Management of Acneiform Rashes Related to Gefitinib Therapy

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Question: What is the best strategy for the management of acneiform rashes resulting from gefitinib (Iressa®, AstraZeneca, Wilmington, DE) therapy?

Answer: In May 2003, gefitinib, an oral cancer agent, was granted accelerated approval by the U.S. Food and Drug Administration as monotherapy for patients with locally advanced or metastatic non-small cell lung cancer whose disease had failed to respond to platinum-based and docetaxel chemotherapies. Gefitinib also is under investigation in many research studies for the treatment of various epithelial cancers such as breast, colon, head and neck, brain, and gynecologic.

This is an exciting and challenging time for nurses as they are presented with new and innovative treatments for patients with cancer. Nurses also are faced with new side-effect profiles. Few published studies about the etiology of the toxicities with epidermal growth factor receptor (EGFR) inhibitors such as gefitinib are available, but the exact mechanism for these toxicities still is not known. Only a few published recommendations are available on how to treat these toxicities, and these are based on individual practitioners' experience (Herbst, LoRusso, Purdom, & Ward, 1998; Herbst, Maddox, & Rothenberg, 2002; Riddle, Lee, & Purdom, 2002). Nurses are left to draw on these reports and their experience to determine the best treatment for these side effects.

Gefitinib belongs to a class of drugs called EGFR-tyrosine kinase inhibitors. Gefitinib blocks EGFR, which prevents activation of tyrosine kinase and switches off signals from EGFR. Tyrosine kinase transmits cell-to-cell signals concerning growth, differentiation, adhesion, motility, and death. The human EGFR family is overexpressed or dysfunctional in many human malignancies, including lung cancer. These receptors are targets for cancer therapy, hence the term "targeted therapies." Gefitinib works differently from chemotherapy drugs. Gefitinib is a targeted therapy; the side effects are less toxic than those of conventional chemotherapy drugs, but they are unique.

Gefitinib received approval based on the phase II Iressa Dose Evaluation in Advanced Lung Cancer 2 Trial in patients with advanced non-small cell lung cancer whose disease failed to respond to platinum- and docetaxel-based regimens. The study treated 216 patients. Patients in one arm of the study (n = 102) received 250 mg per day, and patients in the other arm of the study (n = 114) received 500 mg per day. Patients' tumor responses and duration of responses were clinically significant. Tumor response rates for the 250 mg and 500 mg per day groups were 11.8% (95% confidence interval, 6.2%–19.7%) and 8.8% (95% confidence interval, 4.3%–15.5%), respectively, with tumor response duration ranging from three to seven or more months. Stable disease was seen in 31% and 27% of the 250 mg and 500 mg per day arms, respectively (Kris, Natale, & Herbst, 2002). Favorable symptom responses were seen in 78% of patients, with approximately 60% of the patients reporting improvement by the second week of treatment (Kris et al.). Symptom response was measured by means of the Functional Assessment of Cancer Therapy lung and lung cancer subscales. These patient questionnaires are designed to measure the patients' own assessment of their quality of life. The dose-limiting toxicities of gefitinib, diarrhea and skin rash, were determined in early phase I trials. These same toxicities were seen once again in the phase II trials. Most drug-related adverse events were mild, including reversible grade 1 or 2 diarrhea and skin rash. Approximately 0.33% of patients taking gefitinib died from interstitial lung disease, a lung condition that the manufacturer has reported as a possible side effect of this treatment (AstraZeneca Pharmaceuticals, 2003).

The cutaneous adverse effects of gefitinib are similar to those of other EGFR-targeted agents. The most common toxicities result from direct interference with the functions of EGFR's signaling in the skin and include skin manifestations such as rash (macular, papular, or pustular), dry skin, and pruritus. (See Figures 1 and 2 for a view of a patient experiencing rashes related to gefitinib administration.) Also commonly reported as an adverse side effect of gefitinib is diarrhea, which generally is well tolerated and treatable with over-the-counter antidiarrheals. All of these side effects are reversible upon discontinuation of the drug. Patients must realize that they are not having an allergic reaction to the drug, and they should seek treatment for side effects as soon as they occur.

In the author's experience treating patients receiving gefitinib, clindamycin T gel (Cleocin T® gel, Pfizer Inc., New York, NY) in combination with washing with soap and water and using an unscented moisturizing cream for the management of individual pustules has worked very well. For widespread pustules, clindamycin lotion may be easier to apply. Patients should be cautioned that clindamycin T gel may work only on the pustules and is not appropriate for a macular rash. Overuse of clindamycin T gel may cause the skin to become too dry. If that happens, patients should stop the gel and use a nonperfumed moisturizer, and the physician may consider use of an oral antibiotic. Oral antibiotic treatment such as minocycline hydrochloride (Minocin®, Wyeth, Madison, NJ) or sulfamethoxazole-trimethoprim (Bactrim DS®, Roche Pharmaceuticals, Nutley, NJ) also may be considered when the rash is widespread (i.e., more than 50% of the body surface area) or bothersome. Very few bacteria have been found in skin biopsies of pustules, but antibiotics have been

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