**Diet-Acne Association Gains Footing in Literature**

In a pooled analysis of more than 3,000 acne patients with known glucose 6-phosphate dehydrogenase deficiency recently persuaded the Food and Drug Administration to rescind its requirement that all acne patients be tested for G6PD deficiency before prescribing Azelion (dapsone gel).

That requirement, which came as a condition of FDA approval of Azelion in 2009, had convinced the drug's manufacturer, QLT Inc., that topical dapsone was not a marketable drug. Azelion has languished ever since.

Dr. Pariser of Eastern Virginia Medical School, Norfolk, was an investigator in the phase IV safety study, which involved 56 evaluable acne patients with G6PD deficiency and showed no safety problems. Hemolytic is a concern with systemically administered dapsone in G6PD-deficient patients, but there is virtually no systemic absorption of topical dapsone gel, he said. In a pooled analysis of more than 3,000 patients, 40.3% of acne patients were clear or almost clear after 12 weeks of twice-daily dapsone dosing. Both inflammatory and noninflammatory lesion counts were significantly reduced, with inflammatory lesions responding within the first 2 weeks.

FDA marketing approval is anticipated for another novel topical acne therapy: the combination of the retinoid adapalene 0.1% and benzoyl peroxide 2.5% in a fixed-dose gel formulation applied once daily, according to Dr. Pariser. The combination, known as Epiduo, showed rapid efficacy in a 517-patient, double-blind, 12-week Galderma-sponsored randomized trial in which it outperformed each of its separate constituents as well as vehicle alone.

At 12 weeks, 42.5% of patients in the fixed-dose combination therapy group were clear or almost clear; the primary study end point required by the FDA. That was significantly better than the 34.5% rate with adapalene only 34.5% with benzoyl peroxide only and 14.5% with vehicle. Fifty-three percent of patients on Epiduo experienced at least a 50% reduction in total lesion count, compared with about 35% with either agent alone and 25% with vehicle (J. Am. Acad. Dermatol. 2007;57:79-95).

Dr. Pariser led a 12-month safety and efficacy study of the fixed-dose combination in 452 acne patients. The study showed clinically significant reductions in both inflammatory and noninflammatory lesions as early as week 1, with sustained reductions of 75%-80% at 1 year. Only 2% of subjects discontinued the therapy because of adverse events (J. Drugs Dermatol. 2007;6:989-905).

He disclosed that he is a consultant to QLT and has been paid to conduct research by Galderma. SDEF and this news organization are wholly owned subsidiaries of Elsevier.

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**Removal May Not Alter Outcome**

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visit for a mean of 3.5 years (maximum 6 years). None of the AKs were treated. Lesions were biopsied only when they developed some concern signaling progression to malignancy.

During the study period, the 169 patients had 7,784 AKs documented on their face and ears, one-quarter of which were present at baseline. Fifty-five percent were not present 1 year after diagnosis. Thirty-two percent of those present 1 year after initial diagnosis were absent at the 6-month visit but were noted again 6 months later. Four years after initial diagnosis, 31% of AKs were still present; however, 87% of them had disappeared for one or more interim examinations.

"There are a lot of these things coming and going," Dr. Weinstock said at a meeting of the European Society for Dermato logical Research, the Japanese Society for Investigative Dermatology, and the Society for Investigative Dermatology.

Biopsies were obtained on 411 suspicious lesions. Thirty percent proved to be SCCs, 18% were BCCs, 39% were AKs, and 13% were seborrheic keratoses or other lesions.

Overall, 0.6% of clinically diagnosed AKs progressed to SCC at 1 year and 2.6% at 4 years. Three-quarters were in vasive and the remainder in situ SCCs. This progression rate is nearly 10-fold greater than the often-quoted 0.075%/year progression rate from a 20-year-old British study, the dermatologist observed (Lancet 1988;8589:795-7).

AKs present at the initial examination had a higher rate of progression to SCC. AKs also progressed to BCC at a rate of 0.5% in 1 year and 1.6% at 4 years. That was unexpected, said Dr. Weinstock. Dermatologic dogma holds that AKs give rise to SCCs. It’s unlikely these lesions were predominantly BCCs that had initially been misdiagnosed as AKs because a steady increase in BCC risk over the follow-up period was noted. Had it been largely a matter of misdiagnosed BCCs, the risk of developing BCC would likely have increased sharply early in the study and then remained stable, he said.

Two-thirds of SCCs and one-third of BCCs on the face and ears of study participants arose in lesions diagnosed clinically as AKs in prior examinations.

Dr. Joel M. Gelfand of the University of Pennsylvania, Philadelphia, pronounced the new insights into the natural history of AKs gained through this study "really important," particularly since there is no persuasive data to show any of the modalities used to treat AKs actually alter the risk of developing SCC. That observation prompted Dr. Weinstock to note that a new VA chemoprevention trial, this one involving topical 5-fluorouracil for AKs, is now underway.

Audience members said a key limitation of the Oklahome City study was the reliability of clinical diagnosis of AKs. Dr. Weinstock agreed that the reliability of clinical diagnosis is poor—"better than flipping a coin, but not what anyone would hope for." He noted that based upon a comparison of AK counts by seven dermatologists participating in the tretinoin trial that showed substantial interobserver variability, it was clear that patient management decisions in routine practice are typically based upon clinical diagnosis of AKs.