

Shalita, M.D., professor and chair of dermatology at the State University of New York, Brooklyn, and an acne researcher. "We'll just have to live with whatever restrictions they impose."

Dr. Shalita's colleague, Dr. Baldwin, said she too thought the new program would mean that fewer physicians would be willing to prescribe isotretinoin. That will probably drive patients to the Internet to get their medication, she added, leaving more patients without any medical supervision at all.

There are more than 30 brands of isotretinoin made and sold worldwide, she noted.

"I'm also worried that they are going to get 'Pete's' isotretinoin, and it is not even going to have isotretinoin in it," she said.

Thalidomide may not have had as many pregnan-

cy exposures as isotretinoin, but that does not necessarily mean the thalidomide program will work the same way for isotretinoin, Dr. Baldwin said.

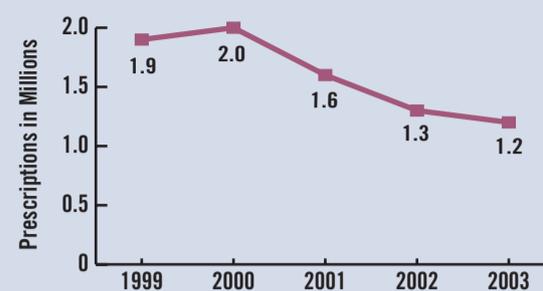
Most patients treated with thalidomide are older, and they are being treated for multiple myeloma. Therefore, they are very sick and probably not inclined to have sexual intercourse.

The FDA's action also prompted a statement from Rep. Bart Stupak (D-Mich.), a well-known critic of isotretinoin, whose son committed suicide while taking the drug.

Stupak's statement suggested that the wrangling over isotretinoin may continue. The congressman vowed to respond if the FDA's final risk management program was not strict enough, and he called for hearings specifically on isotretinoin. ■

DATA WATCH

Isotretinoin Prescribing Declines



Note: Based on data for more than 2 billion pharmacy, hospital, and medical transactions per year in the United States.
Source: Verispan

KEVIN FOLEY, RESEARCH/JULIE KELLER, DESIGN

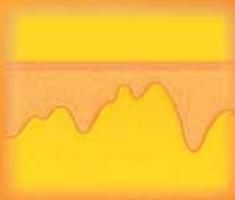
Immunosuppressant Targets for immune response modifiers

types: pyrimidine pyrimidone photoproducts between adjacent pyrimidine residues, and cyclobutane dimers between adjacent thymine or cytosine residues.¹ In fact, accumulations in the form of single (C → T) or tandem (CC → TT) transitions are known as the "UV signature."⁶ The *p53* mutation in keratinocytes plays a key role in the process of carcinogenesis in the skin. In addition to the *p53* gene, mutations in another tumor-suppressing gene, the *patched* (*PTCH*) gene, seem to be implicated in the formation of skin carcinomas.⁷

How immune modification combats skin lesions

Immune response modifiers promise to play an exciting and interesting role in the destruction of precancerous and cancerous lesions. When applied topically, immune response modifiers activate a newly discovered family of pathogen recognition receptors called

Toll-like receptors. Located on the surface of antigen-presenting cells, such as Langerhans and other dendritic cells, Toll-like receptors are a family of 10 members, each of which recognizes signals of damaged cells or microbes.⁸ Activation of Toll-like receptors leads to production of cytokines and chemokines, such as INF- α , TNF- α , IL-12, MCP-1, and MIP-1 α .^{9,10} The



Immune cells clear precancerous and cancerous lesions.

chemokines attract immune cells to the site of application, and the cytokines cause activation of immune cells. Toll agonists have been found to promote cytokine and chemokine release from dendritic cells that reside in the dermis and the epidermis.⁹ Activation of

immune cells and release of cytokines by these dendritic cells can rally the immune system back into action, overcoming the Langerhans cell deficit.¹¹ Mechanism of action studies with immune response modifiers show posttreatment increases in activated dendritic cell and CD4 T-cell numbers when applied to actinic keratosis or basal cell carcinoma lesions, coincident with the destruction of malignant cells.¹²

Ongoing research demonstrates that immune response modifiers are capable of becoming an integral part of the treatment regimen for actinic keratosis and basal cell carcinoma.

3M Pharmaceuticals

References: 1. Soehnle H, Ouhit A, Ananthaswamy HN. Mechanisms of induction of skin cancer by UV radiation. *Front Biosci.* 1997;2:538-551. 2. Freedberg IM, Eisen AZ, Wolff K, et al, eds. *Fitzpatrick's Dermatology in General Medicine.* Vol 1, 2. 5th ed. New York, NY: McGraw-Hill; 1999. 3. Fisher MS, Kripke ML. Systemic alteration induced in mice by ultraviolet light irradiation and its relationship to ultraviolet carcinogenesis. *Proc Natl Acad Sci U S A.* 1977;74:1688-1692. 4. Baron ED, Stevens SR. Sunscreens and immune protection. *Br J Dermatol.* 2002;146:933-937. 5. Vink AA, Moodycliff AM, Shreedhar V, et al. The inhibition of antigen-presenting activity of dendritic cells resulting from UV irradiation of murine skin is restored by in vitro photorepair of cyclobutane pyrimidine dimers. *Proc Natl Acad Sci U S A.* 1997;94:5255-5260. 6. Ouhit A, Ananthaswamy HN. A model for UV-induction of skin cancer. *J Biomed Biotechnol.* 2001;1:5-6. 7. Lacour JP. Carcinogenesis of basal cell carcinomas: genetics and molecular mechanisms. *Br J Dermatol.* 2002;146(suppl 61):17-19. 8. Hemmi H, Kaisho T, Takeuchi O, et al. Small anti-viral compounds activate immune cells via the TLR7 MyD88-dependent signaling pathway. *Nature Immunol.* 2002;3:196-200. 9. Kadowaki N, Ho S, Antonenko S, et al. Subsets of human dendritic cell precursors express different Toll-like receptors and respond to different microbial antigens. *J Exp Med.* 2001;194:863-870. 10. Gibson SJ, Imbertson LM, Wagner TL, Testerman TL, Miller RL, Tomai MA. Cellular requirements for cytokine production in response to the immunomodulators imiquimod and S-27609. *J Interferon Cytokine Res.* 1995;15:537-545. 11. Suzuki H, Wang B, Shivji GM, et al. Imiquimod, a topical immune response modifier, induces migration of Langerhans cells. *J Invest Dermatol.* 2000;114:135-141. 12. Data on file. 3M Pharmaceuticals.

Electronic Health Records Reduced Clinic Visit Length

SAN FRANCISCO — Adopting an electronic health records system reduced the mean length of visits at five outpatient clinics by 4 minutes per patient, a difference that was not statistically significant but that should allay physicians' fears that the technology might be a burden, Lisa Pizziferri said.

The results come from a time-motion study in which observers shadowed primary care physicians before and after implementation of the electronic health records (EHR) system and timed their activities, she said in a poster presentation at the triennial congress of the International Medical Informatics Association.

They studied 20 physicians before EHR implementation, 16 of those after adoption of the system, and 4 newly recruited physicians after EHR implementation, for a total of 20 physicians before and after the system change. The urban and suburban outpatient clinics included neighborhood health centers, hospital-based practices, and community practices.

Talking to or examining a patient (direct patient care) took about 14 minutes in the pre-EHR era of paper-based records and 13 minutes using EHR, said Ms. Pizziferri of Partners HealthCare System Inc., Wellesley, Mass.

Indirect patient care, which involved reading, writing, or other tasks in support of direct patient care, took 9 minutes before EHR and 10 minutes after EHR. Physicians spent about half a minute reviewing schedules before EHR and 1 minute with EHR. Time spent eating, walking, or performing other miscellaneous tasks decreased from 4 minutes to 3 minutes per patient after EHR implementation.

The mean overall time spent with each patient decreased by 4 minutes, and was calculated independently, not by adding up the times of individual tasks, she said. During an average 4-hour observation period per physician, physicians saw 9 patients while using paper records and 10 patients while using EHR. E-mail surveys of the physicians suggested that the time they spent on documentation outside of clinic hours increased from 9 to 10 minutes per established patient after EHR. Future research should study the impact of EHR on nonclinic time, she said.

—Sherry Boschert