A RECENT META-ANALYSIS confirms cyclosporine as the most effective atopic dermatitis (AD) treatment at the molecular level, although dupilumab (Dupixent, Sanofi Genzyme and Regeneron Pharmaceuticals) achieves broad cutaneous changes beyond those expected with specific Th2 inhibition.

Focusing on biomarkers, moreover, may facilitate future development of personalized medicine in AD, authors add.

Unlike psoriasis, says co-author Emma Guttman-Yassky, M.D., clinical trials in AD typically produce high placebo response rates. However, she says that instead of focusing solely on clinical response, examining changes in immune and barrier mechanisms in skin — as the meta-analysis did — provides a more objective, granular picture of the differential effects of specific drugs. She is the Clara Kest professor and vice chair of dermatology at the Icahn School of Medicine at Mount Sinai in New York.

The future of AK treatment

It is estimated that 0.025% to 16% of all actinic keratosis (AK) lesions may progress into invasive SCC per year, and there is still no marker to predict which lesions will progress, according to a recent paper that outlined diagnostic challenges as well as current and pipeline treatment approaches.

“The prevalence of AK is already high and expected to rise even further in the next years,” write authors Philip Cramer, M.D., and Eggert Stockfleth, M.D., from St. Josef Hospital, University Hospital of the Ruhr-University of Bochum, Bochum, Germany. “Actinic keratosis, apart from immune-suppressed patients, mainly is a chronic disease which affects the older third of the population.”

Molecular study highlights drug differences

Unlike psoriasis, says co-author Emma Guttman-Yassky, M.D., clinical trials in AD typically produce high placebo response rates. However, she says that instead of focusing solely on clinical response, examining changes in immune and barrier mechanisms in skin — as the meta-analysis did — provides a more objective, granular picture of the differential effects of specific drugs. She is the Clara Kest professor and vice chair of dermatology at the Icahn School of Medicine at Mount Sinai in New York.
Updates on COVID-19 & clinical care advances

by MIKE HENNESSY, SR

WHILE COVID-19 IS STILL TOP OF MIND for all of us, we continue to keep you informed about how the pandemic is and will continue to affect you and your practice. You can find much of this coverage on our website at dermatologytimes.com/coronavirus as well as recaps of discussions from our recent webcasts: Survival of the private practice: bit.ly/telepracticecounsel
Reopening the private practice: bit.ly/reopeningpractice

This month, as you’re likely in the midst of utilizing teledermatology, Dr. David Goldberg discusses HIPAA compliance concerns (pg 10), and the changes in perceived privacy given the pandemic. In our guest commentary, Dr. Bobby Buka who practices in New York City offers his insights on the role of phototherapy in the treatment of atopic dermatitis as researchers noticed that S. aureus levels appear to decrease during the treatment and increase at treatment termination in a portion of patients (pg 13). Another analysis (pg 27) has indicated some differences in skin microbiota, though not significant, in a small group of patients before and after oral antibiotic therapy. The researchers conclude that a better understanding of cutaneous changes relevant to therapy could help clinicians hone in on microbes that may cause rosacea symptoms. In Dr. Zoe Draeoles’ Cosmetic Conundrums column (pg 11), she shares insights on the role of ‘biotics’ in skin care; however she underscores the need for more research, noting “normalizing the microbiome to achieve skin health sounds wonderful until you realize the normal microbiome has yet to be defined!”

Another theme we captured this month is the role of devices in skin disorders. In “Device-based Tx strategies,” on pg 20, Dr. Fernando Sakamoto-Shigeta shares results from a study that examined targeting the sebaceous glands with high-dose red light PDT to treat acne. And, Dr. Mark Nestor looks at the role of phototherapy in the treatment of psoriasis on pg 16. We hope this issue finds you staying healthy and safe! 🌶️

MIKE HENNESSY, SR., IS CHAIRMAN AND FOUNDER OF DERMATOLOGY TIMES PARENT COMPANY, MJH LIFE SCIENCES.
An IL-23 inhibitor for adults with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy

NOTHING IS EVERYTHING

DURABLE
Most patients achieved PASI 90 at Week 16 and maintained it at Week 52.

RAPID
Co-primary endpoints of PASI 90 and sPGA 0/1 at Week 16, including response 4 weeks after first dose.

CLEAR
The majority of patients achieved PASI 100 at Week 52.

4 DOSES PER YEAR
Reliable 3-month dosing after 2 initiation doses at Weeks 0 and 4 (150 mg per dose).

Nothing less than the opportunity for durable skin clearance.

For your patients, that’s everything.

SAFETY CONSIDERATIONS
SKYRIZI may increase the risk of infection. Instruct patients to report signs or symptoms of clinically important infection during treatment. Should such an infection occur, discontinue SKYRIZI until infection resolves. Evaluate patients for tuberculosis infection prior to initiating treatment with SKYRIZI. Avoid use of live vaccines in SKYRIZI patients.

Please see additional Important Safety Information on the inside spread.
Please see the Brief Summary of the full Prescribing Information on the last page of this ad.
**ACHIEVEMENTS AT WEEK 16 IN ULTIMMA-1 & ULTIMMA-2 (NRI)**

**CO-PRIMARY ENDPOINTS**

<table>
<thead>
<tr>
<th>PASI 90 at Week 16</th>
<th>sPGA 0/1 at Week 16</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ULTIMMA-1</strong></td>
<td><strong>ULTIMMA-2</strong></td>
</tr>
<tr>
<td>75% (229/304)</td>
<td>88% (267/304)</td>
</tr>
<tr>
<td>5% (5/102)</td>
<td>8% (8/102)</td>
</tr>
</tbody>
</table>

**SECONDARY ENDPOINT**

<table>
<thead>
<tr>
<th>PASI 100 at Week 16</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ULTIMMA-1</strong></td>
</tr>
<tr>
<td>36% (109/304)</td>
</tr>
<tr>
<td>0% (0/102)</td>
</tr>
</tbody>
</table>

**CONSISTENT PASI 90/100 RATES AT 2.5 YEARS IN OPEN-LABEL EXTENSION**

**INTEGRATED RESULTS FROM ULTIMMA-1 AND 2—ALL DATA ARE AS OBSERVED**

Participants received treatment at Week 0, Week 4, and every 12 weeks thereafter.

**INDICATION**

SKYRIZI™ (risankizumab-rzaa) is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy.

**IMPORTANT SAFETY INFORMATION**

**Infection**

- SKYRIZI™ (risankizumab-rzaa) may increase the risk of infection. Do not initiate treatment with SKYRIZI in patients with a clinically important active infection until it resolves or is adequately treated.

- In patients with a chronic infection or a history of recurrent infection, consider the risks and benefits prior to prescribing SKYRIZI. Instruct patients to seek medical advice if signs or symptoms of clinically important infection occur. If a patient develops such an infection or is not responding to standard therapy, closely monitor and discontinue SKYRIZI until the infection resolves.

**Pre-Treatment Evaluation for Tuberculosis (TB)**

- Prior to initiating treatment with SKYRIZI, evaluate for TB infection and consider treatment in patients with latent or active TB for whom an adequate course of anti-TB therapy cannot be confirmed. Monitor patients for improvement in clinical signs and symptoms of TB infection and consider a new anti-TB regimen.

**LEARN MORE ABOUT SKYRIZI AT SKYRIZIHCP.COM**
### MAINTENANCE OF RESPONSE

#### AT WEEK 52

In the randomized controlled trials, among patients who achieved PASI 90 or PASI 100 at Week 16, level of response was maintained at Week 52 by 88% (n=398/450) and 80% (n=206/258), respectively.¹

#### AT WEEK 136

In an observed analysis,* among patients who achieved PASI 90 or PASI 100 at Week 52 and had available data at Week 136 in the open-label extension, level of response was maintained at Week 136 by 94% (n=375/398) and 82% (n=232/282), respectively.⁴

*Analysis conducted 8/6/2019.

---

**KEY VARIABLES (AS MEASURED EVERY 12 WEEKS THROUGH WEEK 172) OF OLE**

- sPGA 0/1, sPGA 0, PASI 75, PASI 90, and PASI 100

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

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

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

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**Immunizations**
- Prior to initiating SKYRIZI, consider completion of all age appropriate immunizations according to current immunization guidelines. Avoid use of live vaccines in patients treated with SKYRIZI.

**Adverse Reactions**
- Most common (≥1%) adverse reactions associated with SKYRIZI include upper respiratory infections, headache, fatigue, injection site reactions, and tinea infections.

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The following adverse reactions are discussed in greater detail in other sections of the labeling:

- **Immunizations**
  - Avoid use of live vaccines in patients treated with SKYRIZI. No data are available on the response to live or inactivated vaccines.

- **Live Vaccinations**
  - Do not administer SKYRIZI to patients with active TB. Therapy prior to initiating SKYRIZI in patients with a past history of latent or active TB in whom an adequate treatment regimen was not received prior to initiation of therapy.

- **Pre-treatment Evaluation for Tuberculosis**
  - Monitoring tuberculosis (TB) infection status is essential for patients with psoriasis who were previously microbiologically confirmed as having latent TB exposure or with history of TB prior to initiating therapy. Pre-treatment evaluation should be conducted prior to initiating therapy. Evaluation should include a history of TB exposure and clinical evaluation of risk factors for reactivation. In patients with a positive history or clinical signs, a diagnostic test (e.g., QuantiFERON Gold TB test) should be performed. Prophylaxis to prevent reactivation should be administered to patients with a positive test result. If the test result is negative, it should be repeated at 12 weeks and then annually thereafter.

- **Pediatric Use**
  - There are no data on the presence of risankizumab-rzaa in human milk, the effects on the breastfed infant, or on the potential for adverse effects on the breastfed infant from SKYRIZI. There are no data on the effects of SKYRIZI on the breastfed infant from the underlying maternal condition.

- **Pregnancy**
  - Avoid use of live vaccines in patients treated with SKYRIZI. There are no data on the presence of risankizumab-rzaa in human milk, the effects on the breastfed infant, or on the potential for adverse effects on the breastfed infant from SKYRIZI. There are no data on the effects of SKYRIZI on the breastfed infant from the underlying maternal condition.

- **Drug Interactions**
  - SKYRIZI is a humanized monoclonal antibody to IL-23p19 and is therefore expected to share many of the same neutralizing antibodies as other monoclonal antibodies. Higher antibody titers in approximately 1% of subjects treated with SKYRIZI were associated with lower risankizumab-rzaa concentrations and reduced clinical response. Instruct patients or caregivers to administer two 75 mg single-dose syringes to achieve the 150 mg dose of SKYRIZI.

- **Pediatric Use**
  - There are no data on the presence of risankizumab-rzaa in human milk, the effects on the breastfed infant, or on the potential for adverse effects on the breastfed infant from SKYRIZI. There are no data on the effects of SKYRIZI on the breastfed infant from the underlying maternal condition.

- **Infections**
  - Review peripheral blood differential counts of patients who may be at risk for infectious adverse reactions, such as those with a history of neutropenia or patients with a history of recurrent infections, at least monthly and consider repeat testing if signs or symptoms of infection are clinically apparent or at the time of new infection diagnoses.

- **Carcinogenicity and Mutagenicity**
  - Carcinogenicity and mutagenicity studies have not been conducted with SKYRIZI. Carcinogenicity and mutagenicity studies have not been conducted with SKYRIZI. Carcinogenicity and mutagenicity studies have not been conducted with SKYRIZI. Carcinogenicity and mutagenicity studies have not been conducted with SKYRIZI.

- **Effect on Fertility Parameters**
  - Carcinogenicity and mutagenicity studies have not been conducted with SKYRIZI. Carcinogenicity and mutagenicity studies have not been conducted with SKYRIZI. Carcinogenicity and mutagenicity studies have not been conducted with SKYRIZI. Carcinogenicity and mutagenicity studies have not been conducted with SKYRIZI.
“EVERY INJECTOR NEEDS TO ATTEND THE AESTHETIC EXTENDER SYMPOSIUM! IT IS BY FAR THE MOST VALUABLE RESOURCE AVAILABLE IN THE US FOR AN IN-DEPTH REVIEW OF CLINICAL PRACTICE AND SAFETY STANDARDS.”
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Future of AK Tx

Diagnostic challenges & pipeline approaches

Skin Cancer

ATOPIC DERMATITIS
Molecular study highlights drug differences

PSORIASIS
IL-23 antagonist demonstrates long-term safety
Addressing the Challenges of Managing Atopic Dermatitis
Pathogenesis of atopic dermatitis

What do we—and don’t we—know about the pathogenesis of atopic dermatitis?

In this Dermatology Times® podcast, Emma Guttman, MD, PhD, discusses familial predisposition for atopic dermatitis, hypothesized links between the disease and the Atopic March, prevention of comorbidities through treatment, and variables of adult onset.

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www.dermatologytimes.com/atopicdermatitis
"Unlike other catastrophes that have struck our region, this pandemic is unique in the way that it distances us."

Practicing dermatology in the time of COVID-19

by BOBBY BUKA, M.D., J.D.

Dr. Buka is a board-certified dermatologist and is the CEO and co-founder of The Dermatology Specialists, a full-service dermatology practice with locations all across New York City. Dr. Buka is a contributing founder of the First Aid Beauty skincare line. He’s also the author of Buka’s Emergencies in Dermatology and the newly launched Top 50 Dermatology Case Studies for Primary Care.

I am the CEO and co-founder of one of the largest dermatology practices in New York, and I write this month from the epicenter of the COVID-19 crisis. We have 17 dermatology offices here, all on ground-floor locations throughout New York City. We have always prided ourselves on making dermatology more accessible for folks who may have previously felt apprehensive about visiting a skin doctor. It is this same easy accessibility — this high visibility — that now places us on the front lines of a national health crisis.

I believe that our COVID-19 experience can be instructive for dermatology practices across the country who are understandably concerned about how this pandemic will affect their own offices, and what will happen if their regions also become hot zones. I hope to provide some helpful insight as to how you can better prepare for challenging times ahead.

Unlike other catastrophes that have struck our region (for example, 9/11 or Hurricane Sandy), this pandemic is unique in the way that it distances us. Caring for others is suddenly made more difficult when the inherent trust between patient and physician is compromised by the potential risk of contagion. As a result, patient census drops fast. One day, we had all of our offices open, the next we had volume enough to support only five locations for non-elective dermatology. The lights go out faster than expected — fewer patients will seek skincare and, for the ones that do, state governments will often mandate that they stay-at-home.

This moment in your practice will prove an inimitable inflection point. In our experience, we believe taking more drastic steps, with a subsequent longer outlook to then scale these changes back, will be more successful than stepwise reactivity. In order for our practice to survive and for us to continue taking care of our patients during the crisis, we made the following moves:

DOUBLE-DOWN ON PRECAUTIONS. The Dermatology Specialists is known for its superlative safety record. We take our OSHA-standards for cleanliness, infection-control and inter-patient sanitization very seriously. The new coronavirus disease has given us an opportunity to move many of these back-stage processes to front-and-center in order to reassure our patient population, “this is a safe space.” We room patients quickly, so as to avoid waiting room contagion. We space out waiting room access, in many instances closing front doors and texting patients to enter once we’ve had the opportunity to wipe down surfaces. We direct all incoming patients to the bathroom to wash hands prior to their visit. All registration pens are single use. Re-emphasizing these processes visibly is key to patient retention.

Of note, it is helpful to talk to your medical equipment vendors early — while they may already be out of PPE, ask that you be placed on their re-stock list as additional supplies become available.

STRENGTHENING YOUR TEAM. As difficult as it was, we acted quickly to furlough many employees whom we could not continue to keep on payroll. Putting team members on temporary leave is a gut-wrenching, emotional process among colleagues who have become friends. Like many of you, our staff is the winning recipe for our practice. We look to the stimulus package to help support our practice family until we can all be reunited.

For everyone in the practice, overcommunication is essential. Many have only “doom and gloom” live-streamed daily from their televisions or devices. Our team is resilient, but leadership must check in regularly. We set up a Zoom call every week for our 200+ employees. When information becomes available, we share it transparently along with any helpful updates. Our video calls are for office logistics, to share hopes for and challenges to reopening, and also close with musings on “Tiger King” and homemade haircuts. Those moments of humanity are worth 1,000 emails. I am wholly grateful to our providers who have risked their own health to remain on the front lines — and now is the time to show it. Their efforts have kept patients out of urgent care centers and emergency rooms, preserving precious resources for COVID-19.

For many, this pandemic is also an opportunity to embark on a journey of self-discovery. We are seeing a surge in interest in new dermatology services, with patients out of urgent care centers and emergency rooms, preserving precious resources for COVID-19: CONTINUES ON PAGE 35.
"Historically, confidentiality issues have always been a concern. This all changed with COVID-19."

Teledermatology and HIPAA compliance in the era of COVID-19

by DAVID J. GOLDBERG, M.D., J.D.

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 Mt. Sinai; and, adjunct professor of law, Fordham Law School in New York City.

Dr. NY is a practicing dermatologist in New York City. He has spent the last several years looking for new revenue sources. He has a very interactive website and associated blog. Recently, because of the COVID-19 pandemic, he has markedly increased his use of telemedicine (teledermatology). He consults a long-term 70-year-old patient on FaceTime, something she has used countless times before to keep in touch with her grandchildren.

She tells her youngest son, a law student, how happy she was using FaceTime to communicate with her physician.

He is horrified and tells his mother that FaceTime is not HIPAA compliant. He files a federal complaint, as well as a complaint with local state regulatory authorities against Dr. NY. The dermatologist is horrified. His practice was decimated by COVID-19, he tried to help his patient, and still ends up with legal issues.

“Telemedicine” is a term that covers any use of electronic communication technology to convey medical information. It can be as basic as seeking a consultation or as advanced as robotic surgery. Teleradiologists and telepathologists use electronic communication to send radiographs and specimen images for diagnostic or consultation purposes. Teledermatology can be practiced in the role of a consultant or as a seeker of consultation. However, this practice is fraught with liability issues.

Legal: (i) Is the dermatologist exceeding the license granted by his/her state? If so, the physician can be subject to disciplinary action in the state if the license is used inappropriately as a predicate to practice telemedicine. (ii) Are you engaging in the unlicensed practice of medicine in other states?

Licensure (i) Is the dermatologist exceeding the license granted by his/her state? If so, the physician can be subject to disciplinary action in the state if the license is used inappropriately as a predicate to practice telemedicine. (ii) Are you engaging in the unlicensed practice of medicine in other states?

There is no national consensus on what states demand from physicians located outside their borders and are practicing telemedicine within any one state. Some states demand full licensure, some offer restricted licenses for telemedicine, and some offer licensing by endorsement under reciprocity agreements with neighboring states.

Despite the wide range of options, there is a common thread to keep in mind: If there is a regular, ongoing practice of telemedicine in the state (as opposed to an occasional consultation), the state will want some degree of licensure. A physician who lacks such licensure can be subject to prosecution for the unlicensed practice of medicine.

Insurance coverage (i) Most malpractice policies specifically exclude coverage for unlicensed activities. Some states require insurers to cover work that extends beyond state borders and some do not. (ii) Does the carrier cover you for telemedicine practice? Telemedicine consulting may not be covered by your malpractice insurer, and you may need to obtain surplus lines coverage.

Negligence liability (i) Can a medical malpractice action be brought in the setting of telemedicine? Yes. (ii) Where can the action be brought? The issue of “forum shopping” comes into play if the doctor provided the telemedicine service in a state different from where the patient lives. Most jurisdictions will permit a resident to bring
“Normalizing the microbiome to achieve skin health sounds wonderful until you realize the normal microbiome has yet to be defined!”

The role of ‘biotics in skincare

by ZOE DIANA DRAELOS, M.D.

Dr. Draelos is a consulting professor of dermatology, Duke University School of Medicine, Durham, NC.

WHAT IS PREBIOTIC SKINCARE?
The biotics are the newest ingredients in skincare based on normalizing the microbiome to achieve skin health. This sounds wonderful until you realize the normal microbiome has yet to be defined! Nevertheless, an evaluation of biotic products is worthwhile. These skincare products can be classified as prebiotics, probiotics and postbiotics.

Prebiotics are substances that promote the growth of beneficial bacterial organisms and inhibit harmful bacteria on the skin surface. Oral prebiotics are nondigestible carbohydrates found in fibrous foods, such as legumes, whole wheat, garlic, onions, oats, berries, etc. These foods contain fructo-oligosaccharides (FOS) and galacto-oligosaccharides (GOS), which are nonabsorbable sugars providing nutrition for beneficial bacteria in the gut.

Prebiotic skincare products are based on these sugars or plant oils that are able to provide nutrition for bacteria on the skin surface, which constitute the microbiome. Thus, prebiotic skincare products contain botanically based sugars and oils that provide bacterial nutrition.

WHAT IS PROBIOTIC SKINCARE?
Probiotic skincare contains living organisms placed on the skin from sprays or creams. Probiotic foods that contain bacterial fermentation products include yogurt, kefir, kombucha tea and sauerkraut. The bacteria most commonly used in probiotic skincare products include the dairy propionic acid bacteria (PAB) lactobacillus and bifidobacterium.

True probiotic skincare products must be refrigerated, as they cannot contain preservatives. The preservatives would destroy the beneficial bacteria meaning probiotic skincare is bacterially contaminated! This is the basis for the controversy surrounding these products.

For a probiotic skincare product to be effective, the bacteria must demonstrate adhesion to the skin, transient colonization, resistance toward potential pathogens, and production of antimicrobial substances. In vitro studies show PAB stratum corneum adhesion rates of 4-16%, so it’s possible probiotic skincare might hold some promise. However, putting live bacteria in skincare products is challenging, so most probiotic skincare products contain ultrasound-inactivated bacterial extracts from PAB, which can exist in unrefrigerated, preservative-containing formulations. In addition, many probiotic skincare products contain bacterially fermented ingredients, not necessarily live bacteria inducing fermentation.

One mechanism of action for the effect of bacterial extracts on the skin is bacterial interference. Since bacteria must touch the skin surface for nutrients and reproduction, if the dead bacteria extracts take up space on the skin surface, they can inhibit the growth possible pathogenic organisms through competitive inhibition of binding sites.

If prebiotics and probiotics are combined in the same skincare formulation, the resulting product is known as a synbiotic. Synbiotics contain both the nutrients for bacterial growth and the bacteria.

WHAT IS POSTBIOTIC SKINCARE?
Postbiotic skincare products contain non-viable bacterial products or metabolic by-products from probiotic bacteria. Postbiotics are produced during the fermentation process of probiotic bacteria.

Examples of postbiotics include enzymes, peptides, peptidoglycan-derived muropeptides, polysaccharides, cell surface proteins and organic acids. Postbiotics are really nothing new to dermatology, as many currently marketed skincare products contain bacterial fermentation products, such as lactic acid and glycerol. The therapeutic value of these ingredients has been well established.
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With advancements in deep next-generation sequencing (NGS) and bioinformatics analysis, the skin microbiome may hold promise as a clinical biomarker in atopic dermatitis (AD) management, according to the authors of a recent study.

Researchers published data in The Journal of Allergy and Clinical Immunology that examines the bacterial skin microbiome composition and discusses bacterial measurement methods with technological pitfalls.

“…we see promises, but also missing navigation and technological pitfalls to overcome, for the possibility of using the skin microbiome as a biomarker in AD clinical management,” the authors write.

“Skin microbiome dysbiosis, measured either as microbiome diversity or more reliably as abundance of S. aureus, was clearly shown to correlate with AD severity,” the authors write, noting that this may have possible prognostic value.

S. aureus levels have been shown to decrease during the treatment of AD and then return after the end of treatment in a portion of patients.

A noninvasive measurement of S. aureus may become a successful treatment biomarker, indicating a sustained microbial response (SMR), and lead to a better determination of an optimal treatment.

To use this as a sustainable clinical option, however, the study authors explain that additional information is needed to select the most suitable bacterial measurement method and a standardized quantitative methodology.

“It is critical to develop standardized quantitative methodologies for skin bacterial microbiome analysis, which can be tested, compared and validated in these studies.”

Dr. Matthias Reiger and colleagues UNIKA-T, Technical University of Munich, Germany

They note that the currently relied upon microbiome sequencing method to measure the 16S gene measures the frequency of the 16S gene copies, not species frequency. New methods for measuring the real microbiome distribution need to be developed for analysis.

Various kits are used for DNA extraction from a skin sample, which leads to taxonomic selectivity bias in the yield of DNA extraction, they note.

“For example, bacteria from certain families are more easily disrupted to provide DNA through each method,” they write. “Thus, the obtained microbiome distribution is distorted through any extraction method used.”

These current methods and procedures are also prone to produce differing results based on the lack of standardization in practice and can easily become contaminated from the sampling tool, extraction kit or amplification reagents, among others.

“The great disadvantage of skin sampling is the low amount of input material, in particular the low amount of bacterial DNA,” write the authors. “Furthermore, in contrast to blood or stool samples, skin sampling lacks standardization of the input material; for example, skin swab yield is highly dependent on the examiner, the material used for the swab, the applied pressure during sampling, and the size of the area sampled.”

Authors conclude that to further the research in this area, needs to include advanced technologies and the development of a standard of practice that can be implemented in clinical trials and large longitudinal registries.

“It is critical to develop standardized quantitative methodologies for skin bacterial microbiome analysis, which can be tested, compared and validated in these studies,” authors write.

“In addition, new promising technologies, such as single-molecule real-time sequencing, which could improve skin microbiome analysis with greater accuracy and/or longer sequencing length, and more advanced bioinformatic tools needs to be further developed and tested.”

Reference:

KATIE HOBBINS | Associate Editor
A study in *Journal of the American Academy of Dermatology* reports findings that support dupilumab (Dupixent, Sanofi Genzyme and Regeneron) as a safe long-term treatment in patients with moderate to severe atopic dermatitis (AD).

The phase 3, multicenter, open-label extension study examined the long-term treatment of AD with dupilumab in adults (18 years and older) who had previously participated in phase 1, 2 and 3 clinical trials. The study’s primary endpoint was long-term safety, evaluated as incidence and rate of adverse events (AEs).

A total of 1,491 patients from North America, Europe and the Asia-Pacific region participated in the study. Exclusion criteria included AEs related to dupilumab and serious AEs (SAEs) that led to discontinuing dupilumab treatment in previous clinical trials.

Patients received a dupilumab loading dose of 600 mg, then 300 mg weekly, or a loading dose of 400 mg, then 200 mg weekly, before the protocol was amended to 300 mg weekly. Data was collected for up to 76 weeks of treatment. Most patients (98.6%) were at least 80% adherent to treatment.

According to the authors, 4,384 AEs were reported. Many patients (70.7%) had at least one AE. Few patients (5%) had one or more SAEs. The most common AEs included conjunctivitis, nasopharyngitis, upper respiratory tract infection, AD and headache. Study drug-related SAEs included Hodgkin disease, prostate cancer, enterocolitis, serum sickness, eczema herpeticum, herpes ophthalmic, epilepsy, and eczema.

There were no deaths reported.

This is the first study to evaluate safety in patients receiving dupilumab treatment for more than 52 weeks, write the authors. Although previous studies of the immunosuppressive agents cyclosporine and azathioprine have experienced limitations due to high rates of patient discontinuation, this study had a very low (1.8%) discontinuation rate.

The study results are consistent with findings of other studies analyzing the safety and efficacy of dupilumab, according to the authors. Efficacy was sustained for the treatment period of 76 weeks, thereby improving QoL, study authors report. Less than half of patients used additional treatment for AD during the study.

“This, combined with the relatively small numbers of patients requiring systemic rescue therapy, supports the idea that dupilumab monotherapy or concomitant with topical AD medications provides long-term disease control in patients with moderate to severe AD,” they write.

Authors note limitations to the study include the proportion of patients that were able to reach 76 weeks of treatment and a lack of a control arm but add that the results suggest the benefits of this long-term treatment.

“The favorable benefit-risk profile in this study supports the long-term role of dupilumab treatment for patients with moderate to severe AD and shows that blocking IL-4 and IL-13 signaling can achieve sustained control of AD signs and symptoms with an acceptable safety profile in patients with significant disease burden and for whom conventional topical treatments are inadequate,” they write.

**References:**

Quick TAKES
- Meta-analysis shows cyclosporine as most effective AD treatment at the molecular level.
- Dupilumab showed the highest overall improvement in Th2-specific genes.
- Data illuminate relative improvement achieved by different treatments in various immune and barrier mechanisms, highlighting the unique advantages of targeting a particular axis.
- Focusing on biomarkers may facilitate future development of personalized medicine.

Molecular-level analysis of treatment efficacy

While differences in clinical response between placebo and drug may be minimal in some studies, she says, tissue responses can vary significantly.

“This tells us that for early, small proof-of-concept studies, it’s very important to incorporate biomarkers when companies need to make a decision of go or no go. This way you can ascertain whether your drug is doing what it’s supposed to do compared to placebo,” she says.

For the meta-analysis, investigators included only trials in which Human Genome U133 Plus 2.0 gene arrays (Affymetrix) were available from lesional and/or non-lesional skin of patients with AD treated with broad or specific targeting agents. Overall, cyclosporine showed the highest improvements in AD-related gene signatures, significantly outperforming all other drugs/placebos in most gene subsets (i.e., upregulated and downregulated meta-analysis-derived AD/MADAD transcripts, immune genes, epidermal differentiation and lipid genes, negative regulators and Th1/Th17/Th22/interleukin-22-regulated genes; P<0.01).

However, dupilumab showed the highest overall improvement in Th2-specific genes (median 209%), while significantly outperforming other drugs and placebos at week 16 in terms of MADAD, immune genes, negative regulators and Th2 genes (P<0.05).

Study data also illuminate the relative improvement achieved by different treatments in various immune and barrier mechanisms, highlighting the unique advantages of targeting a particular axis. Targeting the Th22 axis with fezakinumab (an anti-IL-22 monoclonal antibody, Pfizer), for instance, produced major improvement in genes related to barrier dysfunction, but only modest improvement in inflammatory signatures.

Along with giving a more granular view of how particular treatments perform clinically, says Dr. Guttman-Yassky, the study’s approach helps researchers ascertain mechanistically which immune pathways and biomarkers are relevant for each trial.

“Atopic dermatitis is very complex. It has both barrier and immune abnormalities. And it is important to understand how each of the drugs is affecting the immune abnormalities and barrier abnormalities, and what are the differences between them,” she says.

The meta-analysis allows researchers to compare different drugs and their effects in AD — not only versus placebo, but against different drugs even though the studies were done at different times and locations, Dr. Guttman-Yassky adds.

“This paper showed that some drugs are good at affecting specific immune abnormalities. Some other drugs may not be as good at addressing immune abnormalities, but they are as good or even better at improving the barrier defects of atopic dermatitis.”

**Personalized medicine for AD?**

Th2-driven disease may primarily benefit from dupilumab, whereas a patient with high Th2 and Th1 involvement may benefit from JAK inhibition.

In the future, she says, optimal treatments might require a combination of drugs — some that will have more effect in inhibiting the immune abnormalities and some that will improve the barrier.

“It’s very important for us as dermatologists to understand and compare the effects of various drugs on barrier abnormalities and effects on different immune axes that characterize atopic dermatitis,” she says.

The foregoing approach may facilitate future development of personalized medicine in AD by identifying optimal treatments for individual phenotypes based on immune and barrier profiles, says Dr. Guttman-Yassky.

For example, a patient with Th2-driven disease may primarily benefit from dupilumab, whereas a patient with high Th2 and Th1 involvement may benefit more from JAK inhibition.

**Disclosure:**

Dr. Guttman-Yassky has received research funds (grants paid to Mount Sinai) from Abbvie, Amgen, AnaptysBio, Axona Biocarena, Boehringer Ingelheim, Cubist, Daiichi Sankyo, Eli Lilly, Glenmark, Galderma, Gilead, GSK, Hanmi, Janssen, Kyowa, Lexicon, Leo Pharma, LG, MannKind, Mitsubishi Tanabe, Novartis, Pfizer, Regeneron, Roche/Genentech, Sanofi, UCB and Unitx Therapeutics. She is also a consultant for Abbvie, Almirall, Amgen, Arena Pharmaceuticals, Asana, Astellas, Boehringer Ingelheim, CaniTherapeutics, Cubist, Daiichi Sankyo, Esai, Eli Lilly, LG, MSD, Mylan, Novartis, Otsuka, Gilead, Omeros, Appteos, Rand D, Sanofi, Sierra Biopharma and Luminx Therapeutics.

**Reference:**

Beyond biologics

Phototherapy remains a valuable treatment

JOHN JESITUS | Staff Correspondent

Phototherapy remains a valuable psoriasis treatment, according to Mark S. Nestor, M.D., Ph.D., director, Center for Cosmetic Enhancement and the Center for Clinical and Cosmetic Research in Aventura, Fla., and voluntary professor at the Phillip Frost department of dermatology and cutaneous surgery, University of Miami Miller School of Medicine.

For focal areas of plaque psoriasis, the 650-microsecond 1064 Nd:YAG laser provides equivalent efficacy to the more widely used excimer laser, according to study data co-authored by Dr. Nestor and published in the *Journal of Drugs in Dermatology.*

“Fewer people are doing mainstay full-body phototherapy as in the past, as biologics and other systemic therapies have proven to be safe and much more effective,” he says. This is especially true of psoralen and UVA (PUVA), which can have side effects including burning, photoaging and increased skin cancer risk.

“Additionally,” Dr. Nestor adds, “laser has largely taken over for individual and spot treatment of specific areas because you don’t have the same issue of systemic problems with burning.”

Lasers also offer high efficacy on smaller areas that do not require biologic treatment, and as a complement to biologic or systemic therapies, he says.

The 308 nm excimer laser has been the gold standard for psoriasis phototherapy, Dr. Nestor says. It’s effective; however, there have been issues with skin burns, he adds.

Blistering may help clear psoriasis faster, according to Dr. Nestor, although it can result in hyperpigmentation, which is usually reversible (most fades upon completion of therapy).

For physicians who frequently treat psoriasis with light-based devices, he says, excimer laser increasingly may be supplanted by lasers such as the 650-nm Nd:YAG (LightPod Neo, Aerolase). In a 15-patient bilateral comparison study by Dr. Nestor, this laser provided equivalent efficacy to excimer on the trunk and limbs. After 15 treatments, average overall Modified Psoriasis Area and Severity Index (mPASI) scores for both lasers fell from approximately 2.4 at baseline to 1.5.1

Because the 650-nm Nd:YAG laser uses a different mechanism of action than does excimer laser, he says, the former does not cause burns.

“Additionally,” Dr. Nestor adds, “laser has largely taken over for individual and spot treatment of specific areas because you don’t have the same issue of systemic problems with burning.”

Lasers also offer high efficacy on smaller areas that do not require biologic treatment, and as a complement to biologic or systemic therapies, he says.2

The 308 nm excimer laser has been the gold standard for psoriasis phototherapy, Dr. Nestor says. It’s effective; however, there have been issues with skin burns, he adds.

Blistering may help clear psoriasis faster, according to Dr. Nestor, although it can result in hyperpigmentation, which is usually reversible.

In comparison study, tolerance was equivalent and there were no significant differences for redness, thickness, scaliness, or overall mPASI scores for treated plaques.

The key for treatment of psoriasis — it’s not just about biologics. There are other modalities that work well.”

Mark S. Nestor, M.D., Ph.D.
Center for Clinical and Cosmetic Research, Aventura, Fla.

References:
Combining topical agents yields unpredictable results

JOHN JESITUS | Staff Correspondent

Although combination therapy remains a pillar of psoriasis treatment, improvised topical combinations can yield mixed results, says David M. Pariser, M.D., community faculty member at Eastern Virginia Medical School, Norfolk, Va.¹

“Most dermatologists use combination therapy for psoriasis, regardless of whatever treatment they’re giving,” he says. “Even the new biologics, which have extremely high efficacy, still don’t give everybody 100% clearance,” he adds. Therefore, most patients need spot therapy with topical steroids, calcineurin inhibitors or sometimes localized phototherapy.

Guidelines from both the American Academy of Dermatology and the National Psoriasis Foundation support combination therapy for psoriasis. Accordingly, says Dr. Pariser, dermatologists often combine multiple topical agents on their own, and have been doing so for many years. However, he says, extemporaneous compounding of topical agents may not necessarily yield what dermatologists anticipate.

“When you combine something 50-50 with another product,” he explains, “you’re diluting each one in half. So the efficacy may not be what you expect. Also, in extemporaneously compounded combination products, one is not really sure about whether the vehicle that the product is suspended in is the best vehicle for that particular product.”

For drugs with different mechanisms of action, Dr. Pariser says, vehicles often differ significantly, yielding a significant vehicle effect.

“And we don’t know what that effect is in extemporaneously compounded preparations,” he says.

In a meta-analysis of seven clinical trials of combination topicals for psoriasis, for example, adding a class I or class II steroid to a vitamin D analog increased the likelihood of clearance by 28% and 14%, respectively, versus vitamin D analog monotherapy. But adding a class III corticosteroid produced no additive effect. The overall impact of adding any class corticosteroid was a 20% improvement over vitamin D monotherapy.

“Combining topical agents with each other can sometimes yield significant results,” Dr. Pariser explains. “However, it’s important to understand that the effect of each agent may be different, and that the vehicle plus the two active ingredients may not necessarily yield what dermatologists anticipate.”

When you combine something 50-50 with another product, you’re diluting each one in half. So the efficacy may not be what you expect.

David M. Pariser, M.D.
Eastern Virginia Medical School, Norfolk, Va.

Compared to fixed-combination products, says Dr. Pariser, extemporaneously compounded vitamin D-steroid combinations allow treatment regimen flexibility and may reduce corticosteroid usage. Conversely, he says, fixed-combination vitamin D-steroid products can increase adherence because there’s only one product to use, and these products’ safety and efficacy have been tested out to one year. Additionally, combinations such as calcipotriene with either halobetasol or betamethasone have data dating back more than a decade.

For years, dermatologists have compounded topical steroids with other agents such as salicylic acid or calcineurin inhibitors, as well as other older agents, he adds.

“And when you compound something like that, you don’t really know what the functional concentration of the products is,” Dr. Pariser explains. “Nor do you know how well those products are suspended, dissolved or carried in the vehicle and how well they are released in the skin.”

Although many people have used these kinds of compounded products, many of which work fairly well, it’s important to use officially studied compounded products that have been rigorously designed and manufactured, he says.

“Such products have been studied to show that the ingredients in the vehicle, in fact, are effective, and that the vehicle plus the two active ingredients works better than any of the individual active ingredients,” Dr. Pariser notes. “The only way you can know that is through clinical trials.”

Halobetasol-tazarotene lotion represents a relatively new combination. As with betamethasone-calcipotriene, both ingredients have demonstrated efficacy and earned approvals in psoriasis both separately and together.

“But this new combination product has the advantage of a vehicle that has been tested and proven effective where both of the active ingredients are equally therapeutic in this new vehicle,” he says.

In two eight-week studies, the proportions of patients on the combination product who achieved Investigator Global Assessment success (clear or almost clear with at least a two-grade improvement over baseline) were approximately 45% and 35%, versus 12% or less for vehicle (P<0.001).

The trend toward combination products in psoriasis will continue to grow, says Dr. Pariser.

“We’re seeing more of these combination products being tested and marketed. It’s taking advantage of the long-standing practice of dermatologists to do compounding. It’s a natural extension of dermatology that we’ve been doing for a long time.”

Reference:
¹ David M. Pariser, MD, “Combination Therapy in Managing Psoriasis Patients.” South Beach Symposium, February 8, 2020.

Disclosure:
Dr. Pariser is a current or previous investigator and/or consultant for AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, LEO Pharma, Merck, Novartis, Ortho Dermatologics, Pfizer, Promius and Sun Pharma.
Psoriasis

Quick Takes

The interleukin-23 antagonist guselkumab demonstrated greater efficacy compared with adalimumab and secukinumab at week 48 in controlled clinical trials investigating treatment of moderate-to-severe plaque psoriasis.

Long-term data show consistent PASI90 rates over time with 81% of patients at PASI90 at year one and 84% of patients at year four.

Guselkumab had a favorable safety profile compared with placebo after 16 weeks in clinical trials and in patients treated for up to four years.

IL-23 antagonist demonstrates favorable long-term safety from page 1

Dr. Feldman

MECHANISM OF ACTION

Guselkumab inhibits the activity of IL-23 by selective binding to its p19 subunit without binding to the p40 subunit, which is shared with IL-12.

Although theories based on differences in effects on the immune system have been proposed to explain why a pure IL-23 antagonist may have greater efficacy for treating psoriasis than a biologic that blocks IL-12 and IL-23, the reason remains unclear. The important message about the IL-23 antagonist guselkumab is that it is very effective and also has an excellent safety profile," says Dr. Feldman, Director, Psoriasis Treatment Center, Wake Forest University Baptist Medical Center, Winston-Salem, N.C.

It also has an acceptable long-term safety profile, straightforward dosing, and a convenient administration schedule. Furthermore, there is good access for its use thanks to assistance from manufacturer-supported programs.

SAFETY PROFILE

Safety is a key issue for any treatment. Approved for marketing by the FDA in July 2017 as the first IL-23 inhibitor indicated for the treatment of moderate-to-severe plaque psoriasis, guselkumab has accumulated an appreciable safety database that includes more than 1,800 patients, which builds confidence in its use, Dr. Feldman says.

"The length of time that guselkumab has been available and the number of treated patients add to my confidence for using it," Dr. Feldman says.

In the 16-week placebo-controlled period of the VOYAGE trials, the overall adverse event rate in the guselkumab group (49%) was similar to that in the placebo group (47%). Serious adverse events occurred in 1.9% of guselkumab-treated patients and 1.4% of placebo-treated patients. The overall infection rate was 23% for guselkumab and 21% for placebo, while in both groups, the rate of serious infections was <0.2%.

In the long-term safety analysis, the serious infection rate in patients treated with guselkumab was stable at about 1% per year.

"In my opinion, one possible explanation for the slightly higher rate of common infections—like upper respiratory tract infection—in the guselkumab group is that moderate-to-severe plaque psoriasis is a socially disabling disease. With greater improvement in their psoriasis, it is conceivable that patients in the guselkumab group were likely to have more human contact than their counterparts in the placebo group and therefore be at greater risk for exposure to colds and other communicable diseases," Dr. Feldman says.

"The 1% annual rate of serious infections in the guselkumab group is, from what I can tell from my research, similar to that observed in patients with moderate-to-severe plaque psoriasis who are not on systemic therapy. I also find it reassuring to see there was no cumulative increase in the rate of serious infections with continued guselkumab treatment over time."
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Device-based Tx strategies

CHERYL GUTTMAN KRADER, B.S., PHARM. | Staff Correspondent

High-dose red light photodynamic therapy (PDT) offers highly effective and durable treatment for acne by selectively destroying the sebaceous gland. However, a search for alternative light-based strategies has continued because high-dose PDT causes significant side effects.

Speaking about device-based acne treatments at MauiDerm 2020, Fernanda Sakamoto, M.D., Ph.D., discussed PDT and other approaches for targeting the sebaceous gland.

PROS AND CONS OF HIGH-DOSE PDT
Discussing high-dose PDT, Dr. Sakamoto says that when the treatment is performed using 20% aminolevulinic acid (ALA) with a three-hour incubation period followed by high fluence red light exposure, PDT is one of the most efficacious treatments available for acne. Severe acne can be cleared in 80% to 90% of patients, and significant acne improvement can persist for longer than six months.

“In fact, in my clinical practice, acne remission following high-dose PDT can last longer than after isotretinoin treatment. In addition, results of a recently published trial comparing ALA 20% with red light PDT versus adapalene gel 0.1% plus oral doxycycline for patients with moderate inflammatory acne showed that the PDT approach was more effective than what we usually do,” says Dr. Sakamoto, assistant professor of dermatology, Harvard Medical School, Boston.

Nevertheless, high-dose PDT is not widely used because of its side effects that can be very difficult for patients to tolerate. The procedure causes significant pain during treatment, a sunburn-like reaction, and intense blistering and oozing.

“These clinicians also report difficulty with billing. Therefore, economics may be another factor in the underutilization of PDT for acne,” Dr. Sakamoto says.

LASER TREATMENTS
Historically, there is no evidence that lasers are more effective for treating acne than conventional therapies. Dr. Sakamoto proposes that failure to target the correct chromophore limited the potential for achieving better results with laser therapy.

“Because acne is an inflammatory disease of the pilosebaceous unit, optimization of selective photothermolysis could be achieved by targeting lipids in the sebaceous glands rather than water, melanin and blood that are the targets of lasers that have been tried to treat acne,” she says.

To develop selective photothermolysis using non-selective wavelengths as a treatment for acne, Dr. Sakamoto, R. Rox Anderson, M.D., and colleagues at the Wellman Center for Photomedicine, Massachusetts General Hospital, Boston, implemented the use of micro gold shells that can penetrate the sebaceous gland and serve as a laser light-absorbing chromophore. The shells have a silica core that is covered in gold. Changing the thickness of the gold layer on the shells allows wavelength tuning, Dr. Sakamoto explains. Initial work using the micro gold shells for acne treatment was done with a near infrared 810-nm hair removal laser. A 1064-nm laser offers deeper penetration and has the additional advantage of not being absorbed by melanin.

Sebacia has received FDA 510(k) clearance for the use of its gold microparticles (Sebacia) as an accessory to 1064 nm lasers to facilitate photothermal heating of sebaceous glands for the treatment of mild-to-moderate inflammatory acne.

The company plans to limit initial commercial availability to California and Washington, DC. Clinical trial results showed that inflammatory lesion count was reduced by a mean of 85% from baseline. In addition, 56% of patients became medication-free after the treatment and 86% were able to avoid use of systemic medications, Dr. Sakamoto reports.

Another strategy is focusing on the development of a laser that will directly target sebum. Using the free electron laser at the Jefferson National Accelerator in Newport News, Va., Dr. Sakamoto in collaboration with Dr. Anderson determined that sebum had an absorption peak at around 1729-nm. They also found using that wavelength that laser-induced heating of sebaceous glands was approximately 1.5-fold higher than heating of water.

Dr. Sakamoto says further work and advances in fiber laser technology led to the development of a user-friendly 1726-nm laser that is now being investigated in a clinical trial.

The treatment is performed using a multiple dose strategy that aims to preferentially heat and destroy the sebaceous glands without causing damage to the epidermis and dermis. Preliminary data from the clinical trial are promising.

“We have been asked what happens when sebaceous gland activity is turned off. We know that babies have non-active sebaceous glands, and so the answer to that question is that you end up with baby-like skin,” Dr. Sakamoto says. “Destroying the sebaceous glands as a treatment for acne may be a good idea.”

Disclosure:
Dr. Sakamoto is a consultant to Sebacia and to Acure Laser. Both companies have licensed patents from Dr. Sakamoto’s employer, Massachusetts General Hospital, Boston.
Quick TAKES

Newer and pipeline treatments showing promise and improve outcomes for patients with moderate-to-severe acne.

Newer retinoid therapies are aimed at improving treatment compatibility.

A unique topical minocycline 4% foam preparation may address some concerns with antibiotic resistance.

We have not seen new product line and a pipeline like this in a very long time. We have a toolbox now that is amazing, and in my opinion, many of these new drugs are really going to change the way in which we treat acne.\(^1\)

Hilary E. Baldwin, M.D. Rutgers Robert Wood Johnson Medical Center, Piscataway, N.J.

Newer therapies aim to improve outcomes

ILYA PETROU, M.D. | Staff Correspondent

A ntibiotic resistance is an ever-increasing issue, sometimes making therapeutic decisions challenging. Although one of the cornerstones of acne therapy, clinicians must nevertheless be wary when contemplating antibiotic therapy for their acne patients, says Hilary E. Baldwin, M.D., medical director, The Acne Treatment and Research Center, Brooklyn, N.Y., and clinical associate professor of dermatology, Rutgers Robert Wood Johnson Medical Center, Piscataway, N.J. The ubiquitous abuses of topical clindamycin and erythromycin of years past led, in part, to the antibiotic resistances seen today, reducing the efficacy of clindamycin and rendering erythromycin relatively useless in the United States.

It is widely believed that minocycline is one of the best drugs that clinicians have for treating acne, and it has also found utility in the treatment of Methicillin-resistant Staphylococcus aureus (MRSA). A unique topical minocycline 4% foam preparation, developed by Foamix, now a wholly owned subsidiary of Menlo Therapeutics, may be a game changer in the treatment of acne, according to Dr. Baldwin.

“While the blood level of the Foamix product is nearly undetectable, the cutaneous levels are extremely high, and those two things in terms of the concept of a mutant selection window suggest that use of this topical preparation of minocycline may not be associated with the development of resistant organisms,” Dr. Baldwin explains. “More work needs to be done to prove this concept for C. acnes, but also common commensal organisms such as staphylococcus and streptococcus. It may be that our concerns of topical minocycline following in the footsteps of clindamycin and erythromycin are unfounded.”

However, she adds, clinicians need to be good stewards with minocycline, and prescribe oral minocycline only in combination with benzoyl peroxide to prevent the development of resistant organisms.

RETNIOIDS

Newer retinoid therapies are aimed at improving treatment compatibility and outcomes in acne patients. According to Dr. Baldwin, Altreno, a 0.05% tretinoin lotion from Ortho-Dermatologics, has demonstrated improved tolerance with the addition of humectants and other hydrating agents.

The 4th generation retinoid trifarotene (Aklief, Galderma) has full selectivity for the gamma receptor in the skin. For years, clinicians have made the assumption that what works on the face works on the back, but according to Dr. Baldwin, this may not be true due to differences in skin thickness and sebaceous gland distribution. With trifarotene, she adds, clinicians have a large phase 3 study that demonstrates good truncal efficacy for the first time.

“Trifarotene works well on both the face and the trunk with good tolerability, which is what researchers were hoping that the selectivity for the gamma receptor was going accomplish,” Dr. Baldwin says.

One of the exciting drugs in the pipeline is clascoterone 1% cream (Winlevi, Cassiopea SpA) which aims to help improve outcomes for patients with moderate-to-severe acne. The anti-androgen topical medication converts to a non-androgenic cream upon application, making it possible to use in the male population as well as female.

Absorica LD (low dose, Sun Pharma), which launched in the United States in February, is a micronized isotretinoin topical preparation that has been shown to result in higher serum plasma level compared with other existing isotretinoins. The major advantage with this formulation, Dr. Baldwin says, is that the patient can take the medication at any time of day with or without food and it still results in good bioavailability.

Other recent developments include sarecycline (Searsara, Almirall), which is approved by the FDA for the treatment of non-nodular inflammatory lesions in moderate-to-severe acne in patients nine years of age and older. It is a newer tetracycline-class antibiotic taken once daily and has demonstrated good efficacy and tolerability.

Arazlo (Ortho Dermatologics), approved by the FDA for the topical treatment of acne vulgaris in patients nine years of age and older, is a tazarotene 0.045% lotion. According to Dr. Baldwin, its novel vehicle formulation that has been shown to provide strong efficacy with favorable tolerability, reducing the tolerability issue that is prominent with tazarotene use.

Two companies have combination tretinoin/ benzoyl peroxide products in development (Sol-Gel, OrthoDermatologics) in which they’re looking at solving — in different ways — the stability issues that have prevented this combination in the past.

“We have not seen new product line and a pipeline like this in a very long time. We have a toolbox now that is amazing, and in my opinion, many of these new drugs are really going to change the way in which we treat acne,” Dr. Baldwin says.\(^1\)

Disclosures: Dr. Baldwin reports no relevant disclosures.
New direction: Mast cell activity

CHERYL GUTTMAN KRADER, B.S., PHARM | Staff Correspondent

Although it is now accepted that rosacea is a chronic inflammatory condition, the pathogenesis of this skin disease remains unclear. Complicating determination of the etiology of rosacea is the need to account for its multiple subtypes, i.e., erythematotelangiectatic, papulopustular, phymatous and ocular.

It is likely indisputable that better understanding of rosacea etiology could offer new targets for developing better treatments, says Guy F. Webster, M.D., Ph.D., who proposes a focus on controlling mast cell activity. This concept is based on findings from several lines of research that point to a role for histamine and other chemical mediators released by mast cells.

“Altering the foods that are leading causes of the blush response in rosacea patients shows histamine content as a common thread,” says Dr. Webster, Webster Dermatology, Hockessin, Del.

THE MAST CELL CONNECTION

Looking at the foods that are leading causes of the blush response for rosacea patients shows histamine content as a common thread. Dr. Webster notes that in a survey conducted by The National Rosacea Society, yogurt, cheese, sour cream, soy, yeast extract, and chocolate were some of the most common foods reported by rosacea patients.

“These are all fermented foods that have a relatively elevated level of free histamine that causes a vasodilatory response,” he says.

In the body, histamine plus other mediators that cause vasodilation and an inflammatory response are released by mast cells that have been shown to be increased in numbers and activity in the facial skin of patients with rosacea. Furthermore, research by Richard Gallo, M.D., Ph.D., and colleagues at the University of California, San Diego performed in a preclinical model showed that treatment with a mast cell stabilizer effectively decreased the development of rosacea-like inflammation when the animals were challenged with cathelicidin LL-37, a known enabler of rosacea pathogenesis.
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2A randomized clinical trial with 426 patients, ≥18 years of age, that investigated the effectiveness of Enstilar® or the vehicle alone for the treatment of psoriasis vulgaris on the trunk and/or limbs. Efficacy was assessed using a 5-point IGA at Week 4, with treatment success defined as the percentage of patients who achieved at least a 2-step improvement to reach “Clear” or “Almost Clear” disease severity. Patients with “Mild” disease were required to be “Clear” to be considered a treatment success.1,2


INDICATION AND USAGE
Enstilar® (calcipotriene and betamethasone dipropionate) Foam is indicated for the topical treatment of plaque psoriasis in patients 12 years and older. Apply Enstilar Foam to affected areas once daily for up to 4 weeks. Discontinue use when control is achieved. Instruct patients not to use more than 60 grams every 4 days.

IMPORTANT SAFETY INFORMATION
For topical use only. Enstilar Foam is not for oral, ophthalmic or intravaginal use and should not be applied on the face, groin or axillae or if skin atrophy is present at the treatment site. Do not use with occlusive dressings. Patients should wash hands after application.

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INDICATIONS AND USAGE

Enstilar® (calcipotriene and betamethasone dipropionate) Foam is indicated for the topical treatment of plaque psoriasis in patients 12 years and older.

DOSE AND ADMINISTRATION

Instruct patients to shake prior to using Enstilar Foam and to wash their hands after applying the product. Apply Enstilar Foam to affected areas once daily for up to 4 weeks. Rub in Enstilar Foam gently. Discontinue Enstilar Foam when control is achieved.

Patients should not use more than 60 grams every 4 days. Enstilar Foam should not be:

- Used with occlusive dressings unless directed by a healthcare provider.
- Used on the face, groin, or axilla, or if skin atrophy is present at the treatment site.
- Enstilar Foam is not for oral, ophthalmic, or intranasal use.

DOSE FORMS AND STRENGTHS

Enstilar Foam: 0.005%/0.064% - each gram contains 50 mcg calcipotriene and 0.643 mcg of betamethasone dipropionate in a white to off-white opalescent liquid in a pressurized aluminum spray can with a continuous valve and actuator. At administration the product is a white to off-white foam after evaporation of the propellants.

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

Flammability

The propellants in Enstilar Foam are flammable. Instruct the patient to avoid fire, flame, and smoking during and immediately following application.

Hypercalcemia and Hyperparathyroidism

Hypercalcemia and hyperparathyroidism have been observed with use of Enstilar Foam. If hypercalcemia or hyperparathyroidism develops, discontinue treatment until parameters of calcium metabolism have normalized. The incidence of hypocalcemia and hyperparathyroidism following Enstilar Foam treatment of more than 4 weeks has not been evaluated.

Effects on Endocrine System

- Hypothalamic-Pituitary-Adrenal Axis Suppression

Systemic absorption of topical corticosteroids can cause reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for clinical glucocorticosteroid insufficiency. This may occur during treatment or upon withdrawal of treatment. Factors that predispose a patient to HPA axis suppression include the use of high-potency steroids, large treatment surface areas, prolonged use, use of occlusive dressings, altered skin barrier, liver failure, and young age.

Evaluation for HPA axis suppression may be done by using the adrenocorticotropic hormone (ACTH) stimulation test. If HPA axis suppression is documented, gradually withdraw Enstilar Foam, reduce the frequency of application, or substitute with a less potent corticosteroid.

The following trials evaluated the effects of Enstilar Foam on HPA axis suppression:

- In a trial evaluating the effects of Enstilar Foam on the HPA axis, 35 adult subjects applied Enstilar Foam on the body and scalp. Adrenal suppression was not observed in any subjects after 4 weeks of treatment. In another trial, 33 pediatric subjects aged 12 to 17 years applied Enstilar Foam on the body and scalp. Adrenal suppression occurred in 3 (9%) of the subjects.

Cushing’s Syndrome and Hyperpigmentation

Systemic effects of topical corticosteroids may also include Cushing’s syndrome, hyperpigmentation, and hypertrichosis.

Additional Considerations for Endocrine Adverse Reactions

Pediatric patients may be more susceptible to systemic toxicity due to their larger skin surface to body mass ratios.

Use of more than one corticosteroid-containing product at the same time may increase the total systemic corticosteroid exposure.

Allergic Contact Dermatitis

Allergic contact dermatitis has been observed with topical calcipotriene and topical corticosteroids. Allergic contact dermatitis to a topical corticosteroid is usually diagnosed by observing a failure to heal rather than a clinical exacerbation. Corroborate such an observation with appropriate diagnostic patch testing.

Ophthalmic Adverse Reactions

Use of topical corticosteroids, including Enstilar® Foam, may increase the risk of posterior subcapsular cataracts and glaucoma. Cataracts and glaucoma have been reported with the postmarketing use of topical corticosteroid products. Avoid contact with Enstilar Foam with eyes. Enstilar Foam may cause eye irritation. Advise patients to report any visual disturbance to an ophthalmologist for evaluation.

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.

Clinical Trials Conducted in Subjects 18 years and older with Psoriasis

The rates of adverse reactions described below were from three randomized, multicenter, vehicle and/or active-controlled clinical trials in adult subjects with plaque psoriasis.

Subjects applied study product once daily for 4 weeks, with the median weekly dose of Enstilar Foam was 25 grams. Adverse reactions reported in <1% of adult subjects treated with Enstilar Foam included: application site irritation, application site pruritis, folliculitis, skin hyperpigmentation, hypercalcemia, urticaria, and exacerbation of psoriasis.

Clinical Trials Conducted in Subjects 12 to 17 years with Psoriasis

In one uncontrolled clinical trial, 106 subjects aged 12 to 17 years with plaque psoriasis of the extremities and body applied Enstilar Foam once daily for up to 4 weeks. The median weekly dose was 40 grams. Adverse reactions reported in <1% of pediatric subjects treated were acne, erythema, application site pain, and skin reactions.

Postmarketing Experience

Because adverse reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Postmarketing reports for local adverse reactions to topical corticosteroids included atrophy, skin fragility, seborrhea, secondary infection, and skin candidiasis.

Ophthalmic adverse reactions of cataracts, glaucoma, increased intraocular pressure, and central serous chorioretinopathy have been reported with the use of topical corticosteroids, including topical betamethasone products.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

Available data with Enstilar Foam are not sufficient to evaluate a drug-associated risk for major birth defects, miscarriages, or adverse maternal or fetal outcomes. Although there are no available data on use of the corticosterine component in pregnant women, systemic exposure to calcipotriene after topical administration of Enstilar Foam is likely to be low.

Observational studies suggest an increased risk of having low birth weight infants with the maternal use of potent or super potent topical corticosteroids. Advise pregnant women that Enstilar Foam may increase the potential risk of having a low birth weight infant and to use Enstilar Foam on the smallest area of skin and for the shortest duration possible.

In animal reproduction studies, oral administration of calcipotriene to pregnant rats during the period of organogenesis resulted in an increased incidence of minor skeletal abnormalities, including enlarged fontanelles and extra ribs. Oral administration of calcipotriene to pregnant rabbits during the period of organogenesis had no apparent effects on embryo-fetal development. Subcutaneous administration of betamethasone dipropionate to pregnant rats and rabbits during the period of organogenesis resulted in fetal toxicity, including fetal deaths, reduced fetal weight, and fetal malformations (cleft palate and/or crooked or short tail). The available data do not allow the calculation of relevant comparisons between the systemic exposures of calcipotriene and betamethasone dipropionate observed in animal studies to the systemic exposures that would be expected in humans after topical use of Enstilar® Foam.

The estimated background risk of major birth defects and miscarriage of 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% to 4% and 15% to 20%, respectively.

Data

Human Data

Available observational studies in pregnant women did not identify a drug-associated risk of major birth defects, preterm delivery, or fetal mortality with the use of topical corticosteroids of any potency. However, when the dispensed amount of potent or super potent topical corticosteroids exceeded 300 grams during the entire pregnancy, maternal use was associated with an increased risk of low birth weight in infants.

Animal Data

Embryo-fetal development studies with calcipotriene were performed by the oral route in rats and rabbits. Pregnant rats received doses of 0, 6, 18, or 54 mcg/kg/day (0, 36, 108, and 324 mcg/m²/day, respectively) on days 6-15 of gestation (the period of organogenesis). There were no apparent effects on maternal survival, behavior, or body weight or on litter parameters, and no effects on the incidence of major malformations in fetuses. Fetuses from dams dosed at 54 mcg/kg/day exhibited a significantly increased incidence of minor skeletal abnormalities, including enlarged fontanelles and extra ribs. Pregnant rabbits were dosed daily with calcipotriene at exposures of 0, 4, 12, or 36 mcg/kg/day (0, 48, 144, and 432 mcg/m²/day, respectively) on days 6-18 of gestation (the period of organogenesis). Mean maternal body weight gain was reduced in animals dosed at 12 or 36 mcg/kg/day. The incidence of fetal deaths was increased in the group dosed at 36 mcg/kg/day; reduced fetal weight was also observed in this group. The incidence of major malformations among fetuses was not affected. An increase in the incidence of minor skeletal abnormalities, including incomplete ossification of sterna, pubic bones, and forelimb phalanges, was observed in the group dosed at 36 mcg/kg/day. Embryo-fetal development studies with betamethasone dipropionate were performed via subcutaneous injection in mice and rabbits. Pregnant mice were administered doses of 0, 156, 625, or 2500 mcg/kg/day (0, 468, 1875, and 7500 mcg/m²/day, respectively) on days 8 through 13 of gestation (the period of organogenesis). Betamethasone dipropionate induced fetal toxicity, including fetal deaths, reduced fetal weight, malformations (increased incidence of the cleft palate and/or crooked or short tail), and minor skeletal abnormalities (delayed ossification of vertebra and sterna). Fetal toxicity was observed at the lowest exposure that was evaluated (156 mcg/kg/day).

Clinical Trials Conducted in Subjects 12 to 17 years with Psoriasis

Pregnant rabbits were injected subcutaneously at doses of 0, 0.625, 2.5, and 10 mcg/kg/day (0, 7.5, 30, and 120 mcg/m²/day, respectively) on days 6 through 18 of gestation (the period of organogenesis). Betamethasone dipropionate induced fetal toxicity, including fetal deaths, reduced fetal weight, external malformations (including malformed ears, cleft palate, umbilical hernia, kinked tail, club foot, and club hand), and skeletal malformations (including absence of phalanges of the first digit and cranial dysplasia) at doses of 2.5 mcg/kg/day and above.

Calcipotriol was evaluated for effects on peri- and postnatal development when orally administered to pregnant rats at doses of 0, 6, 18 or 54 mcg/kg/day (0, 36, 108, and 324 mcg/m²/day, respectively) from gestation day 15 through day 20 postpartum. No remarkable effects were observed on any parameter, including survival, behavior, body weight, litter parameters, or the ability to nurse or reaps.
Betamethasone dipropionate was evaluated for effects on peri- and post-natal development when orally administered to pregnant rats at dosages of 0, 100, 300, and 1000 mcg/kg/day (0, 600, 1800, and 6000 mcg/m²/day, respectively) from gestation day 6 through day 20 postpartum. Mean maternal body weight was significantly reduced on gestation day 20 in animals dosed at 300 and 1000 mcg/kg/day. The mean duration of gestation was slightly, but statistically significantly, increased at 100, 300, and 1000 mcg/kg/day. The mean percentage of pups that survived to day 4 was reduced in relation to dosage. On lactation day 6, the percentage of pups with a reflex to right themselves when placed on their back was significantly reduced at 1000 mcg/kg/day. No effects on the ability of pups to learn were observed, and the ability of the offspring of treated rats to reproduce was not affected.

Carcinogenesis, Mutagenesis, Impairment of Fertility
When betamethasone dipropionate was applied topically to CD-1 mice for up to 24 months at dosages approximating 1.3, 4.2, and 8.5 mcg/kg/day in females, and 1.3, 4.2, and 12.9 mcg/kg/day in males (up to 26 mcg/m²/day and 39 mcg/m²/day, in females and males, respectively), no significant changes in tumor incidence were observed when compared to control.

When betamethasone dipropionate was administered via oral gavage to male and female Sprague Dawley rats for up to 24 months at dosages of 20, 60, and 200 mcg/kg/day (120, 360, and 1200 mcg/m²/day, respectively), no significant changes in tumor incidence were observed when compared to control.

Calcipotriene did not elicit any genotoxic effects in the Ames mutagenicity assay, the mouse lymphoma TK locus assay, the human lymphocyte chromosome aberration test, or the mouse micronucleus test. Betamethasone dipropionate did not elicit any genotoxic effects in the Ames mutagenicity assay, the mouse lymphoma TK locus assay, or in the rat micronucleus test.

Studies in rats with oral doses of up to 54 mcg/kg/day (324 mcg/m²/day) of calcipotriene indicated no impairment of fertility or general reproductive performance. Studies in male rats at oral doses of up to 200 mcg/kg/day (1200 mcg/m²/day), and in female rats at oral doses of up to 1000 mcg/kg/day (6000 mcg/m²/day), of betamethasone dipropionate indicated no impairment of fertility.

PSCIENTIFIC INFORMED
Flammability
Instruct patients that Enstilar® Foam is flammable; avoid heat, flame, or smoking when applying this medication.

Administration Instructions
• Shake before use and spray the foam by holding the can in any orientation except horizontally.
• Do not use more than 60 grams every 4 days.
• Discontinue therapy when control is achieved unless directed otherwise by the healthcare provider.
• Avoid use of Enstilar Foam on the face, underarms, groin or eyes. If this medicine gets on face or in mouth or eyes, wash area right away.
• Do not occlude the treatment area with a bandage or other covering unless directed by the healthcare provider. Instruct the patients not to use other products containing calcipotriene or a corticosteroid with Enstilar Foam without first talking to the healthcare provider.
• Wash hands after application.

Flammability
Carcinogenesis, Mutagenesis, Impairment of Fertility

When calcipotriene was applied topically to mice for up to 24 months at dosages of 3, 10, and 30 mcg/kg/day (9, 30, and 90 mcg/m²/day, respectively), no significant changes in tumor incidence were observed when compared to control.

A 104-week oral carcinogenicity study was conducted with calcipotriene in male and female rats at doses of 1, 5, and 15 mcg/kg/day (6, 30, and 90 mcg/m²/day, respectively). Beginning week 71, the dosage for high-dose animals of both genders was reduced to 1, 5, and 15 mcg/kg/day (6, 30, and 90 mcg/m²/day, respectively), no significant changes in tumor incidence were observed when compared to control.

When betamethasone dipropionate was administered via oral gavage to male and female Sprague Dawley rats for up to 24 months at dosages of 20, 60, and 200 mcg/kg/day (120, 360, and 1200 mcg/m²/day, respectively), no significant changes in tumor incidence were observed when compared to control.

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PATIENT COUNSELING INFORMATION
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• Wash hands after application.

Local Reactions and Skin Atrophy
Advise patients that local reactions and skin atrophy are more likely to occur with occlusive use, prolonged use or use of higher potency corticosteroids.

Pregnancy and Lactation
• Advise patients that Enstilar® Foam may increase the potential risk of having a low birth weight infant and to use Enstilar Foam on the smallest area of skin and for the shortest duration possible.
• Advise breastfeeding women not to apply Enstilar Foam directly to the nipple and areola to avoid direct infant exposure.

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Local Reactions and Skin Atrophy
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Hypercalcemia and Hypercalciuria
Advise patients that hypercalcemia and hypercalciuria have been observed with the use of Enstilar Foam.

HPA Axis Suppression, Cushing's Syndrome, and Hyperglycemia
Advise patients that Enstilar Foam can cause HPA axis suppression, Cushing's syndrome, and/or hyperglycemia.

Ophthalmic Adverse Reactions
Advise patients to avoid contact of Enstilar Foam with eyes and to report any visual symptoms.

Pregnancy and Lactation
• Advise pregnant women that Enstilar® Foam may increase the potential risk of having a low birth weight infant and to use Enstilar Foam on the smallest area of skin and for the shortest duration possible.
• Advise breastfeeding women not to apply Enstilar Foam directly to the nipple and areola to avoid direct infant exposure.

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Examination of mast cells in pathophysiology

ILONA PETROU, M.D. | Staff Correspondent

Mast cells appear to play an intricate role in the pathophysiology of rosacea and could serve as potential targets for future therapies, according to recent study findings.

Impacting approximately 5% of the adult population worldwide, rosacea can significantly impact a patient’s quality of life and lead to self-hatred, depression, anxiety and social phobia.

Heralded by transient/persistent erythema and inflammatory papules/pustules with or without telangiectasia, rosacea is further divided into four subtypes including erythematotelangiectatic rosacea, papulopustular rosacea, phymatous rosacea or rhinophyma, and ocular rosacea.

“Rosacea is a complex disorder caused by immune dysfunction and neurovascular dysregulation involving many types of inflammatory cells,” writes Lin Wang, M.D., and fellow colleagues, department of dermatology, West China Hospital, Sichuan University, Chengdu, China, in the paper that recently appeared in Frontiers in Medicine.

“Mast cells participate in the pathogenesis of diverse inflammatory diseases.”

Lin Wang, M.D., et al., West China Hospital, Sichuan University, Chengdu, China

“Once activated, the mast cells can promote the release of different mediators and have a considerable effect on the pathophysiology of diverse inflammatory diseases.”

Disclosures:

The authors reported no relevant disclosures.

References

The imbalance of the skin microbiota has been thought to play a key role in the development of rosacea symptoms.

Researchers compared the makeup and diversity of the skin microbiota in a small group of patients before and after taking oral antibiotics.

Rosacea severity increased with age; however, bacterial diversity was not altered significantly by the antibiotic treatment.

Better understanding the changes that occur in the skin microbiota following therapy can help clinicians home in on the potential relevant microbes that can cause the development of rosacea symptoms.

Systemic antibiotics impact skin microbiota

ILYA PETROU, M.D. | Staff Correspondent

The precise etiology of rosacea is still a mystery; however, it is thought that an imbalance of the skin microbiome may play a role in the pathogenesis of the disease. A recent study published in the *Journal of Clinical Medicine* evaluated the changes seen in the skin microbiota of patients following antibiotic therapy to elucidate which organisms might play the biggest role in development of rosacea symptoms.

In healthy skin, the microbiota helps protect the body from harmful pathogens, but when the skin becomes compromised in some way, such as through injury or inflammation, the makeup of the microbiota may change.

Skin microbiome composition is crucial for correct skin immune functions, and the imbalance of the skin microbiota and/or the perturbation of its microbial populations have long been thought to play a key role in the development of rosacea symptoms. Moreover, the efficacy of antibiotics in rosacea treatment suggests a role for microbiota in its pathophysiology.

In the study, researchers compared the makeup and diversity of the skin microbiota in a small group of Asian patients with rosacea before and after taking oral antibiotics, as well as comparing the skin microbiota at baseline according to age and rosacea severity. The longitudinal cohort study included 12 rosacea patients who presented with papules and pustules and no recent use of oral and topical antimicrobials or retinoids.

A total of eleven females and one male (average age of 51 years) with a median age of 51 years) with a median Investigator’s Global Assessment score of 3 (moderate) were enrolled in the study. Study participants were sampled for 16S ribosomal RNA gene sequencing at baseline, and after six weeks of doxycycline treatment.

Results showed that at baseline, *Staphylococcus epidermidis* was the most dominant species (28%) followed by *Cutibacterium acnes* (13%) (formerly known as *Propionibacterium acnes*). The prevalence of *Cutibacterium acnes* was lower in the 60 years and over age group compared to the 60 years and under-age group of patients.

Data showed that rosacea severity increased with age and was associated with a decrease in the relative abundance of *Cutibacterium acnes* and an increase of *Staphylococcus epidermidis*. In all of the study patients, antibiotic therapy reduced clinical rosacea grades and was associated with an increase in the relative abundance of *Weissella confusa*. Results also showed that bacterial diversity was not altered significantly by the antibiotic treatment. Principal coordinates analysis demonstrated mild clustering of samples by patient and scant clustering with treatment.

Various topical and/or oral antibiotics including metronidazole, ivermectin and erythromycin are commonly used to treat the papules and pustules seen in rosacea patients, and according to the researchers, the disappearance of rosacea papules and pustules with systemic antibiotics has been attributed to their anti-inflammatory activity.

“Antibiotics leading to complete abolition of the lesions rather than just blunting, as well as being more effective than agents with much more potent anti-inflammatory effect such as steroids and nonsteroidal anti-inflammatory drugs suggest that bacteria play a role in the papules and pustules of rosacea,” write authors Yu Ri Woo, M.D., and colleagues, from the department of dermatology, Incheon St. Mary’s Hospital, The Catholic University of Korea, Seoul, South Korea.

The severity of rosacea appears to be age-dependent the study authors note, and although a specific causative microbiota could not be pinpointed, a more in-depth understanding of the skin’s microbiota and its modulation through systemic antibiotic therapy can help clinicians better treat and manage this chronic inflammatory skin disease.

*Disclosure:* Dr. Woo et al. report no relevant disclosures.

*Reference:*

**Medical therapy for advanced melanoma**

CHERYL GUTTMAN KRADER, B.S., PHARM. | Staff Correspondent

Systemic therapies for melanoma were first approved for the management of stage IV disease. Subsequently, several agents gained an indication for use as adjuvant therapy for stage III melanoma, and some therapies are now being investigated for high-risk stage II disease.

Although treatment of melanoma with these systemic therapies in the United States is mostly directed by medical oncologists, dermatologists are important collaborators because treatment-related adverse events include a range of cutaneous reactions, says Jean Bolognia, M.D.

She also points out that in addition to their broadening use for treating melanoma, immune checkpoint inhibitors are being used to treat a litany of other cancers. The list of cutaneous side effects associated with their use is also growing.

“Early identification and appropriate management of these cutaneous side effects will allow patients to remain on effective treatment for their cancer. In addition, knowledge of systemic side effects is important so we can discuss them with our patients, especially as immunotherapy is being considered for patients with earlier stages of melanoma who have a better long-term prognosis,” says Dr. Bolognia, professor of dermatology, Yale University, New Haven, Conn.

**THERAPEUTIC OPTIONS**

Given the multiple systemic therapies that have been approved over the past several years, it is helpful to broadly divide them into two categories: the kinase inhibitors and the immune checkpoint inhibitors.

The immune checkpoint inhibitors include the anti-CTLA-4 antibody ipilimumab and the anti-programmed cell death-1 protein (PD-1) antibodies nivolumab, pembrolizumab, and cemiplimab-rwlc.

The three immune checkpoint inhibitors used to treat melanoma differ in clinical efficacy and associated with their use is also growing.

The selective BRAF inhibitors, which include vemurafenib, dabrafenib, and encorafenib, and the MEK inhibitors, which include trametinib, cobimetinib, and binimetinib.

The most common cutaneous side effects associated with the selective BRAF inhibitors include morbilliform or scarlatiniform exanthems, phototoxicity reactions (in particular with vemurafenib), and keratoacanthomas and squamous cell carcinomas (SCCs). However, the incidence of the latter side effect is markedly reduced when the selective BRAF inhibitor is combined with a MEK inhibitor, Dr. Bolognia says.

“Palmar and/or plantar fibromatosis is a lesser known cutaneous side effect of vemurafenib that dermatologists need to recognize,” she adds. “Clinicians should also note that they may be the first to describe a novel side effect of systemic cancer therapies.”

The three immune checkpoint inhibitors used to treat melanoma differ in clinical efficacy and associated with their use is also growing.
I mmunotherapy is a quickly evolving field. Patients with advanced cutaneous squamous cell carcinoma (cSCC) are benefitting from the research for a number of other conditions, as novel agents demonstrate efficacy, according to an expert who spoke earlier this year at the ODAC Dermatology, Aesthetic & Surgical Conference, Orlando, Fla.
Recent advances in immunotherapy have led to the development of cemiplimab (Libtayo, Regeneron and Sanofi Genzyme), the first drug approved by the U.S. Food and Drug Administration (FDA) for the treatment of locally advanced cutaneous and metastatic squamous cell carcinoma. As high mutational and neoantigenic burdens are believed to be strong predictors of responsiveness to immunotherapy, cutaneous squamous cell carcinoma is expected to be responsive to immune checkpoint inhibitors. Cemiplimab is a programmed death receptor-1 (PD-1) blocking antibody with demonstrated efficacy in treating patients with advanced squamous cell carcinoma, particularly where other treatment modalities have failed.

“For those patients with advanced squamous cell cancers in whom surgical intervention and radiation therapy are not an option or contraindicated, novel immune checkpoint inhibitor agents such as cemiplimab are now available and can have a very positive impact in the quality of life of these patients,” says Desiree Ratner, M.D., clinical professor, Ronald O. Perelman department of dermatology, NYU Skin and Cancer Clinic, New York.

According to Dr. Ratner, cemiplimab is one of the first immunotherapeutic drug available to treat advanced squamous cell carcinoma disease effectively, with response rates of approximately 50%.

“While other immunotherapy drugs in this class, such as pembrolizumab and nivolumab, have the potential to be effective, cemiplimab has been the most studied agent to date in cutaneous squamous cell carcinoma,” she says. “The outcomes achieved with this drug are remarkable and time will tell us about the durability of the results achieved so far.”

Pembrolizumab (Keytruda, Merck), which was approved by the FDA for the treatment of advanced melanoma, has also been approved for first line treatment of head and neck SCC. Now that cemiplimab has received approval, it will likely be the PD-1 inhibitor of choice until studies of other agents are performed that show equivalent effects, Dr. Ratner says.

Not every patient is an ideal candidate for immunotherapy though, as side effects can be significant and sometimes intolerable for some. According to Dr. Ratner, immune response modulators can have a negative impact on patients’ thyroid or pituitary function or can generate other types of immune responses that are unrelated to the tumor. Nevertheless, Dr. Ratner says that the benefit of immunotherapy for these patients is usually much greater when compared to the other treatment options currently available.

Immunosuppressed patients such as those with lymphoma or organ transplant recipients may not be ideal candidates for this type of immunotherapy. Clinicians must therefore carefully weigh all treatment options and the risk/benefit ratio of each patient individually.

“Immunotherapeutic agents have become an important treatment option for patients with advanced squamous cell carcinoma. The next frontier of research will likely be combining immunotherapy with chemotherapy or radiation therapy, bridging treatments and initiating immunotherapy or other agents in those patients who may have developed resistances or failed multiple therapies,” Dr. Ratner says.

Disclosures:
Dr. Ratner reports no relevant disclosures.

"For those patients with advanced squamous cell cancers in whom surgical intervention and radiation therapy are not an option or contraindicated, novel immune checkpoint inhibitor agents such as cemiplimab are now available and can have a very positive impact on the quality of life of these patients.”

Desiree Ratner, M.D., NYU Skin and Cancer Clinic, New York
Cosmetic Surgery Forum
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December 2-5, 2020

- HONEST -
“What I like about this particular meeting is that it’s so intimate and it’s so interactive. You have the opportunity to ask questions of the panelist and have this whole interaction about their experience. I really like that because it’s about sharing what everybody is actually doing in their practices, not just evidence-based but anecdotal and experiential.”
- CHYTRA ANAND, MD

- INSIGHTFUL -
“I think one of the best aspects of Cosmetic Surgery Forum is everyone talks about their experience, especially experiences in their practice that are not necessarily on-label, but off-label. I learn so much about what other people are doing that I can apply to my own practice that’s safe, great for patients and that everyone can benefit from.”
- LAWRENCE GREEN, MD

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This is primarily due to high chronic lifetime sun exposure, limited sun protection, and limited awareness of the sunlight’s carcinogenic potency.”

The quality of life of patients with AKs can greatly be impacted and, according to the authors, there are two sides to the social implications related to AK.

“One hand, the feeling of losing control and the speculation about the risk of getting skin cancer may impact a patient’s quality of life as well as the pain associated with many AK treatments. On the other hand, due to the clear correlation between UV-related activities and AK, the necessary change in behavior might also impact a patient’s quality of life, including social circles and social acceptance, as well as self-esteem correlated to tanning,” the authors write.

The primary treatment goals are the eradication of as many clinical and subclinical AK lesions as possible, the authors say, as well as keeping the disease-free intervals as long as possible and decreasing the risk of developing an invasive SCC.

“A practical treatment algorithm” was recently proposed to help clinicians better address AK lesions. Here, treatment was broken down into lesion-directed therapy, cluster directed therapy for a small field (< 25 cm²) and cluster to directed therapy for a larger field (> 25 cm²).

Cryotherapy, curettage and excision are the currently used lesion-directed therapies; however, they do not adequately address field carcinization or subclinical lesions. These treatments are mostly reserved for suspicious single lesions to exclude the possibility of an invasive SCC, the authors write.

In cluster directed therapy, modalities like 5-fluorouracil and 9% imiquimod are readily used, with only the latter finding utility in addressing field carcinization and subclinical lesions.

For large field-directed therapy, 5-fluorouracil, diclofenac and PDT are all used, but according to the authors, imiquimod 3.75% has the highest expert agreement of any field directed therapy and a long-term sustained reduction in AK lesions. Nevertheless, often a combination of approaches is used to successfully control AK lesions.

There are a number of experimental treatments currently under investigation such as Sinecatechin, Tirbanibulin, and Tuvatexib to be the most promising drugs,” the authors write.

Disclosures:
Dr. Cramer and Stockfleth report no relevant disclosures.

References:

Advanced melanoma therapeutic options

risk for severe adverse events (grade 3/4).

The combination of ipilimumab plus nivolumab is associated with a higher clinical response rate than nivolumab or pembrolizumab alone that, in turn, are more effective than ipilimumab monotherapy. However, the risk of grade 3/4 immune-related adverse events is greatest using the combination of ipilimumab and nivolumab, less with ipilimumab alone, and even lower when using nivolumab or pembrolizumab as monotherapy, Dr. Bolognia says.

The most common cutaneous side effects associated with the immune checkpoint inhibitors include pruritus, lichenoid dermatitis, morbilliform and eczematous eruptions, and vitiligo-like leukoderma. Interestingly, bulbous pemphigoid as well as sarcoïdosis have also been reported.

Managing immune-related adverse events

In 2018, guidelines for the management of immune-related adverse events in patients treated with immune checkpoint inhibitors were published in the Journal of Clinical Oncology.1 The skin toxicities were divided into three categories: rash/inflammatory dermatitis, bullous dermatoses, and severe cutaneous adverse reactions (e.g. Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms).

The recommendations for management were based on severity grade and generally consisted of increasing the intensity of systemic corticosteroid treatment as severity increased, in addition to drug holidays. However, there are other interventions that dermatologists can offer, Dr. Bolognia says.

“Rather than initiating oral corticosteroids to manage a grade 2 lichenoid, eczematous or psoriasiform reaction, acitretin, apremilast or methotrexate can be considered,” she explains. “Similarly, whereas the guidelines recommend initiating an oral corticosteroid to treat a grade 2 bullous pemphigoid eruption, oral dicyclomine with or without tacrolimus can be administered instead.”

Importantly, patients with melanoma who develop immunotherapy-related cutaneous adverse reactions, in particular vitiligo-like depigmentation, have been shown to have an improved survival. However, it is important to distinguish whether the vitiligo-like depigmentation (“leukoderma of melanoma”) is spontaneous or treatment-related.

“If the leukoderma is spontaneous, the patient needs to be restaged even though it is not always a reflection of metastatic disease,” Dr. Bolognia says.

References:

skin cancer
A variety of topical and injectable therapies are showing promise for addressing the problem of hair loss in both men and women, says Matt Leavitt, D.O.

“This is an exciting time in the world of hair restoration. There are many new and emerging products and techniques for the treatment of hair loss,” says Dr. Leavitt, Founder and CEO, Advanced Dermatology and Cosmetic Surgery, Maitland, Fla., who is a hair loss and hair restoration specialist. He is joined at his practice location by Natalie Kash, M.D., who is completing a hair loss and restoration fellowship.

**TOPICAL TREATMENTS**

Clascoterone (cortexolone 17-alpha propionate; Breezula, Cassiopea) is an androgen receptor inhibitor that is being developed as a treatment for both male and female androgenetic alopecia (AGA). It is a novel steroid that is rapidly hydrolyzed in plasma to an inactive metabolite. Therefore, it appears to be associated with minimal to no risk of steroid-related systemic side effects.

A phase 2, vehicle-controlled dose-ranging study investigated different concentrations and dosing regimens for clascoterone in males with mild-to-moderate AGA. Its results showed that the treatment had a favorable safety profile and they also provided evidence supporting efficacy. Based on the results, clascoterone 7.5% solution was selected as the best candidate for further study, and a pivotal trial was initiated early in 2020. In addition, a phase 2 study is underway investigating clascoterone in females.

“The results achieved in men in the phase 2 study were pretty dramatic and comparable to some of the best results seen in the past with minoxidil,” Dr. Leavitt says. “More women today are wanting to be treated for hair loss and at an earlier stage, and we often struggle to find safe and effective treatment for women. Oral spironolactone and topical minoxidil have been the primary drugs used for female pattern hair loss, but clascoterone and other topical treatments are showing promise.”

Given the desire for the benefits of finasteride without the potential for systemic side effects, topical use of the anti-androgen has also garnered significant interest. Finasteride blocks the conversion of testosterone to dihydrotestosterone and blocks androgen receptor function. It acts to reduce hair miniaturization and hair inflammation, Dr. Leavitt says.

Findings of a systematic review published in 2018 supported the efficacy of topical finasteride as a treatment for AGA in men and women. The review included seven studies, all of which showed that the topical treatment was associated with increased terminal hair counts, decreased rates of hair loss, and positive hair growth assessments.

“The most common side effects included scalp irritation, erythema and contact dermatitis. There were a number of systemic side effects, but they were rare, and there were no serious side effects.

“The concentrations of finasteride used in these studies varied widely, and there were also...”

**PHASE 2 DOSE RANGING TOPICAL CORTEXOLONE 17 ALPHA PROPIONATE FOR ANDROGENETIC ALOPECIA**

July 2018: Phase 2 interim analysis results very positive

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<th>Clascoterone 5% BID</th>
<th>Clascoterone 7.5% BID</th>
<th>Clascoterone 7.5% QD</th>
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<td>58%</td>
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<td>61%</td>
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</table>

**PHASE 3 CLASCOTERONE 7.5% FOR ANDROGENETIC ALOPECIA**

January 2020: Study results support efficacious and safe use

An expanded pivotal trial was initiated in early 2020. In addition, a phase 3 study is underway investigating clascoterone 7.5% for AGA in women, and a phase 3 study is currently underway to investigate the safety and efficacy of clascoterone 7.5% for AGA in men.

**INNOVATION CONTINUES ON PAGE 34**
New vehicle may effectively deliver tranexamic acid

MELASMA responds well to oral and locally injected tranexamic acid treatments, but clinical results from topical tranexamic acid administration have been disappointing, researchers report in a study published January 21 in the *Journal of Cosmetic Dermatology.*

The lack of efficacy in topical preparations could be from the inability of tranexamic acid topicals to achieve epidermal therapeutic concentrations needed to lighten the pigmented disorder, the authors write.

Researchers in Singapore conducted an *in vitro* study comparing human epidermal and dermal tranexamic acid skin concentrations after applying Fairence T-Complex (TDF Derma Formula), a co-enhancer cream they developed, and a Japanese branded cream as a control. Each topical had a tranexamic acid concentration of 2%.

They found tranexamic acid concentrations in the skin six and 24 hours after applying the co-enhancer cream were well within the required estimated concentration range for efficacy. They looked at interpolated concentrations at a depth of 100 µm, which is at about the dermo-epidermal junction and the therapeutic target for tranexamic acid. At six hours, interpolated concentrations for the Fairence topical were about 4 µg/mL at 100 µm tissue depth.

“A similar interpolation for Japanese branded tranexamic acid cream places 24 hour 100 µm concentrations in the lower part of the predicted efficacy range,” they write.

The co-enhancer cream showed greater skin tissue bioavailability than the control cream and achieved greater therapeutic concentrations at the viable epidermal target.

In the tissue samples studied, tranexamic acid concentrations diminished with skin depth for both formulations. Results from this preclinical study support more research on melasma treatment with Fairence T-Complex co-enhancer cream, they write.

In the last decade, researchers have extensively studied tranexamic acid treatment for melasma. Authors of systematic review and meta-analysis of tranexamic acid treatment for adult melasma concluded that tranexamic acid appeared to be a promising therapeutic approach for melasma.

But they note that data is limited on topical tranexamic acid, which has been applied alone and along with intra-dermal injection, microneedling, fractionated CO2 laser and more.

“Debate exists about whether topical water-soluble [tranexamic acid] is trans-dermally absorbed by the lipid-soluble surface of the skin. In addition to bridging the knowledge gaps in our understanding of topical as an option for melasma patients, further studies on clinical efficacy and side effects comparisons among different administrations of [tranexamic acid] should be carried out,” the review authors write.

Authors of the current study write that topical bioavailability is a concern, as it tends to be lower and more variable with topical administration than with oral tranexamic acid.

Tranexamic acid is not easy to partition into the stratum corneum barrier’s lipid domain.

“Here we formulated 2% tranexamic acid into a glycol co-enhancer drug delivery system, dispersed in silicone elastomer continuous phase, with the objective of combining pharmaceutical topical drug delivery technology with the technology of cosmetic science,” according to the authors.

While more studies, including a double-blind placebo-controlled clinical study, are needed, the authors predict the *in vitro* results will reflect *in vivo* levels. They think that by using the co-enhancer silicone cream in melasma patients to more effectively deliver tranexamic acid to the intended target, especially refractive melasma patients will achieve better treatment outcomes. The co-enhancer technology in Fairence T-Complex has been shown to increase skin penetration for other actives, they write.

**Disclosures:**

Authors report no relevant disclosures.

**Reference:**

1. Ng, SP, Marcon, M, Davis, AF. *In vitro human skin concentrations following topical application of 2% tranexamic acid in co-enhancer cream and branded cream formulations.* *J Cosmet Dermatol.* 2020;0:1–7.

innovation expands hair loss treatment options  FROM PAGE 32

variations in the application regimen. In addition, there is evidence that greater efficacy can be achieved by combining topical finasteride with other treatments, including oral finasteride, topical minoxidil and ketoconazole shampoo,” Dr. Leavitt says. “Clearly there is a need for larger studies with longer follow-up to investigate the efficacy and safety of topical finasteride as well as the optimal vehicle, formulation, concentration, and frequency.”

INJECTABLE TREATMENTS

More than 50 studies have reported on injections of platelet rich plasma (PRP) for hair loss. Similar to the situation with topical finasteride, these studies also varied in methodology, including the method for PRP preparation, timing for PRP injection, and outcome measures, Dr. Leavitt says.

“Despite promising results, there are a lot of questions regarding the ideal preparation technique and regimen for using PRP that might provide the best outcomes,” he observes.

“There is good biologic rationale for interest in PRP. Because it contains a high concentration of platelets in a small volume of plasma, it represents a rich source of growth factors and cytokines that have been shown to promote vascularization and angiogenesis, trigger and extend anagen, reduce inflammation and oxidative stress, trigger hair stem cell regeneration, activate fibroblasts and stimulate extracellular matrix, Dr. Leavitt says.

“I also think that the promise of stem cell therapy is making some hair transplant surgeons turn their attention toward combining PRP with hair transplant procedures,” he says.

Also in the realm ofinjectable therapy, exosomes are the focus of a lot of attention as an emerging treatment for hair loss. Exosomes are extracellular cell-derived vesicles that transport micro RNA, mRNA, and transcription factors or other proteins from cell to cell, thereby allowing intercellular communication. Their use can promote hair restoration and prevent hair loss via several mechanisms, including by stimulating anti-inflammatory, proangiogenic, regenerative and healing pathways.

Studies done in animal models showed that exosomes derived from dermal papilla cells promoted anagen, delayed catagen and regulated hair follicle stem cell growth and differentiation.

However, there are no basic science data from studies investigating the effects of dermal papilla-derived exosomes and exosomal micro RNA on the human hair follicle and hair follicle stem cells, Dr. Leavitt says.

Currently, several companies are producing exosome products for treating hair loss, although none are FDA-approved.

“There is a need for more clinical data on the long-term efficacy and safety of this approach,” he says. •

Disclosure:

Dr. Leavitt is Executive Medical Advisor for Bosley. He has received financial support grants and has received research support regarding class III to Ila finasteride, minoxidil, spironolactone, ketoconazole, exosomes, platelet rich plasma (PRP) or any companies associated with these medications/therapies.

References:


Tattoo-removal device receives 510(k) premarket notification

MORGAN PETRONELLI | Assistant Editor

SOLITON, A MEDICAL DEVICE COMPANY based in Houston, announced March 11, 2020, that the U.S. Food and Drug Administration (FDA) has given special 510(k) premarket notification clearance for the company’s Generation II Rapid Acoustic Pulse (RAP) device.¹

Soliton initially filed the 510(k) application with the FDA on Feb. 10, 2020, noting that the device’s intended use is as an accessory for the 1064 nm Q-Switched laser on black ink in Fitzpatrick Skin Types I-III.

Chris Capelli, M.D., founder, president and CEO of Soliton, says the company intends to distribute the new version of the device to 20-25 of the top U.S. dermatologists for physician feedback and market data on cartridge usage.

“The FDA clearance of our Generation II RAP device marks yet another milestone on Soliton’s path towards commercialization, specifically this year’s strategic launch for tattoo removal,” he says.

The company also announced its recent Manufacturing Services Agreement with Sammina Corporation, an integrated manufacturing solutions provider. The agreement will allow Sammina to produce Soliton’s Rapid Acoustic Pulse (RAP) device and its replaceable cartridges, effective March 6.²

“Sammina’s expertise and world-class service are a great match for Soliton’s innovative device, which is FDA-cleared for tattoo removal and we believe has potential in additional aesthetic indications including cellulite removal and fibrotic scarring, and we look forward to working with them in the years ahead,” says Dr. Capelli, M.D.

The RAP devices utilize rapid pulses of acoustic shockwaves for the removal of tattoos. The company is also investigating other uses for the device, including fat reduction, cellulite improvement and fibrotic scar treatment, and has already presented promising study results for the latter. Currently, the device is only cleared by the FDA for tattoo removal. •

References:


those in need of critical care due to COVID-19.

STRENGTHENING YOUR PATIENT BASE.

Communication is not just for employees; you have a captive patient audience waiting at home. Patients want to know you are a central part of this recovery effort. You’ve got plenty of time now to focus on patient outreach, and patients have more time than ever to listen. Share hand-washing tips, share skincare at-home tips, share new research on COVID-19 you’ve vetted. Your content is good enough - get it out there - outreach is most important. The same calming presence that has kept patients coming back to you year after year - that’s the one they need to hear from today. It is imperative that folks know that they can count on you and the practice for the long term.

There’s been plenty written about teledermatology recently, so I will not belabor this point. Suffice it to say, virtual care is an important initiative both for patient reassurance and engagement. Most of us practice dermatology with our hands, and while that is not possible, it is just as important to reach out with our hearts and minds. I’ve done more education and talk therapy in the last couple weeks than I would have ever done over several months of face-to-face encounters with patients (and doctors) running late for their next appointments. We adopted password-protected Zoom rooms for use in own practice and continue to take notes within our EMR system. It has been met with more demand than I could have imagined.

WRESTLING WITH RENT.

Make these calls now, not next month when every other tenant is also late on rent. We reached out to our landlords early to discuss the pressures on our system. It has been met with more demand than I could have imagined.

Legal: Teledermatology & COVID-19

a lawsuit where the patient received care or where the defendant physician’s office is located.

Telemedicine obviously expands the scope of venue exposure. The plaintiff can bring the telemedicine consultant into a court in his state. A state may also require venue. For example, Montana and North Carolina both require that any medical malpractice claims by their residents that are based on telemedicine must be brought within their state.

A physician who practices in a state with a short Statute of Limitations should not assume that time limit will apply if he is sued for telemedicine consult. Different states also take different approaches to the Standard of Care. Some use a national standard, and some use a local one. The consulting telemedicine physician should therefore become acquainted with the standards used in the states they extend their practice to.

HIPPA Confidentiality. Since teledermatology is clearly the practice of medicine, historic confidentiality issues have always been a concern. This all changed with COVID-19. The federal Office of Civil Rights (OCR) at the U.S. Department of Health and Human Services (HHS) issued a bulletin in March that stipulated that physicians can serve patients through commonly used applications such as FaceTime, Skype and Zoom so as to provide telehealth remote communications.

In the end, Dr. NY need not be concerned. His patient’s law student son, unfortunately, was not informed of the recent regulatory changes.

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### GALDERMA INITIATIVES AIM TO SUPPORT PROVIDERS

**MORGAN PETRONELLI | Assistant Editor**

**GALDERMA ANNOUNCED MARCH 4** its plan to invest in their aesthetic portfolio, increase its U.S. salesforce, improve its ASPIRE Galderma Rewards digital program and introduce a collaboration with ZO Skin Health.

According to a press release, the company will alter their ASPIRE Galderma Rewards program by instituting a new app available for Apple and Android devices where consumers can view and manage their reward points on the go while also having the capability to select their preferred provider. Additionally, the rewards program will soon be able to integrate with electronic medical records commonly used in the aesthetic industry and will be launched in the second quarter of 2020.

“At Galderma, we’re relentlessly focused on driving trust and success for our customers. The acceleration of our growth and expansion plans, underscores Galderma’s commitment to the growing aesthetics market,” says Alisa Lask, vice president and general manager of Galderma U.S. Aesthetics.

The company reports a 15% U.S. salesforce increase and says it plans to expand upon that growth by providing its salesforce with new resources and tools, which include a new collaboration between Galderma’s Restylane and ZO Skin Health and an amplified national direct-to-consumer Restylane marketing campaign to aid in the push of consumers to aesthetic providers.

Zo Skin Health, a skincare brand developed and created by Zein Obagi, M.D., provides prescription and over-the-counter skincare products to consumers.

“...this collaboration with Restylane and ZO Skin Health means my patients have an opportunity to experience two premium brands. This innovative offering is a unique and compelling way to bring new patients to my practice,” says Steven F. Weiner, M.D., facial plastic surgeon and Galderma consultant.

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### References:


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