Avoiding Acitretin in Fertile Women a Must

BY DOUG BRUNK

LAS VEGAS — Even though acitretin is labeled as a pregnancy category X drug, Dr. Craig L. Leonardi claimed he sees at least one patient of childbearing potential per month who is referred to him on the agent.

"I think that's a terrifically bad practice," said Dr. Leonardi at a dermatology seminar sponsored by Skin Disease Education Foundation. "You need to think this one through."

The chief risk posed by use of the drug in women of childbearing potential is retinoid embryopathy, which occurs in 33% of preterm infants exposed to the drug in utero. "As a consequence this drug should not be used in females of childbearing potential, which takes the drug off the list for half the population of our younger psoriasis patients," said Dr. Leonardi, clinical professor of dermatology at St. Louis University. "Since there is no teratogenic threshold established for any of the oral synthetic retinoids, this drug just shouldn't be used in females of childbearing potential."

The recommended acitretin pregnancy avoidance period is 3 years in the United States and 2 years in Europe.

Another downside of the drug is that it converts to detectable levels of etretinate in the presence of alcohol ingestion (based on consumption of 8 ounces by a patient weighing at least 75 kg).

A second-generation retinoid, acitretin (Soriatane, Stiefel Laboratories) is available in 10-g and 25-g gel caps. Common doses in psoriasis treatment are 25 mg twice daily, 25 mg twice daily for 1 month followed by 25 mg once daily, or starting off at 25 mg once daily.

Dr. Leonardi said he rarely prescribes acitretin as monotherapy for psoriasis because it has a modest effect on the disease, compared with cyclosporin and methotrexate, resulting in about a 50% reduction of body surface area over a period of 8-24 weeks. In addition, acitretin was approved for psoriasis based on trials involving only 275 patients, and "interpretation of the trial data is difficult," he said. "If this were a biologic drug it would be shelved."

'There is no teratogenic threshold established for any of the oral synthetic retinoids.'

DR. LEONARDI

Adverse events that occur in more than 20% of patients taking 50 mg/day over 8 weeks include chelitis, skin peeling, pruritus, rhinitis, dry skin, and alopecia. "It's a little bit less of an issue if you use the smaller dose, but nonetheless, these are significant numbers," Dr. Leonardi said. "There are some significant, common adverse events while on this therapy."

Despite its modest effect as monotherapy, acitretin "has a very unique mechanism of action," he noted. "It decreases hyperproliferation of keratinocytes, it decreases inflammation directly, and it helps to normalize differentiation of the skin."

He went on to point out that acitretin is most effective when combined with other treatments, particularly psoralen and ultraviolet light radiation (PUVA). One study of this combination demonstrated 89% clearance of psoriatic lesions at 8 weeks and 94% clearance at 12 weeks (Dertmatologica 1988;177:218-24).

A more recent trial evaluated the impact of 25 mg/day acitretin plus narrow band ultraviolet B light three times a week in 40 difficult-to-treat psoriasis patients (J. Dermatolog. Treat. 2003;14[suppl 2]:17-20). It found that 88% of patients had at least a moderate improvement of psoriasis and 73% had an improvement of at least 75%.

Dr. Leonardi disclosed he is a consultant, investigator, and member of the speakers bureau for several pharmaceutical companies. SDEF and this news organization are owned by Elsevier. ■

An interview with Dr. Leonardi can be viewed by visiting www.youtube.com/user/FamilyPracticeNews#p/u/8/XA5NCq4fihQ

Multiple Melanomas a Real Phenomenon

BY DOUG BRUNK

SAN DIEGO — The chances of a patient's developing multiple primary melanomas over a lifetime is a real phenomenon, with an incidence ranging from 2% to 8% among patients who have had a first melanoma, or an average of about 5%.

"That's significantly higher than if we apply the risk of melanoma to all fair-skinned people in the country," Dr. William M. Burrows said at a melanoma update sponsored by the Scripps Clinic.

Of patients who develop more melanomas, about 80% develop two in addition to the original, 15% develop three, and the remainder develop more than three. "In my practice I have about four people I follow who have had five or six primary melanomas," said Dr. Burrows, who has practiced dermatology for nearly 40 years and is currently with the division of dermatology at Scripps Clinic Rancho Bernardo in San Diego.

He went on to note that the risk of multiple primary melanomas is twofold higher among men, and that the majority of subsequent primary melanomas (70%) occur on a different anatomical site, while 30% occur on the same site. "They have the same distribution as melanomas in general," he said.

The majority of subsequent primary melanomas occur after 2 months, while 30% occur within 2 months or less.

Depth of invasion is similar to national statistics for all primary melanomas. "But the second primary melanoma tends to be thinner than the first one, which makes sense," Dr. Burrows said. "After the first primary melanoma we raise our index of suspicion on lesions that are irregular. In addition, the patient has a significant level of worry."

'In my practice I have about four people I follow who have had five or six primary melanomas.'

DR. BURROWS

Recognized risk factors for multiple melanomas include presence of atypical/dysplastic nevi, family history, and early age of onset.

According to a review of 1,258 melanoma patients treated at the Scripps Clinic between 1990 and 2000, 149 (12%) developed multiple primary lesions, which is more than double the national incidence. "This could be due to one of two things," Dr. Burrows said. "One is the criteria that are used in making the diagnosis of melanoma in situ. I wonder if we [at Scripps] diagnose melanoma in situ more often, as opposed to others who might sign it out as atypical melanocytic hyperplasia or another worrisome diagnosis."

The other possibility is that incidence of melanoma is rising. "We know that we are making the diagnosis of primary melanomas at a younger age than we did 20 years ago," Dr. Burrows said.

In the Scripps series, 75% of patients had two primary melanomas, 15% had three, and the remainder had four or more. The average age at initial primary melanoma diagnosis was 64 among men and 56 among women.

Nearly half of the patients (49%) developed subsequent melanomas less than 3 years after their initial primary melanoma diagnoses.

At this point, Dr. Burrows does not recommend testing for the CDKN2A and CDK4 gene mutations in most patients. "It's not a good screening tool for the general population or fair-skinned population with multiple nevi, but it has potential use in screening patients with a family history of melanoma," he said.

As for managing patients with multiple melanomas, a full skin exam during initial work-up and follow-up intervals is essential, he said. "Follow-up should be lifelong."

Dr. Burrows had no relevant conflicts to disclose. ■

NSAIDs Show No Effect on SCC Risk

BY MARY ANN MOON

The use of nonsteroidal anti-inflammatory drugs does not reduce the risk of cutaneous squamous cell carcinoma, according to the findings of a retrospective study.

In a case-control study involving more than 800 subjects, the dose, duration, and type of NSAID exposure exerted "no clear effect" on the risk of developing squamous cell cancer (SCC), said Dr. Maryam M. Asgari of Kaiser Permanente of Northern California, Oakland, and associates.

NSAIDs block the synthesis of proinflammatory prostaglandins and "inhibit neoplastic proliferation by inducing apoptosis and inhibiting angiogenesis," the authors wrote. They have been reported to protect against colorectal, breast, prostate, and lung cancer, and have shown activity against SCCs both in animal and in vitro studies. However, human studies have produced conflicting results.

Dr. Asgari and her colleagues assessed NSAID use during the preceding decade in 415 patients with pathologically confirmed SCC who were diagnosed in 2004 and 415 control subjects matched for age, sex, and race. Only cases of extragenital and nonmucosal SCC were included.

The subjects (aged 43-85 years) completed 3-page questionnaires detailing medication use, health history, skin cancer history, and risk factors. NSAID use was analyzed by four categories: any NSAIDs, aspirin, ibuprofen, and nonaspirin NSAIDs. Regular use was defined as taking the medication at least once per week for at least 1 year.

Most of the subjects (61%) reported regular use of NSAIDs at some time during the preceding 10 years, most commonly aspirin (48%), followed by ibuprofen (18%), naproxen (5%), and nabumetone (4%).

There was no association between self-reported NSAID use and SCC risk.

This finding was validated in a separate analysis of pharmacy records of NSAIDs that were dispensed to the same group of subjects, the investigators said (Arch. Dermatol. 2010 Feb. 15 [doi:10.1001/archdermatol.2009.374]).

Dose and duration of exposure had no effect on the results.

"Our results are largely consistent with" three of the four published articles examining the association of NSAIDs with SCC risk, they added. ■

Disclosures: *This study was funded by the National Institute of Arthritis, Musculoskeletal, and Skin Diseases and the National Cancer Institute. One of Dr. Asgari's associates reported serving on an advisory committee for Roche Laboratories and consulting for law firms serving both plaintiffs and Ortho-McNeil-Janssen Pharmaceuticals in legal cases. No other potential conflicts of interest were reported.*