waśkiew-Burnat, MD, PhD, a dermatologist at Medical University of Warsaw in Poland, said at the 29th European Academy of Dermatology and Venereology Virtual Congress.

“There are numerous hair and scalp diseases that share similar clinical features,” Waśkiew-Burnat said in her presentation. “Trichoscopy is an easy-to-perform diagnostic method that may help identify subtle details and establish the correct diagnosis. For example, it is difficult to distinguish between female androgenetic alopecia [FAGA] and fibrosing alopecia in a pattern distribution [FAPD] based only on the clinical picture. In these conditions, trichoscopy is useful to avoid misdiagnosis.”

Features of FAGA include increased numbers of vellus hairs and single-hair follicular units, along with anisotrichosis and yellow dots. For a diagnosis of FAGA, patients must meet 2 of the following major criteria:

- More than 4 yellow dots in 4 images at 70-fold magnification in the frontal area
- Lower average hair thickness in the frontal area compared with the occiput (calculated from at least 50 hairs from each area)
- More than 10% thin hairs (< 0.03 mm) in the frontal area

Alternatively, dermatologists can establish a diagnosis of FAGA using 1 major criterion and 2 of the following minor criteria (all comparing frontal area with occiput):

- 2:1 ratio of single-hair unit percentage
- 1.5:1 ratio of number of vellus hairs
- 3:1 ratio of hair follicles with perifollicular discoloration

“Another condition that is difficult to diagnose, even with trichoscopy, is alopecia areata [AA] incognita,” Waśkiew-Burnat said. Because this entity is frequently misdiagnosed as telogen effluvium, histopathological examination is important, she said.

Because it is challenging to identify patients with AA who are at risk of rapid disease progression and to determine which patients are likely to respond well to immunosuppressive therapy, Waśkiew-Burnat and colleagues developed the Alopecia Areata Predictive Score.

In a study of 65 patients with patchy AA, the authors conducted trichoscopic examinations at baseline and 2 months after treatment initiation. After 6 months of treatment, investigators classified 27 patients as responders and 38 as nonresponders. Positive predictive trichoscopic factors (observed in control trichoscopy) for hair regrowth in patchy AA included upright regrowing hairs and pigtail hairs. Negative predictive markers for hair regrowth included black dots, broken hairs, exclamation mark hairs, and tapered hairs. Probability of regrowth ranged from 98.3% for patients with the highest AA predictive score to 0% for patients with the lowest score.

For alopecia totalis or alopecia universalis, Waśkiew-Burnat said, she recommends trichoscopic examination 6 weeks after starting treatment and clinical assessment of hair regrowth after 4 months’ treatment. Positive predictive factors (observed in control trichoscopy) for regrowth in patients include pigmented vellus hairs and pigmented upright regrowing hairs. No negative predictive markers are associated with these conditions, she added.

Findings in a recent analysis showed lichen planopilaris accounted for 7.6% of visits to 22 specialist hair clinics. This condition is characterized by perifollicular scaling and erythema, as well as white dots and milky red and white areas on the scalp.

Trichoscopy can be performed with or without immersion fluid (wet vs dry trichoscopy). “It is important to start the trichoscopy examination using the dry method, as it allows one to better visualize scaling and features of blond and gray hairs,” Waśkiew-Burnat said. She suggests performing trichoscopy after hair dyeing for light tones since dark hair is more easily visible.

“In the future, I believe that trichoscopy will focus on general medicine and its usefulness in diagnosis of nondermatological conditions such as connective tissue disorders and hematological diseases,” she said.

Disclosures

Waśkiew-Burnat reports no relevant disclosures or financial interests.

References


For a complete list of references, see dermatologytimes.com
Pediatric Teledermatology Adds Access, Cuts Wait Times

Reimbursement issues remain a challenge.

JOHN JESITUS | Staff Correspondent

Up to 30% of pediatric health care visits involving skin complaints and fewer than 400 board-certified pediatric dermatologists in the United States, teledermatology offers a valuable tool for increasing access and cutting wait times.

Teledermatology varies in diagnostic concordance depending on case type. Rashes and birthmarks have greater concordance, but for pigmented lesions, teledermatology may be better used as a triage tool followed by an in-person visit, for example.

With up to 30% of pediatric health care visits involving skin complaints and fewer than 400 board-certified pediatric dermatologists in the United States, teledermatology offers a valuable tool for increasing access and cutting wait times.

Diseases include decreased accuracy because of the inability to obtain a comprehensive history and total body skin examination. “Diagnostic concordance for telemedicine vs in-person visits varies based on case type,” Khachemoune said. For example, he said, birthmarks, rashes, and acne may be well-suited for remote visits. A previous study found concordance rates of 92% for rashes and 100% for birthmarks. “For pigmented lesions, teledermatology is likely best used as a triage tool followed by an in-person clinic follow-up,” he said.

Best-practice recommendations from the American Telemedicine Association include considering in-person visits for total-body skin examinations, hair-bearing skin, pigmented lesions, and mucosal lesions and for patients with skin of color, depending on lighting and background conditions. For store-and-forward cases, the American Academy of Dermatology recommends that the dermatologist have either previous face-to-face interaction with the patient or an established relationship through live videoconferencing, unless the dermatologist is part of an integrated care-delivery system.

The authors suggested using a template for televisits to collect patient information and histories, supplementing clinical photos with video footage if needed, and ensuring follow-up with a pediatric dermatologist or primary care provider.

“Formal store-and-forward teledermatology may help optimize evaluation and management requests from other specialists, promote reimbursement, enhance communication among multiple providers, and improve workflow if in-person evaluation is not possible,” the authors wrote. At UPMC Children’s Hospital of Pittsburgh in Pennsylvania, a store-and-forward pediatric teledermatology system within the existing EHR enabled dermatologists to respond to ED consults in less than 1 hour and to inpatient and intensive-care unit consults in less than 12 hours.

However, inconsistent reimbursement has created challenges for store-and-forward strategies. “We were surprised by the current incentive structure, which makes teledermatology a less attractive option for providers than in-person visits, especially in the inpatient setting,” Khachemoune said.

Under 2019 Centers for Medicare & Medicaid Services (CMS) rules, outpatient teledermatology was covered only if the patient was already established within a practice. Applicable reimbursement codes for telemedicine ranged from $12 to $14. Responding to the COVID-19 crisis, CMS issued a waiver allowing Medicare to pay for office, hospital, and other telehealth visits starting in March 2020.

Going forward, Khachemoune called for sustainable reimbursement options for all modalities once restrictions stemming from the COVID-19 pandemic are eased. “The current reimbursement model for telemedicine requires modification to ensure appropriate compensation for both asynchronous and synchronous platforms,” he said.

Disclosures
Khachemoune reports no relevant disclosures or financial interests.

References

Quick TAKES
With up to 30% of pediatric health care visits involving skin complaints and fewer than 400 board-certified pediatric dermatologists in the United States, teledermatology offers a valuable tool for increasing access and cutting wait times.
Does molluscum keep him away from his friends?

When left untreated, symptoms last an average of 13 months and can last for as long as 4 years.¹⁻³

Many dermatologists believe that early treatment of molluscum may¹,²,⁴,⁵:

- Reduce disease progression
- Control the number of lesions and decrease the potential for scarring
- Avoid the spread to other areas of the body or to other people
- Prevent onset and exacerbation of comorbidities such as atopic dermatitis
- Reduce discomfort and itching
- Prevent social exclusion from school or extracurricular activities
- Alleviate anxiety in children and caregivers
- Improve quality of life for patients


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The specialty’s key challenges: accessibility, affordability, and skin of color.

Artificial intelligence, stem cell research, and bioengineered skin may offer new solutions.

Biologics, especially those that limit adverse effects and lab monitoring, are making big news for treating a growing number of skin diseases.

Quick Takes

**Biologics**

- Biologics, especially those that limit adverse effects and lab monitoring, are making big news for treating a growing number of skin diseases.

**Artificial intelligence**

- Artificial intelligence, stem cell research, and bioengineered skin may offer new solutions.

**The specialty’s key challenges:** accessibility, affordability, and skin of color.

Wave of Change

**Where do you see the most innovation in dermatology?**

**ROBERTS:** The next big breakthroughs will be in skin cancer. We already use biologics to treat some skin cancers instead of relying only on surgery. We’ve moved from topical chemotherapy and oral chemotherapy injection to superficial radiation therapy. I’m excited about that imaging component, especially using imaging and ultrasound in combination with microscopy because we can image and treat. We’re going into the realm of multiphoton excitation.

**ALEXANDER:** I’m seeing more research on hair disorders in general and scarring hair disorders in particular, especially in regard to the overall number of women and the number of women with skin color affected by these conditions. Genetic-related causes are now areas of interest. Some study findings already have showed that genetic mutations that may play a role. There is a wider range of new treatments for scarring hair disorders, including plasma-rich platelet [PRP] formulations.

**WAIBEL:** I expect a huge jump in laser technology and devices that will go beyond the cosmetic arena into cancers and laser-assisted drug delivery, not just for dermatology, but for all specialties....Artificial intelligence will contribute significantly to our understanding of our specialty.

**Could you describe the biggest challenges ahead?**

**ALEXANDER:** Getting insurance companies to approve some of the specialty treatments that benefit our patients is a major challenge. Take biologics: Many are phenomenal. Patients love them; their lives are changed. But doctors have to go through a lot of red tape to get insurance companies’ approvals...which can limit patients’ access to these treatments. Off-label use of medications is another concern. It can be difficult to get these treatments, so we may have to use compounding pharmacies. Keeping teledermatology alive and well is also an issue. COVID-19 [coronavirus disease 2019] made teledermatology a necessity for many practices. I think that’s great. It helps increase access for all patients. I’m just hoping it will last and that insurance companies will keep it on board.

**ROBERTS:** Telemedicine is great for providing accessible, affordable care. I love it for medication refills, among other things. But it has some inherent challenges. The toughest part is that it doesn’t replace a physical exam, which may mean that the patient has to schedule a second visit to come into the office if the condition warrants a physical exam or testing. I agree with Dr. Alexander about medications, prescribing, and the whole scenario of getting medications to our patients. Our specialty is looped out. We get medications after development. We need to be more involved in how these agents are brought to market.

I also agree that access is a major challenge. Our country really suffers from lack of access to...
The next big breakthroughs will be in skin cancer. I’m excited about...using imaging and ultrasound in combination with microscopy because we can image and treat.”

Wendy E. Roberts, MD, founding director of dermatopathology, Loma Linda University Health, California; double-board-certified dermatologist and dermatopathologist; founder and chair, Generational Dermatology Symposium; private practitioner, Rancho Mirage, California

I expect a huge leap in laser technology and devices that will go beyond the cosmetic arena into cancers and laser-assisted drug delivery, not just for dermatology, but for all specialties. Artificial intelligence will contribute significantly to our understanding of our specialty.”

Jill S. Waibel, MD, medical director & owner, Miami Dermatology and Laser Institute, Florida; subsection chief of dermatology, Baptist Hospital, Miami; and medical director, Multidisciplinary Skin Cancer Clinic, Miami Cancer Institute

Dermatology. That’s something we have to work on—not only in terms of treatment but also preventive care. Skin disorders drive up the price of medicine nationally. If we could get into a more preventive mode, we could help lower the cost of medicine. A lot of patients can’t benefit from good medicine because they can’t afford it. We need to get our patients out in front of potential skin-related problems.

Dermatologists’ access to devices and lasers is another issue. We want to use all the devices; we want to explore what’s possible. But access and economics often prohibit great devices from getting in the hands of great dermatologists.

Waibel: In parts of the country such as Indiana, where I grew up, there’s definitely an access problem. There are so few dermatologists that it may take a patient with skin cancer 8 months to get an appointment. By then, they may have stage III melanoma. In cities like Miami, where I practice now, we have scope-of-practice issues, especially in the cosmetic arena. I do a lot of scar work. I see patients who have been disfigured permanently or have pigmentation issues from nondermatologists who were not properly trained or did not understand the skin tissue interaction. I’ve even had patients who died or committed suicide after problems with treatments administered by nondermatologists. Patients need to understand that a $200,000 laser plugged into 220 V is being used on their face. Sometimes, if the provider is poorly trained, the outcomes don’t turn out well. My heart just goes out to the patients and families when they get harmed by these technologies.

I share Drs Roberts and Alexander’s concerns about costs. I practice in-patient hospital medical and medical dermatology. Reimbursements continue to go lower for a lot of our medical-only colleagues; it’s getting to be very challenging. They can work with a patient for a year, and deductibles have not even been met. Patients can’t sustain that over time. We’re a smart group; we have to solve those problems.

Q: What will be the most exciting new products of 2021?

Alexander: biologics, particularly ones that may not have any adverse effects and may not require lab monitoring—there are so many for psoriasis. More are being developed to treat atopic dermatitis.

Roberts: I look forward to nano-pulse stimulation for the removal of benign lesions. I practice in the Palm Springs, California, area, and I see many patients with sebaceous hyperplasia and seborrheic keratoses. Until now,
Getting insurance companies to approve some of the specialty treatments that benefit our patients is a major challenge. Take biologics: Many are phenomenal. Patients love them; their lives are changed. But doctors have to go through a lot of red tape to get insurance companies’ approvals...which can limit patients’ access to these treatments.”

Says Tiffany Alexander, MD, chief resident, Department of Dermatology, Duke University Medical Center, Durham, North Carolina.

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**Clinical Insights**

We’ve had only liquid nitrogen to treat these pesky lesions. Wouldn’t it be nice to have a cost-effective treatment that finally gets rid of them? I’m also interested in artificial skin or bioengineered skin.

**WAIBEL:** Stem cell research—our friends at Wake Forest University in Winston Salem, North Carolina, are growing new kidneys and bladders from a patient’s own cells in vivo and implanting them in the patient. Another is an invention one of this year’s Giants of Dermatology® honorees, R. Rox Anderson, MD, professor of medicine and director of the Wellman Center for Photomedicine at Harvard Medical School in Boston, Massachusetts. Dr Anderson is the chief medical officer and founder of Accure Acne. He and his team developed a novel 1726-nm laser that can achieve selective destruction of the sebaceous gland. I think we’ll be able to get some basic hyperplasia with that, as well. The device already has the CE mark in the European Union, and I think we’ll be seeing it on the market here this year.

Dr Anderson also worked on developing a combination of the punch biopsy and the fractional laser. For full disclosure, I was part of the clinical trials for this. The aim is to tighten the skin and soften wrinkles, but I truly believe we’ll be able to use it for acne scars, stretch marks, tattoos, and much more. I’m hoping to see that out in 2021, as well. JAK inhibitors are also exciting, as Dr Alexander mentioned. These things are magical. You can take a patient with atopic dermatitis affecting 80% of the body surface area [and see the condition] clear in 2 weeks. I see potential use for vitiligo and alopecia. I think it’s going to help heart disease, lupus, and autoimmune diseases, among others.

**Q: Do you observe new opportunities in dermatology?**

**ALEXANDER:** I’m so glad to see efforts toward including skin of color and making images available. Not long ago, textbooks, presentations, even articles and PowerPoint didn’t include people with skin of color. That’s been brought into the light. A lot of strides were taken to improve that, like with VisualDX [diagnostic clinical support system], which now has a section with skin of color images. At Duke University, we have various lectures about skin of color and disorders that may affect that patient population disproportionately. Even for COVID-19, people are asking for images of patients with skin of color who have coronavirus-related skin affect our skin, and we need to start good habits earlier in our lives. For someone with a family history of hair loss, do we wait until they’re 40 and their hair starts dropping, or do we want to get ahead and maybe give them some PRP when they’re in their 20s and 30s, knowing that they’re at risk of hair loss? Think about not treating only the person who’s presenting. What about their sister, their brother, their mother, their grandmother? Think about bringing multiple generations into the house of dermatology and expanding the lens. We’re looking at those opportunities in my Generational Dermatology symposium (generationaldermatology.com).
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
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**FOR MORE INFORMATION PLEASE CONTACT:**
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Penn State Health Milton S. Hershey Medical Center
c/o Erica Geist | Physician Recruiter
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