

■ Article

# Managing Toxicities Associated With Antiangiogenic Biologic Agents in Combination With Chemotherapy for Metastatic Colorectal Cancer

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Toxicities commonly associated with antiangiogenic agents include hypertension, proteinuria, wound-healing complications, bleeding or hemorrhage, thromboembolic events, hypersensitivity reactions, and gastrointestinal perforation; however, toxicities most often attributed to chemotherapy include nausea, vomiting, diarrhea, constipation, fatigue, neuropathy, mucositis, hand-foot syndrome, hypersensitivity reactions, and myelosuppression. Patients with metastatic colorectal cancer (mCRC) who receive an antiangiogenic agent in combination with chemotherapy may experience toxicities related to both chemotherapy and the antiangiogenic agent. If possible, evidence-based interventions should be used for the management of toxicities. Patient education

about expected toxicities and optimal toxicity management can promote the optimal use of therapy to improve survival and quality of life. Oncology nurses are well positioned to educate patients and their families on anticipated treatment and management of side effects. This article summarizes the incidence of toxicities associated with the antiangiogenic biologic agents aflibercept and bevacizumab, in combination with chemotherapy for patients with mCRC, and provides strategies for managing these toxicities based on clinical practice guidelines.

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Colorectal cancer (CRC) is the third most common cancer in the United States and the third most common cause of cancer deaths; in 2012, an estimated 143,460 new cases were diagnosed with 51,690 deaths (Siegel, Naishadham, & Jemal, 2012). Since 2004, treatment of metastatic CRC (mCRC) has improved with the introduction of targeted agents, including antiangiogenics (Beatty, Winkelman, Bokar, & Mazanec, 2011; Grenon & Chan, 2009; Viale, 2010; Wilkes, 2005). Aflibercept, an antiangiogenic biologic agent, is an engineered protein consisting of high-affinity binding domains of vascular endothelial growth factor (VEGF) receptor (VEGFR)-1 and VEGFR-2 and the Fc portion of immunoglobulin G1; it blocks binding of VEGF-A, VEGF-B, and placental growth factor to VEGFR-1 and VEGFR-2 (Holash et al., 2002; Tew et al., 2010). Aflibercept was approved in 2012 by the U.S. Food and Drug Administration (FDA) as

ziv-aflibercept, trade name Zaltrap®, in combination with 5-fluorouracil (5-FU), leucovorin, and irinotecan (FOLFIRI) for mCRC that is resistant to or has progressed following an oxaliplatin-containing regimen (Regeneron Pharmaceuticals/Sanofi-Aventis U.S., 2012).

Bevacizumab, another FDA-approved antiangiogenic biologic agent, is indicated for treatment of mCRC in combination with fluoropyrimidine-containing chemotherapy: IFL (irinotecan, bolus 5-FU, and leucovorin [LV]) or FOLFOX4 (5-FU/LV and oxaliplatin) (Genentech, 2012). Preclinical data suggest that these agents may prevent tumor angiogenesis, inhibiting tumor growth and metastases (Gaya & Tse, 2012; Gerber & Ferrara, 2005). Adding aflibercept or bevacizumab to chemotherapy has demonstrated improved overall survival in patients with mCRC compared with chemotherapy alone (Giantonio et al., 2007; Hurwitz et al., 2004; Van Cutsem et