Antivascular Endothelial Growth Factor Monoclonal Antibody Therapy: A Promising Paradigm in Colorectal Cancer

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Colorectal cancer is the third most common malignancy in men and women in the United States. The American Cancer Society (2004) estimated that, in 2004, 147,000 new cases were diagnosed and 57,000 died from the disease, accounting for about 10% of cancer deaths. Approximately 30% of patients with colorectal cancer have metastatic disease at the time of diagnosis, and 50% of those with limited disease will develop advanced disease (Coutinho & Lima, 2003). The five-year survival rate for patients with distant metastatic disease is 9% (American Cancer Society).

Currently, chemotherapy-based regimens are first-line treatment for patients with metastatic colorectal cancer, and 5-fluorouracil (5-FU) has been the standard treatment since the 1960s. However, newer chemotherapeutic agents recently have been added to therapies based on 5-FU in an attempt to improve response rates and survival. Irinotecan, oxaliplatin, and capcitabine, in a variety of combinations, have been approved for the treatment of colorectal cancer (Goldberg et al., 2004; Hoff et al., 2001; Saltz et al., 2000; Van Cutsem et al., 2001). A new targeted agent, bevacizumab (Avastin™, Genentech, Inc., South San Francisco, CA) is a humanized monoclonal antibody, designed to directly target VEGF. The agent has shown promising activity in preclinical and phase I and II studies and is well tolerated compared with conventional cytotoxic chemotherapy. The U.S. Food and Drug Administration recently approved bevacizumab in combination with 5-fluorouracil-based chemotherapy as first-line therapy for patients with metastatic colorectal cancer. The approval was based on phase III data demonstrating that patients treated with bevacizumab plus chemotherapy survived approximately five months longer compared with patients treated with chemotherapy alone. This article will focus on the role of VEGF in tumorigenesis and summarize the available data on the use of bevacizumab in the treatment of metastatic colorectal cancer.