Drugs 2004; 64 (1): 119-121
0012-6667/04/0001-0119/$34.00/0

Cetuximab

A Viewpoint by Fortunato Ciardiello

Dipartimento di Endocrinologia e Oncologia Molecolare e Clinica, Università di Napoli 'Federico II', Napoli, Italy

The medical approach to the treatment of advanced, metastatic colorectal cancer has changed in the past 10 years with the availability of novel cytotoxic agents, such as irinotecan, oxaliplatin, capecitabine, and novel chemotherapy regimens of combinations that have significantly improved response rates, the control of symptoms, the quality of life and that, more importantly, have improved survival. However, metastatic colorectal cancer cannot be cured and although patients respond to first-line and, possibly to second-line chemotherapy, they relapse and eventually die of this disease.

The epidermal growth factor receptor (EGFR) pathway has been demonstrated as one of the relevant growth controlling pathways in the development and progression of human colorectal cancer. Therefore, a therapeutic approach to specifically target the EGFR is promising in colorectal cancer. Three phase II clinical trials have been performed with cetuximab, a human-mouse chimeric blocking anti-EGFR monoclonal antibody, alone or in combination with cytotoxic drugs, in colorectal cancer patients with documented progressive and chemo-refractory disease. In a first phase II study, treatment with cetuximab plus irinotecan in EGFR-positive advanced colorectal cancer patients, that had failed a previous treatment with irinotecan, obtained partial responses in 19% of patients, with a median duration of response of 186 days and disease stabilisation for more than 12 weeks in a further 9 patients (7%). A phase II study of cetuximab monotherapy in a similar population of 57 EGFR-positive advanced colorectal cancer patients obtained 6/57 (10.5%) partial responses and disease stabilisation in 20/57 (35.1%) patients. A European, multicenter, randomised phase II study, named BOND (Bowel Oncology with Cetuximab Antibody), evaluated the antitumour activity of cetuximab treatment alone (111 patients) or in combination with irinotecan (218 patients) in advanced colorectal cancer patients with EGFR-positive disease which progressed on an irinotecan-containing regimen as last treatment. In this heavily pretreated patient population, 261/329 (79.3%) patients had received two or more types of chemotherapy before study entry. Moreover, 206/329 (62.6%) patients were also pretreated with an oxaliplatin-containing regimen. Partial responses were obtained in 22.9% of patients treated with irinotecan plus cetuximab as compared to 10.8% of patients treated with cetuximab alone. Similarly, a significantly better disease control (partial response plus disease stabilisation) [55.5% vs 32.4%] and a prolonged median time to progression (4.1 vs 1.5 months) were observed in the combination as compared to cetuximab monotherapy. In all these studies cetuximab treatment did not increase the irinotecan-specific toxicity.

Taken together, the results of the first series of clinical trials with cetuximab in metastatic colorectal cancer are of particular clinical relevance. They clearly demonstrate a significant activity of this anti-EGFR monoclonal antibody in a setting of patients that are resistant to the currently available active cytotoxic agents and suggest that cetuximab in combination with chemotherapy could be used earlier in the clinical history of colorectal cancer patients, such as in second-line and in first-line therapy. In this respect, a series of currently ongoing clinical trials will help to define the role of cetuximab in the management of EGFR-positive colorectal cancer. ▲