practical dermatology NEWS
Volume 14, No. 2 • February 2017

Study Finds Increased Incidence of SCC Among Patients Treated with Biologics for Psoriasis

A recent study published in the *Journal of the American Academy of Dermatology* sought to estimate the overall malignancy rate (excluding non-melanoma skin cancers [NMSC]) and NMSC rate among 5,889 patients with systemically treated psoriasis.

The researchers identified a cohort of adult Kaiser Permanente Northern California health plan members with psoriasis diagnosed from 1998 to 2011 who were treated with at least one systemic antipsoriatic agent and categorized them into ever-biologic or nonbiologic users. Most biologic-exposed members were treated with TNF-alfa inhibitors (n = 2214, 97 percent).

The study found that overall incident cancer rates were comparable between ever-biologic as compared to non-biologic users. NMSC rates were 42 percent higher among individuals ever exposed to a biologic, largely driven by increased cutaneous squamous cell carcinoma risk.

The authors concluded that increased skin cancer surveillance in this population may be warranted.

FDA Approves RHOFADE Cream for Persistent Facial Erythema Associated With Rosacea

The FDA has approved Allergan's Rhofade cream (oxymetazoline hydrochloride) for the topical treatment of persistent facial erythema associated with rosacea in adults. Approval was based on two clinical studies that evaluated the primary efficacy endpoint on day 29.

Among the estimated 16 million Americans with rosacea, persistent facial redness is cited as the most common sign of rosacea. In a National Rosacea Society survey, cited by Allergan, 65 percent of rosacea patients surveyed said their symptoms first appeared between 30-60 years of age.

"Historically, there haven't been many options available to help physicians address persistent facial erythema and often we ended up just helping our patients identify and manage triggers, which can lead to frustration for both the doctor and patient," said Dr. Robert Weiss, Clinical Trial Investigator and Director of Maryland Laser, Skin & Vein Institute, in a statement. "With the approval of Rhofade, doctors will now be able to provide their patients with an effective once-daily treatment option to help manage this condition."

In two clinical trials, a once-daily application of Rhofade was proven to reduce persistent facial erythema associated with rosacea through 12 hours. The primary efficacy endpoint was at day 29 and defined as the proportion of patients with at least a 2-grade reduction in erythema (improvement) from baseline (pre-dose on day 1) on both the clinician erythema assessment (CEA) and subject self-assessment (SSA) (composite success) measured at hours 3, 6, 9 and 12 versus vehicle. CEA and SSA also measured at Days 1 and 15 at hours 3, 6, 9, and 12.

The clinical trials were identical, multicentered, randomized, double-blind, parallel-group, and vehicle-controlled in moderate or severe patients, N=885, 18 years or older.

In both pivotal trials, the primary efficacy endpoint was met. The proportion of patients achieving composite success were as follows: at hours 3, 6, 9, and 12 results in study 1 were Rhofade (N=222) 12 percent, 16 percent, 18 percent, 15 percent versus Vehicle (N=218) 6 percent, 6 percent, 8 percent, 6 percent, and in study 2 were Rhofade (N=224) 14 percent, 13 percent, 16 percent, 12 percent versus Vehicle (N=221) 7 percent, 5 percent, 9 percent, 6 percent. Rhofade was proven more effective than vehicle in reducing persis-

tent facial erythema associated with rosacea in adults.

Rhofade will be available for commercial supply starting May 2017 in the United States.

ZO Skin Health, Inc. Acquires ReFissa from Suneva Medical

ZO Skin Health, Inc. has acquired the worldwide rights to ReFissa as well as its generic equivalent tretinoin from Suneva Medical. Financial terms for the acquisition were not disclosed.

ReFissa is an FDA-approved prescription cream with a 0.05% strength emollient base designed to reduce fine facial wrinkles, correct irregular pigmentation, and smooth substantial skin roughness. A derivative of vitamin A, ReFissa's new formulation of tretinoin works in tandem with the ZO Melamix skin lightener to help blend the skin to create a more even skin tone. "By acquiring ReFissa, we are able to offer to all of our physician partners a product with superior anti-aging and skin tone benefits so they can continue to prescribe in accordance with my protocols," says Zein Obagi, MD, Founder and Medical Director of ZO Skin Health, Inc, in a news release.

Suneva currently markets Bellafill and ReGenica Skincare in the US, Canada, and Hong Kong.

FDA OKs Coolsculpting for Upper Arm Fat Reduction

ZELTIQ Aesthetics, Inc.'s CoolSculpting is now FDA-cleared for fat reduction in the upper arms. The company will be launching the CoolAdvantage Petite applicator to optimize the performance of CoolSculpting in the upper arms, with full commercial release targeted for the middle part of this year. The CoolAdvantage Petite treatment comes with two interchangeable contours designed to uniquely treat the upper arm area in just 35 minutes.

coolsculpting®

"My patients have been asking for a non-invasive solution for their unwanted arm fat so I am thrilled to be able to offer them a proven solution that is safe and effective," says Grant Stevens, MD, FACS, Founder and Medical Director of Marina Plastic Surgery and Medical Director of Body by OrangeTwist, in a news release. "We anticipate a lot of interest from our patients now that there is an FDA-cleared solution to treat this challenging area."

CoolSculpting is now FDA-cleared for the treatment of fat bulges in the submental area, thigh, abdomen, flank, bra and back fat area, underneath the buttocks, and the upper arm.

Alma Lasers' Accent Celebrates 10 Years with a New Campaign

Accent Prime is celebrating a 10-year anniversary with a newly launched campaign. Alma Lasers released the first generation of the Accent branded platform in 2007, with the FDA approval, and technologically enhanced it throughout the past decade up to the newest addition to Alma Lasers' family of body contouring products: Accent Prime. This latest platform combines advanced innovations in ultrasound and Unipolar radio frequency technologies to deliver fast, effective, highly customized treatments with long lasting results. Accent Prime, the fourth generation of Accent platforms launched in a 10 years' timeframe, allows doubling the speed of body contouring and skin tightening treatments.

The Accent 10 year anniversary campaign will run throughout 2017 and generate engagement through Facebook contests, videos and digital content coverage, which will showcase the success of the brand, according to the company.

Valeant Dermatology to Award $10,000 Scholarships for Undergraduate and Graduate Degrees

Valeant Dermatology, a division of Valeant Pharmaceuticals North America LLC, will award nine individual scholarships of up to $10,000 through its annual ASPIRE HIGHER Scholarship Program. The scholarships will be awarded to students who will be attending undergraduate or graduate education programs during the 2017-2018 school year. The aim of the scholarship program is to recognize students who have been diagnosed and treated for a dermatologic condition and are pursuing their goal of a higher education degree. Applicants need not have used a Valeant dermatologic prescription medication to be eligible, nor will the use of a Valeant product increase an applicant's chance of winning the scholarship.

Three scholarships will be awarded in three different categories: Undergraduate Scholar Awards for students pursuing an

undergraduate degree, Graduate Scholar Awards for students pursuing a graduate degree, and Today's Woman Scholar Awards for students who are mothers pursuing either a graduate or undergraduate degree.

Last year's scholarship winners were selected from a pool of nearly 1,000 applicants, the highest number of applications received since the program launched in 2013.

Applicants are required to submit a 500-word essay describing the impact their dermatologic condition has had on their life and the role their healthcare practitioner has played in helping treat their condition. Other application requirements include two letters of recommendation and information on their current school and community activities. Applications will be accepted from February 1, 2017 through April 30, 2017 and the winners will be named on July 10, 2017. Your patients can apply for a scholarship at www.ValeantAspireHigher.com.

Realm Therapeutics Submits Investigational New Drug Application for PR022 for AD

Realm Therapeutics has submitted its first investigational new drug (IND) application to the FDA for PR022 as a novel treatment for atopic dermatitis (AD). Pending acceptance, the IND will enable Realm to initiate a Phase 2a proof-of-concept trial for patients with atopic dermatitis.

The Phase 2a trial will be a randomized, double-blind, vehicle-controlled, multicenter, parallel-group study to assess the safety and efficacy of multiple doses of PR022 in adult patients with mild-to-moderate AD. Based on outcomes of this study, the company says it intends to conduct a Phase 2b study to include adolescent patients with the goal to incorporate pediatric patients in their pivotal Phase 3 trials.

PR022 is a proprietary, non-alcohol based, topical gel, in which the active moiety is a patented high concentration of hypochlorous acid, offering a differentiated mechanism of action for the treatment of a significant disease. The company has demonstrated that PR022 is associated with a statistically significant therapeutic effect in animal models of atopic dermatitis, including down modulation of key pro-inflammatory cytokines and reduced expression of Th2 cytokines, IL-4, IL-13 and IL-31, as well as TARC and TSLP, which are all linked to the signs and symptoms of the disease. Importantly, these results are delivered without the typical negative effects of commonly used AD immunomodulatory or immunosuppressant drugs, including corticosteroids, suggesting an advantageous safety profile for PR022.

Sun Pharma Introduces Leave Acne Behind Patient Initiative

Sun Pharma introduced a new initiative— "Leave Acne Behind" — to educate patients and create awareness of severe recalcitrant nodular acne (SRNA). Sun Pharma reports that out of all prescription-treated acne cases today, 20 percent represent severe acne conditions, and that those who face such conditions often suffer embarrassment, low self-esteem, and other negative emotions that impact their quality of life. Approximately 90 percent of these cases are often teenagers.

The Leave Acne Behind initiative offers educational resources including a website LeaveAcneBehind.com and resources at dermatologists can offer at their offices, including a book (both in hard copy and iBook) and patient brochure to help patients and caregivers navigate through topics that are often not addressed regarding severe acne. All of the program's resources are meant to open the lines of communication between patients and dermatologists in hopes to reduce the long-term effects of acne, the company says.

The website and book addresses variety of topics such as:

- Who gets acne and why
- The different types of acne
- The physical and emotional damage severe acne can cause
- Treatments to help prevent acne from causing permanent skin damage, such as scars
- Questions a patient or caregiver may want to ask during dermatology health care provider appointments

"For anyone looking to educate themselves on acne, including severe recalcitrant nodular acne and help them make informed treatment decisions, the "Leave Acne Behind" initiative is a great resource," said Jeremy Moss, MD, PhD, an associate professor of dermatology at Yale University, in a statement. "Patients and caregivers can use these education and awareness materials to speak to their dermatologist."

Radiesse Hits Double Digits

Merz Aesthetics' flagship brand, Radiesse, turned 10 this year, and was feted in style at a throw-back Thursday media event in New York City.

The party took beauty bloggers and journos back to 2007 when the first iPhone was released to the public, there was no such thing as a hashtag on social media and Miley Cyrus was better known as Hannah Montana. It was also the year that Radiesse hit the US market. Now, more than six million syringes have been sold worldwide, and the filler is available in 60 countries. Radiesse's first approved indication was for

smoothing moderate to severe facial wrinkles and folds, and 2015 brought a nod for hand augmentation.

"It's not a one-trick pony," says dermatologist Terrence Keaney, MD, assistant clinical faculty at George Washington Hospital in Washington, DC. "Radiesse treats the hands and the lower mid-face." Radiesse does more than just add volume, he says. "It's also a a collagen simulator with results lasting for one year or more."

Cheryl Burgess, MD, founder of the Center for Dermatology and Dermatologic Surgery in Washington DC, agrees. She first started using Radiesse to treat HIV-related facial lipoatrophy. "Radiesse is unique in the fact that it offers immediate visible improvement, and the results continue to develop over time," she says. "This product has a thick texture, and excellent resilience. It provides fantastic structure, like scaffolding, to lift and shape the face."

Venus Concept Launches Venus Velocity for Laser Hair Removal

Venus Concept is bringing a new hair removal laser to the US. Venus Velocity is a diode laser for hair removal, permanent hair reduction, and the treatment of razor bumps. The device has two modes of operation (SLIDE and PULSE), three changeable spot sizes of up to 7 cm^2 on an ergonomic applicator, and a real-time cooling system. Other perks include a longer warranty, no disposables, Internet of Things integration, and Venus Concept's unique subscription-based business model.

Lifestyle Choices May Trump Genes When it Comes to Youthful Skin

Nurture has a larger effect on youthful skin appearance than nature, according to a new study by Olay done in collaboration with personal genetics company 23andMe.

Specifically, sunscreen usage and positive attitude were correlated with younger-looking skin, while sunbathing and frequent dry skin have a negative association with skin aging.

Last year, Olay identified biological commonalities among a group of women called "exceptional skin agers." In the Multi-Decade and Ethnicities Study (MDE Study), Olay scientists found that 10 percent of women looked more than 10 years younger than their actual age and shared a unique gene expression fingerprint. Most recently, in a study with more than 155,000 participants conducted in collaboration with 23andMe, Olay researchers learned that women can take control to achieve exceptional skin aging.

The new findings are slated to be presented at the 2017 American Academy of Dermatology Annual Meeting in Orlando.

In the study, women who almost always used sunscreen were 78 percent more likely to be an exceptional skin ager, compared to women who almost never do. In addition, women who reported they had a positive attitude towards themselves were 30 percent more likely to be an exceptional skin ager. Similarly, women with less than ideal skincare habits were less likely to achieve successful skin aging. Women who frequently sunbathed were 35 percent less likely to be an exceptional skin ager and those women who frequently or always suffered from dry skin were 30 percent less likely to be an exceptional skin ager, the study showed.

Additional positive predictors included activity and energy levels, living in an urban area, regular exercise, eight or more hours of sleep a night, multi-vitamin usage, and high self-rated health. Additional negative predictors included smoking cigarettes and a body mass index of over 25.

Study: Umbrellas Plus Sunscreen Needed to Stave Off Sunburns

When it comes to preventing sunburns, neither beach umbrella or SPF 100 sunscreen are enough on their own, according to a new study in *JAMA Dermatology* that suggests both are needed for sufficient sun protection.

The study — conducted over a few days in August 2014 in Lake Lewisville, TX — included 81 participants, with 41 who used an umbrella and 40 who used SPF 100 sunscreen for protection on a sunny beach for 3½ hours at midday. The beachgoers were examined for sunburn on their bodies (face, back of neck, upper chest, arms and legs) about a day after sun exposure.

Seventy-eight percent of participants who were under the shade of a beach umbrella developed sunburn compared with 25 percent of participants who used SPF 100 sunscreen. There were 142 sunburn incidences in the umbrella group and 17 in the sunscreen group, the study found.

"Umbrella shade alone may not provide sufficient sun protection during extended exposure to UV rays. Although the SPF 100 sunscreen was more efficacious than the umbrella, neither method alone prevented sunburn completely under actual use conditions, highlighting the importance of using combinations of sun protection practices to optimize protection against UV rays," conclude researchers led by Hao Ou-Yang, Ph.D., of Johnson & Johnson Consumer, Inc., Skillman, N.J. Johnson & Johnson Consumer Inc. is the parent company of Neutrogena Corp. and manufacturer of the sunscreen tested in this study.

Limitations of the study include that only one type of beach umbrella was evaluated.

ISDIN: Broad Spectrum Sun Protection Cream with DNA Repair Beneficial Post AK Treatment

ISDIN has reported promising results of a nine-month, randomized, investigator-blinded parallel-group study in a poster presentation at the Winter Clinical Conference. The study was designed to evaluate clinical effects of a high SPF film-forming emulsion containing photolyase, in comparison to a general sunscreen without photolyase, in patients successfully treated with photodynamic therapy (PDT), for actinic keratosis (AK). The film-forming emulsion containing photolyase, a DNA-repairing enzyme, with a high broad photo-protection action (Ery), was assessed in comparison with a comparable high broad photo-protection sunscreen (SS) in AK subjects after a successful PDT for the treatment of AK lesions of the scalp.

At baseline the mean (SD) number of AK lesions was 6.6(2.8) in Ery group and 8.4(3.0) in SS. Immediately after PDT residual lesions, mean (SD) were 2.6 (2.0) in Ery group and 0.6 (0.5) in SS group (NS). A progressive increase of AK lesions was observed in SS group with a mean lesion number of 3.6(3.8) at the end of study period. In contrast, no increase in AK lesions was observed at the end of the study period in Ery group with a mean (SD) number of 1.0 (1.1) lesion in comparison with baseline and with the comparator group (P=0.001). During the 9 month treatment period, while no patients in the Ery group needed a new PDT session, 10 patients out of 15 (66 percent) in SS group needed a new PDT (P=0.004). No severe skin adverse events related to the study products were observed during the trial.

Scarless Wound Healing

Scientists can now transform myofibroblasts found in wounds into adipocytes, paving the way toward scarless healing. Researchers began this work at the Perelman School of Medicine at the University of Pennsylvania, which led to a large-scale, multi-year study in connection with the Plikus Laboratory for Developmental and Regenerative Biology at the University of California, Irvine.

Adipocytes, which don't cause scarring, are normally found in the skin, but they're lost when wounds heal as scars. The study showed hair and fat develop separately but not independently. Hair follicles form first, and the researchers previously discovered factors necessary for their formation. Now they've discovered additional factors actually produced by the regenerating hair follicle to convert the surrounding myofibroblasts to regenerate as fat instead of forming a scar. That fat will not form without the new hairs, but once it does, the new cells are indistinguishable from the pre-existing fat cells, giving the healed wound a natural look instead of leaving a scar.

"Essentially, we can manipulate wound healing so that it leads to skin regeneration rather than scarring," says George Cotsarelis, MD, the chair of the Department of Dermatology and the Milton Bixler Hartzell Professor of Dermatology at Penn, and the principal investigator of the project, in a news release. "The secret is to regenerate hair follicles first. After that, the fat will regenerate in response to the signals from those follicles."

As they examined the question of what was sending the signal from the hair to the fat cells, researchers identified a factor called Bone Morphogenetic Protein (BMP). It instructs the myofibroblasts to become fat. This signaling changed what was previously known about myofibroblasts.

"Typically, myofibroblasts were thought to be incapable of becoming a different type of cell," Dr. Cotsarelis says. "But our work shows we have the ability to influence these cells, and that they can be efficiently and stably converted into adipocytes." This was shown in both the mouse and in human keloid cells grown in culture.

"The findings show we have a window of opportunity after wounding to influence the tissue to regenerate rather than scar," adds the study's lead author Maksim Plikus, PhD, an assistant professor of Developmental and Cell Biology at the University of California, Irvine. Plikus began this research as a postdoctoral fellow in the Cotsarelis Laboratory at Penn, and the two institutions have continued to collaborate.

The first and most obvious use would be to develop a therapy that signals myofibroblasts to convert into adipocytes – helping wounds heal without scarring, but the increase of fat cells in tissue can also be helpful for more than just wounds. Adipocyte loss is a common complication of other conditions, especially treatments for HIV, and right now there is no efficient strategy for treatment. "Our findings can potentially move us toward a new strategy to regenerate adipocytes in wrinkled skin, which could lead us to brand new anti-aging treatments," Dr. Cotsarelis says.

The Cotsarelis Lab is now focusing on the mechanisms that promote skin regeneration, especially with respect to hair follicle regeneration. The Plikus Laboratory is focusing on other aspects of cell reprogramming in skin wounds. Researchers there are examining the role of other signaling factory beyond BMP as well as conducting further studies using human cells and human scar tissue.

The findings appear online in the journal *Science*. ■