A PHASE 2b STUDY investigating gusacitinib (ASN002, Asana Biosciences) as a treatment for moderate-to-severe chronic hand eczema (CHE) met its primary and key secondary endpoints, demonstrating that the investigational oral janus kinase/spleen tyrosine kinase (JAK/SYK) inhibitor provided statistically significant improvements in multiple measures of disease severity compared with placebo. In addition, data on adverse events and treatment discontinuations show that gusacitinib was well-tolerated and had an acceptable safety profile.

Emma Guttman-Yassky, M.D., Ph.D., Sol and Clara Kest Professor of Dermatology, director of the Center for Excellence in Eczema, and director of the Laboratory of Inflammatory Skin Diseases Icahn School of Medicine at Mount Sinai, New York City.

ATOPIC DERMATITIS

Dual JAK/SYK inhibitor a promising systemic treatment for chronic hand eczema

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

A PHASE 2b STUDY investigating gusacitinib (ASN002, Asana Biosciences) as a treatment for moderate-to-severe chronic hand eczema (CHE) met its primary and key secondary endpoints, demonstrating that the investigational oral janus kinase/spleen tyrosine kinase (JAK/SYK) inhibitor provided statistically significant improvements in multiple measures of disease severity compared with placebo. In addition, data on adverse events and treatment discontinuations show that gusacitinib was well-tolerated and had an acceptable safety profile.
BRAND ENHANCEMENTS SUPPORT YOUR PATIENT CARE MISSION

by MIKE HENNESSY, SR

THIS MONTH WE’re EXCITED to announce an upgraded website and a launch of new digital features that we hope you’ll find both valuable and educational. DermatologyTimes.com serves as the hub of this brand. As such, the website will now provide insight into new data and technologies through a variety of communication channels and supporting resources designed to provide complementary and comprehensive industry education.

You’ll find the content has been arranged to highlight key therapeutic areas to simplify navigation and access to pivotal developments. Among an expanding resource area of video and audio products, you’ll find the launch of a new bi-monthly podcast series, “The Cutaneous Connection.” This new series features interviews with industry experts who will explore the impact of new data and technologies to support practitioners in optimizing patient care and practice management. The episodes can be found at www.dermatologytimes.com/podcasts.

In the first episode, Adam Friedman, M.D., FAAD, professor and interim chair of dermatology at the George Washington University School of Medicine and Health Sciences, discusses the rising use of endocannabinoids in the treatment of inflammatory skin diseases and why you may opt not to recommend these ingredients in sunscreen and the use of social media influence on sun protection.

Our cover features share insight from studies conducted in accordance with a recommendation found in the proposed rule on sunscreen drug products for over-the-counter human use that was issued by the U.S. Food and Drug Administration last year. However, David Strous, M.D., Ph.D., director, Division of Applied Regulatory Science, US FDA, Silver Spring, Md., stresses that these findings indicate a need for further study and should not be interpreted as meaning the ingredients have been deemed unsafe. Patients should still be counseled to continue using sunscreen. Another report provides insight into beliefs about UV exposure and sunscreen use.

We’ve also enhanced our video offerings to include expert interviews on timely social topics, as well as key takeaways from today’s virtual meeting activity, which can be found at dermatologytimes.com/expert-interviews. We’ve highlighted one of our early interviews, in which Catherine DiGiorgio, M.D., a cosmetic and laser dermatologist in Boston, shares insights into new devices and procedures for non-invasive body contouring. Many of these videos are part of our Medical World News online network, programming in which you will find breaking news across healthcare as well as discussions on multi-specialty treatment approaches. This is accessible 24 hours a day at www.mjlifesciences.com/news-network.

We hope you find our enhancements valuable. As always, we welcome any feedback to continue to provide the information you need to manage your practice and support your patient care mission.

MIKE HENNESSY, SR, IS CHAIRMAN AND FOUNDER OF DERMATOLOGY TIMES’ PARENT COMPANY, MH LIFE SCIENCES.

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

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An IL-23 inhibitor for adults with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy

NOTHING IS EVERYTHING

Nothing less than the opportunity for durable skin clearance.
For your patients, that’s 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).

TURN THE PAGE TO VIEW THE LONG-TERM DATA

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.
**An IL-23 Inhibitor for Adults with Moderate to Severe Plaque Psoriasis**

**Achievements at Week 16 in Ultimma-1 & Ultimma-2 (NRI)**

<table>
<thead>
<tr>
<th>PASI 90 at Week 16</th>
<th>sPGA 0/1 at Week 16</th>
<th>PASI 100 at Week 16</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ULTIMMA-1</strong></td>
<td><strong>ULTIMMA-2</strong></td>
<td></td>
</tr>
<tr>
<td>75% (229/304)</td>
<td>88% (267/304)</td>
<td>36% (109/304)</td>
</tr>
<tr>
<td>5% (5/102)</td>
<td>8% (8/102)</td>
<td>0% (0/102)</td>
</tr>
<tr>
<td><strong>ULTIMMA-2</strong></td>
<td><strong>ULTIMMA-2</strong></td>
<td></td>
</tr>
<tr>
<td>75% (220/294)</td>
<td>84% (246/294)</td>
<td>51% (149/294)</td>
</tr>
<tr>
<td>2% (2/98)</td>
<td>5% (5/98)</td>
<td>2% (2/98)</td>
</tr>
</tbody>
</table>

**Consistent PASI 90/100 Rates at 2.5 Years in Open-Label Extension**

In the randomized controlled trials, 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 84% (246/294) and 88% (267/304), respectively. In an open-label extension, level of response was achieved at 84% (149/294) and 82% (232/282), respectively.

**Indication**

SKYRIZI® (risankizumab-rrzaa) 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-rrzaa) 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

**Explore Long-Term Data at ViewTheData.com**

[Image of a graph showing consistent PASI 90/100 rates at 2.5 years in open-label extension]

[Graph showing patients who achieved PASI 90 and PASI 100 (%)]

* NRI=Non-Responder Imputation.

Studied Design: Ultimma-1 (N=506) and ultimma-2 (N=491) were replicate phase 3, randomized, double-blind, placebo- and active-controlled studies to evaluate the efficacy and safety of SKYRIZI (150 mg) vs placebo over 16 weeks and biologic active control over 52 weeks in adult patients with moderate to severe plaque psoriasis. SKYRIZI (150 mg) was given as 2 subcutaneous injections at Weeks 0, 4, and every 12 weeks thereafter.

**References**


3. Data on file, Academy of Dermatology Annual Meeting; March 1-5, 2019; Washington, DC.

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 LIMMithless (OLE) and include only patients from ultIMMa-1 and 2 who were originally randomized to SKYRIZI, completed the RCT, and enrolled in the OLE. LIMMithless is an open-label extension for which patients who completed either ultIMMa trial, IMMhance, or IMMvent were eligible to participate.

Treatment cannot be confirmed. Monitor patients for signs and symptoms of active TB during and after SKYRIZI treatment. Do not administer SKYRIZI to patients with active TB.

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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North Chicago, IL 60064
US-SKZD-200177
May 2020
Printed in U.S.A.

SKYRIZI® (sky-RIZZ-ee) (risankizumab-raa) Injection, for subcutaneous use

INDICATIONS AND USAGE

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

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

Infections

SKYRIZI® may increase the risk of infections. In clinical studies, infections occurred in 22.3% of the SKYRIZI group compared to 14.4% of the placebo group through the first 16 weeks of treatment. Serious infections, sepsis, and serious opportunistic infections occurred in 0.6% of patients in the SKYRIZI group and 0.4% of the placebo group. Serious infections included cellulitis, osteomyelitis, sepsis, and herpes zoster.

Infections occurred at any site in 6.7% of patients in the SKYRIZI group and 4.6% of the placebo group.

The rate of serious infections for the SKYRIZI group and the placebo group was ≤ 0.4%. Treatment with SKYRIZI should be discontinued in patients with clinically apparent infection until the infection is controlled.

Infections were observed in 6.8% of patients in the SKYRIZI group and 4.8% of the placebo group.

In patients with a chronic bacterial or a history of recurrent infection, consider the risks and benefits prior to initiating therapy with SKYRIZI.

In patients with a history of viral infection, consider the risks and benefits prior to initiating therapy with SKYRIZI.

Data from placebo- and active-controlled studies were pooled to evaluate the safety of SKYRIZI for up to 16 weeks, 52 weeks, and 104 weeks of treatment in 2174, 1208, and 24 subjects, respectively. Adverse drug reactions that occurred at a rate of at least 1% and at a higher rate in the SKYRIZI group than the placebo group during the 16-week controlled period of pooled clinical studies are summarized in Table 1. Adverse drug reactions occurring in 1% of patients on SKYRIZI through Week 16 are listed below.

Table 1. Adverse Drug Reactions Occurring in >1% of Patients on SKYRIZI through Week 16

<table>
<thead>
<tr>
<th>Adverse Drug Reactions</th>
<th>SKYRIZI (N=2174)</th>
<th>Placebo (N=1208)</th>
</tr>
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<tbody>
<tr>
<td>Upper respiratory tract infectionsd</td>
<td>17.3 (198)</td>
<td>22.7 (271)</td>
</tr>
<tr>
<td>Infectionsb</td>
<td>45.6 (96)</td>
<td>39.0 (47)</td>
</tr>
<tr>
<td>Injection site reactions</td>
<td>33.1 (357)</td>
<td>31.5 (377)</td>
</tr>
<tr>
<td>Neutrophil count decrease</td>
<td>18.7 (39)</td>
<td>17.8 (21)</td>
</tr>
<tr>
<td>Decrease in lymphocytes</td>
<td>14.1 (29)</td>
<td>13.0 (16)</td>
</tr>
</tbody>
</table>

■ Includes: respiratory tract infections, sinusitis, rhinitis, pharyngitis, pharyngitis viral, nasopharyngitis, otitis media.

■ Includes: sinusitis, rhinitis, pharyngitis, sinusitis acute, coryza, cervical lymphadenopathy.

■ Includes: cellulitis, pneumonia, otitis media, conjunctivitis, meningitis, sepsis.

■ Includes: acute otitis media, cellulitis, periostitis, wound infection, pharyngitis.

■ Includes: fever, pharyngitis, headache, sinusitis, rhinitis, pharyngitis, tonsillitis.

■ Includes: headache, fever, influenza-like illness, sinusitis.

■ Includes: neutrophilia, neutropenia, lymphopenia, leukocytosis.

■ Includes: lymphopenia, neutropenia.

■ Includes: nasopharyngitis.

■ Includes: pharyngitis, rhinitis, sinusitis, conjunctivitis.

■ Includes: cellulitis, pharyngitis.

■ Includes: conjunctivitis.

■ Includes: neutrophilia.

■ Includes: rhinitis.

■ Includes: pharyngitis.

■ Includes: nasopharyngitis.

■ Includes: cellulitis, rhinitis.

■ Includes: mastocytosis, lichen planus, viral exanthem, psoriasis.

■ Includes: cellulitis.

■ Includes: cellulitis, sepsis, osteomyelitis, dental abscess.

■ Includes: cellulitis, wound infection.

■ Includes: cellulitis, pharyngitis, nasopharyngitis, rhinitis.

■ Includes: cellulitis, pharyngitis, sinusitis.

■ Includes: cellulitis, rhinitis.

■ Includes: conjunctivitis.

■ Includes: cellulitis.

■ Includes: cellulitis, wound infection.

■ Includes: cellulitis, sepsis.

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Mount Sinai, New York City

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Messaging on UV exposure

Survey reveals insight into impact of climate and health beliefs on skin cancer risk and sun protective behaviors
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Are your patients looking for a well-tolerated treatment they can depend on for the long haul?

RESPONSE THAT LASTS THROUGH WEEK 148

Based on responders at Week 28 who participated in the extension study (reSURFACE 1 and 2)

MAINTAINED PASI 75 THROUGH WEEK 148

Co-primary endpoints: PASI 75 and PGA 0/1 with at least a 2-point improvement, both at Week 12

- After 2 doses, by Week 12, 64% and 61% achieved PASI 75 (reSURFACE 1 and reSURFACE 2, respectively)
  - vs placebo: 6% (reSURFACE 1) and 6% (reSURFACE 2)
- After 2 doses, by Week 12, 58% and 55% achieved PGA 0/1 (reSURFACE 1 and reSURFACE 2, respectively)
  - vs placebo: 7% (reSURFACE 1) and 4% (reSURFACE 2)

DURABLE SAFETY PROFILE

ADVERSE EVENTS

<table>
<thead>
<tr>
<th>Placebo</th>
<th>ILUMYA™</th>
</tr>
</thead>
<tbody>
<tr>
<td>54%</td>
<td>48%</td>
</tr>
</tbody>
</table>

SERIOUS ADVERSE EVENTS

<table>
<thead>
<tr>
<th>Placebo</th>
<th>ILUMYA™</th>
</tr>
</thead>
<tbody>
<tr>
<td>2%</td>
<td>1%</td>
</tr>
</tbody>
</table>

LOW DISCONTINUATION RATE DUE TO AEs

Only 3.4% and 2.3% of patients who entered the extension studies discontinued due to singular-event AEs (reSURFACE 1 and reSURFACE 2, respectively).

*From a post hoc pooled analysis extension study of reSURFACE 1 and 2. No imputation of missing data.

†From the placebo-controlled period of the trial: Weeks 0–12.

‡AEs of interest include: Serious infections, malignancies, non-melanoma skin cancer, melanoma, extended MACE, deaths, injection site reactions, and drug-related hypersensitivity AEs.

All results based on the recommended 100 mg dose of ILUMYA™.

AE=adverse event; MACE=major adverse cardiovascular events; PASI=Psoriasis Area and Severity Index; PGA=Physician Global Assessment.

reSURFACE 1 and 2 were Phase 3, double-blind, placebo-controlled trials of ILUMYA™ given at Weeks 0, 4, and every 12 weeks thereafter. Patients in reSURFACE 1 (N=463) and reSURFACE 2 (N=465) with moderate-to-severe plaque psoriasis who were candidates for phototherapy or systemic therapy were randomized to ILUMYA™ 100 mg or placebo. At Week 28, patients in reSURFACE 1 initially randomized to ILUMYA™ who achieved at least PASI 75 were re-randomized to either continue initial treatment or to receive placebo up to 64 weeks. The co-primary endpoints of both trials were: 1) the proportion of subjects who achieved at least PASI 75 and 2) the proportion of subjects with a PGA 0/1 and at least a 2-point improvement, both at Week 12. Other evaluated outcomes included PASI 90/100 at Week 12 and PASI 75 at Week 28. reSURFACE 1 also measured maintenance of efficacy in responders up to Week 64.

INDICATION

ILUMYA™ (tildrakizumab-asnm) is indicated for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

ILUMYA™ is contraindicated in patients with a previous serious hypersensitivity reaction to tildrakizumab or to any of the excipients.

WARNINGS AND PRECAUTIONS

Hypersensitivity

Cases of angioedema and urticaria occurred in ILUMYA™-treated subjects in clinical trials. If a serious allergic reaction occurs, discontinue ILUMYA™ immediately and initiate appropriate therapy.
Illumya™ (tildrakizumab-asmn) is indicated for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for phototherapy or systemic therapy. Patients in reSURFACE 1 (N=463) and reSURFACE 2 were randomized to Illumya™ 100 mg or placebo. At Week 28, patients in reSURFACE 1 initially randomized to Illumya™ who achieved at least PASI 75 were re-randomized to either continue initial treatment or to receive placebo up to 64 weeks. The co-primary endpoints of both trials were: 1) the proportion of subjects who achieved at least PASI 75 and 2) the proportion of subjects with a Physician Global Assessment 0 or 1 and at least a 2-point improvement, both at Week 12. Other evaluated outcomes included PASI 75 at Week 28. reSURFACE 1 also measured maintenance of efficacy in responders up to Week 64. 

**Infections**

Illumya™ may increase the risk of infection. Treatment with Illumya™ should not be initiated in patients with a clinically important active infection until the infection resolves or is adequately treated.

Consider the risks and benefits of treatment prior to prescribing Illumya™ in patients with a chronic infection or a history of recurrent infection. Instruct patients receiving Illumya™ to seek medical help if signs or symptoms of clinically important chronic or acute infection occur. If a patient develops a clinically important or serious infection, or is not responding to standard therapy, closely monitor and consider discontinuation of Illumya™ until the infection resolves.

**Pretreatment Evaluation for Tuberculosis**

Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with Illumya™. Do not administer Illumya™ to patients with active TB infection. Initiate treatment of latent TB prior to administering Illumya™. Consider anti-TB therapy prior to initiation of Illumya™ in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Patients receiving Illumya™ should be monitored closely for signs and symptoms of active TB during and after treatment.

**Immunizations**

Prior to initiating therapy with Illumya™, consider completion of all age-appropriate immunizations according to current immunization guidelines. Patients treated with Illumya™ should not receive live vaccines.

**Adverse Reactions**

The most common (≥1%) adverse reactions associated with Illumya™ treatment that were more frequent than in the placebo group are upper respiratory infections, injection-site reactions, and diarrhea.

Please see Brief Summary of Full Prescribing Information on the next page or visit IllumyaPRO.com.

**References:**

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ADVERSE REACTIONS

The following serious adverse reactions are discussed elsewhere in the labeling:

Hypersensitivity Reactions [see Warnings and Precautions]

Infections [see Warnings and Precautions]

Clinical Trial Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In clinical trials, a total of 946 subjects with plaque psoriasis were treated with ILUMYA, of which 418 subjects were treated with ILUMYA 100 mg. Of these, 76% subjects were exposed for at least 12 months, 58% for 18 months, and 49% for 24 months. Data from three placebo-controlled trials (Trials 1, 2, and 3) in 705 subjects (mean age 46 years, 71% males, 81% white) were pooled to evaluate the safety of ILUMYA (100 mg administered subcutaneously at Weeks 0 and 4, followed by every 12 weeks [Q12W]) [see Clinical Studies].

Placebo-Controlled Period (Weeks 0-16 of Trial 1 and Weeks 0-12 of Trials 2 and 3)

In the placebo-controlled period of Trials 1, 2, and 3 in the 100 mg group, adverse events occurred in 48.2% of subjects in the ILUMYA group compared to 53.8% of subjects in the placebo group. The rates of serious adverse events were 1.4% in the ILUMYA group and 1.7% in the placebo group.

Table 1 summarizes the adverse reactions that occurred at a rate of at least 1% and at a higher rate in the ILUMYA group than in the placebo group.

Table 1: Adverse Reactions Occurring in ≥1% of Subjects in the ILUMYA Group and More Frequently than in the Placebo Group in the Placebo Pairs: Trials 1, 2, and 3

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>ILUMYA 100 mg (N=705) N (%)</th>
<th>Placebo (N=355) N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper respiratory infections†</td>
<td>98 (14)</td>
<td>41 (12)</td>
</tr>
<tr>
<td>Injection site reactions†</td>
<td>24 (3)</td>
<td>7 (2)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>13 (2)</td>
<td>5 (1)</td>
</tr>
</tbody>
</table>

* Upper respiratory infections include nasopharyngitis, upper respiratory tract infection, viral upper respiratory tract infection, and pharyngitis.
† Injection site reactions include injection site urticaria, pruritus, pain, reaction, erythema, inflammation, edema, swelling, bruising, hematomas, and hemorrhage.

During the placebo-controlled period of Trials 1, 2, and 3, adverse reactions that occurred at rates less than 1% but greater than 0.1% in the ILUMYA group and at a higher rate than in the placebo group included dizziness and pain in extremity.

Specific Adverse Reactions

Hypersensitivity Reactions

Cases of angioedema and urticaria occurred in ILUMYA-treated subjects in clinical trials [see Warnings and Precautions].

Infections

Infections were slightly more common in the ILUMYA group compared to the placebo group. The frequency of infections in the ILUMYA group was less than 1% during the placebo-controlled period. The most common (≥1%) infections were upper respiratory infections. The rates of severe infections for the ILUMYA group and the placebo group were ≤0.3%.

Safety Through Week 52/64

Through Week 52 (Trials 1 and 3) and Week 64 (Trial 2), no new adverse reactions were identified with ILUMYA use and the frequency of the adverse reactions was similar to that observed during the placebo-controlled period.

Immunogenicity

As with all therapeutic proteins there is the potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of incidence of antibodies to tildrakizumab in the studies described below with the incidences of antibodies in other studies or to other products may be misleading.

Up to Week 64, approximately 6.5% of subjects treated with ILUMYA 100 mg developed antibodies to tildrakizumab. Of the subjects who developed antibodies to tildrakizumab, approximately 2% of all subjects receiving ILUMYA had antibodies that were classified as neutralizing. Development of neutralizing antibodies to tildrakizumab was associated with lower serum tildrakizumab concentrations and reduced efficacy.

DRUG INTERACTIONS

Live Vaccinations

Avoid use of live vaccines in patients treated with ILUMYA [see Warnings and Precautions].

USE IN SPECIFIC POPULATIONS

Pregnancy: Risk Summary

Limited available data with ILUMYA use in pregnant women are insufficient to inform a drug-associated risk of adverse developmental outcomes. Human IgG is known to cross the placental barrier; therefore, ILUMYA may be transferred from the mother to the fetus. An embryofetal developmental study conducted with tildrakizumab in pregnant monkeys revealed no treatment-related effects to the developing fetus when tildrakizumab was administered subcutaneously during organogenesis to near parturition at doses up to 115 times the maximum recommended human dose (MRHD). When dosing was continued until parturition, a small increase in neonatal death was observed at 59 times the MRHD [see Data]. The clinical significance of this nonclinical finding is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. The background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data: Animal Data

In an embryofetal developmental study, subcutaneous doses up to 300 mg/kg tildrakizumab were administered to pregnant cynomolgus monkeys once every two weeks during organogenesis to gestational day 118 (22 days after parturition). No maternal or embryofetal toxicities were observed at doses up to 300 mg/kg (159 times the MRHD of 100 mg based on AUC comparison). Tildrakizumab crossed the placenta in monkeys.

In a pre- and postnatal developmental study, subcutaneous doses up to 100 mg/kg tildrakizumab were administered to pregnant cynomolgus monkeys once every two weeks from gestation day 50 to parturition. Neonatal deaths occurred in the offspring of one control monkey, two monkeys at 10 mg/kg dose (6 times the MRHD based on AUC comparison), and four monkeys at 100 mg/kg dose (59 times the MRHD based on AUC comparison). The clinical significance of these nonclinical findings is unknown. No tildrakizumab-related adverse effects were noted in the remaining infants from birth through 6 months of age.

Lactation: Risk Summary

There are no data on the presence of tildrakizumab in human milk, the effects on the breastfed infant, or the effects on milk production. Human IgG is known to be present in human milk. Tildrakizumab was detected in the milk of monkeys [see Data].

The developmental and health benefits of breastfeeding should be considered along with the maternal clinical need for ILUMYA and any potential adverse effects on the breastfed child from ILUMYA or from the underlying maternal condition.

Pediatric Use: Safety and effectiveness of ILUMYA in pediatric patients (<18 years of age) have not been established.

Geriatic Use: A total of 1083 subjects were exposed to ILUMYA 100 mg during Phase 2 and 3 trials. A total of 92 subjects were 65 years or older, and 17 subjects were 75 years or older. Although no differences in safety or efficacy were observed between older and younger subjects, the number of subjects aged 65 and over is not sufficient to determine whether they respond differently from younger subjects.

OVERDOSAGE: In the event of overdose, monitor the patient for any signs or symptoms of adverse reactions and administer appropriate symptomatic treatment immediately.

PATIENT COUNSELING INFORMATION: Advise the patient and/or caregiver to read the FDA-approved patient labeling (Medication Guide).

Instruct patients and/or caregivers to read the Medication Guide before starting ILUMYA therapy and to reread the Medication Guide each time the prescription is renewed. Advise patients of the potential benefits and risks of ILUMYA.

Hypersensitivity

Advise patients to seek immediate medical attention if they experience any symptoms of serious hypersensitivity reactions [see Warnings and Precautions].

Infections

Instruct patients of the importance of communicating any history of infections to the doctor and contacting their doctor if they develop any symptoms of infection [see Warnings and Precautions].

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PLR-00015 RX ONLY
“Private equity has ... provided a business model with demonstrated success that we should now adopt.”

A new business model for dermatology

by ZOE DIANA DRAELOS, M.D.

Dermatology has always been a fascinating, fun area of medical practice. So much so, that everyone wants a piece of the action. Dermatology is unique in that it encompasses patients of both sexes of all ages who are in need of medical, surgical and/or aesthetic services.

Income is derived from the government, private insurance and patient cash pay. No other field of medicine has such diversity in scope or income. These observations caught the attention of big business that spotted an opportunity to make some quick money through investment. Hence, the current expanding trend for purchase of established dermatology practices to undergo consolidation into large conglomerates controlled by private equity.

With a five-year horizon based not on patient care or the practice needs of physicians, the goal of this consolidation is to make money for big business at the expense of all else. The profit that is made for investors is from the dermatologist generated and used to take home. This potentially leaves control of dermatology in the hands of businessmen who are keeping an eye on the bottom line and know little about the practice of medicine, except that it makes money.

However, I believe the battle for control of dermatology is not yet over. There is still time to preserve the joy of independent private practice that has been the hallmark of my medical career, but the opportunity is rapidly disappearing. I would like to propose an alternative model for dermatology practice that I believe would preserve physician autonomy, income and job satisfaction.

I think private equity has nicely provided a business model with demonstrated success that we should now adopt. A nonprofit corporation should be set up as the new business framework. The nonprofit status is important, as demonstrated by the business model used by Blue Cross Blue Shield insurance that has allowed them to become a dominant force in health insurance by becoming more profitable due to their tax-free status. Dermatologists throughout the United States would join their practices to regional groups, much like the current status of private equity groups to avoid FTC issues. These groups would be part of the nonprofit corporation, which would need to be structured carefully to avoid a monopoly. U.S. board-certified licensed dermatologists would hold stock in the new corporation based on their practice value with additional stock purchase both possible and encouraged. Twenty percent of practice income would be shared and 80% would be based on productivity. This would provide for investment in areas where dermatology growth was necessary to generate additional financial returns that would be shared by all stockholders.

Further, young dermatologists, mid-career dermatologists, late-career dermatologists, and retiring dermatologists all would benefit from job and economic satisfaction.

It would be a private equity fund directed by and for dermatologists with a strong dedication to preservation of the specialty and philanthropy. In time, a research arm could be instituted where new technologies could be developed and patented by the dermatology private equity nonprofit and then introduced into practices that are members throughout the United States. Patents would be shared between the inventor dermatologist and the corporation.

Dermatologists are some of the brightest and most entrepreneurial of all physicians. We can do better than to sell the future of our specialty to business investors. We can be business investors! We can set up our own private equity firm and maintain control of our specialty. I believe it is possible. What do you think?
How to eat for healthy skin

by ZOE DIANA DRAELOS, M.D.
Dr. Draelos is a consulting professor of dermatology, Duke University School of Medicine, Durham, NC.

How do I tell patients to eat for healthy skin?
What constitutes a healthy diet has to be one of the greatest enigmas in medicine. Food is more abundant in the United States than ever; yet diet-related disease is rampant as evidenced by the dramatic increase in obesity. An attempt at understanding nutrition developed during WWII was named the recommended daily allowance (RDA), which is still found on food packaging today. The first RDA was accepted in 1941 to establish the minimal nutrition needs for military troops with revisions occurring every five to 10 years. However, the RDA is the minimum dietary requirements, not the optimal diet for health. As a matter of fact, the lack of controlled trials as it relates to diet was recognized at the 2007 meeting. It is well recognized that certain nutrients are essential for skin health. These include Vitamins A, C, and E. It has also been suggested that these nutrients are best consumed as foods, rather than supplement pills. What foods should be recommended?

- Vitamin A is an antioxidant necessary for gene transcription and immune function that can be obtained by eating 2/3 cup of carrots daily.
- Vitamin C, necessary for collagen production and immune function, is a water-soluble antioxidant best consumed by eating one raw tomato daily.
- Vitamin E, the fat-soluble skin antioxidant, can be obtained by eating one-half avocado daily.

These are easy dietary recommendations that can be shared with the patient who wants to get plenty of “skin vitamins” daily.

On a limited calorie diet, how can patients get all the antioxidants they need?
One of the current diet challenges affecting the United States is the consumption of too many calories and not enough antioxidants. This makes it challenging to get adequate antioxidants while minimizing caloric consumption, but it can be accomplished.

- One half-cup of dried blueberries contains 13,427 antioxidants, including anthocyanidin and quercetin.
- One raw apple with skin contains 8,000 phytochemicals.
- One slice of watermelon provides the daily allowance of lycopene.
- One-half avocado provides the daily allowance of lutein/zeaxanthin, which are important water-soluble antioxidants.

All of these foods are low calorie and widely available year-round in the United States.

Do patients need mineral supplementation for great skin?
Most minerals in the diet come from the soil in which plants are grown. If the soil is mineral depleted, so will the foods. A very important mineral antioxidant is selenium obtained from wheat grown in the selenium-rich soil of the Midwestern United States. However, new growing technique and genetically modified wheat with smaller stalks and larger grain heads is depleting the soil. An excellent source of selenium is one Brazil nut daily. Zinc and calcium are necessary for matrix metalloproteinase (MMP) functioning. Calcium can be easily obtained from milk products while two prunes daily will provide sufficient zinc.

Special skin mineral supplementation is not necessary as long as patients make educated dietary choices.
WE WILL CHALLENGE THE STATUS QUO.
WE WILL DELIVER ON OUR PROMISES.
Dr. Joe’s patients are in a euphoric post-COVID-19 quarantine mood, and they are all returning for aesthetic treatments. Before the pandemic, Dr. Joe acquired a new laser. Because he is conscientious, he included a clause in his laser purchase contract that provided that laser expert Dr. Doe would come to Dr. Joe’s office to help him with his first day of treatment. Dr. Joe had three patients scheduled for his first day. He had told all three patients that world-renowned laser expert Dr. Doe would be assisting with the treatments.

One of the three patients was very anxious and scheduled the treatment only because Dr. Doe would be assisting. In addition, because of this patient’s anxiety, each of the three patients signed a general consent form that stipulated their agreement to undergo the procedure by Dr. Joe.

Unfortunately, on the actual day of treatment, Dr. Doe had to cancel his visit because he was made aware that several of his own employees had tested positive for COVID-19. Dr. Joe treated the three patients alone, and there were no complications. However, soon after the procedure date, the anxious patient learned that the new procedure was performed solely by Dr. Joe. This caused him great distress. He sued Dr. Joe for battery.

The basis of the suit was that although no untoward event happened during the procedure (malpractice), a procedure was performed on him for which he never provided consent. The plaintiff expected Dr. Doe to be present during the procedure.

Dr. Joe has now determined that a lawsuit based in battery is not be covered by his medical malpractice insurance. He has conceded that the patient had been told that the procedure would be performed by both he and Dr. Doe. However, he cannot understand how a battery cause of action could proceed against him. He knows that such a lawsuit against him, if successful, could cause him to lose his medical license even though no untoward event occurred. Can the difficulties related to COVID-19 be an excuse?

Many legal cases have now examined the issue of whether a plaintiff can recover for the substitution of a healthcare provider.
absent actual harm. In a well-known New Jersey case, a patient consented to undergo spinal fusion by his physician knowing that the procedure would be performed by both his doctor and another world-renowned surgeon who would be spending the day with his doctor.

On the day of the procedure, the famous physician was not available. His physician substituted an associate to help him with the surgery. The signed consent form never stipulated that the procedure was to take place under the guidance of the famous surgeon. Unfortunately, there were numerous post-operative complications, none of which led to any permanent injury.

The patient chose to sue on a theory of battery and not medical malpractice based on negligence. Negligence would have required proving damages. The battery cause of action could be brought absent any injury. It was based solely on a procedure being performed without the patient’s consent.

The New Jersey court looked at cases based on a lack of informed consent and noted that in order to be successful, the patient must prove that the doctor withheld pertinent medical information concerning the risks of the procedure, the alternatives, or the potential results if the procedure or treatment was not undertaken.

The suing plaintiff must also prove causation, which requires a showing by the plaintiff that a reasonably prudent person in the plaintiff’s position would have declined to undergo the treatment if informed of the risks that the defendant doctor failed to disclose. Thus, the court required damages for informed consent lawsuits, much like it did for negligence lawsuits.

True battery, based on a lack of informed consent, was reserved solely on those instances where the patient consented to one type of operation, but the physician performed a substantially different one from that for which authorization was obtained or where no consent was obtained.

The New Jersey court assumed that the surgeon had made the promise of having the expert surgeon present—even though this was not contained in the signed consent form. The suing plaintiff, in fact, had consented to the surgery and to his physician performing that surgery. The court found that there was no evidence that the surgeon had deviated from the standard of care. The plaintiff had also suffered no harm.

Since this claim was based on informed consent, and not medical battery, the plaintiff was entitled to nothing.

Similarly, Dr. Joe had obtained consent from his patients for the new laser procedure. The procedures were performed without complication. There is no basis for a medical malpractice claim based on informed consent there was also no basis for a suit based in battery. A COVID-19-related defense is not required.

The Dermatology Foundation Funds Research with the Greatest Potential to Lead to Advances in Patient Care.

Every disease seen in the practice of dermatology has new therapies, or even cures, awaiting development—that’s why the work of the DF is so important.

Thanks to our members and supporters over the last 56 years, we have:

- Deepened the understanding of diseases and conditions including psoriasis, atopic dermatitis, inflammatory dermatoses, and autoimmune skin disorders.
- Developed innovations including topical therapies for skin cancer, outcomes research, and biologic therapies.
- Kept talented emerging researchers working in our field by supporting their work at critical points where private funding was key to their continued success.

The innovations your patients need are waiting to be developed. They begin today, with you. Join the DF today and help shape the future of dermatology—for patients everywhere.
No added benefit combining CaHA, HIFU

Study finds monotherapies effective for acne scarring

ILYA PETROU, M.D. | Staff Correspondent

Combination therapies are often employed to help achieve superior clinical outcomes in the treatment of acne scars. Both calcium hydroxyapatite (CaHA) and high intensity focused ultrasound (HIFU) are effective monotherapies; however, the combination of these two modalities did not demonstrate any enhancement clinical efficacy in terms of a synergistic treatment effect, according to findings from a recent study.1

Researchers assessed the safety and efficacy of CaHA monotherapy and its association with HIFU for the treatment of moderate-to-severe atrophic acne scars. The study included 20 female patients (median age 39 years) who were evenly randomized to receive either 3.0-ml CaHA (Radiess, Merz) treatment (0.1 ml at each injection point) or 3.0-ml normal saline solution serving as placebo control. After four weeks, all patients received 400 lines of HIFU (Hifu Finesse, Biotec Italia) therapy delivered by a 10 MHz transducer at a 1.5-mm focal depth able to reach the deep dermis. Patients were followed-up and results were compared to baseline at one, three and six months after the first treatment.

The treatment was performed in a double-blinded manner, as the physician performing injections and the patients did not know whether CaHA or placebo was administered. Each patient received a full-face treatment except for the upper third (forehead and eyebrows), lower lids and submental area. Improvement assessments were made using before and after digital photographs and Antera 3D (Miravex), providing qualitative and quantitative analysis of wrinkles, texture and hemoglobin.

No side effects were reported during the study, underscoring the safety of each individual treatment modality, and all patients completed the study. Results showed that at one month, patients treated with CaHA significantly improved from their baseline wrinkles and skin texture compared with those who received placebo. At the three and six-month follow-up, all patients showed significant improvement in their wrinkles, skin texture and hemoglobin when compared with baseline. Patient satisfaction questionnaires (PSQ) revealed that patients were moderately satisfied at one month and satisfied at three and six months post-treatment.

“Patients receiving CaHA monotherapy demonstrated a significant improvement in wrinkles and skin texture when compared with the control, but its combination with HIFU failed to show any difference with HIFU alone. The lack of apparent synergy may be explained by the fact that HIFU was already so effective as a monotherapy in regenerating dermal tissue that the adjunct of the CaHA was not clinically relevant,” said Antonino Araco, M.D., cosmetic surgeon at University Tor Vergata of Roma, Aesthetic Medicine Department, Rome, Italy, and head-author of the study.

In the placebo control group, wrinkles, skin texture and hemoglobin failed to improve at the one-month follow-up; however, there was improvement in these parameters at the three and six-month follow up time points. According to the PSQ, patients were not satisfied at the one-month follow-up but were moderately satisfied at three and six months post-treatment. Data also showed that there were no differences recorded among the two treatment groups for any of the parameters assessed at the three and six-month follow-up time points when compared to the one-month follow-up treatment assessment.

The HIFU treatment regenerated collagen and increased vascularity of the targeted tissue when used as a monotherapy. Calcium hydroxyapatite treatment alone has been proven effective as a dermal bio-stimulant and, according to Dr. Araco, there is rationale for its association with HIFU. From a scientific perspective, Dr. Araco says that it would be necessary to investigate this potential synergy with a larger cohort of patients.

“We believe that our study proves that both CaHA and HIFU in monotherapy are safe and effective treatment modalities for the improvement of atrophic acne scarring. However, this is a preliminary study and further randomized prospective studies are needed to address the study’s limitations and explore such combination treatment approaches for acne scars,” Dr. Araco says.

Disclosures:
Dr. Araco reports no relevant disclosures.

References:
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Researchers encourage hormone therapy reporting

ILYA PETROU, M.D. | Staff Correspondent

Many of the current acne clinical trials do not consider those acne patients already on hormone therapy when compared to patients not receiving hormones.

Many current acne clinical trials do not consider those patients already on hormone therapy.

Researchers encourage this reporting in future studies to help clinicians better assess how the data might represent a practice population.

Quick TAKES

Acne patients on concomitant hormone therapy may not achieve the same positive treatment outcomes for their acne when compared to patients not receiving hormones.

As these cases can be challenging without recognizing the clear link between hormone therapy and acne, clinicians need to be mindful when contemplating treatment in these patients.

This can be very challenging sometimes because the current guidelines for acne are quite broad and presumably applicable to everyone with acne whether it’s of hormonal etiology or not.

According to Dr. Yeung, a lot of the hormone patients already on hormone therapy.

“I am hopeful that as more and more data is being used regarding what is the optimal treatment for hormonal acne as well as some newer therapies in the pipeline that specifically target the hormonal pathogenesis of acne, hopefully we will have a more streamlined approach to evidence-based strategies for this patient population,” Dr. Yeung says.

As the current data regarding the best way to treat acne in the setting of hormone therapy is lacking, Dr. Yeung encourages all future acne clinical trials researchers to explicitly report how many patients are on oral contraceptives or other hormone therapy in the trial demographics so that clinicians can know how representative their data might be in real-life scenarios for patients who are on hormone therapy.

Disclosure:
Dr. Yeung previously received honorarium from GSK. He is currently supported by the NIH Loan Repayment Program 1L30 AR076081.

Reference:

Dr. Yeung and fellow colleagues recently conducted a study to examine the inclusion and exclusion criteria of acne clinical trials to identify any potential barriers to the enrollment of patients receiving hormone therapy.

The researchers queried the clinicaltrials.gov database for interventional studies from 2009-2019 using the search term “acne.” All age groups and genders were included in the search. They analyzed the inclusion and exclusion criteria of acne interventions with a focus on those related to hormone therapy and contraception.

Of the 86 studies that were identified and included in the evaluation, results showed that 37 studies (43%) had exclusion criteria related to hormone therapy. Patients with medication-induced acne were excluded in 10 studies (11.6%) and patients with hormone disorders were excluded in four studies (4.7%). Other exclusion criteria included current use of oral contraceptives (3.5%), androgen blockers (4.7%), hormone-replacement therapy (2.3%), or use of any medication (7%). The researchers also found that overall, patients receiving consistent oral contraceptives and/or androgen blocker therapy would be excluded from 15 trials (17.4%).

According to Dr. Yeung, a lot of the hormone providers appear to under-recognize the impact of acne among at least 9.1 million women using oral contraceptive pills in 2015-2017 and 2.3 million cisgender and transgender men receiving testosterone replacement therapy.

Despite the many guidelines on acne treatment and management, Dr. Yeung says that there is a lack of high-quality data on the treatment of acne among patients receiving hormone therapy. According to Dr. Yeung, in the United States alone, this potentially impacts the treatment of acne among at least 9.1 million women using oral contraceptive pills in 2015-2017 and 2.3 million cisgender and transgender men receiving testosterone replacement therapy.

As these cases can be challenging without recognizing the clear link between hormone therapy and acne, clinicians need to be mindful when contemplating treatment in these patients.

“I believe that a large part of these patients do not even see a dermatologist, protracting the long-term suffering associated with acne. For those that do, they may receive acne treatments that do not specifically target the underlying hormonal cause. As these cases can be challenging without recognizing the clear link between hormone therapy and acne, clinicians need to be mindful when contemplating treatment in these patients,” Dr. Yeung says.

Despite the many guidelines on acne treatment and management, Dr. Yeung says that there is a lack of high-quality data on the treatment of acne among patients receiving hormone therapy. According to Dr. Yeung, in the United States alone, this potentially impacts the treatment of acne among at least 9.1 million women using oral contraceptive pills in 2015-2017 and 2.3 million cisgender and transgender men receiving testosterone replacement therapy.

As these cases can be challenging without recognizing the clear link between hormone therapy and acne, clinicians need to be mindful when contemplating treatment in these patients.”

Howard Yeung, M.D., M.Sc.
Emory University School of Medicine, Atlanta
Insomnia may predict patients vulnerable to psychiatric effects

Study IDs 'biomarker' for isotretinoin AEs

Illya Petrou, M.D. | Staff Correspondent

Isotretinoin, while very effective for acne, is associated with higher odds of insomnia, which could be a red flag for further potential psychiatric vulnerability in the patient, researchers who presented data in an eposter during the AAD VMX Virtual Meeting Experience 2020, June 12-14.1

“Insomnia is a comorbidity in over 80% of psychiatric disorders. When you look at epidemiologic or clinical studies, patients using isotretinoin experience overall improvement in their acne and this improvement is associated with positive mental health and improved quality of life. However, although in larger clinical studies acne patients typically report feeling a lot better after isotretinoin treatment, it remains very difficult to predict in which patient isotretinoin use may be associated with these idiosyncratic neuropsychiatric reactions. The development of insomnia with isotretinoin use may prove to be a ‘biomarker’ for a vulnerability to develop serious psychiatric adverse effects with isotretinoin.”

Dr. Gupta and fellow colleagues conducted a study to assess the impact of isotretinoin on sleep dysfunction and the potential consequences thereof in a group of acne patients. Researchers examined the U.S. Food and Drug Administration Adverse Event Reporting System (FAERS) database from 2004 to 2019 for the adverse event insomnia with the use of isotretinoin in acne patients, where isotretinoin was considered the primary suspect for the adverse event. All available generic and trade names for isotretinoin were used in the search, and the baseline odds of insomnia was calculated with the use of isotretinoin for the indication of acne versus all other acne treatments in the FAERS database.

Of the 218,594 Individual Safety Reports that were identified (average patient age 23 years) where isotretinoin was used for the indication of acne and specified as a primary suspect for an adverse event, results showed that 1,095 Individual Safety Reports (average patient age 20 years) were associated with the adverse event of insomnia. Also, the Reporting Odds Ratio (ROR) for insomnia when isotretinoin was used for acne versus all other acne treatments was 2.19 and highly significant (p<0.0001), reflecting higher odds for insomnia in this patient subgroup using isotretinoin.

“It is unusual for a young acne patient with an average age of late adolescence or early adulthood to have insomnia as a major complaint,” Dr. Gupta says. “Insomnia is a sign of autonomic dysregulation/activation, which in turn has a high association with impulsive behaviors like suicide and aggression. There seems to be a link between isotretinoin use and insomnia; the onset of insomnia in the acne patient using isotretinoin may suggest a vulnerability for other psychiatric adverse events.”

“Clinicians could try and incorporate symptoms of insomnia in their acne patient screening questions and during the course of treatment with isotretinoin. Perhaps even prior to prescribing isotretinoin, clinicians could specifically ask about any sleep disorders the patient may have, as this may be a red flag suggesting vulnerability for other psychiatric adverse events,” Dr. Gupta suggests. “At the same time the clinician must recognize that, generally, the mental health of the patient improves when given isotretinoin likely due to the significant improvement in acne symptoms.”

“Due to the concern regarding the potential for psychiatric adverse events with isotretinoin, clinicians may be hesitant to prescribe it, particularly in patients with a history of any psychiatric issues. As such, Dr. Gupta says that it is possible that some patients do not get the ideal treatment (i.e., isotretinoin) that they would really benefit from. “It is possible that isotretinoin may be associated with autonomic dysregulation in some patients which may explain symptoms of insomnia. Prospective studies of insomnia and isotretinoin use are necessary to further evaluate this. The results of our study suggest that it may be important to communicate to the acne patient taking isotretinoin that insomnia may be an early sign that something is ‘off,’ and they should inform their prescribing doctor for further evaluation and monitoring,” Dr. Gupta says.

Disclosures: The authors report no relevant disclosures.

References:
Daily topical minocycline foam appears to be safe, was well-tolerated and did not result in adverse events according to pooled data presented during the AAD VMX Virtual Meeting Experience 2020, June 12-14.1

"Topical therapies such as metronidazole, azelaic acid and ivermectin are considered first-line therapies for papulopustular rosacea. Oral tetracyclines, specifically doxycycline and minocycline, are mainstays of treatment for moderate-to-severe disease; however, they are associated with significant systemic side effects," writes Linda Stein Gold, M.D., director of dermatology clinical research, Henry Ford Health System, Detroit, and colleagues in the poster.

The researchers examined data from a pooled analysis of two identical phase 3, randomized, double-blind, vehicle-controlled studies that investigated efficacy, safety and tolerability of FMX103 1.5% topical minocycline foam in patients with papulopustular rosacea.2

The studies included a total of 1,521 patients (mean age: 50 years) who were randomized 2:1 to receive FMX103 1.5% or vehicle once daily for 12 weeks. Data showed that 341 (22.4%) patients reported treatment-emergent adverse events (TEAE). The most frequently reported TEAEs in the FMX103 1.5% vs vehicle groups, respectively, included viral upper respiratory tract infection (2.4% vs 2.3%), upper respiratory tract infection (1.9% vs 2.5%) and headache (1.4% vs 1.9%). The majority of the TEAEs reported by patients were mild in severity. No differences were observed between the treatment groups in the incidence of TEAEs. At week 12, the researchers found that all facial tolerability assessments had higher percentages of “none” compared to baseline and trended toward improving scores in the FMX103 1.5% treatment group.

For patients with moderate-to-severe papulopustular rosacea, FMX103 1.5% minocycline foam not only proves to be effective but a favorable safety profile could be maintained during the studies. As such, the novel foam application could represent a viable treatment alternative to current standard oral treatment regimens for patients with more advanced papulopustular rosacea disease.

Disclosures:
Dr. Stein Gold is an advisor and investigator for Foamix, Galderma, LEO Pharma, Novartis, and Valeant and is an investigator for Janssen, AbbVie, and Solgel.

References:

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Skin microbiome altered in some rosacea subtypes

ILYA PETROU, M.D. | Staff Correspondent

A n imbalance of the microbiome may play a role in the pathogenesis of some subtypes of rosacea, a recent study finds. While Cutibacterium appears to play a protective role in maintaining healthy skin, Staphylococcus and Streptococcus appear to be factors in disease pathogenesis, researchers write.

Yan Wu, M.D., professor of the department of dermatology, Peking University First Hospital, Peking, China, and fellow colleagues, presented a poster during the AAD VMX Virtual Meeting Experience 2020, June 12-14.

Their study aimed to characterize the different microorganisms found in the skin microbiome of rosacea patients compared to those of healthy controls in the hope of finding an association between the varying microorganism counts and the presentation of disease.

The composition of the skin's microbiome is understood to be crucial for homeostatic skin immune functions, and the current conventional wisdom for the development of rosacea is that the innate immune system cannot appropriately recognize the commensal organisms which live and breed naturally on the skin such as C. acnes, S. epidermidis, as well as Demodex folliculorum. The subsequent inflammatory response to these microorganisms by the innate immune system results in the typical spectrum of symptoms seen in rosacea patients.

In their case-control study, Dr. Wu and colleagues sought to characterize the skin bacterial and fungal microbiome in different subtypes of rosacea patients compared with those of healthy individuals. Of the 58 participants enrolled in the study, 21 patients had erythematotelangiectatic rosacea, 15 had papulopustular rosacea, and 22 participants were healthy subjects who served as the control. Researchers extracted DNA from skin samples collected from the cheeks of study participants, and the 16S rRNA V3/V4 genes and internal transcribed spacer one region were sequenced. There were no significant differences in age and gender among the three study cohorts.

Results showed that the alpha diversity index in the patients with papulopustular rosacea was elevated compared to that of healthy controls. In addition, the weighted Unifrac-principal coordinates analysis (Unifrac-PCoA) of bacterial microbiome revealed that the skin samples of erythematotelangiectatic and papulopustular rosacea patients tended to cluster but were separated from those of healthy controls.

“Our study revealed an alteration in the burden of certain pathogenic and protective bacteria in the facial skin microbiome of rosacea patients,” wrote Dr. Wu and colleagues, in the study poster.

Researchers found that rosacea is specifically associated with an alteration in the relative abundance of specific taxa. Results showed that at the phylum level, Actinobacteria and Firmicutes were the most abundant in the facial skin and compared to controls. Actinobacteria demonstrated an obvious decreasing trend in both erythematotelangiectatic and papulopustular rosacea patients. At the genera level, Cutibacterium was significantly decreased in rosacea patients compared to control subjects. Data also showed an increase in the abundance of Staphylococcus in those patients with papulopustular rosacea.

Disclosure: The authors report no relevant disclosures.

Reference:
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Pilot study examines facial microbiome diversity

ILYA PETROU, M.D. | Staff Correspondent

Patients with rosacea show a less diverse facial skin microbiome, according to study results presented in an e-poster during the AAD VMX Virtual Meeting Experience 2020, June 12-14.

Depending on the subtype, patients with rosacea can present with symptoms of flushing, redness, pimples, pustules, and dilated blood vessels typically located on the central face. Among factors associated with symptoms is a possible inflammatory reaction to the skin microbiome. Researchers highlighted some of these exacerbating factors and the importance of the microbiome in the treatment and management of rosacea patients.

“What we’ve learned over the last few years is that rosacea is so much more than just inflammation of the face, suggesting that there may be other types or more systemic inflammation,” says Justin W. Marson, M.D., department of medicine, University of California at Irvine, Orange, Calif., and head-author of the study. “Past studies have already associated the disease with inflammatory bowel disease, metabolic disorders, type 1 diabetes, dementia as well as mixed data on systemic cardiac events such as heart disease. There’s more than just inflammation in rosacea and what exactly drives that inflammation is becoming clearer.”

Dr. Marson and fellow colleagues recently conducted a study during the 2017 Twins Day Festival in which identical and fraternal twins with and without rosacea, who attended the 2017 Twins Day Festival, included history of disease, environmental factors and microbiome data.

“Data collected on identical and fraternal twins with and without rosacea who attended the 2017 Twins Day Festival, included history of disease, environmental factors and microbiome data.”

Results showed that individuals with rosacea are more likely to currently own pets, have a lower Fitzpatrick score, and consume more alcohol than their control counterparts. Researchers found that although individuals with rosacea demonstrated a decreased variation in facial cutaneous microbiome compared to control, there was no significant difference in bacterial load in the facial cutaneous microbiome or enteral microbiome between rosacea or their counterpart controls.

“What we’ve learned over the last few years is that rosacea is so much more than just inflammation of the face, suggesting that there may be other types or more systemic inflammation.”

Justin W. Marson, M.D.
University of California at Irvine, Orange, Calif.

“Beyond an elusive probiotic pill to attempt to restore balance, one of the best things rosacea patients can do is to practice good skin hygiene, regularly using sunscreen and moisturizer, and maintain a well-balanced diet. This way, patients could hopefully develop a healthy and even microbiome inside and outside of their body.”

Disclosure: Dr. Marson reports no relevant disclosures.

Reference:
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AV2001064
No increased cancer risk in children using topical tacrolimus

ILYA PETROU, M.D. | Staff Correspondent

Pediatric patients with atopic dermatitis (AD) do not have an increased risk of developing malignancies after receiving topical tacrolimus therapy, according to results from a recent study. These findings may lay to rest any concern that the popular topical calcineurin inhibitor may cause cancer, one expert says, potentially paving the way for a reversal of the associated U.S. Food and Drug Administration (FDA) black box warning.

The topical calcineurin inhibitors including pimecrolimus and tacrolimus have been long proven as effective at addressing the AD symptoms and have become essential therapeutic tools. In contrast to topical corticosteroids that can be used for acute flares, calcineurin inhibitors are often used as a long-term therapy. Because of the history of systemically administered tacrolimus for transplant patients and its association with malignancies, tacrolimus received a black box warning from the FDA due to its theoretical risk of increased malignancies, specifically lymphoma and nonmelanoma skin cancer.

“At the time the black box warning was put into effect almost 15 years ago, there was no clinical evidence to support the concern that topical tacrolimus use could lead to an increase in the incidence of cancer and studies had suggested that the drug largely remained in the skin. While we have never personally seen a malignancy develop in a patient prescribed topical tacrolimus, it is important to have long-term data in a large group of prospectively studied children,” says Amy S. Paller, M.D., chair of the department of dermatology and professor of pediatrics, Northwestern University School of Medicine, Chicago.

Dr. Paller and colleagues recently completed the APPLES study, “A Prospective Pediatric Longitudinal Evaluation to assess the long-term Safety of tacrolimus ointment for the treatment of atopic dermatitis”, which examined whether topical treatment with tacrolimus 0.03% or 0.1% ointment increases children’s long-term risk of malignancy under actual-use conditions.

The international study quantified incident malignancies including lymphoma and other cancers over a 10-year period in children with atopic dermatitis who used topical tacrolimus for six or more weeks. At baseline and annually thereafter, patients underwent a physical examination, including skin and lymph node evaluation. Atopic dermatitis severity was evaluated every other year. Standardized Incidence Ratios for cancer events were analyzed relative to sex- and age-adjusted control data from national cancer registries.

Of 8,071 patients who enrolled in the study, 7,954 eligible patients at 314 sites in nine countries were included in the analysis. In total, 2,125 (26%) patients could complete the study, including 1,176 who completed with 10 years of follow-up and 949 who were censored at study completion. Results showed that in over 44,629 person-years, only six confirmed incident cancers had occurred, none of which were lymphomas or nonmelanoma skin cancers.

“This evidence complements other evidence suggesting that there is no increased risk. While these results will likely make dermatologists and other practitioners even more comfortable with prescribing topical calcineurin inhibitors for their AD patients, I hope it will convince the FDA to reconsider the black box warning,” Dr. Paller says.

The black box warning has made it challenging for physicians to prescribe tacrolimus. The prescribing physician must always explain the black box warning to the patient, which is time-consuming and a difficult conversation, given that any risk of cancer for a child is frightening to parents. According to Dr. Paller, these results add an important set of 10-year data that dispute the theoretical risk of increased cancer incidence.

Disclosures:
Dr. Paller is an investigator for AbbVie, Amgen, Celgene, Eli Lilly, Galderma, Incyte, Loxo, Janssen, Novartis, Sanofi Regeneron, and is consultant with Amgen for AbbVie, Amgen, Asana, Celgene, Dermovant, Derma, Galderma, Eli Lilly, Forte, LEGO, Pramoreme, Merck, Novartis, PIazo, Regeneron, and Sanofi Genzyme.

Reference:
Challenges with treating eyelid eczema

LISETTE HILTON | Staff Correspondent

ike the name implies, eyelid eczema is fairly common among patients with eczema, or atopic dermatitis. But it also affects patients with no real history of skin problems and can impact quality of life significantly, according to Peter Lio, M.D., clinical assistant professor of dermatology and pediatrics at Northwestern University Feinberg School of Medicine and founding partner, Medical Dermatology Associates of Chicago.

“Doing our best to get to the root of it is important for safe and effective therapy, but is not always easy,” says Dr. Lio, a Scientific Advisory Committee member of the National Eczema Association.

He likens the eyelids to the “canary in the coal mine.” They’re delicate and can be affected with signs of inflammation and allergy when other areas may not, he says.

“For example, a relatively common cause of eyelid eczema is allergic contact dermatitis to a cosmetic or cleanser. In this case, one might expect the entire face — even the scalp when the culprit is a shampoo or conditioner to be involved. However, many times, it is largely limited to the eyelids. For our patients with atopic dermatitis, it is an even tougher mystery. We have to figure out if it is just another manifestation of their atopic dermatitis or if there is another issue that is complicating it.”

Dr. Lio says he has seen patients who have been to several different physicians, have applied steroids to the eyelid area for as long as months; yet, they haven’t been patch tested. That’s a big concern given that skin in the area is so delicate, he says.

“It’s a very sensitive area with some of the thinnest skin on the body, so we have to be extra-careful in the eyelid area. It is also very close to the eyes, so longer-term side effects such as cataracts and glaucoma are much more likely when treating in this area,” he says.

Detective work can take time. It can be tempting to just throw some steroids at it and hope for the best, he says. And steroids might do the trick with an acute irritant dermatitis, but in the setting of allergic contact dermatitis, underlying eczema or even less-common diagnoses such as connective tissue disease, steroids are not a long-term solution, he says. A careful examination, a good history and often patch tests to discover the root of the problem are required, according to Dr. Lio.

**BEST PRACTICES**

Dr. Lio says his general approach is to identify it as “eyelid dermatitis” and explain to patients the goal to determine if there is an underlying driver of the disease.

“I take a careful history, do a full exam to see if they have other suggestive lesions of eczema or contact dermatitis or connective tissue disease on the body and usually will explain patch testing. I then have a template for an ‘eyelid dermatitis plan’ that has a super gentle shampoo, conditioner, facial cleanser [and] moisturizer built in,” he says.

The aim of this plan is to remove common allergens, such as cocamidopropyl betaine and fragrance. He then often uses a mild topical steroid for a few days to cool things down, since mild steroids work quickly, reliably and usually don’t sting or burn.

Then, I will transition them to a non-steroidal topical such as tacrolimus, pimecrolimus or crisaborole,” he says. “For milder cases, this might be all they need. But usually I am going to have them schedule patch testing ASAP so that we can be sure there are no contactants playing a role. Even if negative, of course, there still may be allergens that we have not tested. But I explain we test for 80 of the more common ones and that helps us pick up a fair number without going overboard.”

**AVOID TREATING AROUND EYELIDS**

Prescribing potent corticosteroids or even milder corticosteroids over long periods is not safe for the eyelids, according to Dr. Lio. Dermatologists and other providers have to be extra careful treating patients around the eyes. Dr. Lio recommends against starting with non-steroidal topicals, as they seem much more likely to sting and burn. And, in his opinion, nonsteroidal topicals do not work as quickly or reliably in this context — especially for more severe disease.

Sometimes the very treatments used to control atopic dermatitis can cause eye issues. Researchers report of a case of an adult patient with severe atopic dermatitis who was prescribed dupilumab (Dupixent, Sanofi Genzyme and Regeneron) and developed blepharoconjunctivitis, published December 2019 in the *American Journal of Ophthalmology Case Reports.*

Eye problems can occur with dupilumab use, according to Dr. Lio. It has been a tremendous advance for many patients with moderate and severe disease, but it is not without adverse effects, either, he says.

“The eye issues seem to occur in around 10% of patients and include conjunctivitis, eye pruritus, blepharitis, keratitis and dry eye. In addition, there have been reports of head and neck dermatitis that has developed in patients on dupilumab,” he says. “These findings may or may not be related, but they represent a significant therapeutic challenge for those patients, and it can be refractory to treatments. Many people are working to better understand the etiopathogenesis of these and to find optimal treatments.”

There are many new topical and systemic medications in the pipeline that should greatly help patients with atopic dermatitis and more on the eyelids. Dr. Lio says that the investigational medications most likely to help eyelid issues will probably be topical drugs like topical Janus kinase (JAK) inhibitors, tapinarof and many others that could be approved within the next few years.

In the meantime, not treating, incorrectly treating or undertreating eyelid eczema or dermatitis can result in significant patient suffering, according to Dr. Lio.

“They rub their eyelids. They sometimes get infected. They can actually cause damage to their eyes with enough chronic rubbing. It’s pretty terrible!” he says. “And I have had patients who have been suffering for months and even years. Eczema is pretty crummy anywhere, but on the eyelids I’d argue it’s even worse.”

**Disclosure:**

Dr. Lio has served as an investigator, speaker and advisor for Regeneron and Genzyme and an advisor for AbbVie and AOBiome, an advisor and speaker for CosRx and Medline; was a speaker and investigator for Brolan; has served as an investigator for SanoGen; and an advisor and investigator for Allergan, AbbVie, Alcon, Allergan, Amgen, Dermot, Dermis, Johnson & Johnson, Kinerase, L'Oreal, Perrigo, LEO, Merck, Rhodia, Elastol, ImpDerm, Johnson & Johnson, Nihal, L'Oréal, Pfizer, Procter & Gamble, Pioneer, Perrigo, Genzyme, Pierre Fabre, Sanofi, Trevigen, TopMD, and an advisor to Altus Labs.

Dr. Lio has also served as an advisor to the American Academy of Dermatology; a member of the National Eczema Association’s Medical Advisory Board; an advisor to the American Veterinary Medical Association; a member of the Scientific Advisory Committee for the National Eczema Association; an advisor to the American Academy of Allergy, Asthma & Immunology; a member of the educational program committee for the American Academy of DERMatology; a member of the scientific committee for the American Academy of Dermatology; a member of the educational program committee for the American Academy of Ophthalmology; and a member of the education committee for the American Academy of Optometry.

**References:**

Quick Takes

Gusacitinib, an investigational oral janus kinase/spleen tyrosine kinase inhibitor, demonstrated statistical superiority compared with placebo for improving chronic hand eczema in a phase 2b study. The onset of benefit occurred quickly, and gusacitinib had a favorable safety profile.

Gusacitinib promising for chronic hand eczema

Mount Sinai, New York, is a leading expert on CHE. She notes that the inflammatory skin disorder has an estimated prevalence of up to 10% and ranks as the leading complaint among patients seen in dermatology practice. Importantly, there has been an unmet need for a good treatment to offer patients with moderate-to-severe disease.

“The pathogenesis of CHE is varied in terms of its immune pathways because the etiology of CHE is multifactorial. In some patients, CHE is associated with atopic dermatitis. In other individuals, CHE can be the result of an allergic or irritant contact dermatitis, and in these subgroups, CHE can persist even with avoidance of identified triggers,” she says.

“As a combined pan-JAK/SYK inhibitor, gusacitinib blocks the Th1, Th2, Th17, and Th22 pathways and modulates immunoreceptor signaling in innate immune system cells as well as in keratinocytes. Its ability to target such a broad range of cytokines and cells suggests it would have activity for treating CHE regardless of its underlying cause, and the topline efficacy results from the phase 2b trial are very encouraging. If they are confirmed with additional study, gusacitinib would be the first systemic medication able to provide significant benefit to the large and heterogenous population of patients who require systemic therapy to address their suffering from CHE.”

Sandeep Gupta, Ph.D., is founder, president, and chief executive officer of Asana Biosciences. He tells Dermatology Times that the protocol for a phase 3 study investigating gusacitinib for the treatment of moderate-to-severe CHE will be finalized after meeting with US and European regulatory agency authorities.

“We are excited by the results of this study and believe that gusacitinib will provide benefit to all CHE patients who currently don’t have good and safe treatment options for this often-debilitating disease,” he says.

STUDY DESIGN

The phase 2b trial investigating gusacitinib has a double-blind, dose-ranging design and total duration of 36 weeks. It randomized 97 patients 1:1:1 to treatment with gusacitinib 40 mg, gusacitinib 80 mg, or placebo once daily for 16 weeks. Beginning at week 16 and through week 32, patients originally assigned to placebo are switched to gusacitinib 80 mg while the patients in the gusacitinib groups continue with their same treatment. Patients are returning for a final visit at week 36, four weeks after stopping their assigned treatment.

The study enrolled adults with CHE that was refractory to high potency or ultra-high potency topical corticosteroids. The participants had a mean age of approximately 45 years, the majority were white (~84%), and the majority of patients in each treatment group were judged to have severe CHE (54% to 63%) as defined by a Physician Total Lesion Symptom Score (mTLSS) that investigated it as a treatment for atopic dermatitis and various types of cancer.

The onset of benefit with gusacitinib occurred quickly. Reductions in mTLSS and PGA scores that were clinically relevant and statistically significant were already achieved at the follow-up visit four weeks after treatment randomization.

The safety data showed that the most common treatment-emergent adverse events in the gusacitinib groups were upper respiratory tract infection, headache, nausea, and nasopharyngitis. There were no cases of pulmonary embolism, opportunistic infections, malignancies, major adverse cardiovascular events, or deaths.

Dr. Gutman-Yassky says, “The favorable safety demonstrated by gusacitinib so far in the phase 2b study of patients with CHE is consistent with data reported for it in previous clinical trials that investigated it as a treatment for atopic dermatitis and various types of cancer.”

Disclosure: Dr. Gutman-Yassky has scientific advisory board members for Asana.
Biologics enter post-PASI era

JOHN JESITUS | Staff Correspondent

With newer biologic drugs for psoriasis generally offering excellent and near-equivalent efficacy, an expert says, choosing the best drug for a particular patient requires considering additional factors.

“In the old days,” says George Han, M.D., Ph.D., “you could say ustekinumab (Stelara, Janssen) works better than etanercept (Enbrel, Amgen), and ixekizumab (Taltz, Lilly) works better than ustekinumab. There were bigger differences stratifying the medications, so you might make your choice based on efficacy as the main factor. But nowadays that isn’t so true anymore.” He is system medical director and chief of teledermatology for Mount Sinai Health System and assistant professor of dermatology at the Icahn School of Medicine at Mount Sinai.

With newer biologics consistently posting Psoriasis Area and Severity Index (PASI) improvements greater than 90% in pivotal trials, says Dr. Han, dermatologists need to consider additional factors such as speed of onset, durability, safety, patient comorbidities and dosing regimens.

Real-world comparative studies consistently show that ustekinumab response lasts longer than that of TNF inhibitors. Based partly on ustekinumab data, he adds, many dermatologists expect the interleukin (IL)-23 blockers guselkumab (Tremfya, Janssen), tildrakizumab (Ilumya, Sun Pharma) and risankizumab (Skyrizi, Abbvie) to perform well long-term, although these drugs do not yet have the long track record of ustekinumab.

“In the old days… there were bigger differences stratifying the medications, so you might make your choice based on efficacy as the main factor. But nowadays that isn’t so true anymore.”

George Han, M.D., Ph.D., Icahn School of Medicine, Mount Sinai, New York

In a comparison against ustekinumab and TNF inhibitors published in the February 2018 British Journal of Dermatology, secukinumab (Cosentyx, Novartis) fared worst.

“It is important to note, however, that this is just one study cohort, and many factors impact real-world efficacy and durability of biologics,” Dr. Han adds.

Regarding long-term safety, says Dr. Han, TNF inhibitors are generally believed to be more immunosuppressive than newer medications.

“That’s especially relevant right now as everybody’s thinking about infectious risk,” he says. “Ustekinumab, IL-17 inhibitors and IL-23 inhibitors all look better than the TNF alpha inhibitors from a safety standpoint.”

It is well-known that IL-17 inhibition can worsen inflammatory bowel disease (IBD). “It seems to be primarily IL-17A that drives the negative effects. Inhibiting IL-17A seems to knock out this regulatory function of IL-17 in the gut, which may worsen IBD,” he says.

With newer medications, though, even more nuanced differences between the same drug class could be teased out, says Dr. Han. A mouse study published in the June 2018 Nature Immunology showed that ustekinumab response lasts longer than IL-17F could help IBD.

“Consistently, blocking IL-17A in this animal model worsened IBD, while blocking IL-17F ameliorated it. Furthermore, when researchers blocked both IL-17A and F, it was helpful — it seemed that the function of IL-17F predominates over IL-17A,” Dr. Han says. “This is particularly relevant because a new dual inhibitor of IL-17A and F is coming to the market soon.”

Similarly, he says, blocking IL-23 is likely to help IBD as early phase trials of IL-23 inhibitors have shown promise.

Brodalumab (Silq, Ortho Dermatologics) and ixekizumab provide the quickest response — PASI 50 in under two weeks. For patients with psoriatic arthritis (PsA), most dermatologists choose TNF inhibitors or IL-17 inhibitors. Guselkumab phase 3 data — the first released for an IL-23 inhibitor — are also fairly impressive in this regard, adds Dr. Han, who expects this drug to earn PsA approval soon.

Disclosure:

Dr. Han has received research funds (grants paid to Mount Sinai) from and/or been a consultant for AbbVie, Amgen, Boehringer Ingelheim, Bond LifeScience, Bristol-Myers Squibb, Celgene, Eli Lilly, Novartis, Janssen, Eli Lilly Pharma, MC2, OrthoDerma- tologics, PellePharm, Pfizer, Regeneron, Sanofi Genzyme, SUN Pharmaceuticals and UCB.

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Ozenoxacin cream 1% in clinical practice

By Lawrence A. Schachner, MD; Adelaide A Hebert, MD; Pearl Kwong, MD

Antimicrobial resistance in skin and soft tissue infections

Dermatological conditions often treated by dermatologists include skin and soft tissue infections (SSTIs), such as atopic dermatitis, impetigo and angular cheilitis. Strategies for preventing, managing and treating SSTIs typically include the prescription of antibiotics. An analysis of pharmaceutical sales data has indicated that global antibiotic consumption has risen nearly 40% since 2000.1 Associated with the increase in prescription use, rates of antimicrobial resistance (AMR) are also on the rise, worldwide.2 Despite antibiotic stewardship and infection prevention and control, AMR is associated with a large clinical and public burden. By the year 2050, it is estimated that ~10 million people per annum will die due to AMR-related causes, globally.2, 3 Moreover, this continued rise will cost over 100 trillion United States (U.S.) Dollars.4Given the increasing rates of AMR to commonly prescribed antibiotics for SSTIs (e.g. mupirocin, fusidic acid), there is a need for new therapies.4

SSTIs caused by Staphylococcus aureus and Streptococcus pyogenes

Impetigo is a highly contagious bacterial skin infection characterised by eroding, erythematous pustules that eventually develop a brownish-yellow crust.5 Over three million people in the U.S., are affected by impetigo, each year.6 The main causative pathogens of impetigo are S. aureus and/or Streptococcus pyogenes, although S. aureus alone is observed in most cases. S. aureus and/or Streptococcus pyogenes, although S. aureus alone is observed in most cases.6

Atopic dermatitis is a common inflammatory skin disorder that affects up to 20% of the world population.7 While its pathogenesis remains largely unclear, genetic predisposition and environmental factors influence its eventual development.8 Atopic dermatitis is characterized by itchy, recurrent eczematous lesions. Skin colonization by Staphylococcus aureus correlates with increased severity of the condition and a worsened prognosis.9

Angular Cheilitis presents with erythematous, nonvesicular lesions that radiate from the angle(s) of the mouth. This condition can be accompanied with or without fissure formation. A microbial study found that S. aureus and Streptococci were present in 75.5% and 13.5% of cases, respectively.10

For the above SSTIs, clinical practice guidelines recommend the use of topical antibacterial agents for localized infections; whereas systemic antibiotics should be used for treatment of numerous or extensive lesions, or those not responding to topical therapy.11

Ozenoxacin 1% Topical Cream

Ozenoxacin [(OZN; Ferrer International S.A.; Biofrontera Inc., (United States)] 1% topical cream is the first non-fluorinated quinolone indicated for the topical treatment of impetigo due to S. aureus and S. pyogenes. OZN is indicated for use in adult and pediatric patients two-months of age and older.12 OZN has been shown to display strong bactericidal activity against Gram-positive pathogens associated with SSTIs and is less prone to resistance than the commonly prescribed mupirocin and fusidic acid.13-17 While indicated for impetigo, the low dosing frequency of OZN and its five-day treatment regimen is expected to offer significant benefits for other SSTIs. This case series examines OZN use in clinical practice, for the treatment of various SSTIs.

Case 1

A three-year old female presented with atopic dermatitis with secondary impetiginization and early furunculosis. She was prescribed cephalexin and OZN for five days, but did not take the cephalexin. At the five-day follow-up, the infection was largely gone. Results of the five-day regimen are depicted in Figure 1.

Figure 1. The patient presented with secondary impetigo and early furunculosis on the lower abdomen (top). She was prescribed a twice-daily, five-day regimen of Ozenoxacin 1% topical cream; which cleared her skin (bottom).

Case 2

A five-year old female presented with a one-week history of a facial lesion on her left jawline and a new onset lesion on her left upper-medial cheek. At baseline, the infection was causing an impact on the child’s daily life. Her mother was using Band-Aids to cover the lesions and she was refused access to daycare. She was currently taking mupirocin and not responding. Her dermatologist then prescribed OZN. Results of the five-day regimen are depicted in Figure 2.

Figure 2. The patient presented with a facial lesion on her left jawline and a new onset lesion on her left upper-medial cheek (left). She was prescribed a twice-daily, five-day regimen of Ozenoxacin 1% topical cream; which subsided the infection (right).
CASE 3
A twelve-year old male patient presented with atopic dermatitis on the hands and knees. The condition had been present since early childhood and he had previously been treated with topical steroids, emollients and an antihistamine to aid with pruritus. OZN was prescribed because the dermatologist felt colonization was driving the flare-ups and preventing the control of atopic dermatitis. Improvement was observed after five days of use of OZN. At baseline, the infection was causing an impact on the child’s daily life. The patient did not want to attend school or social activities due to concerns of social stigma. Results of the five-day regimen are depicted in Figure 3.

FIGURE 3. The patient presented at the clinic with atopic dermatitis on the knees (left). He was prescribed a twice-daily, five-day regimen of Ozenoxacin 1% topical cream (right), which resulted in clearing the infection.

CASE 4
A five-year old female patient presented with angular cheilitis in the right labial commissure. Previous treatment included chap stick, taken as needed. OZN was chosen as a treatment strategy as the child’s parents preferred a topical treatment over an oral therapy. Results of the five-day regimen are depicted in Figure 4.

FIGURE 4. The patient presented with angular cheilitis in the right labial commissure (left). She was prescribed a twice-daily, five-day regimen of Ozenoxacin 1% topical cream; which resulted in clearing her skin completely (right).

CONCLUSIONS
The selection of suitable candidates for OZN includes an age minimum of two months; bullous or non-bullous impetigo due to S. aureus or S. pyogenes, including Methicillin-resistant S. aureus; other localized SSTIs characterized by S. aureus or S. pyogenes; and a preference for a topical therapy. OZN is not recommended for systemic infections.

AUTHORS

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Dr. Adelaide Hebert has been the Chief of Pediatric Dermatology at McGovern School of Medicine and Children’s Memorial Hermann Hospital for the past 30 years. Dr. Hebert has specialty clinics in Pediatric Dermatology, Hyperhidrosis, and Vascular Anomalies. She is a past President of the Society for Pediatric Dermatology.

Dr. Pearl Kwong is a pediatric dermatologist. She works in Jacksonville, Florida and specializes in Pediatric Dermatology and Dermatology. Dr. Kwong is affiliated with Wolfson Childrens Hospital.

REFERENCES:
Oraleprenilast effective for scalp psoriasis

LISETTE HILTON | Staff Correspondent

Oraleprenilast (Otezla, Amgen) rapidly and significantly improved disease severity, itch and quality of life compared with placebo in patients with moderate-to-severe scalp psoriasis, according to an article in press in the *Journal of the American Academy of Dermatology.*

Eight in 10 psoriasis patients have scalp involvement, making the scalp the most commonly affected area in psoriasis. People who have scalp psoriasis often suffer significantly when it comes to their mental health, quality of life and social functioning. Despite the condition’s impact, patient adherence to first-line topical therapies tends to be low.

“There is a need for effective, well-tolerated systemic therapies for patients with moderate to severe scalp psoriasis or patients whose scalp psoriasis is inadequately controlled with topical therapies,” the authors write.

In this phase 3b, double-blind, placebo-controlled study, researchers randomized 201 patients with moderate-to-severe scalp psoriasis to receive 30 mg twice daily of apremilast, a phosphodiesterase 4 inhibitor, or placebo for 16 weeks. The patients at 41 sites in the United States and Canada were 18 years and older, had Scalp Physician Global Assessment scores of three or more, 20% or more of scalp surface area involvement and had not tolerated or had inadequate response to one or more topical therapies for scalp plaque psoriasis.

They found that 43.3% of patients taking apremilast achieved the primary endpoint of clear or almost clear with a two or greater point reduction on the Scalp Physician Global Assessment. That was compared to 13.7% in the placebo group.

More than 45% of patients in the apremilast arm achieved a four-point or greater improvement according to the Whole Body Itch Numeric Rating Scale, compared to 22.5% of placebo. And 47.1% in the apremilast group achieved a four-point or greater improvement according to the Scalp Itch Numeric Rating Scale, versus 21.1% in the placebo group.

Patients taking apremilast also had a significantly greater average improvement in the Dermatology Life Quality Index than those in the placebo arm.

More than 30% of patients on apremilast had diarrhea. Other common adverse events in the apremilast group were nausea, headache and vomiting.

This is the first prospective, randomized, placebo-controlled phase 3 study looking at apremilast for treatment for moderate-to-severe scalp psoriasis, the authors note.

“Scalp psoriasis can be a very distressing manifestation of psoriasis, as it is in a highly visible location and often causes intense pruritus,” they write. “The clinically meaningful improvements in Scalp and Whole Body Itch [Numeric Rating Scale] are supported by the significantly greater improvements in quality of life among patients treated with apremilast versus placebo.”

Psoriasis location is one of many factors that providers must consider when prescribing treatment. Results from this study might not be generalizable to patients with other psoriasis forms, according to the paper.

As the analysis did not provide long-term efficacy data and the study did not compare apremilast to other potential treatments for scalp psoriasis, the authors note these as limitations.

Disclosure:
Celgene Corporation, which sold Otezla to Amgen in 2019, funded the study and the authors received additional support from a company sponsored by the Celgene Corporation. The authors of the study have ties to Celgene and other corporations, including as researchers, consultants and advisory board members.

Reference:
This September 12,
Make it an American Dermoscopy Saturday.
From the comfort of your home.

Questions? nicole@nmgmeetings.com
IxEKIZUMAB PROVIDES RELIEF FOR GENITAL PSORIASIS

LISSETTE HILTON | Staff Correspondent

Treatment with ixekizumab (Taltz, Eli Lilly and Company) resulted in quick and lasting relief of genital psoriatic lesions and symptoms. A post-hoc subgroup analysis of the IXORA-Q study examined clinical response to ixekizumab vs placebo. Data offer evidence of the profound impact genital psoriasis, which may increase awareness and rates of diagnosis, monitoring and treatment for this disease.

They found surface disruption signs in genital psoriasis are common. Fifty-seven of the 149 patients, or 38%, presented at baseline with genital erosions, fissures and/or ulcers. Most of those patients had genital fissures, followed by erosions and ulcers.

Secondary lesional changes were associated with significantly higher scores for disease severity and pain but not for sexual health. In the ixekizumab treatment group, 62% of patients had complete resolution of erosions, fissures and/or ulcers in the first week, compared to 25% of the placebo group. Eighty-three percent of patients treated with ixekizumab had complete resolution of the signs at week 12, compared to 21% of patients treated with placebo.

Patients in the ixekizumab group reported significant improvements in pain, itch, disease severity and sexual health compared to those in the placebo group. That was whether or not they had secondary lesional signs at baseline.

“According to our data, signs of surface disruption have a greater impact on patient-reported measures in patients with limited [body surface area] involvement (<10%), highlighting the importance of assessing disease severity and treatment outcomes from both physician and patient perspectives,” the authors write.

Researchers have found that up to 63% of patients with plaque psoriasis have genital involvement at some point. And the signs of genital psoriasis are often painful and pruritic. Genital psoriasis can impact patients’ sexual health and quality of life. Yet, proven treatments for genital psoriasis are limited.

Genital psoriasis often is under-reported, under-diagnosed and under-treated, according to the authors.

Ixekizumab is approved by the U.S. Food and Drug Administration for the treatment of plaque psoriasis. Systemic therapies are recommended when other treatment options fail for genital psoriasis, according to the paper.

While this analysis is limited by its duration and small number of patients, the authors wrote the data offers evidence of genital psoriasis’s profound impact on patients and may increase awareness and rates of diagnosis, monitoring and treatment for this disease.

Disclosure: Eli Lilly and Company funded the study. The authors include consultants, investigators, employees and shareholders of Eli Lilly.

Reference:

“According to our data, signs of surface disruption have a greater impact on patient-reported measures in patients with limited [body surface area] involvement (<10%), highlighting the importance of assessing disease severity and treatment outcomes from both physician and patient perspectives.”

Joseph Merola, M.D., Brigham and Women’s Hospital, Harvard Medical School, Boston, and colleagues
Gene expression profiling has the potential to improve melanoma prognostication, says an expert, but shortcomings remain.

GEP tests specifically look at messenger RNA (mRNA) levels expressed in tumors, an indicator of which target genes are “on,” says Elizabeth Berry, M.D. She serves as an assistant professor and director of the Multidisciplinary Pigmented Lesion Clinic in the Oregon Health & Science University Department of Dermatology, Portland.

“The thought is that gene expression profiling tests might be able to tell which patients will develop metastases in the future,” Dr. Berry says. Conversely, a portion of patients with thick melanomas never develop any further disease. GEP could provide an additional level of testing to identify such patients, she says, and to help determine which patients may benefit from adjuvant therapy or increased surveillance.

In dermatology, says Dr. Berry, the key question with thin melanomas is determining which patients would benefit from sentinel lymph node (SLN) biopsy and which could avoid this procedure.

“Each specialty has its own set of questions,” she says. However, she adds, GEP test developers are trying to address all these questions simultaneously.

Leading melanoma GEPs include DecisionDx-Melanoma, also called the 31-GEP (Castle Biosciences), the eight-GEP (MelaGenix) and the clinical-pathologic (CP)-GEP (SkylineDx and Mayo Clinic). All three tests very have promising early data, says Dr. Berry.

“But we need to proceed with caution,” she says. “We need to look carefully at the data to find where they fit best so that we are not hurting people in the process of trying to propel the field forward.”

Shortcomings that presently affect GEP tests to one extent or another include small sample sizes (often lacking power calculations), study populations that do not represent real-world stage distributions, follow-up times insufficient to track delayed metastases and inconsistent use of multivariate models that make between-study comparisons impossible.

“The most frustrating part is the inability to look under the hood. When you’re looking at the statistical analysis, are they using a dichotomous or continuous variable? And it’s hard to tell in some of the tests what cut-offs they are using for significance in GEP levels. That lack of transparency makes the data difficult to interpret,” she says.

Warts notwithstanding, says Dr. Berry, the GEP platforms coming to market should not be discounted.

“As clinicians, we have a duty to ensure promising technology with the potential to benefit our patients is implemented both rapidly and safely,” she says. “This may include tolerating some uncertainties while we find the best uses for the tests. The ordering provider needs to be well-versed in these uncertainties and limitations to best counsel his or her patients.”

Next steps, she says, should include larger validation studies of the type that have happened in GEP tests for breast cancer.

Disclosure: Dr. Berry reports no relevant financial interests.

Reference:
Nanotechnology may advance skin cancer Tx

ILYA PETROU, M.D. | Staff Correspondent

Novel and emerging nanotechnology approaches used in the treatment of skin cancer are generating interest as they enable the efficient delivery of drugs and other bioactive molecules to target tissues with low toxic effects. A recent study examined current investigations of nanoparticles and nanosystems and highlighted the therapeutic benefit and potentially larger role in the treatment of skin cancer.

Depending on disease stage, melanoma and nonmelanoma skin cancers can be treated in a variety of ways. However, the limitations of some treatment modalities have led research to explore new delivery systems and approaches to help improve clinical outcomes.

“The molecular mechanisms of melanoma have not been entirely elucidated; therefore, treating the disease is difficult. To overcome this challenge, innovative therapies are required that are mainly based on delivery systems using nanotechnology,” writes Livia Neves Borgheti-Caradoso, Ph.D., School of Pharmaceutical Sciences of Ribeirao Preto, University of Sao Paolo, Ribeirao Preto, San Paolo, Brazil, and fellow colleagues, in a study published in Advanced Drug Delivery Reviews.

One of the many recent advancements in the treatment of cancer has been nanotechnology and the nanosystems that they employ. Nanoparticles efficiently deliver therapeutic agents to the tumor site which can include chemotherapeutics, immune and vaccine molecules, and nucleic acids.

“Nanosystems can be developed to overcome biological barriers and to target drug delivery to the tumor sites, thus enabling the use of lower doses, increasing treatment efficacy and decreasing the number and/or the severity of the side effects,” the study authors write.

Most nanotechnology approaches and systems are still in the research and development phase; however, some have reached the clinical stage and are currently available on the market. There are no commercially available nanosystems to date for bioactive molecule topical delivery for skin cancer, the study authors write that some nanoparticle applications and products are being evaluated in clinical trials for advanced solid tumors as well as nonmelanoma skin cancers. The latter is a dose-rising study currently underway evaluating a topical nanoparticle paclitaxel ointment for safety, tolerability, and the preliminary efficacy of three concentrations (0.15%, 1.0%, and 2.0%) of the nanoparticle for the treatment of cutaneous metastases from nonmelanoma skin cancer.

Nanoparticles are currently being investigated to enhance the drug delivery of different agents in skin cancer therapies such as chemotherapy, immunotherapy including the PD-1 inhibitors, as well as therapeutic vaccines, with the hope of promoting more robust antitumor effects and improved clinical outcomes.

In cancer immunotherapy, nanoparticles can be directed to different cells and tissues related to the immune response including antigen presenting cells, lymphocytes and lymphoid tissues, thereby overcoming the limitations of direct cancer cell targeting. According to the study authors, one important advantage of using nanoparticles for antigen delivery is their capability to carry several adjuvants or neoantigens, which is ideal for treating different cancers.

When used in combination with physical techniques, nanocarriers could also help enhance topical and transdermal drug delivery in the treatment of melanoma and nonmelanoma skin cancers. Physical enhancement methods used include laser irradiation (i.e., phototherapy, thermotherapy, and acoustic therapy), iontophoresis, ultrasound, and microneedling systems.

A promising alternative for overcoming multi-drug resistance, the authors explained that nanotechnology can also help the clinician provide treatment in a specific and orderly fashion, with smaller doses of therapeutic agents and fewer
ICI therapy advances treatment for MCCs

ILYA PETROU, M.D. | Staff Correspondent

Merkel cell carcinoma (MCC) is a cutaneous neuroendocrine tumor with a high rate of metastasis and few effective therapeutic options. Continued research has led to the development and recent approval of novel immune checkpoint inhibitors for advanced MCC, such as pembrolizumab (Keytruda, Merck) and avelumab (Bavencio, EMD Serono and Pfizer), which have changed the way clinicians approach management of advanced MCC patients.

Patients with localized MCC have typically been treated with surgery followed by radiation therapy; though, chemotherapy largely remained the best alternative for patients with advanced MCC. Responses to chemotherapy were mostly short-lived however, begging the need for more effective treatment options.

“When traditional chemotherapy is used to treat advanced MCC, it can result in a good response rate in the short term, but patients will usually relapse relatively quickly. The checkpoint inhibitors are a definite game changer in the treatment of advanced MCC,” says Desiree Ratner, M.D., clinical professor, Ronald O. Perelman Department of Dermatology, NYU Skin and Cancer Clinic, New York, who spoke at the ODAC Dermatology, Aesthetic and Surgical Conference in Orlando.

Avelumab is a human monoclonal antibody that targets the protein programmed death ligand PD-L1 and therefore inhibits binding to its receptor PD-1. Formation of a PD-1/PD-L-1 complex is blocked, resulting in the activation of T-cell mediated immune responses against tumor cells.

In the study that led to approval by the U.S. Food and Drug Administration (FDA), Dr. Ratner says, over half of patients responded well to the drug.

“Advanced MCC patients who have already been previously treated with chemotherapy or other systemic treatments but did not respond can particularly benefit from this novel therapy, with about a third of previously treated metastatic MCC patients still alive at three years after treatment with avelumab,” Dr. Ratner says. “Immune checkpoint inhibitors like avelumab offer patients with advanced MCC a more effective treatment alternative than any other systemic agent previously available.”

The treatment for MCC has been evolving due to the high aggressiveness and metastatic rate of the tumor. According to Dr. Ratner, even patients with localized solitary lesions tend to have sentinel lymph node biopsy (SLNB) followed by adjunctive radiation, not only underscoring the aggressivity of the tumor but the need to meet it head-on with effective therapies. Fortunately, the checkpoint inhibitors appear to meet this challenge and are largely viewed as the new standard of care for patients with advanced MCC.

Although immune response modulating therapy can be associated with negative impacts on a patient’s thyroid and adrenal function as well as other types of immune responses unrelated to the tumor, Dr. Ratner says that the overall benefit for patients is nevertheless likely higher with the medication. Clinicians should look at the risk/benefit ratio of each case individually and have a candid discussion with the patient about potential therapeutic options.

“Avelumab is a welcome tool in our armamentarium for advanced MCC. In my opinion, the drug that has really changed the prognosis and quality of life for a considerable number of those unfortunate patients with advanced MCC,” Dr. Ratner says.

Disclosure: Dr. Ratner reports no relevant disclosures.

References:

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toxic effects.

“The use of nanocarriers enables the effective, targeted delivery of several therapeutic agents made from combinations of molecules aimed at acting synergistically and effectively against cancer types that are resistant and no longer responsive to conventional therapies,” the authors write.

Nanoparticles also used together with high-cost therapies including immunotherapies and gene therapies enable a more efficient administration of treatment, which can result in a more cost-effective approach and improved clinical outcomes.

“The versatility of these nanocarriers grows exponentially because although their use adds to the cost of therapy, it comes with innumerable benefits, which in terms of cost-effectiveness, are worth conceding, as these benefits lead to greater prospects for diagnosis and treatments, in addition to allowing the use of theranostics in cancer patients,” the study authors say.

Disclosures: The authors report no relevant disclosures.
Patients should continue to be counseled to use SPF 15 or higher broad-spectrum sunscreens along with other sun-protective measures because these interventions have known benefit for preventing skin cancer and protecting the skin from sunburn and other ultraviolet light-induced damage.”

David G. Strauss, M.D., Ph.D., U.S. Food and Drug Administration, Silver Spring, Md.

Safety of sunscreen active ingredients examined

and effective (GRASE). The MUsT design captures ingredient absorption into the blood under the condition of maximal recommended use per the product’s labeling, explains Dr. Strauss, director, Division of Applied Regulatory Science, US FDA, Silver Spring, Md.

The results from the initial MUsT showed that all of the sunscreen ingredients tested were absorbed systemically and detectable in plasma for at least three days after the last of 16 applications (four times a day for four days).

Results of a follow-up study involving four sunscreen products containing avobenzone, oxybenzone, octocrylene, homosalate, octisalate, and octinoxate showed those sunscreen ingredients were present at appreciable concentrations in plasma of blood samples collected after a single application and under maximal-use conditions.

In both studies, the plasma concentrations of the sunscreen ingredients exceeded the level set in the FDA’s proposed rule that would potentially waive additional safety studies.

Addressing the clinical relevance of the information, Dr. Strauss says that the fact that the sunscreen active ingredients were detectable in the blood should not be interpreted to mean that the FDA considers the ingredients unsafe. Nor does the fact that the agency is seeking more information through further safety testing indicate that the FDA believes sunscreen ingredients are unsafe, he adds.

“The study findings pointed to a need for further testing to determine the safety of the ingredients for repeated use over a lifetime,” Dr. Strauss explains.

In the meantime, patients should continue to be counseled to use SPF 15 or higher broad-spectrum sunscreens along with other sun-protective measures because these interventions have known benefit for preventing skin cancer and protecting the skin from sunburn and other ultraviolet light-induced damage.”

Quick Takes

Studies investigating the systemic absorption of sunscreen active ingredients were conducted in accordance with a recommendation in an FDA-proposed rule on OTC sunscreen products.

The ingredients tested were detectable in appreciable concentrations in plasma after products were applied just once and under maximal-use conditions.

The results indicate a need for further safety testing but should not be interpreted as unsafe, and patients should continue to use sunscreen.

CONTEXT FOR CONDUCTING THE STUDIES

In light of safety concerns that had emerged pertaining to certain sunscreen active ingredients and the lack of nonclinical safety assessment data for many of those ingredients, the FDA described in the proposed rule specific safety data that would be needed to determine whether an active ingredient is GRASE for use in sunscreens. Because MUsTs had not been performed previously for sunscreens, the FDA undertook two trials to demonstrate the feasibility of these studies and collect preliminary data that covered multiple formulations with seven different sunscreen active ingredients, Dr. Strauss explains.

He notes that the call for further testing to determine the safety of the sunscreen active ingredients for repeated use over a lifetime is part of the standard premarket safety evaluation of most chronically administered drugs that have appreciable systemic absorption.

“The data on absorption are then considered with other data from non-clinical toxicology studies and other clinical testing to inform an overall benefit-risk evaluation,” Dr. Strauss says.

As noted in the proposed rule, the FDA identified 12 sunscreen active ingredients that lack sufficient data to support a positive GRASE determination—cinoxate, dioxybenzone, ensulizole, homosalate, meradimate, octinoxate, octisalate, octocrylene, padimate O, sulisobenzone, oxybenzone, and avobenzone. The FDA determined that additional data on the safety of zinc oxide and titanium dioxide were not needed.

As another update, Dr. Strauss notes that the Coronavirus Aid, Relief, and Economic Security Act that was enacted on March 27, 2020, introduced reformed procedures for establishing requirements for OTC monograph drugs, including sunscreens.

“However, the act did not change the applicable standards for determining safety and effectiveness,” he says.

Further discussion of the FDA-proposed rule, the findings and relevance of the agency’s sunscreen absorption studies, and patient counseling considerations can be found in a recently published commentary on the American Society of Clinical Oncology’s Policy Statement on Skin Cancer Prevention written by Dr. Strauss and his colleague Theresa M. Michele, M.D., director of the Office of Nonprescription Drugs at the FDA. *

References

Survey examines the role of context and its influence on UV exposure behaviors.

Findings suggest that beliefs about sunscreen safety, sun exposure health benefits, and regional weather play a role in college students' protective behaviors.

The findings support the need to educate patients who are concerned about the potential harms of chemical ingredients in sunscreens about the many alternative options for UV protection.

Survey findings inform messaging on UV exposure

sity, which is located in western Oregon, where the weather is predominately cloudy. Of 1,406 students who were contacted, 335 (23.8%) met the eligibility criteria and completed the 125-item survey.

The survey included the 11-item Health Beliefs About UV (HBAU) scale, which measures beliefs about sunscreen toxicity and UV in cloudy climates that encourage UV exposure and discourage protection. In addition, it collected data on sociodemographic characteristics, indoor and outdoor tanning frequency, use of sunscreen and other UV protection behaviors, and perceptions of physical appearance.

Statistical modeling that adjusted for a number of covariates, including self-reported untanned skin color, sun sensitivity, and perceptions of skin cancer susceptibility and severity, found a positive association between beliefs about sunscreen toxicity and reduced sunscreen use. Outdoor tanning frequency was predicted by beliefs that tanning had benefits related to mood and vitamin D production, and indoor tanning frequency correlated with beliefs that tanning through the winter could mitigate negative seasonal effects.

Julian tells Dermatology Times, “The HBAU scale used in our study has not yet been clinically validated, but the factors on the scale may merit consideration in the conversations clinicians have with patients, especially with individuals who have recently relocated from a different climate.”

She continues, “Based on findings, we suggest clinicians be prepared to discuss vitamin D, mood and sunscreen safety as potential determinants of patients’ UV exposure behaviors and take into account perceptions of the regional climate.”

SAMPLE CHARACTERISTICS, BELIEFS AND BEHAVIORS

A majority of the 335 students included in the study had very fair or fair skin (59%). Almost three-fourths had never used indoor tanning, however, only approximately one-fourth had done any outdoor tanning in the previous 12 months. Two-thirds of the participants indicated that they used sunscreen only “sometimes” or less often, and the use of an umbrella or a wide-brimmed hat for UV protection was infrequent.

Results from the HBAU portion of the survey showed that, overall, the majority of students were not very concerned about toxicity and harms from sunscreen ingredients. However, common beliefs were that tanning is a more natural source of vitamin D than taking a supplement and that weather has negative effects, in general, on mood and on vitamin D production.

Julian says, “As most dermatologists are aware, the American Academy of Dermatology as well as the U.S. Food and Drug Administration maintain that sunscreens are safe and that individuals should continue to use sunscreen while further research is being conducted focusing on the toxicologic profile of sunscreen ingredients.”

She adds, “A particularly striking and troubling finding of our study was that while concern about sunscreen safety was associated with reduced sunscreen use, there was not a corresponding increase in other sun protection behaviors.”

The findings support the need to educate patients who are concerned about the potential harms of chemical ingredients in sunscreens about the many alternative options for UV protection.

“Patients should be counseled about the option of choosing a mineral sunscreen, rescheduling outdoor activities to times of day with low UV levels, wearing protective clothing and wide-brimmed hats, and seeking shade when outdoors. Because none of these behaviors is optimal for all contexts, patients should be told that combining UV protective behaviors is key to effective sun safety,” Julian says.

GATHERING MORE EVIDENCE

The researchers note that their study has limitations, including its relatively small sample size, the magnitude of its nonresponse rate, and its cross-sectional nature. Based on these issues, future studies are warranted that should include larger and more diverse samples to validate the findings, Julian says.

“In addition,” she says, “future research should further examine how the role of beliefs about vitamin D deficiency, seasonal mood, and the safety of sunscreen differs by indoor versus outdoor UV exposure and identify what types of messages are effective at countering beliefs that increase risky UV behaviors including indoor/outdoor tanning and the disuse of sunscreen.”

Reference:

Based on findings, we suggest clinicians be prepared to discuss vitamin D, mood, and sunscreen safety as potential determinants of patients’ UV exposure behaviors and take into account perceptions of the regional climate.”

Anne K. Julian, Ph.D., M.A., National Cancer Institute, Rockville, Md.
Consumers can get virtually all of today’s hottest skin, hair and nail nutrients without buying special supplements, says an expert.

Unlike multivitamins designed for overall health, says Zoe Diana Draelos, M.D., supplements marketed for the skin, hair and nails usually include costly specialized vitamins. She is president of Dermatology Consulting Services, PLLC.

“The question I wanted to answer is, do you need a special supplement? What’s unique about skin, hair and nail vitamins?”

Every skin, hair or nail supplement she has examined contained Vitamins A, B (various forms), C, D and E, all of which can be found in multivitamins.

**Vitamin A** is important for vision. We know there are retinoid receptors in the skin that are necessary for skin health,” she says.

**Folic acid (vitamin B9)** helps prevent cardiac disease and supports reproduction of DNA, RNA and red blood cells and is therefore associated with skin, hair and nail health, says Dr. Draelos. Biotin (B7) deficiency causes poor nail and hair growth, she adds, but biotin supplementation is not useful for hair and nail growth in healthy people.

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**Quick TAKES**

- Supplements marketed for the skin, hair and nails usually include costly specialized vitamins.

- Every skin, hair or nail supplement contains various forms of Vitamins A, B, C, D and E, all of which also can be found in multivitamins.

- Instead of specialized supplements, dietary supplements can be found in certain foods.

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**Proprietary supplements largely unnecessary**

**JOHN JESITUS | Staff Correspondent**

Consumers can get virtually all of today’s hottest skin, hair and nail nutrients without buying special supplements, says an expert.

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Every skin, hair or nail supplement she has examined contained Vitamins A, B (various forms), C, D and E, all of which can be found in multivitamins as well.

**SKIN-FRIENDLY VITAMINS, MINERALS**

“Vitamin A is important for vision. We know there are retinoid receptors in the skin that are necessary for skin health,” she says.

Folic acid (vitamin B9) helps prevent cardiac disease and supports reproduction of DNA, RNA and red blood cells and is therefore associated with skin, hair and nail health, says Dr. Draelos. Biotin (B7) deficiency causes poor nail and hair growth, she adds, but biotin supplementation is not useful for hair and nail growth in healthy people.
The nutrition you need can be obtained very easily with a multivitamin or, probably better, through adjusting your diet to include more fruits and vegetables.\footnote{Zoe Diana Draelos, M.D., president of Dermatology Consulting Services, PLLC., High Point, N.C.}

Vitamin C is necessary for producing collagen, boosting immunity and fighting free radicals. Vitamin D is actually a sex hormone. “Deficiencies are quite common,” she says.

But typical multivitamins do not contain enough vitamin D because the actual needs of mature men and women are much higher than the current recommended daily allowance, says Dr. Draelos. She recommends 1,000 to 2,000 international units (IU) daily vitamin D supplementation.

Vitamin E is the most important antioxidant in the skin, she says.

**FOOD SOURCES**

- **Vitamin C**: 2/3 cup of raw carrots
- **Vitamin B9 (folic acid)**: 1 avocado or olive oil
- **Vitamin E**: olive oil or 1/2 raw avocado
- **Collagen**: chicken, fish or collagen supplement

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The take-home message is that these skin, hair and nail supplements are really not necessary from a health standpoint. The nutrition you need can be obtained very easily with a multivitamin or, probably better, through adjusting your diet to include more fruits and vegetables.\footnote{Disclosure: Dr. Draelos reports no relevant financial interests.}

**Related:**

- How to Eat for Healthy Skin [PG. 12]
PRP plays promising role in periorbital rejuvenation

ILYA PETROU, M.D. | Staff Correspondent

Autologous platelet-rich plasma (PRP) therapy is being used more frequently and could play a promising role as a monotherapy or in multimodality regimens for periorbital rejuvenation, according to authors of a recent review.1

Mohamad Goldust, M.D., department of dermatology, University of Rome G. Marconi, Rome, Italy, and fellow researchers recently conducted a collaborative literature review to evaluate commonly used non-surgical and minimally invasive treatment modalities for periorbital rejuvenation. They performed a search of published clinical trials and scientific reviews concerning periorbital rejuvenation in the MEDLINE and PubMed electronic databases.

The periorbital region of the face is central to the creation of the perception of age among all races and age groups, the authors note. Typical cosmetic concerns include periorbital wrinkles, melanosomes and more prominent tear troughs.

Treatment options include chemical peeling, mechanical and laser resurfacing techniques, PRP, neuromodulation, soft tissue fillers, as well as energy-based modalities. Each of these treatment modalities can be effective for periorbital rejuvenation; however, they each have limitations, the authors cite. Clinicians must be able to skillfully navigate among them to best address their patients’ concerns.

Topical agents that can address periorbital pigmentation include tretinoin creams, hydroquinone, kojic acid, azelaic acid, vitamin C, caffeine and peptides.

“Hydroquinone is one of the most commonly used agents for pigmentation reduction in strengths varying from 2% to 6%,” the authors wrote. “In a study performed in Indian patients, 4% hydroquinone was found to be effective and tolerable to treat periorbital hyperpigmentation.”

Chemical peeling has been used for both periorbital pigmentation and wrinkles. The segmental chemical peels with phenol-croton oil is cost-effective, the authors write, and has been associated with lasting neocollagenesis.

While forms of dermabrasion have been used, it still carries scarring risk and has been largely replaced by safer therapies like fractional lasers, the authors say.

Non-ablative lasers like intense pulsed light, pulse dye, Nd:YAG 1320nm, Nd:YAG 1064 nm and Erbium glass 1540 are safer treatment options for periorbital rejuvenation, the authors write. These devices have been associated with improvement in eyelid tightening, improved skin flexibility and wrinkles, increases in collagen and reduced melanin with no major side effects, according to studies the authors cite.

Neuromodulators and soft tissue fillers alone and in combination with other modalities have been useful for reducing wrinkles and filling in the tear trough region; however, use of fillers in this area has been associated with complications. Clinicians should have strong knowledge of anatomy and injection technique.

The researchers found that autologous PRP therapy is increasingly being used in dermatology for skin and hair conditions, and its use is quickly growing in popularity as a modality to achieve skin rejuvenation. The study results also confirm the mechanism by which PRP leads to skin rejuvenation, namely by increasing the dermal fibroblast proliferation, as well as the expression of matrix metalloproteinase and collagen synthesis.

“The mechanism by which PRP leads to skin rejuvenation is by increasing the dermal fibroblast proliferation, expression of matrix metalloproteinase, and collagen synthesis.”

Mohamad Goldust, M.D., department of dermatology, University of Rome G. Marconi, Rome, Italy, and colleagues

References:

Disclosures:
The authors reported no relevant disclosures.

The mechanism by which PRP leads to skin rejuvenation is by increasing the dermal fibroblast proliferation, expression of matrix metalloproteinase, and collagen synthesis.
**Bakuchiol, EXPERTS AGREE, OFFERS RETINOL-LIKE BENEFITS WITHOUT IRRITATION**

Physicians have long considered retinol to be the gold standard topical ingredient for skin rejuvenation. But experts say there’s a new, natural ingredient on the block. Bakuchiol (pronounced bahl-KOH-chee-all), a natural retinol alternative, offers patients the skin renewal benefits of retinol without the irritation, redness, peeling and sun-sensitivity.

Scientists have shown clinically that bakuchiol reduces the appearance of fine lines and wrinkles, improves skin firmness, brightens skin and improves skin tone and texture.

Sound like retinol? So far, but what bakuchiol has also demonstrated in studies is that, when applied to the skin, it does not cause the skin irritation and sun-sensitivity that results in so many patient aversions to using retinol products.

“… bakuchiol is comparable with retinol in its ability to improve photoaging and is better tolerated than retinol. Bakuchiol is promising as a more tolerable alternative to retinol,” authors reported in a research paper published in 2018 in the *British Journal of Dermatology.*

In the 12-week randomized, double-blind study of 44 patients who applied either bakuchiol 0.5%-cream twice daily or retinol 0.5%-cream daily, researchers found both topicals significantly decreased wrinkle surface area and hyperpigmentation, with no statistical difference between the compounds.

But the bakuchiol users reported less facial skin scaling and stinging, according to the study.

Burt’s Bees Renewal line of products features bakuchiol for these very reasons, according to Hemali Gunt, Ph.D., head of clinical and scientific affairs at Burt’s Bees, a leader in evidence-based natural skincare. The search for natural ingredients suitable for use in an aging population with sensitive skin resulted in the development of a bakuchiol-based skincare regimen.

The Renewal line targets aging skin, by providing firming, hydrating and skin brightening benefits, with products including a cleanser, eye cream, spot treatment, night cream and more.

**And it’s natural**

Another plus given today’s consumer demand for natural products is that while retinol in skincare topicals comes from animal sources or is synthetically-derived in the lab, bakuchiol is a natural extract pressed from the seed of the bakuchiol plant, Dr. Gunt said.

Bakuchiol likely is the hottest natural ingredient on the market, according to dermatologist Joshua Zeichner, M.D., director of cosmetic and clinical research in dermatology at Mount Sinai Hospital, New York.

“There’s definitely an increasing consumer demand for natural skincare products,” Dr. Zeichner said. “With the demand has come an influx of natural skincare products. There are many different natural brands available over-the-counter. The problem is many of them are lacking data, so we really don’t know how effective some of these natural products are and which products are making unsubstantiated marketing claims.”

That’s not the case with bakuchiol, which has been well-studied in skin and has been shown to effectively strengthen skin and stimulate collagen, according to Dr. Zeichner.

“While retinol is an outstanding ingredient that I like my patients to use, there are just some people who have sensitive skin and cannot tolerate it. We’re always looking for a retinol alternative for this population of patients. That’s where bakuchiol fills an unmet need,” Dr. Zeichner said.

**A skin renewal symphony**

While bakuchiol is a featured and powerful ingredient in skincare products, it’s not the only ingredient to work toward the goal of skin renewal. And it shouldn’t be the only thing that consumers look for when choosing quality skincare. Rather, it’s a combination of ingredients that make a great product, according to Dr. Gunt.

For example, consumers don’t want harsh ingredients in their skincare products. The ingredients in the Renewal line are of natural origin, and the line is formulated without synthetic fragrances, dyes, parabens, sulfates and phthalates, according to Dr. Gunt.

“Our whole formula approach utilizes natural ingredients,” Dr. Gunt said. “Waxes, oils and butters form a product’s matrix, and to that we add a few specific, well-researched ingredients to correct a particular skin condition. The product matrix or base of waxes, oils and butters is inherently powerful and provides multiple functional benefits.”

In our clinical work, we have shown that the nature-based bakuchiol regimen was well tolerated in a challenging sensitive skin population while producing improvement in smoothness, clarity, radiance, overall appearance, and global anti-aging after four weeks of use. The subjects with eczema/atopic dermatitis did not experience worsening barrier function, the subjects with rosacea did not experience increased flushing or inflammatory papules, and the cosmetic intolerance syndrome subjects were able to use the products without facial sensory discomfort.

Dr. Zeichner said he is a big fan of the Burt’s Bee Renewal Refining Cleanser.

“It uses a unique technology that, to my knowledge, is not in any other cleansers on the market,” he said. “When the cleanser is applied to the skin, it has a gritty sensation. As you lather it and rub it onto the skin, the gums and starches in it dissolve, which releases the cleansing ingredient or surfactant. It gives a very mild physical exfoliation combined with the cleansing ability.”

Up until recently, bakuchiol has only been available in high-priced skincare brands, according to Dr. Zeichner. Burt’s Bees products are affordable, natural and well-studied, he said.

“This is a great time for us to have products that can recommend that will continue to give patients antiaging benefits that they’re looking for without creating more irritation,” Dr. Zeichner said. “In an environment where people are wearing facemasks on a daily basis, an ingredient like bakuchiol will become a staple ingredient in skincare routines.”

Noninvasive body contouring options grow

MORGAN PETRONELLI | Assistant Editor

Over the last 10 years, noninvasive procedures have become increasingly popular in the world of body contouring, according to Catherine DiGiorgio, M.D., a board-certified cosmetic and laser dermatologist at The Boston Center for Facial Rejuvenation located in Boston. She spoke about the heightened popularity during the 2019 American Society of Dermatologic Surgery meeting in Chicago.

Of 623,000 body contouring procedures conducted in 2018, only 18,000 were invasive, such as liposuction, according to recent ASDS data, says Dr. DiGiorgio. She attributes this to patients searching for treatments with minimal pain and downtime.

Today’s noninvasive offerings include injectables and energy-based devices, Dr. DiGiorgio says. For example, deoxycholic acid, a currently available injectable, is often used to dissolve fat in the submental area and can also be used off-label to correct or touch-up pockets of adipose tissue left over such from invasive liposuction. Other noninvasive procedures include cryolipolysis, high and low-intensity focused ultrasound, and 1060 nm laser lipolysis.

Cryolipolysis is a well-known procedure that treats small areas of unwanted adipose tissue by cooling body fat, which breaks down the fat cells without damaging other types of tissue.

“We also have ultrasound treatments: high intensity focused ultrasound and low intensity focused ultrasound, which have been around for a while,” she says. “The low-intensity focused ultrasound uses acoustic waves to create damage to the fat. And the high-intensity focused ultrasound more creates necrosis through heating of the fat.”

Finally, laser lipolysis with a 1060 nanometer laser uses heat to selectively destroy adipose tissue on the body as well as the submental area, according to Dr. DiGiorgio.

NEW TO THE MARKET

Dr. DiGiorgio also highlights new noninvasive offerings coming to the market, which include a collagenase Clostridium histolyticum injection for treatment of cellulite as well as radiofrequency devices and devices that use electromagnetic stimulation.

Collagenase Clostridium histolyticum is a combination of two bacterial collagenases that work to dissolve collagen types one and three. Currently, the injection is in a phase 3 open-label 5-year study investigating its efficacy in dissolving cellulite in women.

“This will be an exciting thing to see in the future if it really provides a new treatment for cellulite for our patients,” she says.

Electromagnetic stimulation works by stimulating muscle contractions, which builds muscle tissue and theoretically decreases fat, according to Dr. DiGiorgio.

“I think that we have a lot to offer our patients in the noninvasive body contouring world and it’s only going to grow from here. As dermatologists we really need to continue to grab hold of this technology and help our patients to look and feel their very best,” Dr. DiGiorgio says. ◆
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First injectable for cellulite approved by FDA

MORGAN PETRONELLI | Assistant Editor

The U.S. Food and Drug Administration (FDA) has approved collagenase clostridium histolyticum-aaes (Qwo, Endo International) for the treatment of moderate-to-severe cellulite in the buttocks in adult women, making it the first FDA-approved injectable cellulite treatment.

“Today’s FDA approval of QWO is a key achievement in the continued execution of Endo’s long-term strategy, especially as it relates to building our portfolio and capabilities for the future,” says Blaise Coleman, president and CEO of Endo. “As Endo embarks on an exciting new journey into medical aesthetics, we look forward to bringing this innovative treatment to market through our Endo Aesthetics organization.”

The injectable combines two collagenases, AUX-I and AUX-II, which are purified enzymes produced naturally by the Clostridium histolyticum bacterium. Together, the enzymes degrade types 1 and 3 collagen by releasing the fibrous septae, which leads to an improvement in appearance and texture of the skin, according to the company.

“QWO could be a game-changer for many women with cellulite,” says Anne Chapas, M.D., board-certified dermatologist at Union Square Laser Dermatology, New York City. “I am thrilled there will now be an FDA-approved injectable treatment option proven to address a root cause of cellulite. What is exciting about QWO is that it is a cutting-edge cellulite treatment, without the cutting.”

The company expects the injectable to be available to aesthetic healthcare providers in the United States beginning in Spring 2021.

For more information about collagenase clostridium histolyticum-aaes, visit www.QWO.com.

References:

Quick TAKES

The novel injectable combines two purified enzymes, AUX-I and AUX-II.

The enzymes degrade type 1 and 3 collagen, leading to improved skin appearance and texture.

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Anne Chapas, M.D., Union Square Laser Dermatology, New York.
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Consider biopsy in patients with certain cancers

LISETTE HILTON | Staff Correspondent

A skin biopsy of a 65-year-old woman’s rapidly progressing facial and scalp lesions helped doctors to diagnose the rare hematological malignancy blastic plasmacytoid dendritic cell neoplasm (BPDCN), according to a case report published last year in the *BMJ*.

While little is known about this cancer and how to treat it, the authors suggest a low threshold for performing a skin biopsy to evaluate skin lesions in patients with hematological cancers, especially when those lesions are quickly progressing, large or involve atypical sites.

BPDCN is thought to account for less than 1% of hematological cancers. Concurrent CD4, CD56, BCL-2 and CD123 expression defines the malignancy. More than 90% of patients present (many early in the disease) with indolent skin lesions. Patients might also present initially with leukemic or systemic involvement. There have been rare reports of bone marrow, lymph node, central nervous system, spleen, liver, lung and other areas of involvement, according to the paper.

In 10% to 20% of BPDCN cases, patients have a history of cancer. Common cancers in their pasts include myelodysplastic syndrome, chronic myelomonocytic leukemia and acute myeloid leukemia. These associations, among other things, suggests BPDCN is a myeloid-related neoplasm, they wrote.

Patients with the cancer have a poor prognosis. The patient in this particular case died four months after her diagnosis. Allogeneic hematopoietic stem cell transplant is the most effective treatment.

In this case, doctors had diagnosed the patient with myeloproliferative disorder and chronic lymphocytic leukemia in 2002. Providers noted an increasing lymphocyte count consistent with early stage chronic lymphocytic leukemia in 2011, so they monitored her blood counts but didn’t treat her. It was in September 2018, when she developed prominent violaceous patches and nodules on her scalp and upper part of the face that doctors diagnosed widespread BPDCN.

They treated her with hyper-cyclophosphamide, vincristine, doxorubicin, dexamethasone (CVAD) and intrathecal methotrexate. But she continued to progress, even after doctors tried another treatment option, decitabine and venetoclax.

Providers have no clear guidelines for treating BPDCN. Among the potentially effective treatment regimens, hyper-CVAD, methotrexate and cytarabine, as well as cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP) or CHOP plus etoposide. Research suggests these patients are at high risk for central nervous system involvement, especially in relapses. As a result, central nervous system prophylaxis using intrathecal therapy is recommended, according to the paper.

The U.S. Food and Drug Administration (FDA) approved tagraxofusp-erzs (Elzonris, Stemline Therapeutics) in December 2018 for BPDCN in adults and children ages 2 years and older. FDA approved tagraxofusp-erzs, a CD123-directed cytotoxin, based a multicenter, multicohort, open-label, single-arm clinical trial of patients with untreated or relapsed/refractory BPDCN.

“In the pivotal cohort, seven (53.8%; 95% CI: 25.1, 80.8) of 13 patients with untreated BPDCN achieved complete response/clinical complete response after a median follow-up of 11.5 months. The median response duration was not reached. In the second cohort, of 15 patients with relapsed or refractory BPDCN, one patient achieved a complete response (duration 111 days) and one patient achieved a clinical complete response (duration 424 days),” according to an FDA release on the approval.

In the case documented in the *BMJ*, doctors offered the patient tagraxofusp-erzs before it was approved as an experimental agent. But because of logistic issues she didn’t receive the drug. She wasn’t a candidate for the drug after its approval due to performance status, according to the authors.

Researchers have shown a greater overall survival after allogeneic hematopoietic stem cell transplant than with chemotherapy alone. Allogeneic hematopoietic stem cell transplant is preferred over autologous stem cell transplant, according to the paper.

“Stem cell transplantation beyond first complete remission … might have an adverse impact on the survival. However, many patients are elderly and frail, or have rapidly progressive disease that never achieves remission. Thus, they are very poor candidates of stem cell transplant.”

In such groups, venetoclax with hypomethylating agents like decitabine or azacitidine has shown some benefit,” they wrote.

**Disclosures:** The authors report no relevant disclosures.

**Reference:**
The Importance of Early, Appropriate Treatment of Atopic Dermatitis

If childhood atopic dermatitis is untreated—or inappropriately treated—what is the potential impact? How do food allergies or asthma correlate to atopic dermatitis in the first year of life? At what age and/or severity of disease does pharmacologic treatment become a consideration?

Lawrence F. Eichenfield, MD, answers these questions and more in an expert discussion of early and appropriate treatment of atopic dermatitis.

The Importance of Early, Appropriate Treatment of Atopic Dermatitis

Why have current topical options fallen short in treating atopic dermatitis? What potential do novel topical therapies show, particularly in the first few years following the approval of crisaborole? Does research data support consideration for Janus kinase or PDE4 inhibitors?

Adam Friedman, MD, FAAD, discusses challenges, advancements and new horizons for topical therapies in the treatment of atopic dermatitis.

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* Treatment success* rates were 26% for ARAZLO Lotion vs 13% for vehicle in study 1 and 30% vs 17%, respectively, in study 2 (P<0.001 in both studies).

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