Clinical and radiological response with FOLFOXIRI and bevacizumab as third-line therapy after mFOLFOX6 and FOLFIRI failure

Julio Vieira de Melo, Mauro Sérgio Vieira de Melo and Mariana Helena Abad

Studies suggest that the continuous use of bevacizumab, a vascular endothelial growth factor inhibitor, may play a crucial role in improving therapy success in patients with metastatic colorectal cancer. This is a case report of a female 60-year-old patient with colon cancer metastases in the liver and lungs refractory to mFOLFOX6 and FOLFIRI given as first and second-line therapy, respectively, who demonstrated a good response to FOLFOXIRI and bevacizumab as third-line therapy. Bevacizumab may be added to first, second and third-line chemotherapy for palliative treatment of metastatic colorectal cancer, and data indicate an increase in patient survival with a good response rate and low toxicity. ***Anti-Cancer Drugs*** **22 (suppl 2):S19–S20 © 2011 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

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Mauro Sérgio Vieira de Melo, Centro de Terapia Oncológica, Rua Dr. Sá Earp, 309 – Morin 25625-073 – Petrópolis – RJ, Brasil

Correspondence to Julio Vieira de Melo, Serviço de Oncologia Clinica do Centro de Terapia Oncológica de Petrópolis-RJ, Brasil
Tel: +55 24 22442005; e-mail: julio@ctopetropolis.com.br

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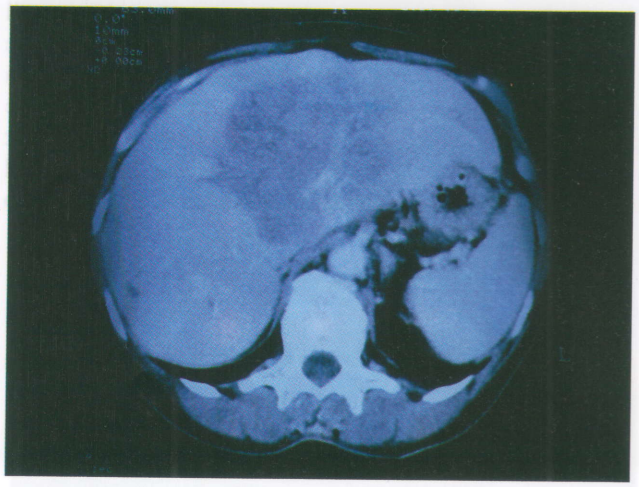
Introduction

Colorectal cancer (CRC) is one of the most common types of cancer worldwide and is the second cause of cancer death in the USA [1]. Surgery may cure 50% of patients, but the other 50% will develop metastases. The most common metastatic sites are lymph nodes, liver and lungs [2]. Chemotherapy schemes with fluoropyrimidines, oxaliplatin and irinotecan are good options for treating metastatic CRC [1,2]. The addition of the anti-angiogenic monoclonal antibody bevacizumab as well as the anti-epidermal growth factor receptor monoclonal antibodies cetuximab and panitumumab has further improved patient outcomes [3,4]. Large prospective trials suggest that the continuous use of bevacizumab, a vascular endothelial growth factor inhibitor, plays a crucial role in the improvement of survival in metastatic CRC patients [5].

Case description

A 60-year-old female patient developed epigastralgia, malaise and lumbar pain in June 2008, which progressed to acute abdomen. She required an exploratory laparotomy, which revealed a perforated sigmoid due to an obstructing tumour. A sigmoidectomy and lymphadenectomy were performed and pathology demonstrated adenocarcinoma in the sigmoid, pT4pN2 grade 2. Immunohistochemistry testing defined a mutated *k-Ras*. Staging revealed several hepatic and pulmonary metastases. Chemotherapy with mFOLFOX6 and bevacizumab was started in October 2008, and after three cycles a computed tomography scan showed a decreased number and size of hepatic lesions and the disappearance of pulmonary nodules. The patient tolerated the treatment well. After 13 cycles of chemotherapy, scans showed progression of hepatic metastases. Treatment was changed to FOLFIRI and bevacizumab. After three cycles of the new scheme clinical deterioration was observed consisting of painful hepatomegaly and further growth of hepatic lesions (Fig. 1). As this patient had tumour tissue with mutated *k-Ras*, she was not a candidate for anti-epidermal growth factor receptor treatment. Therefore, FOLFIRI was switched to FOLFOXIRI while bevacizumab was maintained. Toxicity was tolerable. After the second cycle, the computed tomography scan revealed a major

Fig. 1



May 2010. Progression of liver metastasis after mFOLFOX6 and FOLFIRI plus bevacizumab as, respectively, first and second-line therapy.

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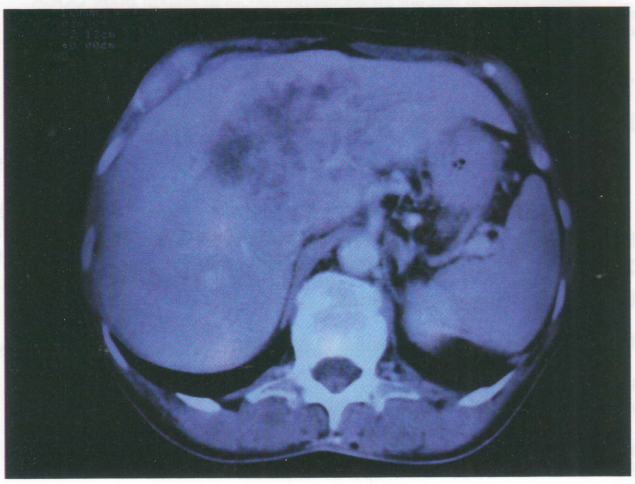
Fig. 2



August 2010. Regression of liver metastasis after the second cycle of FOLFOXIRI plus bevacizumab as third-line therapy.

decrease of liver implants (Fig. 2). The patient received six cycles of FOLFOXIRI and bevacizumab and at present the patient is on bevacizumab every 2 weeks maintaining stable disease.

Discussion/conclusion

Several randomized studies have shown that patients with CRC metastases who received a fluoropyrimidine, oxaliplatin and irinotecan at some point in the course of their disease experienced a significant increase in survival. This emphasizes the need for exposing the patient to the highest possible number of active therapies in order to maximize the survival period. The addition of monoclonal antibodies, such as bevacizumab, cetuximab and panitumumab, increased overall survival to more than 2 years [6,7]. Which antibody or which antibody sequence should be used in patients with metastatic CRC is still unclear. Because of the mutated *k-Ras* in this case [8,9], the only option for monoclonal antibody addition was bevacizumab, which was continued despite disease progression. Bevacizumab is a humanized recombinant monoclonal antibody that blocks vascular endothelial growth factor [10]. As we noted in this case, bevacizumab did not add toxicity to the chemotherapy scheme and showed benefit even given in third-line treatment. Bevacizumab may be as added to first, second and/or third-line chemotherapy for palliative treatment of metastatic CRC, and it appears to increase patient survival with a good response rate and low toxicity [11].

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