Managing skin toxicities related to panitumumab

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Background: Dermatologic toxicities from targeted agents such as panitumumab can interfere with cancer treatment.

Objective: We sought to evaluate the rash assessment and management in a consecutive patient cohort who received panitumumab for colorectal cancer treatment.

Methods: This was a retrospective chart review.

Results: Skin toxicity, consisting of papulopustular rash, was experienced by 32 of 34 patients. The majority (85%) developed the rash by the end of the second infusion cycle. Patients presented with a mild (41%), moderate (38%), and severe (21%) rash, and progressed to an extensive rash without appropriate treatment. A grading system was used for 65% of patients to document severity.

Limitations: Small sample size limited power in analysis. Rash severity had to be inferred based on rash description and management in 11 of the patients.

Conclusion: Dermatologic toxicities related to panitumumab are common; however, the way they are reported and managed varies among physicians. To prevent progression, toxicities must be assessed and treated early and aggressively, according to severity grading. Dermatologists could aid oncologists in choosing the best management strategies. (J Am Acad Dermatol 2014;71:754-9.)

Key words: Common Toxicity Criteria for Adverse Events; epidermal growth factor receptor inhibitors; panitumumab; papulopustular rash; skin toxicity.

Dermatologic toxicities such as a papulopustular rash (acneiform eruption), erythema, skin fissures, and paronychia are common side effects of targeted cancer agents such as the epidermal growth factor receptor (EGFR) inhibitors, panitumumab (Vectibix), cetuximab (Erbitux), gefitinib (Iressa), erlotinib (Tarceva), and afatinib (Gilotrif).[1-4] These toxicities significantly impact patients' quality of life, affecting compliance and clinical outcomes[5-7] with about one-third having discontinuation or dose reductions as a result of rash.[8]

Panitumumab is an EGFR inhibitor used for treatment of metastatic colorectal cancer with a

Abbreviations used:

CTCAE:	Common Toxicity Criteria for Adverse Events
EGFR:	epidermal growth factor receptor
PMCC:	Princess Margaret Cancer Center

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Supported by Cancer Care Ontario and Ontario Patient-Reported Outcomes of Symptoms and Toxicity. Dr Liu is supported by the Alan B. Brown Chair in Molecular Genomics and the Posluns Family Fund. Dr Howell is supported by the Royal Bank of Canada (RBC) Chair in Oncology Nursing Research.

Conflicts of interest: None declared.

Accepted for publication June 4, 2014.

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Published online July 29, 2014.

0190-9622/$36.00

http://dx.doi.org/10.1016/j.jaad.2014.06.011

nonmutated or wild-type KRAS gene after failure of chemotherapy treatment. Research demonstrating the incidence, assessment, and management of drug-related skin toxicities has been limited compared with other EGFR inhibitors.[9-12] In colorectal cancer, panitumumab is administered intravenously every 2 weeks at a dose of 6 mg/kg.[2,13] The associated rash, characterized by papules and pustules ("papulopustular") on the face, scalp, and trunk, typically appears within the first 3 weeks of treatment.[2] Although resembling acne vulgaris and often referred to as an "acneiform" rash, comedones are not observed; it is pathologically and etiologically distinct from true acne.[14] Symptomatically unlike acne, this rash is associated with pruritus and pain. Studies have shown that this papulopustular rash caused by other EGFR inhibitors may be an indicator of biological effect; its presence and severity have been correlated with improved survival.[15]

CAPSULE SUMMARY

- Current recommendations for treating dermatologic toxicities of some targeted cancer agents are based mainly on expert opinion.
- We assessed the skin toxicities and their management in a series of panitumumab-treated patients with cancer.
- Using empiric data, we modified the current clinical guidelines specifically for panitumumab.

Treatment options for EGFR inhibitor-associated skin toxicities remain inconsistent. Few controlled studies have been conducted to investigate the prevention and treatment of this rash. Many current recommendations are based on small studies or case reports.[16-18] In 2011, the Multinational Association for Supportive Care in Cancer skin toxicity study group conducted a thorough literature review of the current studies investigating the management of skin toxicities and suggested specific treatment algorithms.[16] Based on this review, hydrocortisone 1% combined with moisturizer, sunscreen, and doxycycline (100 mg) twice a day for the first 6 weeks of treatment is recommended (level II evidence).[16] Medium- to high-potency topical corticosteroids and oral minocycline or doxycycline are recommended once a rash has developed (level-IV evidence). Other treatment options are being investigated, including pimecrolimus 1% cream,[19] vitamin K1,[20] topical retinoids,[9,21] or prophylactic therapy.[22] In clinical trials, providers follow specific treatment algorithms based on rash severity to make treatment decisions, often using the National Cancer Institute Common Toxicity Criteria for Adverse Events (CTCAE).[23,24] A simplified 3-tier grading system using the mild/moderate/severe toxicity terminology has been proposed but is not well recognized.[25]

In this study we evaluated the management of skin toxicities related to panitumumab in a consecutive cohort of patients who received panitumumab for the treatment of colorectal cancer.

METHODS

Ethics approval was obtained from the university health network research ethics board. The study design was a retrospective chart review of consecutive patients with colorectal cancer receiving panitumumab treatment. Eligible patients, all treated at Princess Margaret Cancer Center (PMCC) (Toronto, Ontario, Canada), a comprehensive cancer center with over 400,000 patient visits every year where 6 medical oncologists treated metastatic colorectal cancer,[26] were identified through the PMCC pharmacy database. Inclusion criteria included age of 18 years or older and receipt of single-agent panitumumab for the colorectal cancer treatment since the PMCC approval of panitumumab in April 2009 until the end of the chart abstraction period (September 1, 2012). Exclusion criteria included panitumumab therapy outside of PMCC, concurrent radiation or chemotherapeutic therapy, receipt of only a single panitumumab dose, or presence of underlying documented skin diseases (eg, blistering skin diseases, psoriasis). Data abstraction was performed by 1 author (H. B.) from electronic medical records. Management of skin toxicities, at the discretion of treating oncologists, were classified into 6 categories, similar to those used in a previous survey of oncologists.[8] For example, 1 category was topical agents alone, which included entities such as clindamycin and 1% hydrocortisone cream for mild rash treatment, whereas another category was topical agents and an oral antimicrobial, as is currently recommended for more severe rashes.[16,17,25] Assessment of severity was divided into 3 methods: oncologists' use of CTCAE grading system, use of a mild/moderate/severe terminology, or use of neither grading system. If neither grading system was used, description of the rash was used to determine severity. For example, an "extensive rash covering the entire body" was interpreted as a severe rash whereas a "typical rash involving part of the face not