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Panitumumab

A Viewpoint by Imtiaz Malik

Division of Hematology-Oncology, Loma Linda University Medical Center, Loma Linda, California, USA

Colorectal cancer is a major public health problem. In the US, it is the third most common cancer in men and women and the second leading cause of cancer death. This is rather unfortunate for a disease that lends itself to prevention and early detection.

The primary treatment of metastatic colorectal cancer (MCRC) is chemotherapy. Although metastatectomy can cure some patients, treatment is palliative. Median survival without therapy is 8 months. For decades, fluorouracil was the only drug available; however, its use had a minimal impact on survival. The last few years have witnessed remarkable progress in the management of MCRC. Two additional chemotherapy drugs, irinotecan and oxaliplatin, are used in patients who fail to respond to fluorouracil or as part of first-line therapy. The addition of either drug to fluorouracil results in improvements in response rates, time to progression (TTP) and overall survival (OS). There are no major differences between the two drugs in terms of efficacy. Furthermore, the sequential use of these three agents allows the patient to derive maximum benefit with median survival ranging from 20 to 24 months.

Recent advances in the management of MCRC also include the success of targeted therapies. Bevacizumab (anti-vascular endothelial growth factor antibody) when added to fluorouracil-based combination chemotherapy results in improvements in response rates, TTP and OS. It has now become an essential component of initial therapy. Another approach undertaken relates to the use of antibodies directed against the epidermal growth factor receptor (EGFR). Cetuximab is a chimeric IgG1 antibody that has efficacy as a single agent or in combination with irinotecan in patients who are refractory or intolerant to irinotecan.

Panitumumab is a human IgG2 antibody presently undergoing extensive evaluation as a single agent in patients who have not responded to systemic chemotherapy. Initial results are encouraging and are described in the article by Hoy and Wagstaff. Interestingly, there is no correlation of response to the intensity of EGFR staining by immunohistochemistry. Panitumumab has documented efficacy in patients with no or minimal EGFR expression. Similar experience, though anecdotal, has been described with cetuximab. Skin rash is the most common treatment-related adverse event of anti-EGFR therapy and the severity of the rash appears to be correlated with the response. Other important adverse events include diarrhoea, infusion reactions, paronychial inflammation, electrolyte disturbances and fatigue. Although no direct comparisons have been made, both drugs appear to have comparable efficacy as a single agent. Cetuximab has documented efficacy when used in combination with irinotecan. The incidence of grade 3/4 infusion-related reactions appears to be lower with panitumumab and the drug can be administered without any pre-medication. Furthermore, panitumumab offers a more flexible dose administration schedule. Any differences related to the type of antibody (IgG1 versus IgG2) and its ability to generate an immunologic reaction remains theoretical at this point.

Overall, panitumumab is an important addition to a clinician's armamentarium in taking care of patients with MCRC. Both cetuximab and panitumumab are effective and generally well tolerated agents. Both require further investigation as part of combination chemotherapy and chemoradiotherapy in colorectal cancer. ▲