# Skin & Allergy News

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## WHAT'S NEWS

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- The American Society for Laser Medicine and Surgery
- The Society for Investigative Dermatology
- And more!

The **June 30 deadline** for e-prescribing compliance is nearing. Are you ready? **7**

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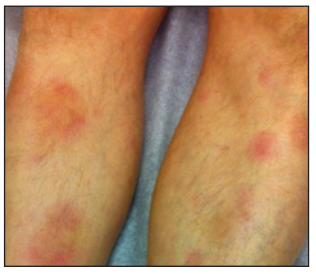
## CASE OF THE MONTH



A 47-year-old male with no significant past medical history presented with a 1-day history of tender lesions on the bilateral anterior portion of his lower legs. Eight days prior to presentation, he reported experiencing nausea, vomiting, diarrhea, and subjective fever. On examination, several scattered erythematous, tender, subcutaneous nodules with surrounding darker erythema were present.

*What's your diagnosis?* **30**

# Melanoma Death Cut In Half After SCREEN

**The landmark German project is considered the most ambitious effort to screen for melanoma ever conducted.**

BY BRUCE JANCIN

FROM THE ANNUAL MEETING OF THE SOCIETY FOR INVESTIGATIVE DERMATOLOGY

RALEIGH, N.C. – A population-based total-body skin cancer screening program reduces melanoma mortality, according to the results of a landmark German project.

"I would argue that this is the most important presentation anywhere at this meeting," Dr. Martin A. Weinstock said during his presentation of the SCREEN (Skin Cancer Research to Provide Evidence for Effectiveness of Screening in Northern Germany) project.

"The reason I make that argument is very simply because melanoma accounts for more deaths than anything else in the dermatology world. If we want to reduce that number of deaths, the best way is [through] early detection – and SCREEN provides the best evidence to date that we can do that," explained Dr. Weinstock, professor of dermatology and epidemiology at Brown University, Providence, R.I., and a SCREEN project organizer.

SCREEN was a population-based skin cancer screening program in which all residents over age 20 in the German federal state of Schleswig-Holstein were encouraged to undergo a standardized whole-body skin examination between July 2003 and June 2004. Nineteen percent of the state's eligible population – 360,288 individuals – participated. Half of the 1,169 melanomas diagnosed in Schleswig-Holstein during the study period were detected via the SCREEN program.

Before the skin cancer screening period (1998-1999), the melanoma mortality rate was 1.9 per 100,000 men and 1.4 per 100,000 women. The key study finding was that melanoma mortality fell by 48% in Schleswig-Holstein by 2008-2009 to 1.0 per 100,000 men to 0.7 per 100,000 women.

JOHN ABROMOWSKI/BROWN UNIVERSITY

**SCREEN provides the best evidence yet that early detection can reduce melanoma death, said Dr. Martin A. Weinstock.**

*See* **Melanoma** *page 6*

# Daily Emollient Prevented Atopy In 67% of High-Risk Infants

**Previous studies have demonstrated that skin barrier dysfunction proceeds eczema.**

BY BRUCE JANCIN

FROM THE ANNUAL MEETING OF THE SOCIETY FOR INVESTIGATIVE DERMATOLOGY

RALEIGH, N.C. – Once-daily application of an emollient from birth through age 6 months has shown considerable promise as a means of preventing atopic dermatitis, according to the Barrier Enhancement for Eczema Prevention study.

BEEP was a multicenter, international, randomized controlled pilot study assessing the feasibility, safety, and effectiveness of a novel approach to the prevention of atopic dermatitis.

The study hypothesis was that protecting the skin barrier early in life can prevent this common skin disease, explained Dr. Eric L. Simpson of Oregon Health and Science University, Portland.

The rationale for this approach lies in previous work demonstrating that skin barrier dysfunction precedes eczema development. And emollients can be effective in treating mild disease and preventing flares, he added.

BEEP involved 124 infants in Portland and at four medical centers in the United Kingdom. All were deemed high risk for atopic dermatitis because they had one or more first-degree relatives with a history of asthma, hay fever, or atopic dermatitis.

Participating families were randomized to either once-daily application of an emollient to the baby's entire body except the scalp and diaper area starting before age 3 weeks and continuing for 6 months, or to a control group that agreed to refrain from regular use of

*See* **Atopy** *page 6*

# ONLINE EXTRAS

NASEEM S. MILLER/IMNG MEDICAL MEDIA

**Reporter Naseem S. Miller talked with Dr. Brett Coldiron, president of the American College of Moh's Surgery, during the society's annual meeting in Chicago, where he explained the ACMS's position on Mohs surgery. He emphasized that Mohs surgery is not being overused; rather, he said that the increase in use is the result of the nation's skin cancer epidemic.**


IMNG MEDICAL MEDIA

**SKIN & ALLERGY NEWS managing editor Amy Pfeiffer and senior editor Terry Rudd highlight trending news in dermatology with leading expert interviews. This month's program takes a look at the American Academy of Dermatology's volunteer and skin cancer awareness programs – like SPOT – plus much more.**

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TOP FIVE 5

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**TOP FIVE Viewed Stories**

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2. First-Ever Acne Treatment Guidelines for Children Revealed
3. Topical Hyaluronic Acid Is Breaking Through Dermis
4. New Results Challenge Laser Effectiveness for Onychomycosis
5. Total Body Exam Reduces Melanoma Mortality

Source: Google Analytics April Statistics


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**Multimedia Producer** Nick Piegari

**Contributing Writers** Christine Kilgore, Mary Ann Moon

**Project Manager** Susan D. Hite

**Assignments Manager** Megan Evans

**Address Changes** Fax change of address (with old mailing label) to 973-290-8245 or e-mail change to subs@elsevier.com

**Editorial Offices** 5635 Fishers Lane, Suite 6000, Rockville, MD 20852, 877-524-9336, sknews@elsevier.com

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**Senior Systems Administrator** Lee J. Unger

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**Sales Director, IMNG Medical Media** Mark E. Altier, 973-290-8220, m.altier@elsevier.com

**Director, Special Projects** Michael Raftery, 973-290-8213, m.raftery@elsevier.com

**Director, eBusiness Development** John Maillard, 973-290-8231, j.maillard@elsevier.com

**National Account Manager** Sally Cioci, 973-290-8215, fax 973-290-8250, s.cioci@elsevier.com

**Advertising Offices** 60 Columbia Rd., Bldg. B, 2nd flr., Morristown, NJ 07960, 973-290-8200, fax 973-290-8250

**Classified Sales Manager, IMNG Medical Media** Robert Zwick 973-290-8226, fax 973-290-8250, r.zwick@elsevier.com

**Classified Sales Representative** Andrea LaMonica, 800-381-0569, fax 914-381-0573, a.lamonica@elsevier.com

**Classified Advertising Offices** 1120 Jensen Avenue, Mamaroneck, NY 10543, 800-381-0569

**Reprints/Eprints** Contact Wright's Media 877-652-5295

**Sr. Program Manager, Customized Programs** Malika Wicks

**Audience Development Manager** Barbara Cavallaro, 973-290-8253, b.cavallaro@elsevier.com

**Manager, Marketing and Research** Jennifer Eckert

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# Majority of Young Adults Report Yearly Sunburn

**VITALS**

**Major Finding:** Up to 66% of young adults reported at least one sunburn and up to 44% of women reported using a tanning bed in 2010.

**Data Source:** The studies included data from 11 years of the National Health Interview Survey.

**Disclosures:** Ms. Hartman, Dr. Siegel, and Dr. Plescia reporting having no relevant disclosures.

BY MICHELE G. SULLIVAN

FROM THE MORBIDITY AND MORTALITY REPORT

Despite the documented increased use of sunscreen and protective clothing in recent years, up to 66% of young adults are still getting sunburned at least once a year.

The use of tanning beds also continues. A review of the National Health Information Survey found that up to 44% of women in a subgroup analysis reported using the devices in 2010, and that those who tan indoors do so up to 28 times each year. Even people with a family history of skin cancer or with recent sunburns are using the devices, said Anne Hartman, a biostatistician with the National Cancer Institute.

The findings are worrisome on a number of levels, said Dr. Daniel M. Siegel, president of the American Academy of Dermatology. "It is distressing that the study found tanning bed use is higher in those with a family history of skin cancer and that sunburn prevalence remains high," he said in an interview. "This emphasizes how important it is to educate the public and encourage them to change their behaviors as they do not necessarily understand the dangers of sun exposure and indoor tanning. If they do, the risks may not be discouraging the behavior."

The sun protection study extracted data from 5 years of the National Health Interview Survey (NHIS). The survey includes detailed questions on sun exposure, the use of sunscreens and protective clothing, and other sun-protective behaviors from the 2000-2010 surveys (MMWR 2012;61:317-22).

Overall, 50% of respondents reported at least one sunburn during the past 12 months. This was highest among whites (66% in 2010) and lowest among blacks (11% in 2010). A similar number of men and women reported getting sunburned, and the prevalence of burning did not differ from 2000 to 2010 (about 50% each year).

**'It is distressing that the study found tanning bed use is higher in those with a family history of skin cancer.'**

DR. SIEGEL

Women were most likely to report sunscreen use and staying in the shade (37% and 35%, respectively). Sunscreen use increased significantly from 2000 to 2010, as did the use of clothing to the ankles (21% in 2000 and 26% in 2010). There were also significant increases in the practice of seeking shade (29% and 35%, respectively). However, there were no significant increases in the use of wide-brimmed hats or long-sleeved shirts.

White women were more likely to report shade use, with a significant increase each year. Black women were least likely to report using sunscreens each year.

Men most often reported using long clothing and staying in the shade (33% and 26%, respectively). Shade use among men increased from 18% in 2000 to 26% in 2010. Long protective clothing use increased from 28% to 33%, but changes in sunscreen use were not significant over that time, nor were changes in wearing a long-sleeved shirt or wide-brimmed hat.

Clinicians and policy makers can help improve these behaviors by continuing to stress the importance of sun protection, Ms. Hartman said. "Evidence from a recent review by the U.S. Preventive Services Task Force suggests that behavioral counseling can increase sun protective behaviors, particularly among persons aged 10-24 years. Additionally, environmental and policy changes (for

*Continued on following page*

# AAD: New Sun Counseling Guidelines Fall Short

BY ALICIA AULT

Counsel patients up to age 24 years on the merits of avoiding sun exposure to reduce the risk of skin cancers, the U.S. Preventive Services Task Force recommended May 8.

The task force stopped short making the same recommendation for patients older than 24 years, saying that the evidence is not sufficient "to assess the balance of benefits and harms." The panel noted in its recommendations the prevalence of skin cancer – affecting more than 2 million Americans yearly – and the rising incidence of melanoma, with 70,000 cases in 2011 and about 8,800 deaths. The USPSTF said there was "convincing" evidence that ultraviolet radiation exposure during childhood and youth is linked to "a moderately increased risk for skin cancer later in life," but that for adults the evidence is only adequate, and, it is associated with just a small increase in risk.

There are potential downsides to counseling – it might lead kids to be less active – but no studies showed such a decrease, according to the recommendations. The document also noted that studies need to be done on whether sun exposure avoidance leads to lower vitamin D levels.

The American Academy of Dermatology praised the recommendation for children and adolescents. "However, we firmly believe that behavior counseling is essential for all populations, including the adult population," said AAD President Daniel M. Siegel, in a statement. "Given this, we will continue our efforts to educate the public on skin cancer prevention, and encourage our members to conduct additional research in this important area," he said. ■

*Continued from previous page*

example, the provision of shade and sunscreen in recreational setting) could be promising strategies for creating social and physical environments that routinely promote sun protection for younger adults and persons of all ages" (Ann. Intern. Med. 2012 May 8 [Epub ahead of print]).

The indoor tanning study used NHIS data from 2010 and included information from 25,233 respondents aged 18 years and older.

Overall, 6% of respondents reported indoor tanning in the past 12 months, reported Ms. Hartman. Tanning was most common among young adults, with 12% of those aged 18-25 years and 9% of those aged 26-29 years using it.

A total of 9% of those with a family history of skin cancer reported indoor tanning, as did 8% of those who had a sunburn within the past 12 months. The associations with cancer and sunburn suggest that many people still don't understand the dangers of indoor tanning, Ms. Hartman said.

Tanning was also related to socioeconomic status; 7% of those with some college or technical school and 7% of those with an income of more than 200% of the federal poverty level reporting indoor tanning.

The highest rates were in white women aged 18-21 years (32%), particularly those from the Midwest (44%). A total of 36% of Southern women aged 22-25 years also reported indoor tanning.

When white women did tan inside, they did so frequently, the report found. Overall, women reported an average of 20 times per year, with 58% reporting that they tanned 10 or more times per year. White women aged 18-21 years had the highest frequency of tanning (28 sessions per year), with 68% reporting a frequency of 10 or more times per year.

The findings from both studies suggest the need for even more education about sun protective behaviors, Dr. Marcus Plescia said in a statement.

"More public health efforts, including providing shade and sunscreen in recreational settings, are needed to raise awareness of the importance of sun protection and sunburn prevention to reduce the burden of skin cancer," said Dr. Plescia, director of cancer prevention and control at the Centers for Disease Control and Prevention. "We must accelerate our efforts to educate young adults about the dangers of indoor tanning." ■

# SCREEN Saves Lives

**Melanoma** *from page 1*

Nothing parallel occurred in the rest of Germany, or in Schleswig-Holstein's neighbor to the north, Denmark. The observed melanoma mortality rate in Schleswig-Holstein during 2008-2009 was 1.0 per 100,000 for men and 0.7 per 100,000 for women, compared with 1.8 and 1.2, respectively, in Germany as a whole excluding Schleswig-Holstein.

During 2000-2009, the most recent 10-year period for which official German mortality statistics are available, melanoma mortality in Schleswig-Holstein declined by 7.4% annually. In contrast, melanoma mortality rates were stable over time in each of the four adjacent states to the north, south, east, and west, none of which had a skin cancer screening program. (See chart.)

A bump in the incidence of melanoma was recorded in Schleswig-Holstein during the screening year, but not elsewhere, according to Dr. Weinstock.

The standardized total-body skin examinations were performed by physicians, who had to complete an 8-hour, day-long training course in order to participate. Of note, 116 of the 118 dermatologists practicing in Schleswig-Holstein participated in SCREEN, as did 64% of primary care physicians. Physicians were paid to perform the screens, and the public was encouraged to undergo screening via an extensive multimedia campaign.

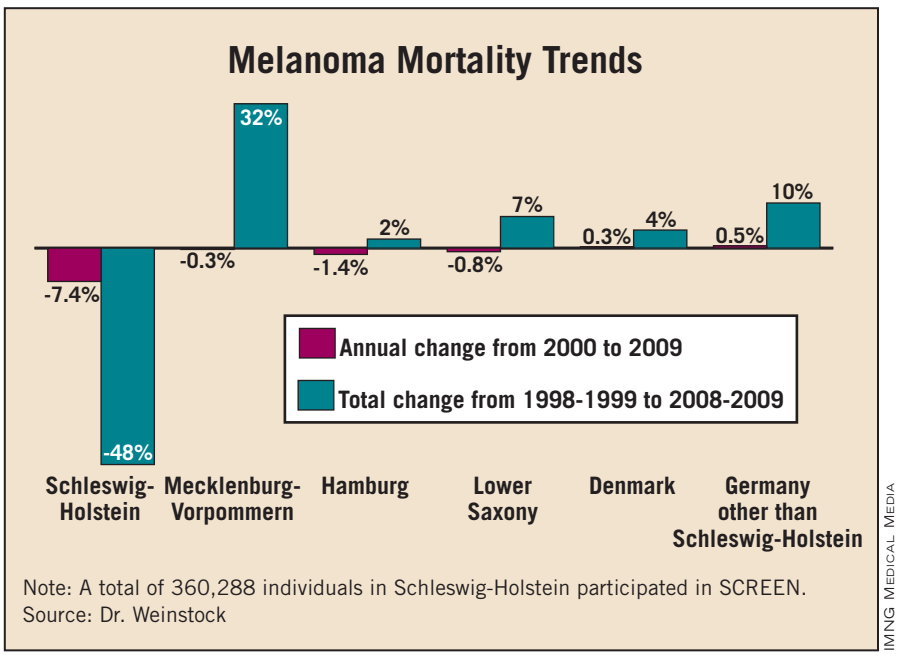
The screening had a two-tiered structure. More than three-quarters of individuals were initially screened by primary care physicians. Participants with suspicious findings were sent to a dermatologist, who performed a second whole-body skin examination and performed biopsies as warranted.

Total-body skin examination as a means of reducing melanoma mortality has long been a controversial issue. The U.S. Preventive Services Task Force has recommended that there is not enough evidence to recommend screening the general adult population (Ann. Intern. Med. 2009;150:188-93). However, according to Dr. Weinstock, the recommendation will need to be revisited in light of the new evidence from Germany.

He observed that although SCREEN was an observational study, and, hence, doesn't constitute absolute proof that a skin cancer screening program saves lives, it was the most ambitious effort to screen for melanoma ever conducted anywhere in the world. And it provides what is probably the strongest evidence that will ever be available, in his view, given the great expense and many years of follow-up required for a randomized controlled trial of skin cancer screening.

As he and his coauthors wrote in a new report from the SCREEN project, "In the public health arena, absolute proof is not necessarily required when lives are at stake" (Cancer 2012 April 19 [doi: 10.1002/ cncr.27566]).

German dermatologists, flush with the SCREEN success, had proposed to follow up the project with a definitive randomized controlled trial of melanoma screening, but were overruled. Federal health officials found the SCREEN results so persuasive that they launched an ongoing national skin cancer screening program. All 45 million Germans aged 35 years and older are now eligible for a total-body skin examination every 2 years.




Note: A total of 360,288 individuals in Schleswig-Holstein participated in SCREEN.
Source: Dr. Weinstock

IMNG Medical Media

**The project also detected basal cell carcinomas at a rate of 5.4 malignancies per 1,000 persons screened.**

DR. BLUM

The SCREEN investigators ruled out improvements in melanoma therapy as a potential explanation for the observed reduction in mortality, since there were none during the study years. Nor were there any changes in coding practices in the Schleswig-Holstein statistics office. And no major melanoma primary prevention programs were introduced. Melanoma mortality rates in Schleswig-Holstein were fairly constant from 1990 to 2003, then dropped during and immediately after introduction of the statewide SCREEN program.

Dr. Weinstock promised there will be much more information and analysis to come from the SCREEN project, including tumor thickness–specific incidence rates.

In a presentation at the Hawaii Dermatology Seminar sponsored by the Skin Disease Education Foundation (SDEF) in Waikoloa, Hawaii, Dr. Andreas Blum noted that while the main purpose of whole-body skin examination is to save lives through early detection of melanoma, the SCREEN project also detected basal cell carcinomas at a rate of 5.4 malignancies per 1,000 persons screened, and squamous cell carcinomas at a rate of 1.1 per 1,000.

Five lesion excisions had to be performed in order to detect one malignancy, according to Dr. Blum, professor of dermatology at the University of Tübingen (Germany). He predicted that the cost involved in routine total-body skin examinations is likely to be a critical source of controversy. Using the U.S. National Cancer Institute's estimate that 12.5% of melanomas are fatal, and assuming the cost of a total-body skin exam to be $50 per person, he estimated that routine total-body skin exams in the SCREEN project cost $240,000 per melanoma death avoided.

Meanwhile, in a recently reported multicenter study in which more than 14,000 subjects underwent a total-body skin exam, 400 patients had to be screened in order to find 1 melanoma (J. Am. Acad. Dermatol. 2012;66:212-9). Again, assuming a cost of $50 per total-body skin exam, that would work out to roughly $140,000 per melanoma death avoided, Dr. Blum said.

He added that in his own clinic, where he and his colleagues see a relatively select patient population, routine total-body skin exams cost an estimated $65,000 per melanoma death avoided.

Dr. Weinstock and Dr. Blum reported having no financial conflicts. SDEF and this news organization are owned by Elsevier. ■

# Result Was Better Than Expected

**Atopy** *from page 1*

emollients. All families received advice on best-practice skin care, namely to minimize the use of harsh cleansers and hot water bathing.

The 6-month cumulative incidence of investigator-diagnosed eczema was 21.8% in the daily emollient group, compared with 43.3% in controls, for a 67% reduction in risk. It was a considerably more dramatic effect than what the investigators had anticipated.

"This was kind of a surprising finding to us," Dr. Simpson admitted. Patients will be followed up at 1 and 2 years to learn whether the early-life treatment actually prevented or simply delayed onset of atopic dermatitis.

In a subanalysis, skin barrier function studies were carried out in 15 patients divided between a control and intervention arm. Children in the control arm showed favorable albeit nonsignificant trends for less transepidermal water loss and a lower skin pH, he said.

Parents in the intervention arm were given a choice of three emollients of various viscosities: sunflower seed oil; Cetaphil cream in the United States or Doublebase gel in the United Kingdom; or Aquaphor in the United States or 50-50 ointment, a white soft paraffin/liquid paraffin product marketed in the United Kingdom. More than two-thirds of families opted for Cetaphil cream or Doublebase gel.

Ninety-six percent of families in the intervention arm found their emollient acceptable, and 80% indicated they used it at least 5 days per week. No cases of irritant or contact dermatitis occurred in the emollient group. Three mild skin infections occurred in each study arm.

Dr. Simpson's BEEP coinvestigators included atopic dermatitis experts such as Dr. Hywel C. Williams, professor of dermatology at the University of Nottingham (England) and Dr. Jon M. Hanifin, professor emeritus of dermatology at Oregon Health and Science University.

The researchers are now planning a larger, definitive, randomized controlled trial of emollient therapy early in life as a means of preventing the development of atopic dermatitis. This study will be powered to look at the relative efficacy of different emollients. Also, it will include objective measures of adherence, such as volume of emollient used, rather than simply relying upon parental report.

Audience members expressed enthusiasm over the BEEP findings. The prevalence of atopic dermatitis has been rising for decades; the disease exacts a steep toll in terms of quality of life; and to date, there has been no established eczema prevention strategy. Moreover, there is the prospect that by preventing eczema via a simple topical therapy it will be possible to halt the "atopic march" to asthma and other comorbidities.

**Ninety-six percent of families in the intervention arm found their emollient acceptable.**

DR. SIMPSON

Dr. Simpson noted that BEEP was a small-scale feasibility study carried out because investigators were initially unsure if families would be willing to participate in a clinical trial where they could be randomized to avoiding emollients. But 28%-59% of the families approached at the participating centers agreed to enroll.

BEEP was funded by the National Institute of Arthritis and Musculoskeletal and Skin Diseases, the Oregon Clinical and Translational Research Institute, and the U.K. National Institute for Health Research. Dr. Simpson reported having no financial conflicts of interest. ■

# Clock Is Ticking Toward E-Prescribing Penalties

BY MARY ELLEN SCHNEIDER

So far, the Centers for Medicare and Medicaid has touted the "carrots" of health information technology. Come June 30, it will start using one of its first "sticks."

Physicians have until June 30 to report on the use of electronic prescribing under Medicare Part B or apply for a hardship exemption (see box for details). Those who fail to do so face a 1.5% reduction in Medicare payments starting Jan. 1, 2013.

For those who aren't already e-prescribing, the decision will be whether to find an inexpensive e-prescribing program and submit the information necessary to avoid the penalty, or to invest in the transition to a full-scale electronic health record (EHR) system.

For a physician with a 2,000-patient panel whose practice is 40% Medicare, the 1.5% penalty could add up to $3,000-$4,000 in 2013, said Neil Kirschner, Ph.D., senior associate for regulatory and insurer affairs at the American College of Physicians.

Last year, Dr. Jasdip Brar, an internist in Glendale Heights, Ill., thought he was well on his way to successful e-prescribing through the Medicare eRx Incentive Program, but the EHR that came free with his billing system never sent the appropriate G codes. He's still waiting to hear from the CMS to find out if it will accept his backup documentation as proof of e-prescribing.

"My experience has been kind of rough," said Dr. Brar, who feels like a "point-and-click data entry clerk."

The American Academy of Dermatology conducted a survey at the end of 2011, and found that the participation rate for the electronic prescribing incentive program went from 24% in 2009, to 58% in 2011, to 67% in 2012 (those planning to participate), according to Dr. Mark D. Kaufmann of the dermatology department at Mount Sinai School of Medicine in New York.

COURTESY MICHELLE KALLEVIK OF THE ADVENTIST GLENOAKS HOSPITAL FOUNDATION

**Dr. Jasdip Brar describes his e-prescribing transition as "kind of rough."**

"I think it is becoming obvious that the whole eRx program was used as 'training wheels' for the Holy Grail – EHR adoption. That is why an exclusion was developed for those implementing an EHR, and why the eRx penalties sunset in 2014, just when the penalties for the EHR incentive program get started," said Dr. Kaufmann.

Those physicians who do adopt EHRs seem to be doing a better job of e-prescribing. Surescripts, which operates the nation's largest health information network, found higher utilization of e-prescribing among EHR users than among physicians with standalone e-prescribing systems. ■

## The Fine Print of E-Prescribing

Under the Medicare Electronic Prescribing (eRx) Incentive Program, eligible providers must submit information on at least 10 e-prescriptions on their Medicare Part B claim forms between Jan. 1 and June 30. The information must be submitted using either a qualified e-prescribing program or a certified EHR. The claim form must include the e-prescribing G code (G8553).

Small group practices participating in the eRx Group Practice Reporting Option must submit codes for 625 e-prescriptions. Large group practices participating in the program are required to submit codes for 2,500 e-prescriptions.

Individuals who are unable to submit information on at least 10 e-prescriptions can seek a hardship exemption under a few circumstances:

- ► If they cannot e-prescribe because of local, state, or federal laws.
- ► If they will write fewer than 100 prescriptions between Jan. 1 and June 30.
- ► If they practice in a rural area with insufficient high-speed Internet access (use code G8642).
- ► If they practice where there are not enough pharmacies that can receive electronic prescriptions (G8643).

Submit hardship requests to the CMS via the Quality Reporting Communication Support Page by June 30. If the hardship has an associated G code, submit the request through the Communication Support Page or use the G code on at least one claim before June 30.

Those who successfully reported on 25 e-prescriptions in 2011 need not worry about the 2013 penalty.

# Women Top Men by 30% in Melanoma Survival

VITALS

**Major Finding:** Compared with men, women with melanoma showed a consistent advantage of approximately 30% for overall survival, relapse-free survival, disease-specific survival, lymph node metastasis, and distant metastasis.

**Data Source:** A pooled analysis of data from four large, randomized clinical trials involving 2,672 adults with localized melanoma who were closely followed for disease progression was conducted.

**Disclosures:** The investigators reported having no relevant financial disclosures.

BY MARY ANN MOON

FROM THE JOURNAL OF CLINICAL ONCOLOGY

Among patients with stage I or II cutaneous melanoma, women have been found to have a consistent 30% advantage over men in overall survival, disease-specific survival, rate of distant metastasis, rate of lymph node metastasis, and rate of relapse.

"The 30% advantage extends to the whole spectrum of melanoma disease behavior," reported Dr. Arjen Joosse of Erasmus University Medical Center, Rotterdam, the Netherlands, and his associates.

Women with melanoma are known to have higher survival rates than men, but the details of the difference had never been thoroughly explored.

Dr. Joosse and his colleagues examined the issue by analyzing the pooled results of four large, randomized phase III clinical trials of localized melanoma performed by the European Organisation for Research and Treatment of Cancer (EORTC). The trials, which investigated different therapies for the disease, involved detailed medical records and "meticulous" follow-up of 2,672 patients (48% men and 52% women).

"Women exhibited an independent, significant, and consistent advantage of approximately 30%" for overall survival, relapse-free survival, disease-specific survival, time to in-transit metastasis, lymph node metastasis, and distant metastasis, the investigators reported (J. Clin. Oncol. 2012 April 30 [doi:10.1200/JCO.2011. 38.0584]).

This sex-based difference persisted across numerous prognostic subgroups of patients, regardless of the location of the initial lesion, Breslow thickness, the presence or absence of ulceration, and whether the patient underwent sentinel node biopsy or elective lymph node dissection. If the hypothesis about sex differences in melanoma detection, screening, and diagnostic delays were true, there should be marked differences in the discrepancy between men and women across such subgroups; but no such differences were found. Moreover, because women showed both a longer delay before relapse and a higher cure rate, "it seems that whatever the cause of the female advantage may be, it causes both a delay in progression and a larger subset of melanomas being cured in women, compared with men," the researchers wrote.

To explore the hypothesis that estrogen might be the source of women's survival advantage, the investigators classified the female patients by age.

Postmenopausal women (defined as those aged 60 years and older) retained the 30% advantage in overall survival, relapse-free survival, time to lymph node metastasis, and time to distant metastasis, compared with premenopausal women (aged 45 and younger). The advantage for disease-specific survival declined significantly in this analysis, but that may be a chance finding because of the small sample sizes and low event rates in these subgroups.

Thus, estrogen alone cannot account for the sex-based differences in survival. Other factors that may be involved include androgen receptors in melanoma cells; differences in oxidative stress between men and women; differences between the sexes in vitamin D metabolism, because vitamin D levels appear to affect melanoma prognosis; and differences in immune homeostasis.

Unravelling the underlying cause of the survival difference between men and women could point the way to targeted therapies, the investigators noted. ■

# Psoriasis Not Independent Cardiac Risk Factor

BY DOUG BRUNK

FROM THE ANNUAL MEETING OF THE AMERICAN ACADEMY OF DERMATOLOGY

SAN DIEGO – A large study has determined that psoriasis is not an independent risk factor for ischemic heart disease, based on Framingham Risk Scores.

While previous studies have demonstrated that cardiac mortality is increased in patients with psoriasis, it is also known that people with the skin condition have a higher prevalence of smoking, alcohol consumption, obesity, diabetes, and dyslipidemia, researchers reported in a poster session at the meeting.

"Is this increase in ischemic heart disease due to traditional risk factors, or is psoriasis an additional independent risk factor?" wrote the investigators, who were led by Dr. Marian T. McEvoy, in their abstract.

**Psoriasis patients are more likely to smoke, drink, and be obese, and have diabetes and dyslipidemia than those without it.**

DR. McEVOY

They performed a population-based analysis of 1,338 adults with psoriasis who resided in Olmstead County, Minn., between 1998 and 2008 to evaluate the validity of the Framingham Risk Score (FRS) in predicting the incidence of ischemic heart disease in the study cohort. The FRS is a validated measure of standard ischemic heart disease risk factors.

Dr. McEvoy, a dermatologist at the Mayo Clinic in Rochester, Minn., and her associates compared the risk of cardiac death and myocardial infarction based on the FRS with the actual incidence of myocardial infarction and cardiac death in the study population, which was limited to patients older than age 30 but younger than age 80. They used Poisson regression models and standardized incidence ratios for statistical analysis.

The researchers reported that full Framingham risk factors were available for 974 of the 1,338 patients (73%). They predicted that the median 10-year risk of cardiac events based on the FRS was 3.8%, while the observed 10-year risk of cardiac events was 5.5%. However, there were 44 observed cardiac events compared with 47.7 FRS-predicted cardiac events, which translated into a standardized incidence ratio between the two groups of 0.9. Standardized incidence ratios also showed no statistically significant differences between the two groups when analyzed by gender, by age greater than 65 years, by age less than 65 years, and by whether patients were receiving systemic treatment or not.

"If psoriasis was an independent risk factor for ischemic heart disease, the observed incidence of cardiac events would have been in excess of predicted," the researchers wrote in their poster. "Since there was no statistical difference between actual and predicted events, psoriasis is not an independent risk factor for ischemic heart disease."

In a later interview, Dr. McEvoy acknowledged limitations of the study, including the fact that the small number of observed cardiac events (44) limited the statistical power of the study. "Since this is a retrospective study, we did not have a good tool to assess severity of psoriasis," she said. "We used surrogates based on therapy to identify those with 'more severe disease.' The Framingham Risk Score was valid for this group also." ■

**VITALS**

**Major Finding:** Among adults with psoriasis who were studied over a 10-year period, there were 44 observed cardiac events, compared with 47.7 cardiac events predicted by the Framingham Risk Score, which translated into a standardized incidence ratio between the two groups of 0.9.

**Data Source:** A study of 1,338 adults with psoriasis who resided in Olmstead County, Minn., between 1998 and 2008.

**Disclosures:** The study was partially funded by a grant from Pfizer, and was made possible by a grant from Amgen/Wyeth and by the Rochester Epidemiology Project.

ALAN ROCKOFF, M.D.

# Under My Skin
# Quality Control

I asked a new acquaintance what he does for a living.

"We make call center software," he said. "When you hear, 'This call may be monitored or recorded for quality and training purposes,' – that's us."

"How do you monitor quality?" I asked.

He ticked off several measures: efficiency, productivity, courtesy, and so forth. "All employees get a report card every day, showing where they stand on several parameters."

"So your quality-control software helps them do their job better," I said.

"Of course," he replied. "If they're falling short, they meet with a supervisor who reviews calls with them in person, step-by-step, so they see what they need to work on."

That sounds sensible enough. It stands in stark contrast to the way we are measured.

I've previously written about how some insurance companies have rated me Tier I (hooray!), then how one of them demoted me to Tier II (the shame!), saddling their patients with a higher copay for choosing a less-efficient, lower-quality doctor like me.

Then last month, I got this year's rating from one of the insurers – still Tier I (hooray!). Showing either that I really persevere or that I refuse to learn from experience, I wrote the medical director who had signed this latest report card:

Thank you for my grade. Could you please help me understand two criteria on which I seem to have excelled: 1) "fungal infection w/o surgery" and 2) "skin cancer, major, w/o surgery." Is there a fungal infection w/surgery? Should there be a major skin cancer w/o surgery? Thanks so much.

To my gratified astonishment, he actually called me!

"As to the two episode treatment groups you questioned," he said, "a diabetic with actinomycosis may need amputation. 'Fungal infection without surgery' would refer to less severe fungi. As to 'skin cancers, without surgery,' that just means you performed a biopsy or simple excision, not Mohs or reconstructive surgery."

I thanked him for the clarification, but pressed on. "For fungal infections," I said, "I make a diagnosis and prescribe a generic cream or, occasionally, prescribe an oral treatment. I rarely do a KOH prep, and in any case don't bill for it because it's not covered. Once in a great while I send a nail biopsy or, even more rarely, a culture. As for skin cancers, I do a biopsy to make the diagnosis, and then either perform a simple removal or send the patient elsewhere.

"If I wanted to improve my performance," I concluded, "how much less could I do?" He had no answer.

"I'm happy you rated me Tier I," I said, "though another insurer rated me Tier II on the basis of the same data. When I asked to see those data, they sent me a spreadsheet with 4,700 rows, half with missing demographics, and 27 columns, each with indecipherable acronyms. Can you honestly tell me that my report card gives me what I need to become a better doctor?" Again, he had no answer.

"I'll tell you what I think," I went on, "You don't send these reports to improve doctors' performance, which they obviously can't. You send them so you can tell your investors, your regulators, and possibly yourselves that you are doing something useful to improve medical quality and efficiency, when in fact you're engaged in an empty ritual that does nothing of the kind." For a third time, he said nothing.

My little speech will have no impact, but it felt good. If my call center friend's software doesn't produce results, his firm will lose sales, revenue, and market share. He, therefore, has to make a product that delivers. ■

DR. ROCKOFF *practices dermatology in Brookline, Mass. To respond to his column, send an e-mail to sknews@elsevier.com.*

## COMMENTARY

# Tattoo You

LARRY GREENBAUM, M.D.

Patient tattoos have always interested me, and this sometimes leads to unexpected discoveries. I've seen plenty of older men, (that is, anyone older than me) with naked women tattooed on their arms. Presumably these tattoos are souvenirs of their wild youth.

One patient has a Celtic cross of protection on his right upper arm. I asked him about it once, and he told me he used to be a cop. He felt more secure with this image permanently on his arm.

I've seen a number of biblical verses too, some of them positioned in less than modest places on the physique. I wonder if it is still called a "tramp stamp" if it comes from the good book.

For a while, it was fashionable to have "love" inscribed on the knuckles of one hand and "hate" on the other hand. I've had a few patients with these tattoos. Flowers and butterflies are generally passé, but foreign language tattoos are interesting. Oriental calligraphy can be lovely, but Hebrew can be tricky. I've seen a few tattoos that had problems because either the tattoo artist, or the tattoo recipient, or both, didn't know that Hebrew goes from right to left, creating an unintentional tattoo dyslexia.

One of my patients has a tattoo of a heart pierced by a dagger dripping blood. He used to consider me a miracle worker because his arthritis improved so nicely with methotrexate and prednisone. He often embarrassed me by referring to me as "Dr. God." In general he was polite to the point of being deferential.

We got along quite well, but then one day he called the office and insisted that I immediately see his wife, also my patient and a heavy smoker, because she was short of breath. My schedule was full and the office nurse offered an appointment with a nurse practitioner. He began yelling that his wife was too short of breath to speak in full sentences and that he was bringing his wife to our office for immediate attention.

As providence had arranged things, Dr. God had a cancellation. After I took one look at his wife, I wished he had taken her to the ER. She was gray, dyspneic, weak, and quite drowsy. She had lost 25 pounds since I last saw her, and her husband informed me that she still smoked two packs a day. I was worried about heart failure, pulmonary embolus, and stroke, but quickly decided this was most likely emphysema.

"I've been in business for 25 years and I know when I'm not being treated right," the man stormed at me.

Then I recalled his tattoo and that he had once confided to me it was a Mafioso tattoo, and that it was "real." He seemed rather pleased explaining this to me, and I didn't ask for any documentation of his right to sport this symbol.

I began to wonder if the mafia has customer service representatives. "All of our assassins are assisting other callers. Your call is very important to us, please stay on the line."

He thought that his wife's condition should guarantee her immediate care. I tried to explain that our office was ill equipped to deal with emergencies.

In a convoluted way it was a compliment that he thought Dr. God's office was the best place to bring his breathless wife. In reality, his reaction was just pigheaded and stupid.

He didn't buy my arguments, and warned me that I didn't want to see him lose his temper. And, yes, he reminded me about his tattoo. ■

DR. GREENBAUM *is a rheumatologist who practices in Greenwood, Ind. You may reach him at sknews@elsevier.com.*

**Correction**

In the article "Instant Glue Safely, Effectively Thwarts Onychotillomania" (February 2012, p. 26), the first name of Dr. Daniel S. Ring was misspelled.

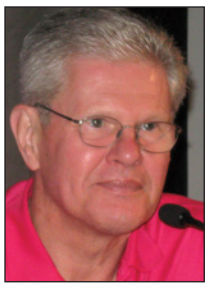
# Topical Botulinum, in Phase III Testing, Predicted to Upend Wrinkle Treatments

BY BRUCE JANCIN

EXPERT ANALYSIS FROM THE SDEF HAWAII DERMATOLOGY SEMINAR

WAIKOLOA, HAWAII – Topically applied botulinum toxin type A may no longer be a pipe dream, as it is now likely full speed ahead for proposed phase III trials of the agent.

The completed phase II program consisted of 11 clinical studies in which 553 patients had their lateral canthal lines treated with the investigational topical product known for now as RT001, under development by Revance Therapeutics. The results were highly impressive, according to Dr. Alastair Carruthers, a dermatologist at the University of British Columbia, Vancouver.



"Watch out for topical botulinum toxin. I think Revance is going to turn the neurotoxin market upside down," he predicted at the seminar, sponsored by Skin Disease Education Foundation (SDEF).

Revance has developed a proprietary platform that enables transcutaneous flux of large medicinal payloads. The company has reported successful proof-of-concept studies for topically delivered insulin, growth factors, and numerous other macromolecules with applications in fields ranging from cardiovascular disease to cancer. But it's the topical botulinum toxin project that has captured Dr. Carruthers' attention.

"Their technology enables you to get the neurotoxin across intact skin, which is something I never thought that we would see. But it really works," he said.

No significant adverse events occurred in the phase II studies. There was no evidence of diffusion of neurotoxin away from the target muscle, and no effect upon the cranial nerves, he said. Laboratory monitoring and ECGs did not yield any evidence of systemic exposure.

**The neurotoxin is able to get across intact skin, 'which is something I never thought that we would see.'**

DR. CARRUTHERS

The median duration of therapeutic effect was 113 days. The response rate was up to 89% based upon a stringent composite end point requiring a 2-point improvement as assessed independently by investigator and patient, he said.

The proposed commercial product that will undergo phase III testing entails mixing the viscous topical gel in a one-step applicator, which is then used in treating the lateral canthal lines. The mixing and application takes only a couple of minutes. The gel is left on for perhaps 30 minutes – the optimal time is yet to be determined – and then removed with a proprietary cleanser.

Dr. Carruthers said that as many know, increasing competition has arrived among the manufacturers of the three Food and Drug Administration–approved injectable botulinum toxin type A products.

"I doubt that the battle, such as it is, will be fought on intellectual, scientific issues. I think it will be fought based upon cost, marketing, and other intangibles," he predicted. Brand loyalty, company sponsorship of medical education, appeals to nationalism – one manufacturer is U.S.-based, the others German and French – these are the sorts of issues he expects to see brought forth.

That's because the things that really matter to clinicians, such as onset of therapeutic effect, its spread, duration, and side effects, are all a function of dose – and there is no agreement as to what the comparable dose is between the various commercial preparations. Despite manufacturers' claims, it's not possible to detect small differences in effectiveness, immunogenicity, or other end points without doing studies that would require enormous numbers of patients, according to Dr. Carruthers.

Dr. Carruthers reported that he has no financial relationship with Revance. He is a consultant to, and paid investigator for, Allergan and Merz, which market Botox and Xeomin, respectively.

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# Ablative Laser Remodeled Scar Collagen

BY SHARON WORCESTER

FROM THE ANNUAL MEETING OF THE AMERICAN SOCIETY FOR LASER MEDICINE AND SURGERY

KISSIMMEE, FLA. – Treatment with a 2,940 Er:YAG ablative fractional laser led to a clinically significant reduction of third-degree burn scars in a prospective study of 11 patients.

Clinical and histologic findings from the laser study provide important clues as to the mechanism of action and appropriate treatment intervals, Dr. Jill S. Waibel reported at the meeting. Scars from fire or thermal injury are among the worst that are seen in clinical practice, and although fractional laser therapy is emerging as the preferred treatment for these injuries, a better understanding of the optimal laser wavelengths, clinical response patterns, scar tissue response, and histologic changes will improve outcomes.

Patients in this study underwent three ablative treatments at 4-week intervals, and – based on blinded evaluation by independent investigators – were found to have an overall modified Manchester score of 2.3 out of 3 points, indicating moderate to excellent improvement. The scores for dyschromia, hypertrophy reduction, vascularity, and scar texture improvement were 1.7, 1.9, 2.0, and 2.0, respectively, indicating mild to moderate improvement, said Dr. Waibel, a physician in private practice in Miami.

The patients, who had third-degree burn scars over an average of 80% of their bodies, were treated with one pass at depths ranging from 400 to 800 microns.

On biopsies taken at baseline, the scars were noted to have thickened, homogenized, dystrophic collagen structures; and on biopsies taken 3 months after the final treatment, a decrease in these dystrophic fibers was seen.

Dr. Waibel hypothesized that scar improvement resulted from the complete replacement of ablated zones by newly synthesized collagen and that the collagen remodeling led to more normal-appearing skin.

She noted that the erbium laser is "very powerful" and caused a great deal of erythema in two patients, leading her to "turn the power down" over the course of the study. Although no worsening of scars was seen, the increased vascularity in the two patients suggested that intervals longer than 4 weeks between treatments – perhaps to between 2 and 3 months - may be warranted.

Although additional study is needed, the findings suggest that the 2,940 Er:YAG laser is effective for clinically improving burn scars. ■

**VITALS**

**Major Finding:** Based on blinded evaluation by independent investigators, patients had an overall modified Manchester score of 2.27 out of 3 points, indicating moderate to excellent improvement.

**Data Source:** A prospective study of 11 patients with third-degree burn scars who underwent three ablative treatments at 4-week intervals.

**Disclosures:** This study was funded by Sciton. Dr. Waibel said she had no other relevant financial disclosures.

**VIEW VIDEO ONLINE**

To view a video interview with Dr. Waibel, scan the QR code or visit www.skinandallergynews.com.

# New Cellulite Therapies Target Fibrous Septae

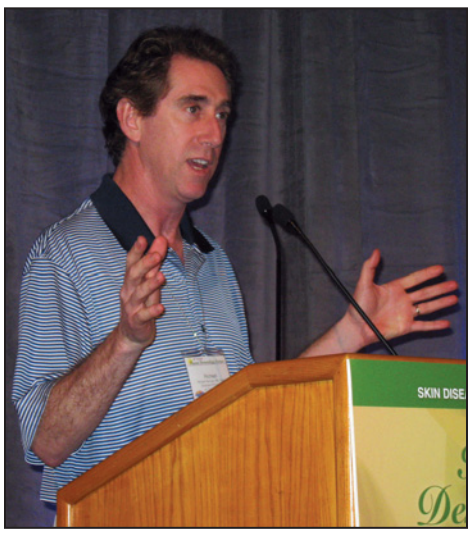
BY BRUCE JANCIN

EXPERT ANALYSIS FROM THE SDEF HAWAII DERMATOLOGY SEMINAR

WAIKOLOA, HAWAII – Cellulite therapy may be moving out of the dark ages of overhyped claims made on behalf of interventions of little or no value to an era of treatments that work.

And what appears to work, according to Dr. Michael S. Kaminer, are therapies that cut the fibrous septae tethering the dermis to deeper tissues.

"I think it's likely that the vertical pull of the fibrous septae tends to pull down on the cellulite in the skin and causes the cellulite dimples," he explained at the seminar sponsored by Skin Disease Education Foundation (SDEF).



Bruce Jancin/IMNG Medical Media

**"Until very recently, there was absolutely no reason to pay attention to cellulite," Dr. Michael S. Kaminer said at the seminar.**

The fibrous septae theory of the etiology of cellulite is relatively new. It has gained substantial credence as a result of encouraging clinical trial data showing long-term effectiveness for two devices targeting cellulite via severing fibrous septae: the Cellulaze 1,440-nm Nd:YAG laser and the Cabochon Aesthetics controlled subcision system for subdermal undermining, according to Dr. Kaminer, who is a managing partner at SkinCare Physicians, Chestnut Hill, Mass.

Cellulaze, developed by Cynosure, recently received Food and Drug Administration marketing approval for the treatment of cellulite. The Cabochon device for subcutaneous release of fibrous septae is still in clinical trials.

"Until very recently, there was absolutely no reason to pay attention to cellulite except to counsel patients as to the fact that they shouldn't waste their money," Dr. Kaminer said.

The situation has changed with the emergence of fibrous septae as the prime therapeutic target. Cellulaze can be used for laser lipolysis; however, in addition, the handpiece for the cannula can be turned in such a way that the laser beam can be used like a saw to cut through the fibrous septae, with resultant long-term improvement in cellulite.

In U.S. clinical trials, the average increase in skin thickness following Cellulaze therapy was 23% at 1 month and 27% at 1 year. Skin elasticity improved over baseline by 32.5% at 1 month and 21% at 1 year. Sixty-eight percent of patients demonstrated significant improvement in cellulite based upon analysis of photographs, as did 65% when assessed by Vectra 3D surface imaging.

Patients rated the results as good to excellent at 1 month in 76% of cases. Physicians judged the results as good to excellent in 69% of cases. The results have held up at 1 year of follow-up, noted Dr. Kaminer, who also is with the dermatology departments of Yale University, New Haven, Conn.; Dartmouth College, Hanover, N.H.; and Brown University, Providence, R.I.

The downside of Cellulaze is that it is an invasive therapy that requires tumescent anesthesia. And given that the history of the field of cellulite therapy is one of hype far in excess of reality, Dr. Kaminer indicated that a healthy skepticism is appropriate. "For me, I'm going to approach this with caution. ... I'd like to see it around for a little longer before we all jump on the bandwagon."

The Cabochon system draws a small section of skin affected by cellulite into a handpiece so that a percutaneously inserted cutting tool can be utilized to cut the fibrous septae. Dr. Kaminer was an investigator in a two-site, 56-patient clinical trial with a 6- to 12-month follow-up.

In independent blinded physician review of before and after photos, 78% of patients were judged to have improved at least one full grade in severity at 6 months, such that, for example, those whose cellulite was rated severe at baseline were judged to have moderate or mild cellulite at follow-up.

At baseline, the average cellulite severity score was about 4.5 on a 0-6 scale. At 90 days, the average severity score had dropped to 3, and at 180 days to roughly 2.5. Ninety-four percent of patients were rated by independent physicians as having improved by at least 1 point on the 0-6 scale. Of the 33 U.S. patients followed for 1 year, 87% felt their appearance was improved and 77% were satisfied with their treatment at all time points.

Seroma formation was an issue early on, until investigators realized the problem resulted from treating adjacent sites at the same depth. But once operators began utilizing the device's automated guidance system to vary the cutting depth at adjacent sites seromas were no longer a problem. None of 25 patients treated in this fashion had a seroma in excess of 2 cc 1 month post treatment, said Dr. Kaminer.

He reported serving as a consultant to Cabochon and receiving funding from Cynosure. SDEF and this news organization are owned by Elsevier. ■

# Cosmeceutical Critique

# Red Light for Acne

LESLIE S. BAUMANN, M.D.

Several light devices based on red light–emitting diodes (LEDs) have made their way to the market in recent years. Although red light is not truly a cosmeceutical, it is a significant emerging adjuvant therapy that, like blue light, has been studied in comparison to and in conjunction with topical options primarily to treat acne. Of course, acne is the most common skin disorder prompting visits to the dermatologist, with an estimated 85% of adolescents affected, many into adulthood (J. Am. Acad. Dermatol. 2008;58:56-9).

This discussion will consider red light when used alone and when used in combination with blue light. Blue light is the most effective light to target *Propionibacterium acnes* (specifically at wavelengths of 407-420 nm). However, many devices are utilizing red light because it has a purported anti-inflammatory effect and penetrates deeper into the skin (Dermatol. Ther. 2005;18:253-66).

## Erythrasma

Darras-Vercambre et al. evaluated the effects of red light for the treatment of erythrasma (a superficial skin infection provoked by *Corynebacterium minutissimum*) in 13 patients. One treatment (80 J/cm$^2$) by red light (broadband, peak at 635 nm) without exogenous photosensitizing molecules was administered to each subject. Therapy was effective and well tolerated, with three patients experiencing complete recovery, and significant reduction of lesions in most other cases. The authors noted that the key to their study, given the absence of an exogenous photosensitizing agent, was capitalizing on the presence of porphyrins in the lesions. They concluded that the use of red light alone for this localized infection is easy and inexpensive, but that an optimal method has not yet been established (Photodermatol. Photoimmunol. Photomed. 2006;22:153-6).

## Acne

In 2007, Na and Suh evaluated the efficacy of red light phototherapy with a portable device in 28 volunteers with mild to moderate acne in a split-face randomized trial. Phototherapy was performed twice daily for 15 minutes for a total of 8 weeks to one side of the face. The investigators concluded that red light phototherapy alone is an effective therapeutic option for acne, as they noted significant reductions in noninflammatory and inflammatory lesion counts on the treated side versus the untreated side, a drop from 3.9 to 1.9 in the visual analog scale on the treatment side, and significant disparities between the treatment and control sides after 8 weeks (Dermatol. Surg. 2007;33:1228-33, discussion 1233).

A 2006 article in the British Journal of Dermatology reported good clinical results from acne treatment with photodynamic therapy (PDT) using methyl aminolevulinate (MAL) and red light, but there were adverse side effects that prompted 7 of 19 subjects to discontinue the study (Br. J. Dermatol. 2006;154:969-76). In response to the study, Mavilia et al. wrote a letter to the journal acknowledging their more effective combination therapy using a lower concentration of MAL and low doses of red light. All 16 patients completed the study, in which the count of inflammatory lesions fell an average of 66% with mild but tolerable side effects, including a subtle sensation of heat, then minimal erythema during the procedure and slight scaling that began 3 days after treatment (Br. J. Dermatol. 2007;157:810-1).

In a small study of patients with moderate facial acne, Zane et al. exposed 15 women to 20 J/cm$^2$ of broadband red light (600-750 nm) twice weekly for 4 weeks.

They also measured skin sebum, pH, hydration, and transepidermal water loss (TEWL). Untreated lesions of the trunk served as controls. The investigators found the treatment safe, well tolerated, and effective, with significant improvement in acne lesions and reduction of sebum excretion and TEWL after 4 weeks of therapy and at the 3-month follow-up visit. They speculated that the improvement was due to the decreased colonization of *P. acnes*, decimated by photoactivated endogenous porphyrin, and concluded that this inexpensive therapy warrants inclusion among treatment options for moderate acne (Photodermatol. Photoimmunol. Photomed. 2008;24:244-8).

**Using an at-home device twice a day that delivers 407-420 nm (with or without the addition of red light), and delivers enough joules (at least 25 J/cm$^2$), is an effective method of treating acne.**

In a 2009 study of 19 patients with moderate to severe facial acne who received a single treatment of low-dose, red light PDT on the left cheek and MAL 3 hours before red light on the right cheek, both therapies yielded significant reductions in acne score. Red light was found to be as effective as MAL-PDT (Acta Derm. Venereol. 2009;89:372-8).

## Combined Blue and Red Light Phototherapy

In 2006, Goldberg and Russell evaluated the combination of blue (415 nm) and red (633 nm) LED phototherapy in 24 patients with Fitzpatrick skin types II-V and mild to severe symmetric facial acne. Twenty-two patients completed the trial, which included two sessions per week (separated by 3 days) alternating between blue and red light for a total of eight sessions. Mild microdermabrasion was used at the start of each session. The mean decrease in lesion count was significant after 4 weeks (46%) and 12 weeks (81%). Inflammatory lesions responded better than did noninflammatory ones, and severe acne responded slightly better than mild acne. The investigators concluded that the combination of blue and red LED phototherapy is free of side effects and pain, and exhibits great potential for the treatment of mild to severe acne (J. Cosmet. Laser Ther. 2006;8:71-5).

In 2007, Lee et al. set out to examine the efficacy of combining blue and red LED phototherapy for acne in a study of 24 patients with mild to moderately severe facial acne. Twice weekly for 4 weeks, patients were treated with quasi-monochromatic LED devices, alternating blue (415 nm) and red (633 nm) light. Fourteen patients self-reported improvements in skin tone and texture. Improvements in noninflammatory and inflammatory lesions were substantial (34.28% and 77.93%, respectively). The researchers concluded that combined blue and red LED phototherapy is a safe and effective option, especially for papulopustular acne (Lasers Surg. Med. 2007;39:180-8).

In 2009, Sadick evaluated the efficacy of the combination of blue (415 nm) and near-infrared (830 nm) LED therapy for moderate acne in 13 females and 4 males ranging in skin type from II to VI and in Burton acne grade at baseline from 1 to 5. Twice-weekly 20-minute sessions were conducted for 4 weeks, alternating between blue and near-infrared light. Eleven patients exhibited improvement ranging from 0% to 83.3%, and six patients discontinued the study. A decreasing trend was observed in the Burton grade. Noninflammatory lesion counts improved in seven patients but increased in four. Sadick noted that these results paled in comparison to the effectiveness of the blue and red combination at lowering inflammatory lesions seen previously, but encouraged the study of the combination phototherapy in a much larger population (J. Cosmet. Laser Ther. 2009;11:125-8).

Several recent reviews have found that red light–activated MAL-PDT, the combination of blue and red light, and aminolevulinic acid as a photosensitizing agent before treatment with blue light, red light, or the 595-nm pulsed dye laser are among the most promising evidence-based laser- and light-based therapies for acne (Semin. Cutan. Med. Surg. 2008;27:207-11; J. Eur. Acad. Dermatol. Venereol. 2008;22:267-78; Dermatol. Surg. 2007;33:1005-26).

In a systematic literature review of randomized controlled trials of light and laser therapies for acne vulgaris (using the Cochrane Central Register of Controlled Trials, MEDLINE, Embase, CINAHL, PsycINFO, LILACS, ISI Science Citation Index, and Dissertation Abstracts International), Hamilton et al. found that trials of blue light, blue-red light, and infrared radiation were more successful, especially when multiple treatments were used. Notably, blue-red light demonstrated better short-term effectiveness than did topical 5% benzoyl peroxide cream (Br. J. Dermatol. 2009;160:1273-85).

Kim and Armstrong have noted that blue light has been demonstrated to photoinactivate *P. acnes*, but it does not penetrate deeply into the skin. It is believed to work synergistically, however, with red light, which is less effective than blue light at exciting porphyrins but can reach deeper sebaceous glands and may impart an anti-inflammatory effect by inciting cytokine release from macrophages (Dermatol. Surg. 2007;33:1005-26). Indeed, Kim and Armstrong found that combined blue-red light therapy was more effective at lowering the number of inflammatory acne lesions than were benzoyl peroxide monotherapy and blue light monotherapy (Lasers Surg. Med. 1989;9:497-505).

## Conclusions

A lengthy review of the literature and personal experience treating patients have convinced me that blue light is an effective treatment for acne. *P. acnes* is most susceptible to the blue light wavelengths of 407-420 nm. Addition of red light may help speed resolution of inflammatory lesions through an anti-inflammatory effect. Blue and red light devices are efficacious when used in the office if the devices deliver enough joules.

Many at-home devices and iPhone apps have hit the market. These are a great alternative to irritating topicals and antibiotics, and they may help increase compliance. However, many at-home light devices are too weak (do not emit enough joules), or emit a broad range of light (rather than 407-420 nm).

The manufacturers of some of these products claim that the heat produced by the devices improves acne, but there is a paucity of research proving this point. In my opinion, using an at-home device twice a day that delivers 407-420 nm (with or without the addition of red light), and delivers enough joules (at least 25 J/cm$^2$), is an effective method of treating acne. For comparison purposes, the in-office Omnilux delivers around 49 J/cm$^2$ but is used only two or three times per week. Know your wavelengths and joules when trying to decide which device to sell in your practice or recommend to patients. ■

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DR. BAUMANN *is in private practice in Miami Beach. She did not disclose any conflicts of interest. To respond to this column, or to suggest topics for future columns, write to her at sknews@elsevier.com.*

Pages 14a—14b

# ICG Augmentation Receives High Patient Rating

BY SHARON WORCESTER

FROM THE ANNUAL MEETING OF THE AMERICAN SOCIETY FOR LASER MEDICINE AND SURGERY

KISSIMMEE, FLA. – Indocyanine green–augmented diode laser treatment appears promising for the treatment of both port wine stains and telangiectatic leg veins, preliminary data have shown.

This novel treatment involves an off-label use of the water-soluble indocyanine green fluorescent dye commonly used in medical diagnostics and approved by the Food and Drug Administration for determining cardiac output, hepatic function, and liver blood flow, and for ophthalmic angiography. Indocyanine green has a peak spectral absorption of 800 nm.

VITALS

**Major Finding:** For port wine stains, ICG+DL treatment was slightly, though not significantly, better than FPDL with respect to clearance rates and cosmetic appearance at 12 weeks. For leg veins, vessel clearance was dose dependent, with "good" (40%-50%) vessel clearance in those receiving a radiant exposure of 100-110 J/cm$^2$, and "excellent" (greater than 50%) clearance when double pulses were used.

**Data Source:** A pilot study of 31 patients with port wine stains and a proof of concept study of 15 women with telangiectatic leg veins.

**Disclosures:** The presenters said they had no relevant financial disclosures to report.

## Port Wine Stains

A randomized, controlled pilot study compared indocyanine green–augmented diode laser (ICG+DL) treatment with standard flashlamp-pumped pulsed-dye laser (FPDL) treatment in split-face fashion in 31 patients with port wine stains. After one treatment, two blinded investigators rated ICG+DL treatment as slightly, though not significantly, better than FPDL with respect to clearance rates and cosmetic appearance at 12 weeks' follow-up (Br. J. Dermatol. 2012[doi:10.1111/j.1365-2133.2012.10950.x]). The patients rated the ICG+DL treatment as significantly superior to FPDL on these measures, Dr. Philipp Babilas reported at the meeting.

ICG+DL was applied at 810 nm with a fluence of 20-50 J/cm$^2$, a spot size of 7 mm, a pulse duration of 10-25 milliseconds, and an ICG concentration of 2 mg/kg of body weight; FPDL was applied at 585 nm with a fluence of 6 J/cm$^2$ and a pulse duration of 0.45 milliseconds, he said noting that the treatments were well tolerated.

Complete clearance of port wine stains is rarely achieved, largely because of the resistance of small blood vessels to laser irradiation. Prior studies suggested that the use of ICG with diode laser treatment could overcome this resistance, but in this study, histology revealed that the approach provided photocoagulation only of blood vessels larger than 20 mcm in diameter with collateral damage of surrounding dermal tissue, said Dr. Babilas of University Hospital Regensburg (Germany).

The results were nonetheless intriguing, he said, noting that histology also showed that there was no epidermal damage at 1 week and that complete remodeling of dermal tissue had occurred by 3 months.

Many smaller blood vessels replaced the larger blood vessels, which could be one reason the treatment was not as effective as expected, he said.

The findings, including the patient assessments of outcomes, suggest ICG+DL represents a promising treatment modality for port wine stains – a treatment that may prove even more effective as laser parameters and ICG concentrations undergo further study and optimization. Such studies, including one that is evaluating an increased concentration of indocyanine green, are underway in an effort to enhance results, he added.

The search for improved treatments for port wine stains is important given that available treatments typically provide only partial clearing, that about 20% of cases are resistant to FPDL treatment, and that port wine stains can be associated with significant adverse psychological effects, he said.

## Leg Veins

In a separate proof-of-concept study, Dr. Babilas and his colleagues evaluated ICG+DL for telangiectatic leg veins, which, like port wine stains, are rarely completely cleared. The treatment was evaluated in 15 women with skin types II or III and telangiectatic leg veins of 0.25-3 mm in diameter. After intravenous administration of ICG, diode laser pulses were applied as a single treatment. The treatment was safe, with no persistent side effects, Dr. Annette Klein, also of University Hospital of Regensburg, reported.

ICG+DL in this study was applied at 808 nm, with a fluence of 50-110 J/cm$^2$ and an ICG concentration of 2 mg/kg of body weight (Lasers Surg. Med. 2012[doi:10.1002/lsm.22022]). Vessel clearance was dose dependent, with "good" (40%-50%) vessel clearance in those receiving a radiant exposure of 100-110 J/cm$^2$ and "excellent" (greater than 50%) clearance when double pulses of the diode laser were used, Dr. Klein said, noting that vessel clearance was rated only as "poor" or "moderate" (only up to 25%) with pulsed-dye laser, which was used in this study as a reference treatment.

"We conclude that ICG-augmented diode laser therapy is a safe and effective new therapy option for the treatment of spider leg veins, and double pulses improved our results," she said, noting that follow-up studies to identify the optimal ICG concentration and laser parameters are underway. ■

# Port Wine–Stain Hypertrophy Common in Patients Over 50

BY SHARON WORCESTER

FROM THE ANNUAL MEETING OF THE AMERICAN SOCIETY FOR LASER MEDICINE AND SURGERY

KISSIMMEE, FLA. – Hypertrophy of port wine stains is more common than not in the majority of patients older than age 50 with the vascular anomaly, and is most often associated with red and purple lesions, according to findings from a retrospective patient-questionnaire study.

"By the age of 50, over 70% had hypertrophy of their port wine stain," said Dr. Anne Margreet van Drooge of the Netherlands Institute of Pigment Disorders at the University of Amsterdam.

VITALS

**Major Finding:** Of the 335 patients included in the review, 68 had hypertrophy of their port wine stains.

**Data Source:** The study was a database review of patients with port wine stains who were referred to a single outpatient clinic between 2005 and 2009.

**Disclosures:** Dr. van Drooge had no disclosures to report.

Hypertrophy is known to be fairly common in port wine stains, but data are lacking on its pathogenesis and development. In this study, the incidence of hypertrophy in port wine stains was about 20% in all patients, and both color and hypertrophy were frequently reported as reasons for seeking treatment.

Only 4% of all hypertrophy cases were associated with pink lesions, Dr. van Drooge said at the meeting.

Of the 335 patients included in the review, 68 had hypertrophy, classified as thickening, nodular, or both. Cases were divided almost equally into age groups of under 18 years, 18-30 years, and greater than 30 years. The median age of those with hypertrophic port wine stains was 50 years, and the median age at the time of hypertrophic development was 31 years, although the ages of onset of nodular hypertrophy and diffuse thickening were 39 years and 12 years, respectively. Nodular hypertrophy was rarely seen in those younger than 18 years.

In all study patients, most of the port wine stains were on the face. Half were red in color, and 44% were purple. No differences were seen between those with and without hypertrophy with respect to gender, lesion size, or lesion location, she noted.

Patients included in the study had been referred to a single outpatient clinic between 2005 and 2009. Medical records and photographs were examined to identify and characterize hypertrophic port wine stains.

PHOTOS COURTESY DR. ANNE MARGREET VAN DROOGE

**Both darker color in a port wine stain and older age were significantly linked to hypertrophy, seen here in a 55-year-old male (left) and a 78-year-old male.**

The findings of different ages at onset for different types of hypertrophy suggest that unique pathomechanics may exist for each type, Dr. van Drooge said. "There is definitely a correlation between the color of the port wine stain and the risk for the development of hypertrophy. In a multivariate analysis of all patient characteristics, we found that both darker color and older age were significantly associated with hypertrophy, independent from each other."

Improved understanding of hypertrophy in port wine stains is important given the adverse psychosocial effects these lesions can have on patients; in this study, 5% of patients said they avoided social interaction because of their port wine stain, she noted, adding that the findings have implications for treatment.

Although this study provided no direct support for the notion that treatment may prevent hypertrophy, some studies have suggested that it may, adding that treatment guidelines should be adapted to include more emphasis on hypertrophy and its prevention, keeping in mind the findings of this study with respect to age and lesion color.

"However, I don't think it is possible to treat only darker port wine stains in the effort to prevent hypertrophy, since pink port wine stains – particularly in younger patients – eventually can darken, and with that, the risk for hypertrophy increases," she noted. ■

# Laser, Light Combo Offers Results in Single Session

BY SHARON WORCESTER

FROM THE ANNUAL MEETING OF THE AMERICAN SOCIETY FOR LASER MEDICINE AND SURGERY

KISSIMMEE, FLA. – The combined use of a nonablative, fractional 1,540-nm laser and optimized pulsed light provided significantly greater improvement in dyspigmentation after a single treatment session, compared with the 1,540-nm laser alone, based on findings from a study comparing the two treatments in 36 patients.

The observation of improved pigment after a single treatment in the combination group represents a reduced time course for achieving outcomes; typically, several treatments are required to produce results, Dr. Chung-Yin Stanley Chan said at the meeting.

The novel combined approach to facial rejuvenation also modestly improved wrinkles, although this outcome did not differ significantly between the two groups, Dr. Chan and his colleagues noted.

The mean pigment improvement score in the 10 subjects assigned to the combination treatment group was 2.4 points on a 1- to 4-point scale, indicating at least 50% improvement, with 96% of patients in that group experiencing improvement. The mean pigment improvement score in the 26 subjects assigned to the laser-only treatment group was 1.2 points.

Fitzgerald wrinkle scores improved from 6.4 to 6.0 (on a scale of 1-9) in the combination group, and from 5.3 to 4.9 in the laser-only treatment group, said Dr. Chan, a dermatologist in private practice in Chestnut Hill, Mass., where the study was conducted.

Both groups received treatment with an Er:Glass laser (at 1,540 nm, with 50 mJ/microbeam and a 15-millisecond pulse duration), and the combination group also received treatment with optimized pulsed light (operated at 500-670 nm and 870-1,200 nm, with a fluence of 32 J/cm$^2$, and with a 20-millisecond pulse duration). The order of treatment in the combination group was randomized, and the order had no effect on the outcome. However, treatment was better tolerated when optimized pulsed light was applied first, followed by the laser treatment, Dr. Chan noted.

The side effects were similar in the two groups, and included only effects "that would be expected with nonablative fractional laser treatment," he said, explaining that erythema and edema occurred in all patients, flaking and xerosis occurred in some patients, and postinflammatory hyperpigmentation was extremely rare. "In fact, all side effects resolved within 1 month, and most resolved within 1 week," he said, adding that no difference was seen in the incidence of adverse effects between the combination and laser-only treatment groups.

All patients reported being satisfied with the outcome, and most reported being "very satisfied," he said.

Outcomes were assessed by three blinded dermatologists trained in the evaluation of wrinkles and pigmentation, one of whom was Dr. Chan. The dermatologists compared clinical photographs taken at baseline and at 1 month following treatment.

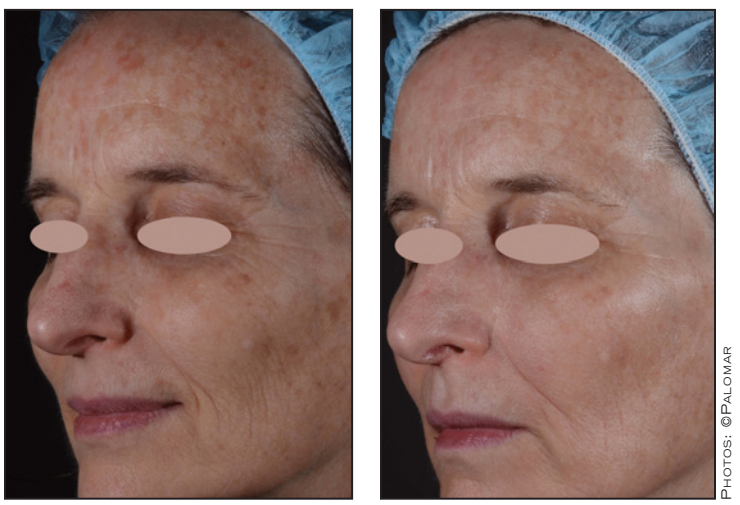
A single treatment with this combined approach to facial rejuvenation can lead to modest improvement in wrinkles and significant improvement in pigmentation, he concluded, noting that multiple treatments using this combined approach could hypothetically lead to further improvements. ■

**VITALS**

**Major Finding:** The mean pigment improvement score in the 10 patients assigned to the combination treatment group was 2.4 points on a 1- to 4-point scale, compared with 1.2 points in the 26 patients assigned to the laser-only treatment group.

**Data Source:** A study comparing combined 1,540-nm laser treatment and optimized pulsed light with 1,540-nm laser treatment alone for facial rejuvenation.

**Disclosures:** This study was sponsored by Palomar. Dr. Chan said he had no other relevant financial disclosures.



PHOTOS: ©PALOMAR

**A patient is shown before (left) and 1 month after undergoing treatment with the combined use of a nonablative, fractional 1,540-nm laser and optimized pulsed light.**

# Broadband Light Halted Signs of Aging in Small Study

BY SHARON WORCESTER

FROM THE ANNUAL MEETING OF THE AMERICAN SOCIETY FOR LASER MEDICINE AND SURGERY

KISSIMMEE, FLA. – Broadband light therapy virtually halted the signs of aging in women treated at least annually for 8 years, according to Dr. Patrick Bitter Jr.

"This really is the closest thing we have to a fountain of youth for delaying skin aging," Dr. Bitter said.

Eleven women underwent treatment of the entire face with the Sciton BroadBand Light system at least once a year over an 8-year period. Blinded evaluators (490), including 51 dermatologists, indicated that the women aged no more than about 6 months during that time, said Dr. Bitter, a dermatologist in private practice in Los Gatos, Calif.

The mean age of the women at the start of treatment was 45 years, and the dermatologists who participated in the evaluations of "before" and "after" photographs rated their age as a mean of 45 years based on the "before" images. At an average of 8 years follow-up, the evaluators rated the age of the participants at a mean of 45 to 45.5 years, which was a mean of 9 years younger than the participants' actual ages, he said.

Study participants included women in Dr. Bitter's practice who received at least one treatment annually with good "before" photos who had not received any laser treatments or cosmetic surgery. Skin care regimens varied among the women.

The evaluators – only the dermatologists' responses were included in the data Dr. Bitter presented –were blinded to any treatments the women underwent, and photos were taken in a way that ensured the evaluation was based entirely on skin appearance and not on other signs of aging (such as graying hair), he noted.

Broadband light technologies are known to be effective for reversing the signs of aging, such as wrinkles, redness, and brown spots, and data have shown that broadband light can improve the skin histologically. However, this is the first blinded evaluation of long-term results among those receiving regular treatments, Dr. Bitter said, noting that this study was prompted in part by a Swiss study published several years ago that speculated that such treatments might actually accelerate aging of the skin when used over time.

His experience in 14 years of using broadband light treatments suggested otherwise, and these findings provide further evidence that long-term use reverses and prevents the signs of aging, he said.

New data from a corollary study to be presented at an upcoming meeting of the Society for Investigative Dermatology will provide additional evidence that light "does more than just make reds and browns go away," he said. "What is seems to do is make skin cells behave like younger skin cells."

Dr. Bitter noted that the difference between a patient's really liking results and not seeing a difference is technique. "This is a great technology, buy you need to know how to use it," he said, explaining that it is important to know the optimal parameters based on skin type, to perform enough passes at each session, and to conduct enough sessions.

In an interview, Dr. Robert A. Weiss of the department of dermatology at Johns Hopkins University, Baltimore, agreed that the technique is critical to success. "Continued sun protection is critical, as well," he said.

Like Dr. Bitter, Dr. Weiss has seen effective long-term results with intense pulsed light technology. In a study published in 2002, he and his colleagues reported on 80 randomly selected patients with skin types I-IV who were treated with filtered flashlamp intense pulsed light between 1996 and 1997. At 4-year follow-up after the first of a median of three treatments, 83% of patients had improved skin texture, 82% had improved telangiectasias, and 79% had improved pigmentation (Dermatol. Surg. 2002; 28:1115-9).

**Technique and continued sun protection are critical to treatment success.**

DR. WEISS

"The end result is clearer, brighter, younger, healthier-looking skin," Dr. Weiss said. ■

**VITALS**

**Major Finding:** After 8 years of at least once-a-year treatment, the women in the study were rated as appearing a mean 9 years younger than their actual age.

**Data Source:** This was a blinded evaluation of long-term outcomes with regular broadband light therapy in 11 women.

**Disclosures:** Dr. Bitter owns the trademark for FotoFacial intense pulsed light treatments. Dr. Weiss reported at the time his study was published he was a consultant and preceptor for Lumenis, and that the devices used in the study were purchased at a discount.

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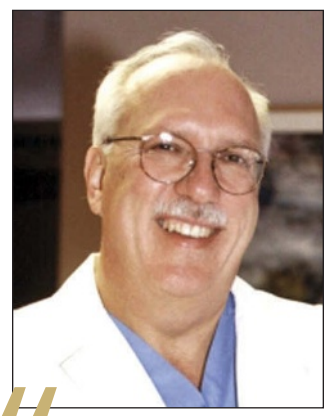
# 60 Years and Counting: A Celebration Of Dermatologic Surgery Milestones

BY SHARON WORCESTER

FROM SEMINARS IN CUTANEOUS MEDICINE AND SURGERY

*"Dermatologic surgery is an important component of nearly all dermatology postgraduate courses."*
–Dr. Hanke



*"The concept of augmentation has moved from simple lines, scars, and wrinkles to revolumizing the aging face."*
–Dr. Glogau

*"The development of fractional photothermolysis was "a milestone in the history of laser technology and cutaneous resurfacing."*
–Dr. Saedi

It was questionable whether in 1952, when Dr. Norman Orentreich performed the first hair transplant and Dr. George Mackee reported on his 50-year experience with phenol chemical peels, anyone envisioned how far the field of dermatologic surgery would advance, but there's no question now: The specialty has come a long way.

"Dermatologic surgery has blossomed into a full and diverse specialty with many elements," Dr. C. William Hanke noted in the June issue of Seminars in Cutaneous Medicine and Surgery (2012;31:52-9). He highlighted key events that shaped the burgeoning specialty.

## Historical Highlights

From the first report on phenol peels by Dr. Mackee (Br. J. Dermatol. 1952;64:456-9), to the coining of the term "tumescent local anesthesia" by Dr. Hanke and his colleagues in 1998 – and publication of a comprehensive text on the tumescent technique 2 years later by Dr. Jeffery A. Klein ("Tumescent Technique: Tumescent Anesthesia and Microcannular Liposuction," St. Louis, Mosby, 2000) – Dr. Hanke chronicled the specialty's evolution.

For example, he noted that in 1961, Dr. Leon Goldman became the first physician to treat patients with lasers. "He is acknowledged as the father of lasers in medicine and surgery," Dr. Hanke, a dermatologist in private practice in Carmel, Indiana, wrote. He added that the pioneer's first medicinal use of a laser launched 3 decades of related leadership, practice, and research.

Among other events that stand out in the history of the specialty, according to Dr. Hanke, are the first reports on cryosurgery with liquid nitrogen in 1966 by Dr. Setrag Zacarian ("Cryosurgery of Skin Cancer and Cutaneous Disorders," St. Louis, Mosby, 1985), and on ambulatory phlebectomy by Dr. Robert Muller the same year (Phlebologie 1966;19:227-9).

And, in 1967, Dr. Frederic E. Mohs founded the American College of Chemosurgery, which is today known as the American College of Mohs Surgery. "Mohs surgery continues to be an important part of the dermatologic surgery curriculum," Dr. Hanke said.

Advancements in vein ablation took pace in 1982 when the first report on hypertonic saline injections for treating leg veins, by Bruce Chrisman, was published (Hawaii Med. J. 1982;41:406-8).

In 1986, Dr. Saul Asken published the "Manual of Liposuction Surgery and Autologous Fat Transplantation Under Local Anesthesia" (Terry and Associates, Irvine, Calif.), and the following year, Dr. Jeffery A. Klein published the first report on the tumescent technique for liposuction (Am. J. Cosm. Surg. 1987;4:263-7).

Dr. Alastair Carruthers and Dr. Jean Carruthers revolutionized the field in 1987 when they began using botulinum toxin for cosmetic purposes. "Their joint observation that botulinum toxin can affect the muscles of facial expression began a revolution in cosmetic dermatology," wrote Dr. Hanke.

He also highlighted the launch of numerous societies and publications that helped to advance the specialty, including the founding of the American Society for Dermatologic Surgery in 1970, the launch of the Journal of Dermatologic surgery in 1975, and the founding of the American Society for Lasers in Medicine and Surgery in 1981. And the specialty has continued to evolve at a rapid pace since that time, he noted.

Work by Dr. R. Rox Anderson and Dr. John A. Parrish on selective photothermolysis, for example, launched research leading to the fractionated laser technology in use today; and ongoing work by the Carruthers on botulinum toxin launched a new era in noninvasive facial rejuvenation, he said.

"Facelift bypass" procedures have satisfied many patients without subjecting them to the expense or morbidity of extensive facial surgery, Dr. Hanke noted, adding that new filler materials can be placed in the subcutaneous or supraperiosteal planes of the face with good results and minimal complications.

"A newly approved hyaluronic acid from Germany will allow treatment of very superficial wrinkles without the risk of the 'Tyndall effect,' " he added.

Also in the last decade, dermatologic surgery–related educational initiatives have been advanced. In 2004, 1-year fellowship training programs were approved by the Accreditation Council for Graduate Medical Education for training in dermatologic surgery; and last year, there were 47 ACGME-accredited procedural dermatology fellowship training programs in place, he said.

"Dermatologic surgery is an important component of nearly all dermatology postgraduate courses," added Dr. Hanke.

The history of fractional laser technology and fillers was addressed in separate articles in the same issue of Seminars in Cutaneous Medicine and Surgery, underscoring the importance of the two recent developments.

## Fillers

The next phase of development in injectable fillers has begun, according to Dr. Richard G. Glogau.

"The concept of augmentation has moved from simple lines, scars, and wrinkles to revolumizing the aging face," noted Dr. Glogau, a clinical professor of dermatology at the University of California, San Francisco. "While seeking extended duration of effect balanced against the safety profile of the injectable, our focus is now directed to extending the lifting or volumizing effect that one can achieve with these fillers."

The initial movement into 3-dimensional correction with injectable fillers began with the dramatic improvement seen in lip volume championed in the 1980s, and each of a litany of fillers that followed, including fat, collagen, silicone, hyaluronic acids, poly-L-lactic acids, calcium hydroxylapatite, and polymethylmethacrylate (Sem. Cut. Med. Surg. 2012;31:78-87).

New fillers, some of which represent refinements of existing technologies, continue to undergo review. Aquamid – a biocompatible, nonabsorbable, permanent injectable hydrogel implant – is currently under review by the Food and Drug Administration and is approved for use in Europe.

It is also possible that fillers will move beyond the traditional concept of inert medical devices and into the realm of true biologics – "materials that will improve the texture, elasticity, radiance, and possibly color, of the skin itself," he added.

"Just as the last 40 years has seen the movement from 2 to 3 dimensions, the next 2 decades will see movement from the macro to the micro level, and fillers will become systems for active metabolic manipulation and protection of the aging skin," he concluded.

## Fractionation

The development of fractional photothermolysis was "a milestone in the history of laser technology and cutaneous resurfacing," according to Dr. Nazanin Saedi, a dermatologist in private practice in Chestnut Hill, Mass, and her colleagues.

The technology, noted the study authors, builds on the knowledge gained from early $CO_2$ and Er:YAG laser treatment experiences, achieving greater optimization of parameters to induce the types of benefits seen with $CO_2$ resurfacing, but without the significant postoperative morbidity, complications, and discomfort associated with the earlier technologies.

Furthermore, the older therapies destroyed the barrier protection, which "significantly increased the risk of infection throughout the recovery period and required extensive home care. The risk of scarring, delayed-onset permanent hypopigmentation, and demarcation lines was significant even in the hands of an experienced operator," they wrote (Sem. Cut. Med. Surg. 2012;31:105-9).

In an en effort to overcome these problems, what followed was nonablative dermal remodeling (with less than impressive results), and ultimately, the "idea of fractionated laser technology," they continued.

First used in hair transplant surgery, the technology led to development of the 1,550-nm nonablative "Fraxel" laser (now called the Fraxel Re:Store by Solta Medical), which debuted in the literature in 2004. This and other fractional laser technologies are now used to treat photoaging, superficial and deep

*Continued on following page*

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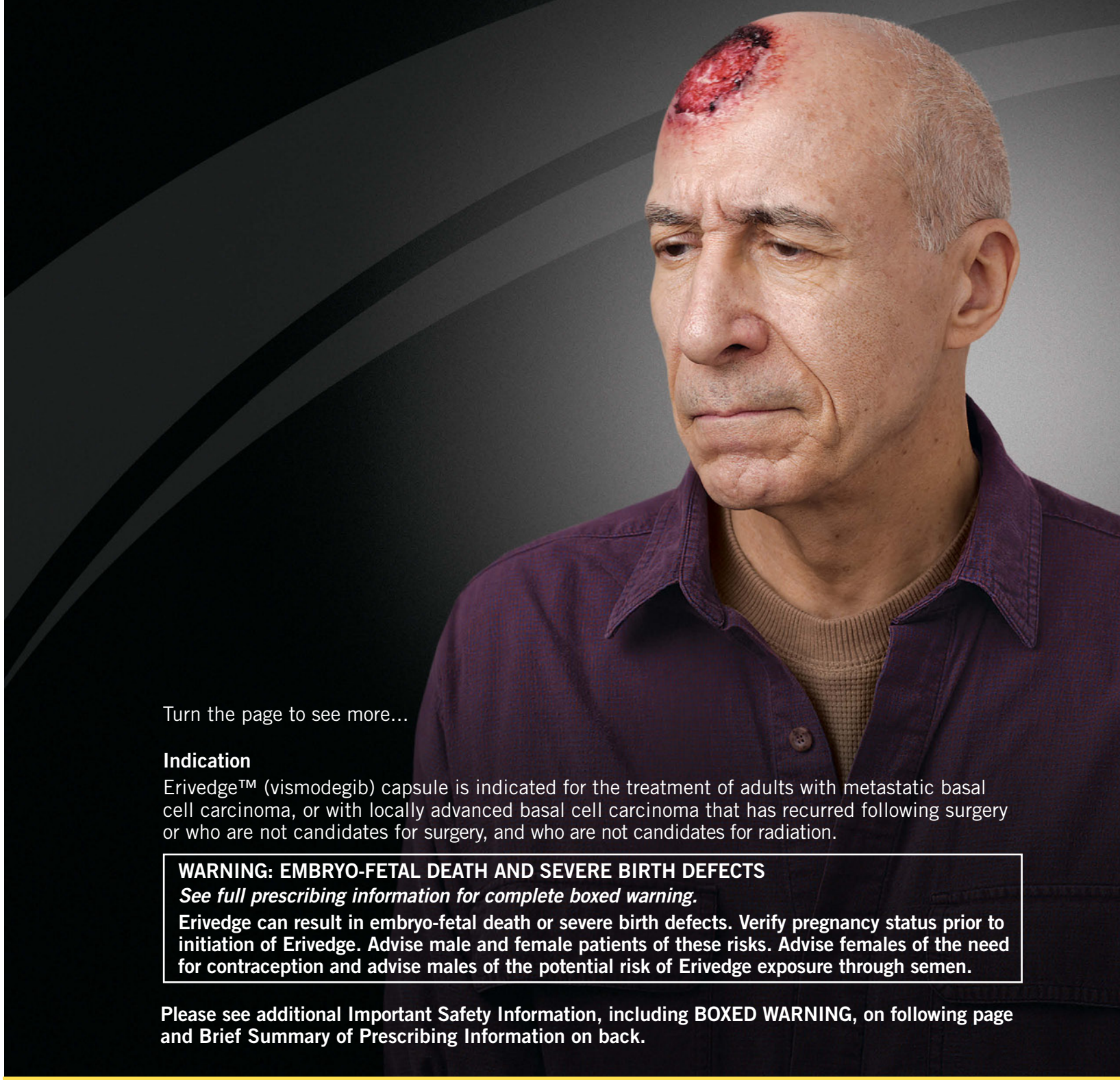

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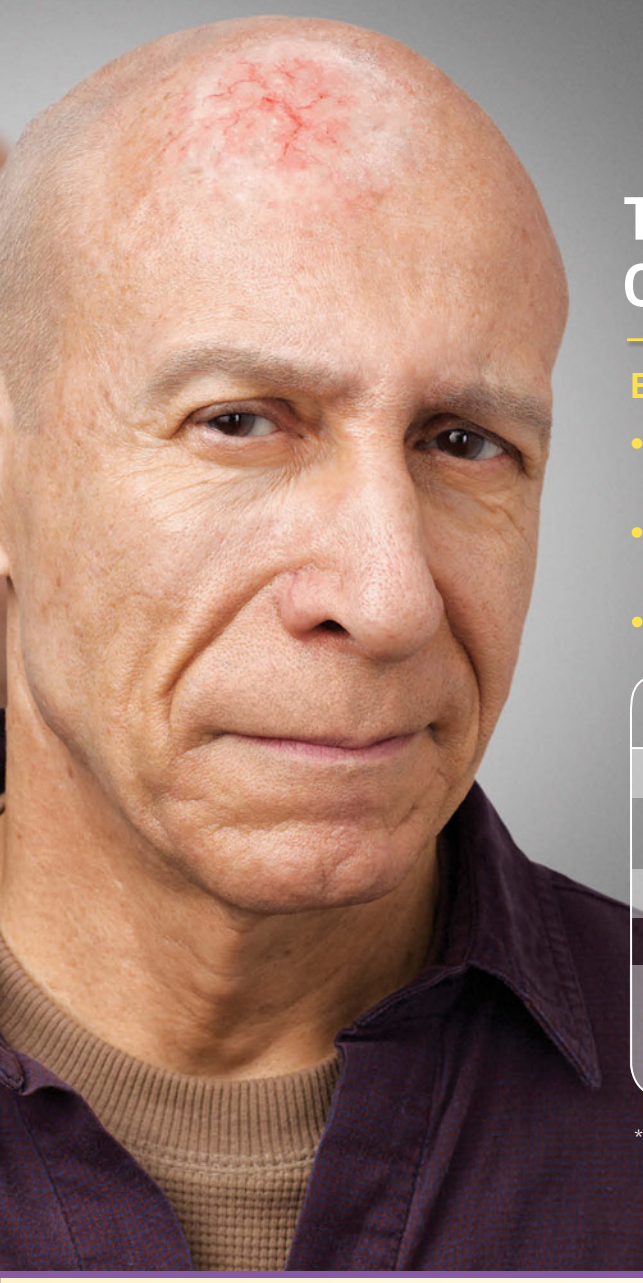
- Advise patients not to donate blood or blood products while receiving Erivedge and for at least 7 months after the last dose of Erivedge

## Nursing Mothers

- Inform female patients of the potential for serious adverse reactions in nursing infants from Erivedge, taking into account the importance of the drug to the mother



# TRANSFORM THE TREATMENT OF ADVANCED BCC

## Erivedge—a unique treatment option

- Systemic therapy that targets dysregulated Hedgehog pathway signaling, a known driver of BCC[1,2]
- One 150-mg capsule a day until disease progression or unacceptable toxicity[1]
- Erivedge reduced lesions in patients with advanced BCC[1]

**Objective response rates (ORR) by IRF from ERIVANCE[1]***

| | laBCC (n=63) | mBCC (n=33) |
|---|---|---|
| ORR (95% CI) | 43% (n=27) (30.5-56.0) | 30% (n=10) (15.6-48.2) |
| Complete response | 21% (n=13) | 0% |
| Partial response | 22% (n=14) | 30% (n=10) |
| Median response duration (months) (95% CI) | 7.6 (5.7-9.7) | 7.6 (5.6-NE) |

* Patients received at least 1 dose of Erivedge with independent pathologist-confirmed diagnosis of BCC. For laBCC, complete response was defined as objective response with no residual BCC on sampling biopsy.

IRF=Independent Review Facility. CI=confidence interval. laBCC=locally advanced BCC. mBCC=metastatic BCC. NE=not estimable.

## Adverse Reactions

- The most common adverse reactions (≥10%) were muscle spasms, alopecia, dysgeusia, weight loss, fatigue, nausea, diarrhea, decreased appetite, constipation, arthralgias, vomiting, and ageusia
- In clinical trials, a total of 3 of 10 premenopausal women developed amenorrhea while receiving Erivedge
- Treatment-emergent grade 3 laboratory abnormalities observed in clinical trials were hyponatremia in 6 patients (4%), hypokalemia in 2 patients (1%), and azotemia in 3 patients (2%)

**Please see Brief Summary of Prescribing Information on following page.**

Erivedge™ (vismodegib) capsule

Treatment Transformed

See what you can offer your patients with advanced BCC at www.Erivedge.com

**References: 1.** Erivedge™ (vismodegib) capsule Prescribing Information. Genentech, Inc. January 2012. **2.** Epstein EH. *Nat Rev Cancer.* 2008; 8:743-754.

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MIX
Paper from responsible sources
FSC® XXXXXXX

Erivedge™
(vismodegib) capsule

ERIVEDGE (vismodegib) capsule
Initial U.S. Approval: 2012

This is a brief summary of information about ERIVEDGE. Before prescribing, please see full prescribing information.

**WARNING: EMBRYO-FETAL DEATH AND SEVERE BIRTH DEFECTS**

**ERIVEDGE (vismodegib) capsule can result in embryo-fetal death or severe birth defects. ERIVEDGE is embryotoxic and teratogenic in animals. Teratogenic effects included severe midline defects, missing digits, and other irreversible malformations.**

**Verify pregnancy status prior to the initiation of ERIVEDGE. Advise male and female patients of these risks. Advise female patients of the need for contraception and advise male patients of the potential risk of ERIVEDGE exposure through semen [see *Warnings and Precautions (5.1), Use in Specific Populations (8.1, 8.6)*].**

## 1 INDICATIONS AND USAGE

ERIVEDGE capsule is indicated for the treatment of adults with metastatic basal cell carcinoma, or with locally advanced basal cell carcinoma that has recurred following surgery or who are not candidates for surgery, and who are not candidates for radiation.

## 2 DOSAGE AND ADMINISTRATION

The recommended dose of ERIVEDGE is 150 mg taken orally once daily until disease progression or until unacceptable toxicity [see *Clinical Studies (14)*].

ERIVEDGE may be taken with or without food. Swallow capsules whole. **Do not open or crush capsules.**

If a dose of ERIVEDGE is missed, do not make up that dose; resume dosing with the next scheduled dose.

## 4 CONTRAINDICATIONS

None.

## 5 WARNINGS AND PRECAUTIONS

### 5.1 Embryo-Fetal Death and Severe Birth Defects

ERIVEDGE capsules can cause fetal harm when administered to a pregnant woman based on its mechanism of action. Vismodegib is teratogenic, embryotoxic, and fetotoxic in rats at maternal exposures lower than the human exposures at the recommended dose of 150 mg/day. In rats, malformations included craniofacial anomalies, open perineum, and absent or fused digits. Fetal retardations and variations were also observed.

Verify pregnancy status prior to the initiation of ERIVEDGE. Advise male and female patients of the risks of embryo-fetal death and severe birth defects and the need for contraception during and after treatment. Advise patients to contact their healthcare provider immediately if they suspect they (or, for males, their female partner) may be pregnant. Female and male patients of reproductive potential should be counseled regarding pregnancy prevention and planning. If ERIVEDGE is used during pregnancy or if a patient becomes pregnant while taking (or for a male patient, if his female partner is exposed to) ERIVEDGE, the patient should be apprised of the potential hazard to the fetus. Report immediately exposure to ERIVEDGE during pregnancy to the Genentech Adverse Event Line at 1-888-835-2555. Encourage women who may have been exposed to ERIVEDGE during pregnancy, either directly or through seminal fluid, to participate in the ERIVEDGE pregnancy pharmacovigilance program by contacting the Genentech Adverse Event Line at 1-888-835-2555 [see *Boxed Warning, Use in Specific Populations (8.1, 8.6)*].

### 5.2 Blood Donation

Advise patients not to donate blood or blood products while receiving ERIVEDGE and for at least 7 months after the last dose of ERIVEDGE.

## 6 ADVERSE REACTIONS

### 6.1 Clinical Trials Experience

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

ERIVEDGE capsule was administered as monotherapy at doses ≥ 150 mg orally daily in four open-label, uncontrolled, dose-ranging or fixed single dose clinical trials enrolling a total of 138 patients with advanced basal cell carcinoma (BCC). The median age of these patients was 61 years (range 21 to 101), 100% were White (including Hispanics), and 64% were male. The median duration of treatment was approximately 10 months (305 days; range 0.7 to 36 months); 111 patients received ERIVEDGE for 6 months or longer.

The most common adverse reactions (≥ 10%) were muscle spasms, alopecia, dysgeusia, weight loss, fatigue, nausea, diarrhea, decreased appetite, constipation, arthralgias, vomiting, and ageusia (Table 1).

**Table 1: Adverse Reactions Occurring in ≥ 10% of Advanced BCC Patients**

| | All aBCC[1] Patients (N = 138) | | |
|---|---|---|---|
| MedDRA Preferred Term[2] | All Grades[3] (%) | Grade 3 (%) | Grade 4 (%) |
| Gastrointestinal disorders | | | |
| Nausea | 42 (30.4%) | 1 (0.7%) | - |
| Diarrhea | 40 (29.0%) | 1 (0.7%) | - |
| Constipation | 29 (21.0%) | - | - |
| Vomiting | 19 (13.8%) | - | - |
| General disorders and administration site conditions | | | |
| Fatigue | 55 (39.9%) | 7 (5.1%) | 1 (0.7%) |
| Investigations | | | |
| Weight loss | 62 (44.9%) | 10 (7.2%) | - |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | 35 (25.4%) | 3 (2.2%) | - |
| Musculoskeletal and connective tissue disorders | | | |
| Muscle spasms | 99 (71.7%) | 5 (3.6%) | - |
| Arthralgias | 22 (15.9%) | 1 (0.7%) | |
| Nervous system disorders | | | |
| Dysgeusia | 76 (55.1%) | - | - |
| Ageusia | 15 (10.9%) | - | - |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | 88 (63.8%) | - | - |

[1]aBCC = Advanced Basal Cell Carcinoma.

[2]MedDRA = Medical Dictionary for Regulatory Activities.

[3]Grading according to NCI-CTCAE v3.0.

*Amenorrhea:*

In clinical trials, a total of 3 of 10 pre-menopausal women developed amenorrhea while receiving ERIVEDGE [see *Non-Clinical Toxicology (13.1)*].

*Laboratory Abnormalities:*

Treatment-emergent Grade 3 laboratory abnormalities observed in clinical trials were hyponatremia in 6 patients (4%), hypokalemia in 2 patients (1%), and azotemia in 3 patients (2%).

## 7 DRUG INTERACTIONS

### 7.1 Effects of Other Drugs on Vismodegib

*Drugs that Inhibit or Induce Drug Metabolizing Enzymes*

Vismodegib elimination involves multiple pathways. Vismodegib is predominantly excreted as an unchanged drug. Several minor metabolites are produced by multiple CYP enzymes. Although vismodegib is a substrate of CYP2C9 and CYP3A4 *in vitro*, CYP inhibition is not predicted to alter vismodegib systemic exposure since similar steady-state plasma vismodegib concentrations were observed in patients in clinical trials concomitantly treated with CYP3A4 inducers (i.e., carbamazepine, modafinil, phenobarbital) and those concomitantly treated with CYP3A4 inhibitors (i.e., erythromycin, fluconazole).

*Drugs that Inhibit Drug Transport Systems*

*In vitro* studies indicate that vismodegib is a substrate of the efflux transporter P-glycoprotein (P-gp). When ERIVEDGE is coadministered with drugs that inhibit P-gp (e.g. clarithromycin, erythromycin, azithromycin), systemic exposure of vismodegib and incidence of adverse events of ERIVEDGE may be increased.

*Drugs that Affect Gastric pH*

Drugs that alter the pH of the upper GI tract (e.g. proton pump inhibitors, $H_2$-receptor antagonists, and antacids) may alter the solubility of vismodegib and reduce its bioavailability. However, no formal clinical study has been conducted to evaluate the effect of gastric pH altering agents on the systemic exposure of vismodegib. Increasing the dose of ERIVEDGE when coadministered with such agents is not likely to compensate for the loss of exposure. When ERIVEDGE is coadministered with a proton pump inhibitor, $H_2$-receptor antagonist or antacid, systemic exposure of vismodegib may be decreased and the effect on efficacy of ERIVEDGE is unknown.

### 7.2 Effects of Vismodegib on Other Drugs

Results of a drug-drug interaction study conducted in cancer patients demonstrated that the systemic exposure of rosiglitazone (a CYP2C8 substrate) or oral contraceptives (ethinyl estradiol and norethindrone) is not altered when either drug is co-administered with vismodegib.

*In vitro* studies indicate that vismodegib is an inhibitor of CYP2C8, CYP2C9, CYP2C19 and the transporter BCRP. Vismodegib does not induce CYP1A2, CYP2B6, or CYP3A4/5 in human hepatocytes.

## 8 USE IN SPECIFIC POPULATIONS

### 8.1 Pregnancy

Pregnancy Category D

ERIVEDGE capsule can cause fetal harm when administered to a pregnant female based on its mechanism of action. Vismodegib is teratogenic in rats at doses corresponding to an exposure of 20% of the exposure at the recommended human dose (estimated $AUC_{0\text{-}24hr}$ steady-state exposure). In rats, malformations included craniofacial anomalies, open perineum, and absent or fused digits. Fetal retardations and variations were also observed. Vismodegib is embryolethal in rats at exposures within the range achieved at the recommended human dose. If ERIVEDGE is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the embryo or fetus. Report immediately exposure to ERIVEDGE during pregnancy to the Genentech Adverse Event Line at 1-888-835-2555. Encourage women who may have been exposed to ERIVEDGE during pregnancy, either directly or through seminal fluid, to participate in the ERIVEDGE pregnancy pharmacovigilance program by contacting the Genentech Adverse Event Line at 1-888-835-2555 [see *Boxed Warning, Warnings* and *Precautions (5.1)*].

In an embryo-fetal developmental toxicity study, pregnant rats were administered oral vismodegib at doses of 10, 60, or 300 mg/kg/day during the period of organogenesis. Pre- and post-implantation loss were increased at doses of ≥ 60 mg/kg/day (approximately ≥ 2 times the systemic exposure (AUC) in patients at the recommended human dose), which included early resorption of 100% of the fetuses. A dose of 10 mg/kg/day (approximately 0.2 times the AUC in patients at the recommended dose) resulted in malformations (including missing and/or fused digits, open perineum and craniofacial anomalies) and retardations or variations (including dilated renal pelvis, dilated ureter, and incompletely or unossified sternal elements, centra of vertebrae, or proximal phalanges and claws).

### 8.3 Nursing Mothers

It is not known whether vismodegib is excreted in human breast milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from ERIVEDGE, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

### 8.4 Pediatric Use

The safety and effectiveness of ERIVEDGE capsule have not been established in pediatric patients.

In repeat-dose toxicology studies in rats, administration of oral vismodegib resulted in toxicities in bone and teeth. Effects on bone consisted of closure of the epiphyseal growth plate when oral vismodegib was administered for 26 weeks at ≥ 50 mg/kg/day (approximately ≥ 0.4 times the systemic exposure (AUC) in patients at the recommended human dose). Abnormalities in growing incisor teeth (including degeneration/necrosis of odontoblasts, formation of fluid-filled cysts in the dental pulp, ossification of the root canal, and hemorrhage resulting in breakage or loss of teeth) were observed after administration of oral vismodegib at ≥ 15 mg/kg/day (approximately ≥ 0.2 times the AUC in patients at the recommended human dose).

### 8.5 Geriatric Use

Clinical studies of ERIVEDGE capsule did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger patients.

### 8.6 Females of Reproductive Potential and Males

ERIVEDGE capsule can cause harm to the embryo or fetus when administered during pregnancy. Counsel female and male patients regarding pregnancy prevention and planning. Advise patients to contact their healthcare provider immediately if they suspect they (or, for males, their female partner) may be pregnant [see *Boxed Warning, Warnings and Precautions (5.1), Use in Specific Populations (8.1)*]

*Female patients*

Determine pregnancy status within 7 days prior to initiation of treatment in females of reproductive potential. For females with a negative pregnancy test, initiate a highly effective form of contraception (failure rate of less than 1%) prior to the first dose. Continue highly effective contraception during therapy and for 7 months after the last dose of ERIVEDGE. If a patient becomes pregnant while taking ERIVEDGE, or during the 7 months after the last dose of treatment, report the pregnancy to the Genentech Adverse Event Line at 1-888-835-2555. Encourage pregnant females to participate in the ERIVEDGE pregnancy pharmacovigilance program by calling the Genentech Adverse Event Line at 1-888-835-2555. Counsel pregnant females about the teratogenic risk to the fetus.

Amenorrhea has been observed in clinical trials in females of reproductive potential. Reversibility of amenorrhea is unknown [see *Adverse Reactions (6), Nonclinical Toxicology (13.1)*].

*Male patients*

Male patients should use condoms with spermicide, even after a vasectomy, during sexual intercourse with female partners while being treated with ERIVEDGE capsule and for 2 months after the last dose to avoid exposing an embryo or fetus to vismodegib.

### 8.7 Hepatic Impairment

The safety and effectiveness of ERIVEDGE capsule have not been established in patients with hepatic impairment [see *Clinical Pharmacology (12.3)*].

### 8.8 Renal Impairment

The safety and effectiveness of ERIVEDGE capsule have not been established in patients with renal impairment [see *Clinical Pharmacology (12.3)*].

## 10 OVERDOSAGE

There is no information on overdosage in humans. In clinical trials, ERIVEDGE capsule was administered at 540 mg orally once daily; exposure did not increase between 150 mg and 540 mg daily.

## 17 PATIENT COUNSELING INFORMATION

***See FDA-approved patient labeling (Medication Guide).***

- Advise patients that ERIVEDGE exposure during pregnancy can cause embryo-fetal death or severe birth defects.
- Instruct female patients of reproductive potential to use a highly effective form of contraception (failure rate of less than 1%) while taking ERIVEDGE and for at least 7 months after the last dose of ERIVEDGE.
- Instruct all male patients, even those with prior vasectomy, to use condoms with spermicide, during sexual intercourse with female partners while taking ERIVEDGE and for at least 2 months after the last dose of ERIVEDGE.
- Instruct patients to immediately contact their healthcare provider if they (or, for males, their female partner) become pregnant or if pregnancy is suspected following exposure to ERIVEDGE.
- Instruct patients to immediately report any pregnancy exposure to ERIVEDGE and encourage participation in the ERIVEDGE pregnancy pharmacovigilance program by calling the Genentech Adverse Event Line at 1-888-835-2555.
- Inform female patients of the potential for serious adverse reactions in nursing infants from ERIVEDGE, taking into account the importance of the drug to the mother.
- Advise patients not to donate blood or blood products while taking ERIVEDGE and for at least 7 months after the last dose of ERIVEDGE.
- Advise patients to swallow ERIVEDGE capsules whole and not to crush or open the capsules.

Genentech
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ERIVEDGE™ [vismodegib] capsule

Manufactured by:
Patheon, Inc.
Mississauga, Canada

Distributed by:
**Genentech USA, Inc.**
A Member of the Roche Group
1 DNA Way
South San Francisco, CA 94080-4990
HED0000832300


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*Continued from previous page*

rhytids, scars (including in patients with darker skin types), and pigmentation.

Both nonablative and ablative fractional resurfacing have proved to be safer than have traditional ablative lasers, Dr. Saedi and her colleagues noted. However, complications can still occur, such as infections (with herpes simplex virus being the most common), acneiform eruptions, prolonged erythema, pigmentary alteration, and scarring (rare, but can also result from infection associated with treatment).

"Counterintuitively, nonablative or ablative fractionated devices at low energies and densities can be useful in the treatment of scarring, including hypertrophic scars" as previously mentioned, they noted.

"While [fractional lasers are] inherently safer due to the pixelated manner of the treatment, complications can be further prevented with attentive surgical technique and judicious use of prophylaxis," they wrote.

The future of fractional laser technology promises to hold exciting developments. For example, since ablative fractional resurfacing creates microscopic vertical holes in tissue, the delivery of topical drugs through these holes is possible. In animal models, the photosensitizer methylaminolevulinic acid has been delivered using this approach, and tests have suggested that low-density treatment would be sufficient for deep dermal drug delivery.

"Treatment of skin in a porcine model showed enhanced depth of photodynamic therapy following porphyrin application after pretreatment with fractional resurfacing. An in vitro study utilizing low fluence fractionated Erbium:YAG demonstrated upward of a 125-fold increase in imiquimod delivery," they noted.

Trials in humans are underway to assess the feasibility and safety of enhanced drug delivery using this approach, and there is speculation that, ultimately, it could be used for delivery of biologic peptides and vaccines.

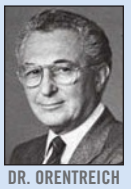
Tattoo removal is another promising use for fractional lasers, with early studies demonstrating good results, noted Dr. Saedi and her colleagues, explaining that ablative fractional lasers, when used in conjunction with a Q-switched laser, appear to provide enhanced tattoo removal capabilities.

"With new devices and wavelengths, the applications of this technology continue to grow," they wrote, concluding that "the future remains bright for fractionated laser devices."

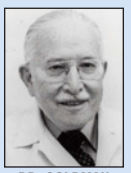
Likewise, the future of dermatologic surgery in general remains promising, Dr. Hanke said. "Many new procedures and advances lie ahead."

Neither Dr. Hanke nor Dr. Saedi had disclosures to report. Another author on the article by Dr. Saedi (Dr. Christopher Zachary) reported receiving an honorarium from Solta Medical. ■

## Milestones in Dermatologic Surgery


DR. ORENTREICH

**1952 –** Dr. Norman Orentreich performed the first hair transplant (published in 1959); Dr. George Mackee reported on his 50-year experience of using phenol chemical peels.


DR. GOLDMAN

**1961 –** Dr. Leon Goldman became the first physician to treat patients with lasers.


DR. MOHS

**1967 –** Dr. Frederic E. Mohs, who earlier developed the "fixed tissue" technique, founded the American College of Chemosurgery; Dr. Theodore A. Tromovitch and Dr. Samuel J. Stegman began using Mohs "fresh-tissue" technique.


**1975 –** The Journal of Dermatologic Surgery was founded by Dr. George L. Popkin and Dr. Perry Robins (renamed the Journal of Dermatologic Surgery and Oncology in 1977 and Dermatologic Surgery in 1995).


DR. ASKEN

**1986 –** Dr. Saul Asken published the Manual of Liposuction Surgery

**1998 –** Dr. C. William Hanke, Dr. Boris Sommer, and Dr. Gerhard Sattler, coined the term "tumescent local anesthesia."


DR. ANDERSON


DR. PARRISH

**2000 (and beyond) –** Dr. R. Rox Anderson and Dr. John A. Parrish continued their work on selective photothermolysis, leading to the fractional technologies being developed today.

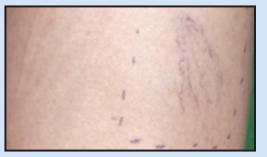
**– 1953** Dr. Abner Kurtin developed modern-day dermabrasion.

**– 1966** Dr. Setrag Zacarian published the first report on cryosurgery using liquid nitrogen; Dr. Robert Muller published the first report on ambulatory phlebectomy.

**– 1970** The American Society for Dermatologic Surgery was founded.

**– 1981** The American Society for Lasers in Medicine and Surgery was founded.

**– 1982** Dr. Bruce Chrisman published the first report on hypertonic saline injections for leg veins.



**– 1987** Dr. Jeffrey A. Klein published the first report on the tumescent technique for liposuction; Dr. Alastair Carruthers and Dr. Jean Carruthers began the cosmetic use of botulinum toxin.


DR. KLEIN

**– 2004** One-year fellowship training programs in procedural dermatology were approved by the Accreditation Council for Graduate Medical Education.

Source: Sem. Cut. Med. Surg. 2012; in press

IMNG MEDICAL MEDIA



# Quasi-Ablative Device Dulls Photodamage

BY SHARON WORCESTER

FROM THE ANNUAL MEETING OF THE AMERICAN SOCIETY FOR LASER MEDICINE AND SURGERY

KISSIMMEE, FLA. – The nonablative 1,540-nm fractional laser can be safely converted to a quasi-ablative device for treating facial actinic keratoses and photodamage, according to Dr. Moshe Lapidoth.

With slight modification of technique, a 50%-75% improvement in actinic keratoses and photodamage was noted in 17 patients who underwent two to three treatments at 4-week intervals, Dr. Lapidoth reported at the meeting. The laser was used in noncontact mode hovering 5-10 mm above the skin rather than in contact mode.

The patients had actinic keratoses and photodamage requiring ablative treatment of the epidermis. Treatment was applied using a fluence of 75 J/cm$^2$, a 15-ms pulse duration, and a 10-mm spot size.

Two blinded assessors and the participants evaluated clinical improvement at 3 months after the final treatment using a quartile grading scale (Lasers Med. Sci. 2012 April 27 [doi: 10.1007/s10103-012-1103-6])

A score of 0 was associated with no improvement; a score of 1 with 1%-25% improvement, a score of 2 with 26%-50% improvement, a score of 3 with 51%-75% improvement, and a score of 4 with 76%-100% improvement. The mean score for actinic keratoses was 3.4, and for skin appearance was 3.2, said Dr. Lapidoth, head of the laser department at Rabin Medical Center in Israel.

Side effects after each treatment included erythema, mild edema, erosion in two patients, and mild desquamation.

Although more current fractional laser devices are designed to be either ablative or nonablative, the 1,540-nm fractional laser was designed to be nonablative.

Dr. Lapidoth reported having no disclosures. ■

# Majority of HIV Patients Don't Get Regular Care

VITALS

**Major Finding:** Only an estimated 36% of HIV-infected adults were receiving regular medical care, but within this group, 89% were on antiretroviral therapy and 72% achieved viral suppression.

**Data Source:** A cross-sectional survey of 4,217 HIV-infected adults in the United States in 2009 (the Medical Monitoring Project).

**Disclosures:** Dr. Skarbinski disclosed that he had no relevant conflicts of interest.

BY SUSAN LONDON

FROM THE CONFERENCE ON RETROVIRUSES AND OPPORTUNISTIC INFECTIONS

SEATTLE – Greater efforts are needed to get people with HIV infection into medical care, a necessary prerequisite to therapy and viral suppression, suggests a cross-sectional survey of 4,217 HIV-positive adults conducted by the Centers for Disease Control and Prevention.

Survey results, reported at the Conference on Retroviruses and Opportunistic Infections, also showed that only an estimated 36% of adults living with HIV in 2009 had at least one medical care visit between January and April of that year.

But within this group, measures of therapy were good: 89% had received at least one prescription for antiretroviral therapy (ART) in the past year, and 72% had achieved a suppressed HIV viral load.

"Increasing the size of the in-care population is critical to increase the overall proportion of HIV-infected persons who are on ART and suppressed," said Dr. Jacek Skarbinski, of the Division of HIV/AIDS Prevention at the CDC.

Analyses have suggested that expanding guidelines regarding when to initiate ART – from the current recommendation (presence of AIDS or a nadir CD4 cell count of 500 cells/mL or lower) to a new one covering all HIV-infected people (regardless of CD4 cell count) – would have only a small impact.

In additional study findings, certain groups of people in care – young adults, blacks, and those living in poverty, among others – were significantly less likely to be prescribed ART, to achieve viral suppression, or both.

Thus, "we need to address disparities in HIV care and treatment, especially by age, race, and income," Dr. Skarbinski said.

To obtain national estimates of these outcomes, he and colleagues analyzed data from the Medical Monitoring Project, a supplemental surveillance system that captures information on nationally representative samples of HIV-infected people in care. In 2009, it collected data from 17 states and territories, 461 facilities within those states and territories, and 4,217 HIV-infected patients receiving care in those facilities.

The patients represented an estimated 421,186 adults in care at the population level, or just 36% of all 1.2 million people living with HIV nationally on the basis of a recent estimate (MMWR 2011;60:689-93). The value was higher, but still only 41%, when analyses were annualized to reflect receipt of care during the whole year and not just the first 4 months.

Patients in care were predominantly 40 years of age or older (75%), male (71%), non-Hispanic black (41%) or white (34%), and men who had sex with men (47%). The majority had more than a high school education (51%) but also lived below the poverty line (54%) and had public health insurance (62%). Half were at least 10 years out from diagnosis, and two-thirds had AIDS.

Multivariate analyses showed that individuals in care were significantly less likely to be prescribed ART if they were aged 18-29, non-Hispanic black, female, in the first 4 years after diagnosis, and did not have AIDS (regardless of nadir CD4 cell count).

Similarly, individuals in care were significantly less likely to be prescribed antiretroviral therapy if they were aged 18-49, non-Hispanic black or of "other" race/ethnicity, were living at or below the poverty level, and did not have AIDS and had a nadir CD4 cell count of greater than 500 cells/mL. ■

# Measles Cases, Outbreaks Hit 15-Year High

BY DIANA MAHONEY

FROM THE CDC MORBIDITY AND MORTALITY WEEKLY REPORT

The number of cases of measles reported in the United States last year was higher than any year since 1996 – an increase the Centers for Disease Control and Prevention attributes primarily to an increase in the importation of the disease from other countries and the vulnerability of susceptible, unimmunized people in the community.

A total of 222 measles cases and 17 measles outbreaks from 31 states were reported to the CDC in 2011, compared with a median of 60 cases and 4 outbreaks reported annually during 2001-2010, Dr. Anne Schuchat, director of the National Center for Immunization and Respiratory Disease's Office of Infectious Diseases reported in a telebriefing.

**VITALS**

**Major Finding:** In 2001, 222 cases of measles and 17 outbreaks in 31 states were reported in the United States.

**Data Source:** Findings came from reports to the Centers for Disease Control and Prevention.

**Disclosures:** Dr. Schuchat said she had no financial conflicts of interest to disclose.

Of the 222 cases, 200 (90%) were associated with importations from other countries, including 52 (26%) cases in U.S. residents who had recently traveled abroad and 20 (10%) in foreign visitors, she said, (MMWR 2012;61:253-7).

Of the patients who contracted the disease in 2011, 86% were either unvaccinated or had unknown vaccination status, underscoring the ongoing risk for measles among unvaccinated individuals and the importance of vaccination, despite the fact that the disease was declared to be eliminated – defined as the interruption of year-round endemic transmission – in the United States in 2000, Dr. Schuchat said.

For the purposes of the CDC report, measles outbreaks were defined as three or more cases linked in time or place, and U.S residents were classified as eligible or ineligible for measles, mumps, and rubella (MMR) vaccination according to the recommendations of the Advisory Committee on Immunization Practices, whereby vaccine-eligible patients were those who were unvaccinated or had unknown vaccination status; did not have vaccination contraindications; and were either born after 1957 and at least 12 months old without documented evidence of measles immunity or 6-11 months with a recent history of international travel, according to the report.

The median age of the infected patients was 14 years (3 months to 84 years). Of the 222, 196 were U.S. residents; of those, 166 were unvaccinated or had unknown vaccination status, 141 of whom were eligible for vaccination, 18 who were too young for vaccination, 6 who were born before 1957 and thus had presumptive immunity, and 1 with previous evidence of presumptive immunity.

In all, 72 of the 200 importation-associated measles cases were imported from other countries and nearly half of the 72 importations occurred among individuals who contracted the disease in the European region, Dr. Schuchat said. "We don't usually think of Europe being associated with measles, but in reality there has been a lot of measles in that region. In 2011, more than 30,000 cases were recorded in Europe, including 8 measles-related deaths. The hardest hit regions were places Americans tend to travel to, including France, Italy, and Spain."

Unvaccinated U.S. residents traveling to regions where measles are endemic put themselves and others in their communities at risk for measles, she said.

Physicians need to keep measles in mind when they encounter persons with a fever and rash, along with symptoms such as cough, coryza, or conjunctivitis, especially in persons who recently have traveled abroad or have had contact with travelers.

Despite the relatively small number of measles cases in the United States, vigilance on behalf of the public and health care providers is critical to avoid a drop in MMR vaccination coverage. ■

# Melanoma Awareness Credited for Rise in Survival

BY BRUCE JANCIN

EXPERT ANALYSIS FROM THE SDEF HAWAII DERMATOLOGY SEMINAR

WAIKOLOA, HAWAII – The improvement in melanoma survival over the past 4 decades can be attributed to effective public education campaigns, increased patient awareness, and improved physician skills and diagnostic tools, according to Dr. Ashfaq A. Marghoob.

It has been nothing short of phenomenal, he said, and it can't be credited to major therapeutic advances because until a couple years ago there weren't any.

Survival at 5 years for all-stage melanomas of the skin climbed from less than 60% in 1970 to 91% in 2011, he said at the seminar sponsored by the Skin Disease Education Foundation (SDEF).

But the statistics are somewhat deceiving, said Dr. Marghoob, a dermatologist at Memorial Sloan-Kettering Cancer Center in New York.

He is among a growing number of experts who believe that many thin melanomas detected through screening efforts are slow-growing, indolent skin cancers that sometimes regress and in any event will never become thick or dangerous – never result in death – within the range of current life expectancy. He noted that there is ample precedence, namely, indolent forms of prostate cancer, lymphoma, and breast cancer.

Dr. Marghoob was part of an international team that demonstrated the existence of a slow-growing subtype of melanoma. In a series of 103 melanomas excised after a median follow-up of 20 months, most of the lesions were still in situ or in an early invasive stage. Only three lesions were 1-mm thick or more. There was no correlation between tumor thickness and follow-up time (Br. J. Dermatol. 2010;162:267-73).

Growing support exists among epidemiologists for the concept that there are three distinct, unrelated melanoma subtypes (Br. J. Dermatol. 2007;157:338-43). One subtype consists of thin, slow-growing melanomas – the kind that have been steadily increasing in incidence for decades. These are associated with intermittent sun exposure and often arise on the trunk among numerous background nevi. These melanomas are amenable to detection via screening or periodic surveillance. But they only rarely metastasize.

A second type of slow-growing melanoma often occurs on the head and neck of individuals with continuous sun exposure. The incidence of this subtype of melanoma is slowly increasing.

The third and most concerning melanoma subtype consist of thick, fast-growing lesions in individuals with many nevi, but that are not associated with sun exposure. The incidence of these fast-growing, high-lethality melanomas has remained steady over time because they often escape detection as a result of their accelerated growth rate. Improved early detection is a high priority, and it will require creative new approaches, he said.

But in terms of celebrating rising 5-year melanoma survival rates, a contributory landmark event, in Dr. Marghoob's view, was the increased awareness about melanoma after introduction of the ABCD mnemonic, devised chiefly for primary care physicians and the general public. This was later enhanced by the "ugly duckling" campaign, which taught physicians and patients that melanomas are generally recognizable as outlier lesions.

Multiple studies have shown that skin cancer specialists using visual examination alone can typically diagnose melanoma with a sensitivity of 70% and specificity of 75%. The number needed to treat (NNT) or benign-to-malignant biopsy ratio is 1:12-15. With the aid of total body photography for assistance in patient follow-up, the NNT improves to 10.

Another advance, dermoscopy, enables physicians to pick up melanomas not detectable by other methods. Skin cancer specialists who supplement visual examination with dermoscopy typically have 90% sensitivity and 86% specificity for the diagnosis of melanoma. The NNT improves to 4-7, Dr. Marghoob said. Studies indicate these numbers get better with the use of confocal microscopy.

Dr. Marghoob reported having no disclosures. SDEF and this news organization are owned by Elsevier. ■

# Patient Dermatoscopes May Help Detect Cancer

BY BRUCE JANCIN

EXPERT ANALYSIS FROM THE SDEF HAWAII DERMATOLOGY SEMINAR

WAIKOLOA, HAWAII – Improved early detection of fast-growing, lethal melanomas will require out of the box thinking, such as providing dermatoscopes for patients to use at home and educating hairdressers and other nondermatologists on how to detect melanoma.

"At least three companies are now designing dermatoscopes for patient use. Patients will be able to buy the dermatoscope at a pharmacy and do self-examination or examine their spouse. That, I think, is going to be a reality within the next 5 years," Dr. Ashfaq A. Marghoob predicted at the seminar sponsored by Skin Disease Education Foundation (SDEF). A key feature of these devices will be the capability of hooking into a smart phone for wireless transmission of suspicious images to a skin cancer expert for assessment.

BRUCE JANCIN/IMNG MEDICAL MEDIA

**Patients will soon be able to buy dermatoscopes at pharmacies, predicted Dr. Ashfaq A. Marghoob.**

Dr. Marghoob and his coworkers first proposed dermoscopy as a tool with untapped potential for skin self-examination in selected patients in an article last year (Arch. Dermatol. 2011;147:53-8).

But patient empowerment is only part of what's needed in order to improve early detection of the fast-growing killer subtype of melanoma. Dr. Marghoob and his coworkers are now conducting a prospective study to evaluate the impact of a 20-minute education session for hair care professionals about how they can aid in detecting skin cancers on the scalp, neck, and face.

This study was a direct outgrowth of a survey the investigators conducted at a Houston convention of barbers and hairstylists. Forty-nine percent of respondents indicated they were highly receptive to participating in a skin cancer education program. During the preceding month, 37% of respondents had looked at more than half of their customers' scalps for suspicious lesions, 29% had looked at more than half of their customers' necks, and 15% had checked more than half of their customers' faces (Arch. Dermatol. 2011;147:1159-65).

Melanoma of the scalp and neck accounted for 10% of all melanoma deaths in the United States from 1973 to 2003. Barbers and hairstylists are in a unique position to detect skin cancers in those locations. In addition to hair professionals, other workers ideally suited to serve as lay skin cancer educators and examiners include massage therapists, manicurists, cosmetologists, and electrologists.

Dr. Marghoob has also been involved in efforts to teach dermoscopy to primary care physicians and other nondermatologist physicians, including ob.gyns., pediatricians, and plastic surgeons. Moreover, he recently conducted a study in which second-year medical students were issued dermatoscopes and trained in their use.

"We found they get better at diagnosing skin cancer and are paying more attention to the skin. All we really want them to do is really look at the skin while they're doing a physical examination," he said.

Another potentially fruitful means of improving upon the gains achieved in early detection of skin cancer would be targeted screening of older men, a high-risk group for fast-growing nodular melanomas, Dr. Marghoob added.

He reported having no financial conflicts. SDEF and this news organization are owned by Elsevier. ■

# Calcinosis Prognosis for Adults Considered Grim

BY PATRICE WENDLING

EXPERT ANALYSIS FROM A SYMPOSIUM SPONSORED BY THE AMERICAN COLLEGE OF RHEUMATOLOGY

CHICAGO – The prognosis for adults diagnosed with calcinosis remains grim, despite some excellent treatment responses reported in children for this often disabling and disfiguring condition, according to Dr. Lisa Christopher-Stine.

"I have not had a lot of success treating calcinosis in adults," she said at the symposium.

Calcinosis is a deposition of insoluble calcium salts in the skin. It can often look like scleroderma, and is divided into four categories based on pathogenesis: dystrophic, metastatic, idiopathic, and iatrogenic. Although rare in adults, it is relatively common in children, affecting up to 40% of patients with juvenile dermatomyositis. Calcinosis is variable in its severity and thought to correlate with poor underlying disease control and a delay in starting therapy, explained Dr. Christopher-Stine, codirector of the Johns Hopkins Myositis Center in Baltimore.

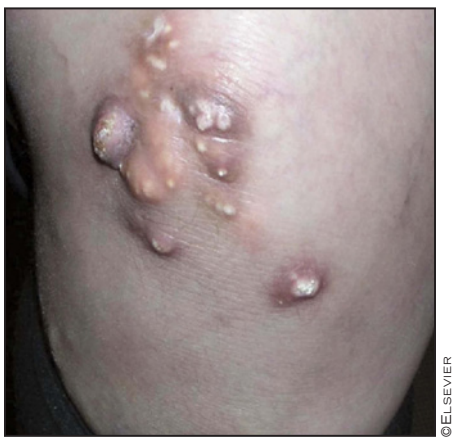
"It's probably true that if we mitigate the disease early, we can actually prevent calcinosis from developing, but even in patients with well-controlled disease, it seems to have a life of its own," she said.

The hallmarks of calcinosis are firm dermal or subcutaneous papules or nodules, frequently found on sites of microtrauma such as the buttocks, elbows, knees, and hands. Large subcutaneous tumoral deposition can occur on the trunk. Calcification of the muscles is generally asymptomatic and only found incidentally on radiographs.

Although the true etiology of calcinosis remains unknown, it is now thought to be an imbalance of calcium and phosphate metabolism. "Once calcinosis starts, it often progresses," she said. "It is unstoppable."

The complications of calcinosis include pain, cosmetic disfigurement, persistent ulceration, infection, and mechanical compromise, particularly contractures in the fingers and elbows.

There are no controlled studies in the treatment of calcinosis, only anecdotal reports. Dr. Christopher-Stine said she recommends starting with the calcium-channel blocker diltiazem (Cardizem) at an average dosage of 360 mg/day, followed by colchicine (Colcrys) 0.6 mg/day, working up to 1.8 mg/day.



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**Hallmarks of calcinosis are firm dermal or subcutaneous papules or nodules.**

Other potential therapies include warfarin, intravenous immunoglobulin, bisphosphonates, sodium thiosulfate plus topical administration of abatacept (Orencia) and extracorporeal shock wave lithotripsy (J. Am. Acad. Dermatol. 2011;65:15-22; Semin. Arthritis Rheum. 2005;34:805-12).

Daily use of the broad-spectrum tetracycline antibiotic minocycline (Minocin) decreased the frequency of ulceration and inflammation associated with calcinosis deposits, but only modestly reduced calcinosis deposits in nine patients with limited cutaneous systemic sclerosis (Ann. Rheum. Dis. 2003;62:267-9).

Dr. Christopher-Stine said that all therapies are worth a trial, but that surgical removal should probably be considered as a last resort, as the trauma from surgery can induce more calcification, poor wound healing, and infections.

The Mayo Clinic reported that excision of symptomatic lesions resulted in 22 complete responses, 5 partial responses, and no response in 1 patient among 28 patients undergoing surgery for calcinosis cutis (Arch. Dermatol. 2012;148:455-62).

Dr. Christopher-Stine reported having no relevant financial relationships. ■

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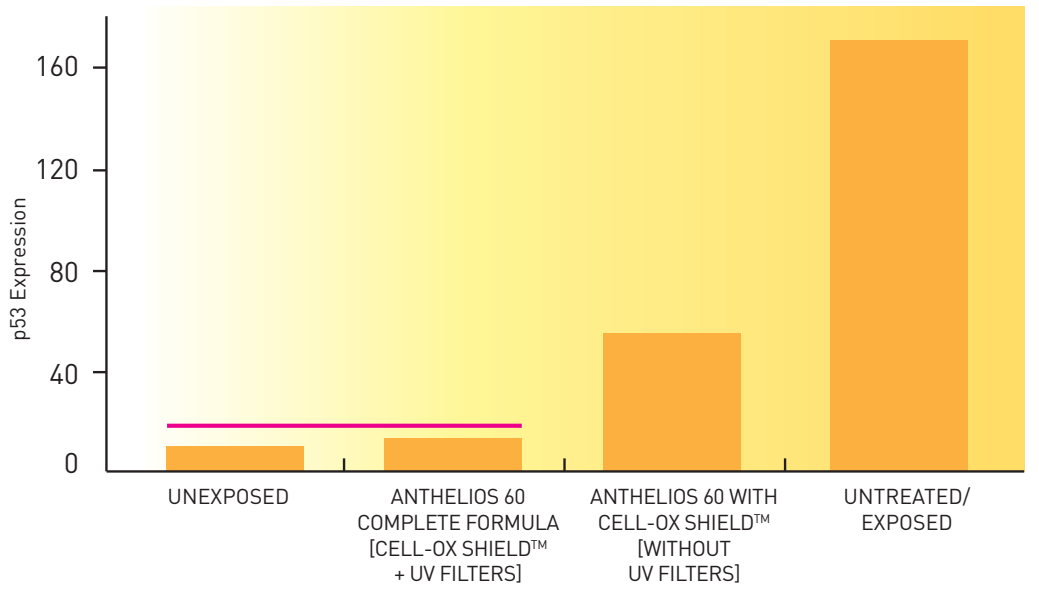


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(1) Upper layers of the skin.
(2) Source: Journal of Cosmetic and Laser Therapy, 2010; 12: 157–162.

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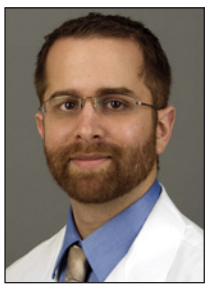
# Thorough Work-Up Crucial in Sarcoidosis Cases

BY DOUG BRUNK

EXPERT ANALYSIS FROM THE ANNUAL MEETING OF THE AMERICAN ACADEMY OF DERMATOLOGY

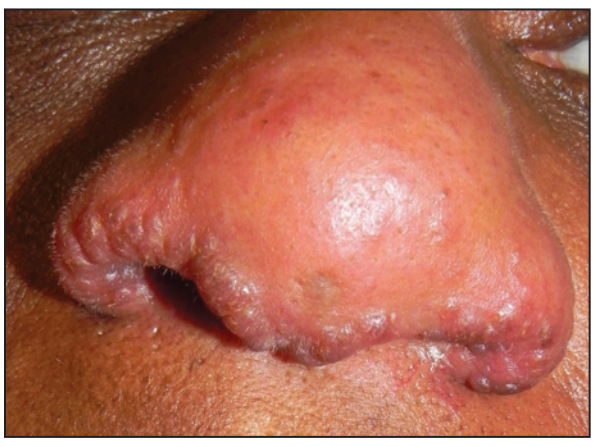
SAN DIEGO – While it's well known that sarcoidosis commonly affects pulmonary function, it's perhaps less known that the disorder can be detrimental to cardiac function in approximately 5% of cases.



"A common way that patients present with cardiac sarcoidosis is with sudden cardiac death," Dr. Misha Rosenbach said at the meeting. "This is a terrible way to present to your doctor with a problem."

A multisystem disorder of unknown cause, sarcoidosis commonly affects young and middle-aged adults and frequently presents with bilateral hilar lymphadenopathy, pulmonary infiltration, and ocular and skin lesions. Other organs may be involved. The diagnosis is established when clinicoradiologic findings are supported by histologic evidence of noncaseating epithelioid cell granulomas.

"Sarcoidosis is primarily a pulmonary disease, but patients can also present with profound systemic symptoms," said Dr. Rosenbach of the departments of dermatology and internal medicine at the University of Pennsylvania, Philadelphia. "When you're evaluating a patient with cutaneous sarcoidosis, and making a diagnosis of granulomatous disease of the skin, and looking for extracutaneous involvement, it's important to know what else can be affected."



**Sarcoidosis is a multisystem disease (cutaneous manifestation on the nose is shown above).**

Although pulmonary function is affected in more than 90% of cases, other commonly affected sites include the eyes (25%-50% of cases), lymph nodes (about 33% of cases), musculoskeletal system (25%-40% of cases), endocrine system (10%-25% of cases), and liver (20%-50% of cases).

The initial evaluation should consist of history and physical exam; chest x-ray; pulmonary function tests (including carbon monoxide diffusing capacity); ophthalmologic examination; complete blood count and serum chemistries (including calcium); urinalysis; EKG (plus additional testing if there is a history of palpitations); tuberculin skin test (TST) or interferon (IFN)–gamma release assay; and thyroid and vitamin D testing.

**'A common way that patients present with cardiac sarcoidosis is with sudden cardiac death.'**

**DR. ROSENBACH**

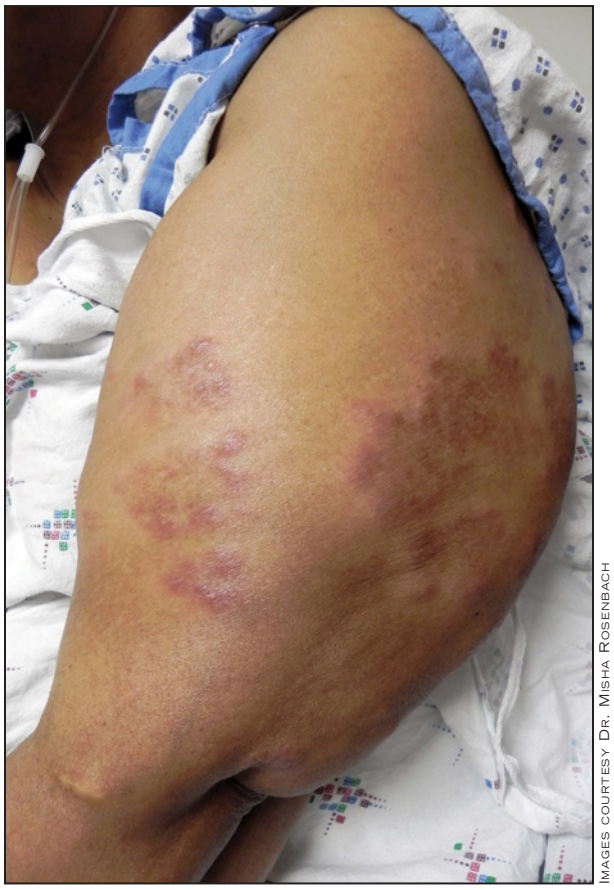
"Patients with sarcoidosis often have low levels of 25-hydroxyvitamin D, but elevated levels of 1,25-dihydroxyvitamin $D_3$," Dr. Rosenbach said. "Inappropriate supplementation can lead to hypercalcemia."

For latent tuberculosis testing, he pointed out that the IFN-gamma release assay (IGRA) is thought to be more accurate than the TST. "IGRA significantly reduces false-positive results" in bacille Calmette-Guérin–vaccinated patients, said Dr. Rosenbach, who is also director of the cutaneous sarcoidosis clinic at the University of Pennsylvania. "Cost-benefit analyses suggest that IGRA [is] cost equivalent to TST, and the Centers for Disease Control and Prevention recommends that IGRA may be used in all circumstances in which the TST is currently used. However, both TST and IGRA have decreased responsiveness and lower sensitivity in patients with impaired immune systems."

In terms of the impact of sarcoidosis on the thyroid gland, a recent analysis of a large database in the United Kingdom found that hyper- and hypothyroidism were twice as common in patients with sarcoidosis, compared with a control population (Postgrad. Med. J. 2009;85:233-7).

A more recent study of 50 patients with cutaneous sarcoidosis conducted by Dr. Rosenbach and his colleagues found that 25% of patients had abnormal thyroid laboratory test results (J. Am. Acad. Dermatol. 2012;66:167-8).

The precise association between sarcoidosis and malignancy remains unclear, he said, but the best available studies suggest that the incidence of lymphoproliferative disorder may be increased in patients with sarcoidosis. Other granulomatous dermatitides may be associated with hematologic abnormalities. Authors of one review found that granulomatous dermatitides may be the first sign of underlying myelodysplastic syndrome (MDS), and recommended that clinicians consider looking for underlying MDS in patients with unexplained or atypical granulomatous skin eruptions (Arch. Dermatol. 2011;147:331-5).



IMAGES COURTESY DR. MISHA ROSENBACH

**Treatment should begin with steroids or injections (cutaneous sarcoidosis on the arm is shown above).**

A common stepwise approach for treating patients, Dr. Rosenbach said, begins with skin-directed therapies in the form of steroids or injections. The second step involves the use of antimalarials and tetracycline-class antibiotics; the third step involves methotrexate and/or prednisone, and the fourth step involves consideration for treatment with infliximab or adalimumab. "At this point, etanercept should probably not be used," Dr. Rosenbach said. "It appears to be less effective, and in a few reports has been associated with worsening of disease."

The data are strongest for infliximab, he said, at a recommended dosage of 5 mg/kg at 0, 2, and 6 weeks, and then with maintenance therapy every 6-8 weeks. Adalimumab appeared to work best at 40 mg every week, he said, "but the addition of low-dose methotrexate is sometimes necessary to either regimen."

Dr. Rosenbach disclosed that he was an investigator for a clinical trial sponsored by Centocor and Johnson & Johnson to investigate biologics for chronic/refractory sarcoidosis. ■

# Urine Analysis May Help Predict Response to Biologics

BY SARA FREEMAN

FROM THE ANNUAL MEETING OF THE BRITISH SOCIETY FOR RHEUMATOLOGY

GLASGOW, SCOTLAND – Urine analysis might help to predict if patients are likely to respond to biologic treatments, the results of a small metabolomics study suggest.

Pretreatment levels of histamine, glutamine, xanthurenic acid, and ethanolamine were consistently correlated to response to anti–TNF-alpha therapy at 12 weeks in the 36-patient evaluation.

Dr. Sabrina Kapoor, an Arthritis U.K. clinical research fellow in the Rheumatology Research Group at the University of Birmingham (England), and her associates obtained frozen urine samples from 16 patients with RA and 20 with psoriatic arthritis (PsA). The samples had been taken during a randomized, three-center clinical study investigating patient responses to treatment with infliximab or etanercept (Rheumatology 2012;51[suppl.3]:abstract O15).

Nuclear magnetic resonance (NMR) spectroscopy was used to analyze the metabolomic profiles of the urine samples that were taken before and 12 weeks after anti-TNF treatment.

All patients in the study received methotrexate and had a disease duration of more than 6 months. RA patients were rheumatoid factor (RF) positive, anti–cyclic citrullinated protein (CCP) antibody positive, or both, and had a DAS28 greater than 4. PsA patients were negative for RF and anti-CCP antibodies, with three or more swollen or tender joints.

Only the samples from the patients with RA could be linked to treatment effect. All the patients with PsA had a good response to treatment according to EULAR criteria. Changes in the DAS28 were used to identify patients with RA who did (n = 7) or did not (n = 9) respond to anti-TNF therapy at 12 weeks.

Good responders were those who achieved a DAS28 lower than 3.2, or an improvement in score greater than 1.2.

"There was a significant [$P = .04$] correlation between baseline metabolomic profiles in the urine samples and the extent of change in DAS28," Dr. Kapoor said. Baseline metabolomic analysis of the urine in RA patients had 85.9% sensitivity and 85.7%, specificity to detect treatment response.

These data need to be confirmed in a larger, independent cohort of patients.

Dr. Kapoor had no financial disclosures. Merck sponsored the original study. ■

Finally in metastatic melanoma

# A PERSONALIZED TREATMENT

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ZELBORAF is not recommended for use in patients with wild-type BRAF melanoma.

## Important Safety Information

### Cutaneous squamous cell carcinoma (cuSCC)

- Cases of cuSCC, including both SCCs of the skin and keratoacanthomas, have been reported in patients treated with ZELBORAF. The incidence of cuSCC in ZELBORAF-treated patients in the Phase III study was 24%. The median time to first appearance of cuSCC was 7 to 8 weeks. Potential risk factors included age ≥65 years, prior skin cancer, and chronic sun exposure.
- All patients should receive a dermatologic evaluation prior to initiation of therapy, every 2 months while on therapy, and potentially for 6 months following discontinuation of ZELBORAF. Any suspicious skin lesions should be excised, evaluated, and treated as per standard of care.

### Hypersensitivity and Dermatologic Reactions

- Serious hypersensitivity reactions, including anaphylaxis, have been reported in association with ZELBORAF and upon re-initiation of treatment. Severe reactions may include generalized rash and erythema or hypotension.
- Severe dermatologic reactions have been reported in patients receiving ZELBORAF, including 1 case of Stevens-Johnson syndrome and 1 case of toxic epidermal necrolysis in the Phase III study.
- ZELBORAF treatment should be permanently discontinued in patients who experience a severe hypersensitivity or dermatologic reaction.

### QT prolongation

- Exposure-dependent QT prolongation has been observed in patients treated with ZELBORAF, which may lead to an increased risk for ventricular arrhythmias, including Torsade de Pointes.
- Treatment is not recommended in patients with uncorrectable electrolyte abnormalities, with long QT syndrome, or who are taking medicines known to prolong the QT interval. ECG and electrolytes should be monitored before initiating treatment with ZELBORAF and after dose modification and routinely during treatment (15 days after treatment initiation, then monthly for first 3 months of treatment and every 3 months thereafter or as clinically indicated). If the QTc exceeds 500 ms, ZELBORAF treatment should be temporarily interrupted, electrolyte abnormalities corrected, and cardiac risk factors for QT prolongation (e.g. congestive heart failure, bradyarrhythmias) controlled. Re-initiation of treatment should occur at a lower dose once the QTc decreases below 500 ms. Permanent discontinuation is recommended if, after correction of associated risk factors, the QTc increase meets both a value of >500 ms and >60 ms change from pre-treatment values.

### Liver laboratory abnormalities

- Liver laboratory abnormalities have occurred with ZELBORAF.
- Liver enzymes (transaminases and alkaline phosphatase) and bilirubin should be monitored before initiation of treatment and monthly during treatment, or as clinically indicated. Lab abnormalities should be managed with dose reduction, treatment interruption, or treatment discontinuation.

### Photosensitivity

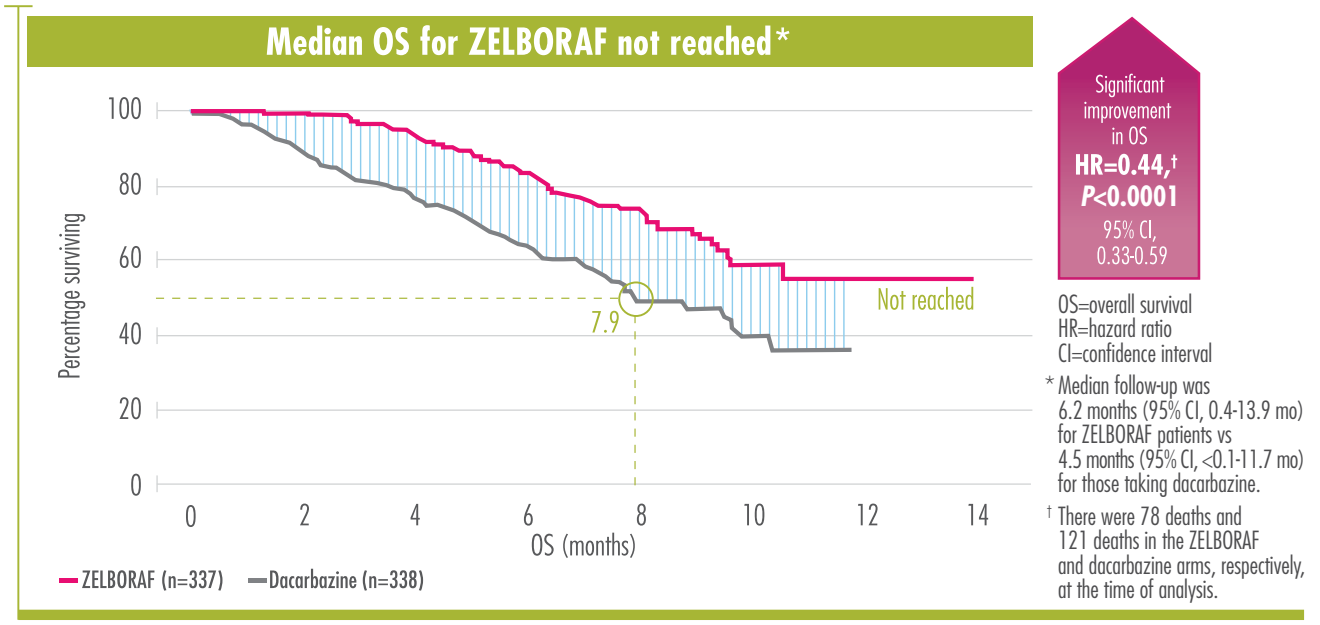
- Mild to severe photosensitivity was reported in patients treated with ZELBORAF in clinical trials.
- While taking ZELBORAF, all patients should be advised to avoid sun exposure and, when outdoors, to wear protective clothing and use a broad spectrum UVA/UVB sunscreen and lip balm (SPF ≥30). For intolerable grade 2 or greater photosensitivity, dose modifications are recommended.

### Ophthalmologic Reactions

- In the Phase III study, 5 cases of uveitis were reported in patients treated with ZELBORAF.

# EXTEND survival

## 56% reduction in risk of death from any cause with ZELBORAF (95% CI, 0.33-0.59)




OS=overall survival
HR=hazard ratio
CI=confidence interval

* Median follow-up was 6.2 months (95% CI, 0.4-13.9 mo) for ZELBORAF patients vs 4.5 months (95% CI, <0.1-11.7 mo) for those taking dacarbazine.

† There were 78 deaths and 121 deaths in the ZELBORAF and dacarbazine arms, respectively, at the time of analysis.

- **~4-month improvement in median progression-free survival** (5.3 vs 1.6 months; HR=0.26, *P*<0.0001, 95% CI, 4.9-6.6 months vs 1.6-1.7 months)
- **Significant improvement in best overall response rate** (48.4% vs 5.5%; *P*<0.001, 95% CI, 41.6%-55.2% vs 2.8%-9.3%)[3]
  - There were 2 complete responses (1%) and 104 partial responses (PRs) (47.4%) with ZELBORAF vs 12 PRs (5.5%) with dacarbazine
- **The most common adverse reactions of any grade (≥30%) reported were arthralgia, rash, alopecia, fatigue, photosensitivity reaction, nausea, pruritus, and skin papilloma; the most common (≥5%) grade 3 adverse reactions were cutaneous squamous cell carcinoma and rash**

- Treatment with steroid and mydriatic ophthalmic drops may be required to manage uveitis. Patients should be routinely monitored for signs and symptoms of uveitis.
- Additionally, 5 cases each of blurry vision and iritis and 6 cases of photophobia were reported in the Phase III study. One case of retinal vein occlusion was reported in the Phase II study.

### New Primary Malignant Melanoma

- Eight skin lesions in 7 patients were reported as new primary malignant melanoma in the Phase III study.
- Cases were managed with excision and patients continued treatment without dose adjustment; monitoring for skin lesions should occur as outlined above *[see cuSCC]*.

### Use in Pregnancy: Pregnancy Category D

- ZELBORAF may cause fetal harm when administered to a pregnant woman based on its mechanism of action. There are no adequate and well-controlled studies in pregnant women.
- If ZELBORAF is used during pregnancy or if the patient becomes pregnant while taking ZELBORAF, the patient should be apprised of the potential hazard to a fetus.

### BRAF Testing

- Confirmation of $BRAF^{V600E}$ mutation-positive melanoma as detected by an FDA-approved test is required for the selection of patients appropriate for ZELBORAF therapy. The efficacy and safety of ZELBORAF have not been studied in patients with wild-type BRAF melanoma.

### Most common adverse events

- The most common adverse reactions of any grade (≥30%) reported were arthralgia, rash, alopecia, fatigue, photosensitivity reaction, nausea, pruritus, and skin papilloma.
- The most common (≥5%) grade 3 adverse reactions were cuSCC and rash. In clinical studies, cuSCC was predefined as a grade 3 event.

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

**References: 1.** Smalley KS, Sondak VK. Melanoma—an unlikely poster child for personalized cancer therapy. *N Engl J Med.* 2010;363:876-878. **2.** Flaherty KT. Next generation therapies change the landscape in melanoma. *F1000 Med Reports.* http://f1000.com/reports/m/3/8. Published April 1, 2011. Accessed July 14, 2011. **3.** Chapman PB, Hauschild A, Robert C, et al. Improved survival with vemurafenib in melanoma with BRAF V600E mutation. *N Engl J Med.* 2011;364:2507-2516.

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# CASE OF THE MONTH

## Diagnosis: Erythema Nodosum

Erythema nodosum is the most common form of panniculitis. Although the acute form of erythema nodosum may occur at any age, it is more common in adult females aged 20-40 years, and usually presents as bilateral, painful, erythematous subcutaneous nodules on the pretibial areas and lateral shins.

Typically, lesions do not ulcerate. Other body areas – such as the upper legs, arms, neck, and face – may be involved, although rare.

Associated symptoms, such as fever, headache, arthralgias, conjunctivitis, gastrointestinal complaints, and malaise, may be present.

The differential diagnosis includes erythema induratum (nodular vasculitis). This condition tends to affect the posterior legs and may ulcerate. Pancreatic panniculitis lesions also ulcerate, and are associated with elevations in amylase and lipase.

There are numerous causes of erythema nodosum, with most being idiopathic. Causes include upper respiratory infections (*Streptococcus* most common), medications (estrogen, sulfonamides, penicillin, bromides, and iodides), sarcoidosis, inflammatory bowel disease, and other infectious causes (such as coccidioidomycosis, hepatitis B, and *Yersinia*). Histopathology may reveal a primarily septal panniculitis with an infiltration of lymphocytes and neutrophils. Miescher's microgranulomas may be seen within the septa.

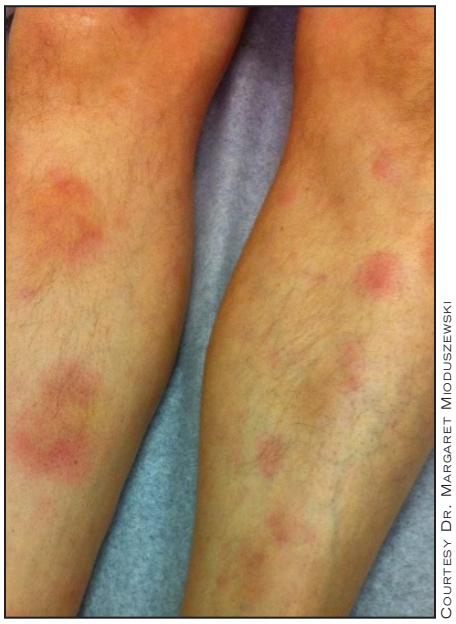
Treatment of erythema nodosum involves investigation of the primary underlying cause, and potassium iodide is usually effective. Improvement of lesions is usually seen in 2 weeks; lesions often involute without scarring.

This patient was treated with bed rest and NSAIDs. An underlying condition was not elucidated.

**–Donna Bilu Martin, M.D.**

Dr. Martin *is in private practice in Miami.*

*This case was submitted by Dr. Margaret Mioduszewski of the University of Ottawa.*



Courtesy Dr. Margaret Mioduszewski

**The condition usually presents as bilateral, painful, erythematous subcutaneous nodules on the pretibial areas and lateral shins.**



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## POLICY & PRACTICE

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### FDA Delays Sunscreen Rule

The Food and Drug Administration announced in May that it was giving sunscreen manufacturers 6 additional months to comply with the final ruling on product labeling and effectiveness testing. That final rule was published in June 2011; soon after, the Personal Care Products Council (PCPC) and the Consumer Healthcare Products Association (CHPA) sought a 6-month delay in the deadline, saying that manufacturers needed more time. The agency agreed and has pushed back compliance dates. Now, products that have sales of less than $25,000 will have until Dec. 17, 2013, to comply; all other products must comply by Dec. 17, 2012. However, the agency is encouraging manufacturers to "introduce individual products bearing the new labeling as it becomes available, even in advance of the revised compliance date." The American Academy of Dermatology also urged sunscreen makers to comply sooner, rather than later, but said in a statement that the extension "allows manufacturers the necessary time to test their products for broad-spectrum protection and properly label them." The Environmental Working Group (EWG) which publishes a database of sunscreen effectiveness, chided the FDA, saying in a statement that it "has caved to industry pressure every step of the way," of getting the rules finalized – a 30-year process. The group estimates that 90% of sunscreens are already in compliance with what it calls the FDA's "low-bar regulations on efficacy and safety."

### Vermont Bans Tanning for Minors

Vermont has become the second state to enact a prohibition on the use of indoor tanning beds by minors. However, Gov. Peter Shumlin (Democratic and Working Families Party) did not support the legislation or sign it; but it became law regardless of his position. The new law levies a $100 fine on tanning salon owners for the first violation, and $500 for each subsequent violation. The AAD supported the bill, as did the American Cancer Society Cancer Action Network. Both groups noted that indoor tanning is linked to an increased risk of melanoma. According to the AAD, between 2004 and 2008, the melanoma incidence in Vermont in women aged 15 years or older increased by 34%. "Prohibiting minors' access to indoor tanning stops this behavior before it can become a habit that continues through adolescence into young adulthood," said AAD President Daniel M. Siegel in a statement.

### EWG Releases Sunscreen Rankings

The EWG has issued its annual ranking of sunscreens, and reported that of more than 1,800 it reviewed, about 25% pass muster. That's up from 20% in 2011 and 8% in 2010. According to the group, children's sunscreens contain the most effective and safest ingredients. Sixty percent of the 180 products marketed for children have ingredients such as minerals, which are considered effective, compared with only 40% of those for the general public. The group recommended that consumers choose products with zinc oxide, titanium dioxide, or 3% avobenzone and that they avoid oxybenzone and vitamin A (retinyl palmitate). Sunscreen sprays and powders are not as effective as creams or lotions, according to the group. And it found that many manufacturers are selling products with escalating SPF values. In a statement from the EWG, Sen. Jack Reed (D-R.I.) said that the FDA needs to move more quickly on instituting sunscreen standards, but in the meantime, "it is good to know Environmental Working Group is providing consumers with the facts about the effectiveness of sunscreen products that are currently on shelves." The AAD refuted much of the EWG claim in a statement, noting that there is no evidence that oxybenzone affects hormones, nor is oxybenzone or vitamin A dangerous in sunscreens, said Dr. Siegel. The AAD continues to back use of a water-resistant, broad-spectrum sunscreen that protects against UVA and UVB, with an SPF 30 or higher, in conjunction with limiting sun exposure and wearing sun-protective clothing.

### Abbott Seeks to Block Biosimilars

Abbott Laboratories has petitioned the FDA to not approve any generic versions of its rheumatoid arthritis drug Humira if the applications were submitted before March 23, 2010. That date is important because it is when President Obama signed into the law the Biologics Price Competition and Innovation Act. That law gives brand-name biologics 12 years of market exclusivity and in exchange, the FDA is able to use proprietary information on their branded products in approving generic versions or biosimilars. In its petition, Abbott is asking the FDA to interpret the law as applying only to applications made after its enactment. If the FDA were to accept applications made before March 23, 2010 it would open itself up to constitutional questions and liability for infringing on trade secrets, according to Abbott's petition.

**–Alicia Ault**

JOSEPH S. EASTERN, M.D.

# Managing Your Dermatology Practice

## A Great Boss

Visitors to my office often ask about the secret to maintaining "such a marvelous" 11-person staff. "You must pay them a fortune," they say.

Yes, they are compensated fairly; but that's not why they stay. Staff turnover is essentially nonexistent. (My most junior employee is going on 18 years.) I know for a fact that many of them have turned down higher salaries at big clinics.

They remain, I believe, because I welcome their ideas; and I let them know on a regular basis that I notice and appreciate their efforts.

**By encouraging my employees to propose solutions and suggest better methods and procedures, I demonstrate to them that they have a stake in the success of the office.**

Soliciting employee input is a win-win; it builds loyalty and a sense of community, and you discover better ways to run your office.

I fancy myself an innovative guy, but I can't think of everything myself. I don't sit at the reception window; I don't handle the phones; I don't put patients in rooms. So, don't let your staff keep good ideas to themselves. Your staff will only make the effort, however, if they understand that there is something in it for them, other than a token salary raise at year's end.

The monthly office meeting is a great vehicle for brainstorming. I like my office manager to run them; or more precisely, we like to let them run themselves. We just moderate the discussion, identify problems, and solicit solutions. Usually the answer will come from the dialogue. In addition, we always leave time for airing of any proposals for general improvement of the office as a whole.

By encouraging my employees to propose solutions and suggest better methods and procedures, I demonstrate to them that they have a stake in the success of the office. And when a solution or a new suggestion is staff conceived, the staff has a stake in ensuring that it is implemented and that it works.

This method also offers the opportunity to identify and work out minor problems before they become major ones.

Even in this digital age, an essential tool for me at office meetings is a good old-fashioned yellow legal pad, on which I note everything discussed.

Each problem identified and each new idea offered is paired with proposed solutions and practical suggestions for implementation, and someone is assigned the responsibility of taking action. Not only does it guarantee that a problem will not continue and a good idea will not die, it also reassures staff that they are not just whistling in the dark when they point out a problem or propose a new office policy.

Some physicians hold meetings away from the office, perhaps at a local restaurant, going on the theory that staff will be more frank when outside of the office. Personally, I have never found my employees reluctant to express themselves in any setting, but if you have, consider that alternative.

Anytime someone comes up with a great idea, or calls attention to a significant issue, I make sure that the person hears – immediately and publicly – the praise that he or she deserves. That goes for all aspects of the office. Whenever I "catch someone doing something right," I note it, and praise that person.

Of course, it is also sometimes necessary to dole out constructive criticism; but as public as praise should be, criticism should be private. And the manner of the criticism is just as important as the setting. I prefer to point out the problem, ask what might have precipitated it, and suggest ways to correct it. After all, nobody is perfect. When you are understanding of your employees' mistakes, they will be more understanding of yours.

The emphasis, however, is always on praise. When I leave at the end of the day I always thank the staff. If I can't think of a specific thing to thank them for, I thank them for a good day. ■

DR. EASTERN *practices dermatology and dermatologic surgery in Belleville, N.J. To respond to this column, email him at our editorial offices at sknews@elsevier.com.*

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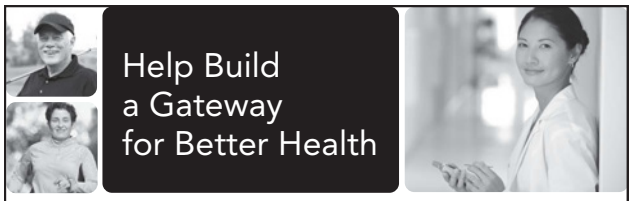


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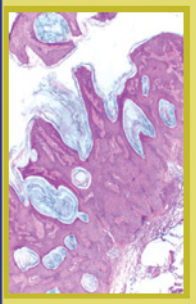

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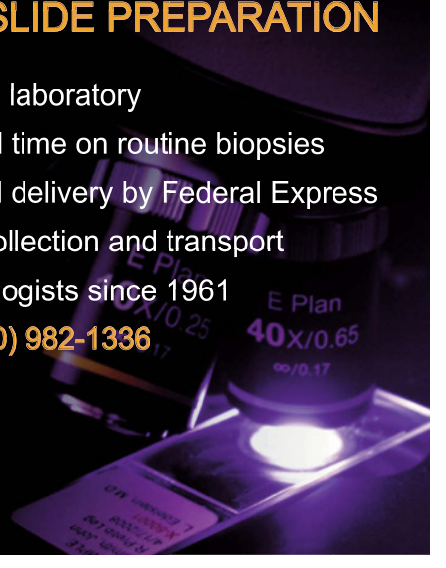


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## NeutraPhase Wound Cleanser

NeutroPhase wound cleanser comprises a patented pure hypochlorous acid (HOCl) solution that mimics the infection-fighting compounds produced naturally by white blood cells. For use in combination with commercially available wound dressings in patients who have chronic nonhealing wounds such as pressure, venous stasis, and diabetic ulcers, the nonantibiotic irrigant and cleanser supports healing by disrupting bacterial biofilm and killing common gram-positive and -negative wound pathogens without harming the healthy fibroblast cells. The cleanser can be used in wet-to-moist dressing techniques and also in negative pressure wound therapy procedures.

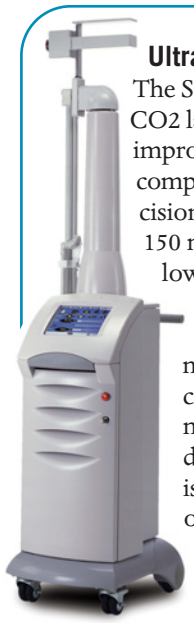

NovaBay Pharmaceuticals
www.neutrophase.com

## Swift Lift Serum

A new formula will be introduced for emerginC Swift Lift skin tightening serum in September. The formula has been improved by adding instalift goji and provides instant, noticeable, all-day face lifting, firming, and tightening. Instalift goji is an isolated active glycopeptides fraction which combines the skin lifting and firming strength of both proteins and polysaccharides. The serum also includes: carrageenan extract, sodium hyaluronate, soybean extract, grape seed extract, glycerin, green tea and myoxinol. The serum retails for $79.


emerginC
www.emerginc.com

## UltraPulse With SCAAR FX



The SCAAR FX module of the UltraPulse CO2 laser penetrates deep into the skin to improve the appearance of conspicuous, complex, and deep skin lesions. Using precision and high energy impact of up to 150 mJ per pulse per spot, SCAAR FX allows direct impact up to 4 millimeters deep into the skin tissue, which is four times deeper than other commercially available $CO_2$ lasers, according to the manufacturer. The module's combination of short pulse durations and high energy per pulse is designed to improve the structure of deep contracted skin lesions, such as surgical scars, leading to increased range of motion and enhanced skin appearance.

Lumenis
www.lumenis.com

## Advanced Eye Cream

Kinerase is launching a new, gentle, nonprescription eye cream, which includes the company's antiaging ingredient, Kinetin, and a new HA$^3$ technology (N-acetylglucosamine-6-phosphate). The new complex is a retinol alternative that supports the skin's ability to produce hyaluronic acid. The product also contains eyeseryl tetrapepdtide and SYN-coll/palmitoyl tripeptide. The cream is formulated to visibly reduce the appearance of fine lines and wrinkles around the eye; reduce puffiness and under eye circles; and moisturize and brighten the eye area. The products will be available in July through ULTA.


Kinerase
www.kinerase.com

## Anti-Aging Serum

Pro+Therapy MD has launched émergence Cell Rejuvenation Complex, an anti-aging serum that contains four anti-aging innovations, along with prosome delivery of kinetin and zeatin. The product helps the skin to appear firmer and less wrinkled, according to the manufacturer. The noncomedogenic and hypoallergenic serum reactivates cellular youth potential for younger looking skin; improves the appearance of photodamage and aging; and provides high levels of kinetin and zeatin via the prosome delivery system, which slowly releases the plant-derived growth factors to nourish cells and help improve the visible signs of aging. The product retails for $130 for 1 fl. oz.

Valeant Pharmaceuticals
www.protherapymd.com

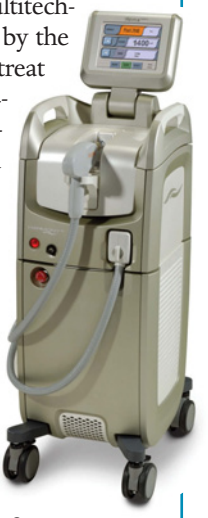
## Promiseb Regimen for Seborrheic Dermatitis

Promiseb Complete is a new two-step regimen available for patients with seborrheic dermatitis. The regimen includes the Promiseb Topical Cream and the Promiseb Plus Scalp Wash. The Promiseb Topical Cream is a nonsteroidal, prescription cream for the treatment of seborrheic dermatitis. In a randomized clinical study the cream had comparable efficacy and fewer relapses than a low-potency topical corticosteroid. The cream has also shown anti-inflammatory and anti-fungal properties, according to the manufacturer. Patients with a known allergy to shea butter or shea nut oil should contact their physician before using the product. The companion product, Promiseb Plus Scalp Wash, is formulated to cleanse the scalp and remove flaky build-up. In a 2-week open study of the scalp wash, patients had a decrease in flakes. The scalp wash is only available as part of the Promiseb Complete regimen.


Promius Pharma
www.promiuspharma.com

## Laser Treatment for Onychomycosis

The Harmony multiapplication, multitechnology laser has received clearance by the Food and Drug Administration to treat nail fungus. The Q-switched 1064-nm Nd:YAG laser creates microcavitations and acoustic shock waves on the surface of the nail plate, which are transmitted to the nail bed – causing mechanical damage in the irradiated fungal colony, which may decapsulate the fungus spores. In addition, yellow and brown streaks that cover the nail are eliminated by the green light of the Q-Switched KTP 532-nm tip. This wavelength is well absorbed by the red and brown pigments of the infected nail microorganism, according to the manufacturer.



Alma Lasers
www.almalasers.com

## NIA 24 Rapid Depigmentation Serum

NIA 24 Rapid Depigmentation Serum is a concentrated serum with Pro-Niacin that helps to diminish the appearance of spots and discolorations. Pro-Niacin, along with tyrosine inhibitors, vitamin C, and hexylresorcinol helps to normalize melanin in the skin to improve the appearance of skin tone, texture, and hyperpigmentation.


The serum helps to visibly diminish the appearance of dark spots and overall discoloration for a significant improvement in skin brightness, clarity, and tone. The serum can be used morning and night. The product retails for $75 for 1 fl. oz. A Depigmentation Spot Repair is also available for targeting individual dark spots. It retails for $45 for 0.135 fl. oz.

Nia 24
www.nia24.com

## Purifying Facial Wash

PUR Purifying Facial Wash is a gentle, foaming cleanser that removes dirt and other impurities while moisturizing and tightening pores. The facial wash is formulated with copper gluconate, aloe, and anti-inflammatory ingredients. The product is suitable for individuals with sensitive skin. The product is a multi-functional cleanser and toner and rinses completely without the use of additional toners or astringents. It is lightly scented with essences of grapefruit and lemon. A 7.6 oz (225 ml) bottle of the facial wash retails for $46 and is available for pre-order online. The facial wash is the latest edition to the LAFACE Laboratories product line, which includes Cellular Regeneration Cream, Hydrating and Purifying Serum, and Hydrating and Firming Body Lotion, EFFACE line erasure concentrate, and BEAUX YEUX beautiful eyes concentrate intensive.

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