Cetuximab Found to Yield Complete SCC Response

BY SUSAN LONDON
Contributing Writer

VANCOUVER, B.C. — The epidermal growth factor receptor inhibitor cetuximab alone has been found to produce complete response in patients with advanced cutaneous squamous cell carcinoma.

"To date, there have been no trials using the epidermal growth factor receptor inhibitors for treatment of patients with cutaneous squamous cell carcinoma," said Dr. Matthew E. Halpern at the annual meeting of the American College of Mohs Surgery. A previous trial found that cetuximab (Erbitux) plus radiation was efficacious for treating locally advanced squamous cell carcinoma (SCC) of the head and neck (N. Engl. J. Med. 2006;354:567-78).

Study patients had advanced SCC of the back, scalp, temple, and chest, according to Dr. Halpern, a dermatologic surgeon at New York–Presbyterian Medical Center. Two patients had in-transit metastasis alone, one had both in-transit and axillary metastases, and one had pulmonary metastases. Their treatment consisted of weekly infusions of cetuximab, with a total of four infusions planned.

Two patients had a complete clinical response to cetuximab (Erbitux), Dr. Halpern reported. "Really, like magic, the in-transit metastasis absolutely melted before our eyes," he said, describing one of the patients. Another patient, who received only half of the planned number of infusions because of comorbidities, had a partial response. The remaining patient had merely a limited response.

'The severity of acneiform eruption ... seemed to be a surrogate marker for therapeutic response.'

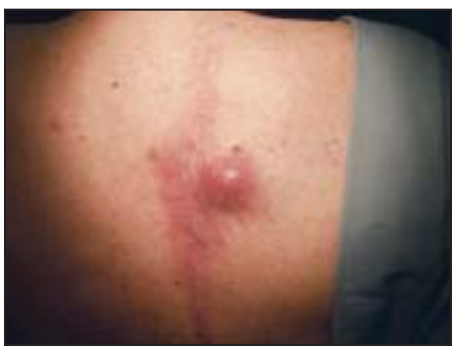
DR. HALPERN

"As you might expect, side effects of this class of medications are largely cutaneous," Dr. Halpern noted, explaining that patients might develop a characteristic acneiform rash, paronychial inflammation, xerosis, pruritus, and trichomegaly. The study's two complete responders developed a severe rash, and the partial responder developed a moderate rash, while the nonresponder did not develop any rash at all. "Interestingly, even though this is a very small series of patients, patient response seemed to correlate with the severity of acneiform eruption," he observed. "It seemed to be a surrogate marker for therapeutic response."

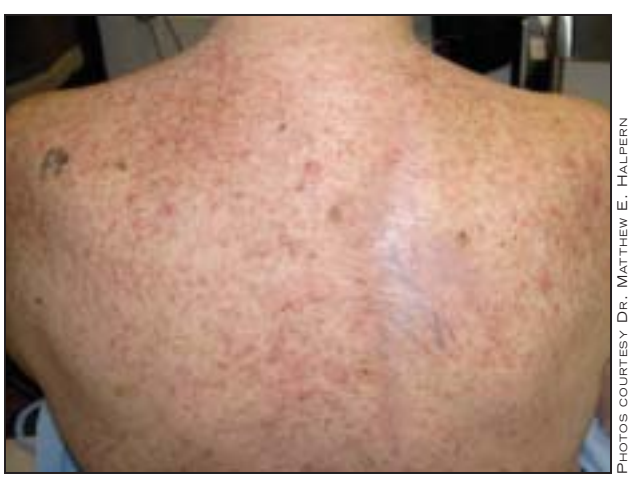
One of the patients with a complete response was alive at 6 months after treatment, while the other died 7 months afterward from a primary lung cancer. The patient with a partial response died 4 months after treatment from chronic rejection of a lung transplant and had additional metastases at that time. The patient who had a minimal response died 4 months after treatment from brain metastases.

The study had limited follow-up related to the recent treatments patients had received and their comorbidities, Dr. Halpern conceded. Nonetheless, he said, "cetuximab has potential benefit for patients with metastatic cutaneous squamous cell carcinoma and is extremely well tolerated in our hands, with minimal side effects, some of which may be predictive of therapeutic benefit."

Dr. Halpern reported that he had no conflicts of interest in association with the study. ■



Biopsy of this nodule revealed infiltrating SCC without epidermal involvement.



PHOTOS COURTESY DR. MATTHEW E. HALPERN

The patient's in-transit metastasis and axillary metastases cleared after the third cetuximab infusion. The acneiform rash is characteristic of this drug class.

Limit Sentinel Node Biopsy to SCC Patients at Highest Risk

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

WILLIAMSBURG, VA. — Sentinel lymph node biopsy should be reserved only for squamous cell carcinoma patients whose primary tumors have a high-risk profile, according to Dr. Merrick Ross.

"Clearly, the routine use of sentinel node biopsy is not indicated in these patients, but its selective use in high-risk squamous cell carcinoma [SCC] seems rational," said Dr. Ross at a meeting of the American Society for Mohs Surgery. "This is why it's important for us to continue to define exactly what constitutes a high-risk squamous cell tumor."

High-risk features of SCC include anatomical location, thickness, size, perineural invasion, and the immunocompetence of the patient.

Increasing size is associated with decreased local control and the increased presence of positive lymph nodes. A size of 2 cm "seems to be the most relevant break point," said Dr. Ross, professor of surgical oncology at the University of Texas M.D. Anderson Cancer Center, Houston. "Studies have shown that up to 50% of SCCs larger than that will have nodal involvement. However, to date there is no multivariate analysis that demonstrates size as an independent predictor of nodal disease."

Most studies identify 4-5 cm as the high-risk break point for tumor thickness, he said. In a large German study of 550 patients, only 3% of those with tumors less than 5 mm thick had nodal metastasis, compared with more than 17% of those with thicker tumors, Dr. Ross noted (Cancer 1997;79:915-9).

High-grade tumors are more likely than low-grade tumors to have nodal disease, said Dr. Ross, with 17% of high-grade tumors showing metastasis, compared with 4% of lower-grade tumors. When the German investigators looked at grade distribution according to nodal involvement, 44% of node-positive patients had high-grade primary tumors, whereas only 5% of node-negative patients had high-grade tumors.

Local recurrence is strongly associated with nodal involvement, just as it is with larger size, thicker tumors, narrow excision margins, and anatomical site. Up to 45% of recurrent presentations will have nodal disease, Dr. Ross said.

Lesions that arise on the lip, around the ear, and in the anogenital region are particularly risky. A 2006 study found that 27% of SCCs on the external ear had nodal disease, as did more than 20% of T3- and T4-stage lip lesions (Aust. J Derm. 2006;47:28-33).

The overall health of the patient is another important risk factor. "Patients with HIV [disease] or other immunodeficiency diseases are at an increased risk for metastasis, as are those with any chronic hematologic malignancy" Dr. Ross said. ■

Skin Cancer Risks Tracked for Immunosuppressant Regimens

BY BRUCE JANCIN
Denver Bureau

KYOTO, JAPAN — Mycophenolate mofetil–based chronic immunosuppression is associated with a markedly lower risk of skin cancer during the first decade post kidney transplant, compared with alternative regimens aimed at preventing graft rejection, Dr. Irma Wisgerhof said at an international investigative dermatology meeting.

By 13 years post transplant, however, the squamous cell carcinoma risk in mycophenolate mofetil–treated organ recipients is equivalent to that of azathioprine, noted Dr. Wisgerhof of Leiden University (the Netherlands) Medical Center.

The mechanisms underlying these very different arcs of skin cancer risk are unclear. Azathioprine (Imuran) has a direct carcinogenic effect and causes accumulation of 6-thioguanine in cellular DNA. Azathioprine begins causing skin cancer in kidney transplant recipients early, and at a rate that remains steady over time. In contrast, mycophenolate mofetil (CellCept) prevents graft rejection by blocking immune surveillance; it suppresses both cellular and humoral immune responses, she explained.

Dr. Wisgerhof reviewed the experience with nonmelanoma skin cancer in 1,111 kidney transplant recipients who received their first donor kidney at the medical center in 1986-2006.

Through 2007, 6.7% of the patients developed a total of 102 invasive squamous cell carcinomas and 121 basal cell carcinomas. The cumulative incidence of nonmelanoma skin cancer was 3% after 5 years, 6% after 10 years, and 10% after 15 years of graft survival, she said.

The risk of SCC varied depending upon the chronic immunosuppression regimen used.

DR. WISGERHOF

The risk of squamous cell carcinoma—but not basal cell carcinoma—varied significantly depending upon the chronic immunosuppression regimen used.

The age- and gender-adjusted risk through the first decade post transplant was 88% lower with mycophenolate mofetil than with azathioprine-based regimens, and 65% less with cyclosporine- or tacrolimus-based regimens than with azathioprine-based immunosuppression, Dr. Wisgerhof said at a meeting of the European Society for Dermatological Research, the Japanese Society for Investigative Dermatology, and the Society for Investigative Dermatology.

Dr. Wisgerhof's study was supported by the Dutch Society of Dermatology and Venereology. ■

Pages 28a—28b