

Cetuximab: Adverse Event Profile and Recommendations for Toxicity Management

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The epidermal growth factor receptor (EGFR, c-ErbB-1, HER-1) is a member of the HER family of receptors, which includes HER-2, a receptor targeted in breast cancer therapy (Baselga, 2002). The EGFR is expressed in many human tumors, including colorectal (Messa, Russo, Caruso, & Di Leo, 1998; Salomon, Brandt, Ciardiello, & Normanno, 1995), bladder, brain, cervical, esophageal (Salomon et al.), head and neck (Rubin Grandis, Melheim, Barnes, & Twardy, 1996), renal cell (Salomon et al.), lung (Rusch et al., 1997), ovarian (Bartlett et al., 1996), pancreatic (Yamanaka et al., 1993), prostate (Salomon et al.), and breast cancers (Bucci et al., 1997; Klijn, Berns, Schmitz, & Foekens, 1992). The activation of the EGFR by its natural ligands, such as epidermal growth factor or transforming growth factor- α , can lead to increased cell proliferation, inhibition of programmed cell death (apoptosis), promotion of angiogenesis, and stimulation of metastasis (Baselga, 2000, 2002; Woodburn, 1999) (see glossary on page 338).

Cetuximab is a chimeric immunoglobulin G1 monoclonal antibody (Mendelsohn, 2000). It is one of several targeted biologic agents that have been developed to selectively inhibit or reverse tumorigenic processes, with relative sparing of normal proliferating cells. Cetuximab has been designed to bind to the extracellular domain of the EGFR, blocking its natural ligands and the oncogenic processes associated with its activation (Mendelsohn).

Cetuximab (ErbixTM, IMC-C225, ImClone Systems Incorporated, New York, NY) is a monoclonal antibody targeted to the epidermal growth factor receptor. Expression of the epidermal growth factor receptor is associated with disease progression, poor survival, poor response to therapy, and the development of resistance to therapy in many solid tumors. Cetuximab blocks the binding of natural ligands to the epidermal growth factor receptor, thus inhibiting oncogenic processes associated with its activation. Infusion reactions, acneform skin rash, and nail disorder are the most clinically relevant adverse events observed. Because infusion reactions can be life threatening when severe, nurses must administer prophylactic treatment with an H₁ antagonist prior to infusion and actively manage cetuximab-related infusion reactions when they occur. Management of infusion reactions typically includes vigilant patient monitoring, appropriate medical supervision, readily available resources for the treatment of infusion reactions, and initiation of institution- or practice-specific protocols when necessary. Acneform skin rash is the most common adverse event, but severe (grade 3 or 4) rash requiring interruption of treatment is not common. Topical and systemic antibiotic therapies may be administered to reduce symptoms. Nail disorder typically is mild to moderate and is observed infrequently; this also may be treated with systemic and topical antibiotics. Overall, the safety profile of cetuximab is favorable compared to that typically seen with chemotherapeutic agents. The acneform skin rash and nail disorder, which may affect quality of life, rarely threaten the general well-being of patients and typically are manageable.

Clinical trials have shown that cetuximab has activity against many tumor types, including head and neck, prostate, lung,

esophageal, pancreatic, kidney, ovarian, and breast cancers, with a generally favorable toxicity profile; the maximum tolerated dose has not been defined (Bos et al., 1996; Falcey et al., 1997). Partial responses and stable disease were reported in more than one-third of the patients with irinotecan-refractory colorectal cancer included in a recently reported trial (Saltz et al., 2004). In a randomized, phase II trial of irinotecan-refractory, metastatic colorectal cancer, patients treated with single-agent cetuximab achieved partial responses in 10.8% of cases, and the disease control rate was 32.4%; patients receiving cetuximab plus irinotecan exhibited partial response and overall disease control rates of 22.9% and 55.5%, respectively; and median times to tumor progression in each arm were 1.5

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