

All SCCs May Not Require Emergent Biopsy

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STOWE, VT. — All squamous cell carcinomas require attention, but not all of them require emergency attention, said Dr. Glenn D. Goldman at a dermatology conference sponsored by the University of Vermont.

Thanks to effective public health campaigns in recent years, there has been a dramatic increase in patient and physician

awareness of the potential seriousness of squamous cell carcinoma. The flip side of this successful educational program has been its contribution to the notion that all patients with a positive biopsy for the cancer must have a dermatology consult within days of the report.

"I can't tell you how many calls we get from patients and providers requesting immediate consultations because when they go through the [appointment office], they're told we are booking out a

couple of months," said Dr. Goldman of the division of dermatology at the University of Vermont. "As a result, I am constantly squeezing people into my schedule for 'emergency' consults, which drives the nurse manager nuts. And a lot of the time, when the patient comes in, it's clear that it's not really urgent, which drives me nuts.

"The truth is, not all squamous cell carcinomas are created equal. Many are minimally invasive and slowly advancing,

whereas others are very invasive and advancing daily," said Dr. Goldman. And although it's important that all squamous cell carcinomas be thoroughly removed and appropriately treated in a timely manner, some require more immediate attention than others, and it's usually not that difficult to tell the difference, he said.

"There are a handful of clues that will let you know you're dealing with a bad squamous cell carcinoma," Dr. Goldman said. When any of these are present, "it's a sign that the lesion is aggressive and needs to be treated quickly and with great care."

The first indicator of a bad lesion is that it is new and has developed rapidly within a short period. "Often, someone will

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come in with a squame that has been sitting there literally for years without changing much, and it could probably sit there for another year without causing a problem," said Dr. Goldman. "It's the person who just noticed this thing

a few weeks ago, and since then it has grown and changed daily, that you have to worry about."

Also of concern is the patient who "is experiencing true neuropathic pain—not just the type of pain caused by a squame that feels like a screw if you put pressure on it—but the dull, searing neuropathic pain that doesn't go away," said Dr. Goldman. Such pain could indicate nerve damage from metastases, he noted.

Immunosuppressed patients, such as transplant patients or those with chronic lymphocytic leukemia, who develop squamous cell carcinomas generally require aggressive treatment because their lesions often multiply and enlarge quickly, said Dr. Goldman.

Finally, "old men with squamous cell carcinoma tend to have bad luck with it, particularly if it is on the temple, which is one of the areas at highest risk for metastases," Dr. Goldman said. "This is fairly well known in the dermatology community, but it's not written about much in the national literature."

There also are several telltale indicators that a squamous cell carcinoma is not going to be difficult to cure and doesn't require immediate action. These include lesions that start as a patch or a plaque and those that are slow growing and non-tender, Dr. Goldman said. Often, with such growths, "the biopsy itself is the cure," he said. "More than 60% of the time, the biopsy will have gotten the whole thing. The clinical exam will reveal no residual squamous cell carcinoma, and the pathology will bear this out."

Although these less serious squamous cell carcinomas do require treatment, "they can easily wait 1 to 2 months before being treated," Dr. Goldman said. ■

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* Shorter duration of episode: in study 1, acyclovir (n=324) 4.3 days vs vehicle (n=346) 4.8 days (P=0.010). In study 2, acyclovir (n=328) 4.6 days vs vehicle (n=343) 5.2 days (P=0.007). Shorter duration of pain: in study 1, acyclovir (n=334) 2.9 days vs vehicle (n=352) 3.2 days (P=0.024). In study 2, acyclovir (n=348) 3.1 days vs vehicle (n=351) 3.5 days (P=0.027).

Reference: 1. Spruance SL, Nett R, Marbury T, Wolff R, Johnson J, Spaulding T, for The Acyclovir Cream Study Group. Acyclovir cream for treatment of herpes simplex labialis: results of two randomized, double-blind, vehicle-controlled, multicenter clinical trials. *Antimicrob Agents Chemother.* 2002;46:2238-2243.

ZOVIRAX® (acyclovir) Cream 5%

INDICATIONS AND USAGE

ZOVIRAX Cream is indicated for the treatment of recurrent herpes labialis (cold sores) in adults and adolescents (12 years of age and older).

CONTRAINDICATIONS

ZOVIRAX Cream is contraindicated in patients with known hypersensitivity to acyclovir, valacyclovir, or any component of the formulation.

PRECAUTIONS

General: ZOVIRAX Cream is intended for cutaneous use only and should not be used in the eye or inside the mouth or nose. ZOVIRAX Cream should only be used on herpes labialis on the affected external aspects of the lips and face. Because no data are available, application to human mucous membranes is not recommended. ZOVIRAX Cream has a potential for irritation and contact sensitization (see ADVERSE REACTIONS). The effect of ZOVIRAX Cream has not been established in immunocompromised patients.

Drug Interactions: Clinical experience has identified no interactions resulting from topical or systemic administration of other drugs concomitantly with ZOVIRAX Cream.

Carcinogenesis, Mutagenesis, Impairment or Fertility: Systemic exposure following topical administration of acyclovir is minimal. Dermal carcinogenicity studies were not conducted. Results from the studies of carcinogenesis, mutagenesis and fertility are not included in the full prescribing information for ZOVIRAX Cream due to the minimal exposures of acyclovir that result from dermal application. Information on these studies is available in the full prescribing information for ZOVIRAX Capsules, Tablets, and Suspension and ZOVIRAX for Injection.

Pregnancy: Teratogenic Effects: Pregnancy Category B. Acyclovir was not teratogenic in the mouse, rabbit, or rat at exposures greatly in excess of human exposure. There are no adequate and well-controlled studies of systemic acyclovir in pregnant women. A prospective epidemiologic registry of acyclovir use during pregnancy was established in 1984 and completed in April 1999. There were 749 pregnancies followed in women exposed to systemic acyclovir during the first trimester of pregnancy resulting in 756 outcomes. The occurrence rate of birth defects approximates that found in the general population. However, the small size of the registry is insufficient to evaluate the risk for less common defects

or to permit reliable or definitive conclusions regarding the safety of acyclovir in pregnant women and their developing fetuses. Systemic acyclovir should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether topically applied acyclovir is excreted in breast milk. Systemic exposure following topical administration is minimal. After oral administration of ZOVIRAX, acyclovir concentrations have been documented in breast milk in 2 women and ranged from 0.6 to 4.1 times the corresponding plasma levels. These concentrations would potentially expose the nursing infant to a dose of acyclovir up to 0.3 mg/kg/day. Nursing mothers who have active herpetic lesions near or on the breast should avoid nursing.

Geriatric Use: Clinical studies of acyclovir cream did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. Systemic absorption of acyclovir after topical administration is minimal (see CLINICAL PHARMACOLOGY).

Pediatric Use: Safety and effectiveness in pediatric patients less than 12 years of age have not been established.

ADVERSE REACTIONS

In 5 double-blind, placebo-controlled trials, 1,124 patients were treated with ZOVIRAX Cream and 1,161 with placebo (vehicle) cream. ZOVIRAX Cream was well tolerated; 5% of patients on ZOVIRAX Cream and 4% of patients on placebo reported local application site reactions.

The most common adverse reactions at the site of topical application were dry lips, desquamation, dryness of skin, cracked lips, burning skin, pruritus, flakiness of skin, and stinging on skin; each event occurred in less than 1% of patients receiving ZOVIRAX Cream and vehicle. Three patients on ZOVIRAX Cream and 1 patient on placebo discontinued treatment due to an adverse event.

An additional study, enrolling 22 healthy adults, was conducted to evaluate the dermal tolerance of ZOVIRAX Cream compared with vehicle using single occluded and semi-occluded patch testing methodology. Both ZOVIRAX Cream and vehicle showed a high and cumulative irritation potential. Another study, enrolling 251 healthy adults, was conducted to evaluate the contact sensitization potential of ZOVIRAX Cream using repeat insult patch testing methodology. Of 202 evaluable subjects, possible cutaneous sensitization reactions were observed in the same 4 (2%) subjects with both ZOVIRAX Cream and vehicle, and these reactions to both ZOVIRAX Cream and vehicle were confirmed in 3 subjects upon rechallenge. The sensitizing ingredient(s) has not been identified.

The safety profile in patients 12 to 17 years of age was similar to that observed in adults.

Observed During Clinical Practice: In addition to adverse events reported from clinical trials, the following events have been identified during post-approval use of acyclovir cream. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. These events have been chosen for inclusion due to a combination of their seriousness, frequency of reporting, or potential causal connection to acyclovir cream.

General: Angioedema, anaphylaxis.

Skin: Contact dermatitis, eczema, application site reactions including signs and symptoms of inflammation.

OVERDOSAGE

Overdosage by topical application of ZOVIRAX Cream is unlikely because of minimal systemic exposure (see CLINICAL PHARMACOLOGY).

DOSAGE AND ADMINISTRATION

ZOVIRAX Cream should be applied 5 times per day for 4 days. Therapy should be initiated as early as possible following onset of signs and symptoms (i.e., during the prodrome or when lesions appear). For adolescents 12 years of age and older, the dosage is the same as in adults.

HOW SUPPLIED

Each gram of ZOVIRAX Cream 5% contains 50 mg acyclovir in an aqueous cream base. ZOVIRAX Cream is supplied as follows:

2-g tubes (NDC 64455-994-42).

5-g tubes (NDC 64455-994-45).

Store at or below 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F) (see USP Controlled Room Temperature).

Manufactured by

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