

# Trans-arterial Chemoembolization (TACE) of Liver Metastases from Colorectal Cancer Using Irinotecan-Eluting Beads: Preliminary Results

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**Abstract.** Purpose: The purpose of the study was to evaluate the feasibility of irinotecan drug-eluting beads (DC Bead™) administered as trans-arterial chemoembolization (TACE) in patients with liver metastases from colorectal cancer (CRC). Patients and Methods: Ten patients with liver metastases from CRC were treated with TACE adopting irinotecan-eluting beads at a dose of 100 mg every 3 weeks. Computed Tomography (CT) was performed 24h before and after TACE. Results: TACE with irinotecan eluting beads was found to be feasible and well-tolerated. Right upper quadrant pain (RUQP) lasting 4 days (range 2-7) was reported by all the patients. After 30 days, a reduction >50% of CEA levels and of the lesional contrast enhancement was observed in all the patients. Conclusion: Irinotecan drug-eluting beads administered as TACE were shown to be active and safe in patients with liver metastases from CRC.

Patients with liver metastases from CRC have a poor prognosis with 1- and 3-year survival rates of 31% and 2.6%, respectively (1-3). Surgery is feasible in only a minority of patients and most patients are treated with systemic chemotherapy. Irinotecan is an active drug in the first- and second-line treatment of advanced colorectal cancer (4). The advantage of delivering chemotherapy by hepatic arterial infusion is the administration of a high-dose of the drug in the target tissue (5-6). The intra-arterial infusion of irinotecan showed to be safe and feasible as reported in phase I and II studies (6-8).

TACE is a combination of local drug infusion with selective embolization of the feeding arteries of the tumor. The use of irinotecan drug-eluting beads seems to optimize this method.

The objectives of this study were to determine the safety, feasibility, tolerance of and response to TACE using

irinotecan loaded DC Bead™ (Biocompatibles UK Ltd) for the treatment of unresectable metastasis to the liver in patients with CRC.

## Patients and Methods

**Patients.** All patients had histologically confirmed colorectal carcinoma with unresectable liver metastases comprising less than 70% of the liver parenchyma and with no evidence of extrahepatic disease. To be eligible, patients were required to have disease measurable by CT, normal metabolic and laboratory conditions, a Karnofsky performance status of 60% or greater and the absence of infection or ascites. Exclusion criteria included a history of inflammatory bowel disease or extensive intestinal resection, central nervous system involvement, uncontrolled infection, and a history of other cancer except adequately treated *in situ* carcinoma of the cervix or basal or squamous carcinoma of the skin. Prior treatment with systemic chemotherapy was required. All the patients submitted written informed consents. CT was used to determine the extent of liver involvement and to assess the responses.

**Treatment.** Irinotecan drug-eluting beads (DC Bead™, Biocompatibles UK Ltd) were administered as TACE every 3 weeks at a dose of 100 mg. The dose was reduced by 50%, after the first cycle, if a significant toxicity grade 3-4 occurred. Other reasons for treatment termination were progressive disease, hematological or non-hematological toxicity persisting for more than 5 weeks (2-week delay), or patient refusal.

**Drug administration.** A diagnostic angiography was performed in all patients. TACE followed the correct positioning of the catheter tip: it was placed either in the left or in the right hepatic artery. Under fluoroscopic guidance a solution of 2 ml of irinotecan drug-eluting beads and non-ionic contrast medium was injected into the artery feeding the lesions. The irinotecan and beads solution was prepared two hours before TACE.

Laboratory tests showed that a complete loading of irinotecan into beads was achieved within 60-120 min. Prophylactic treatment against nausea and pain and intra-venous hydration were administered.

## Results

Ten patients were enrolled in the study. All the patients presented multiple lesions with a median liver substitution

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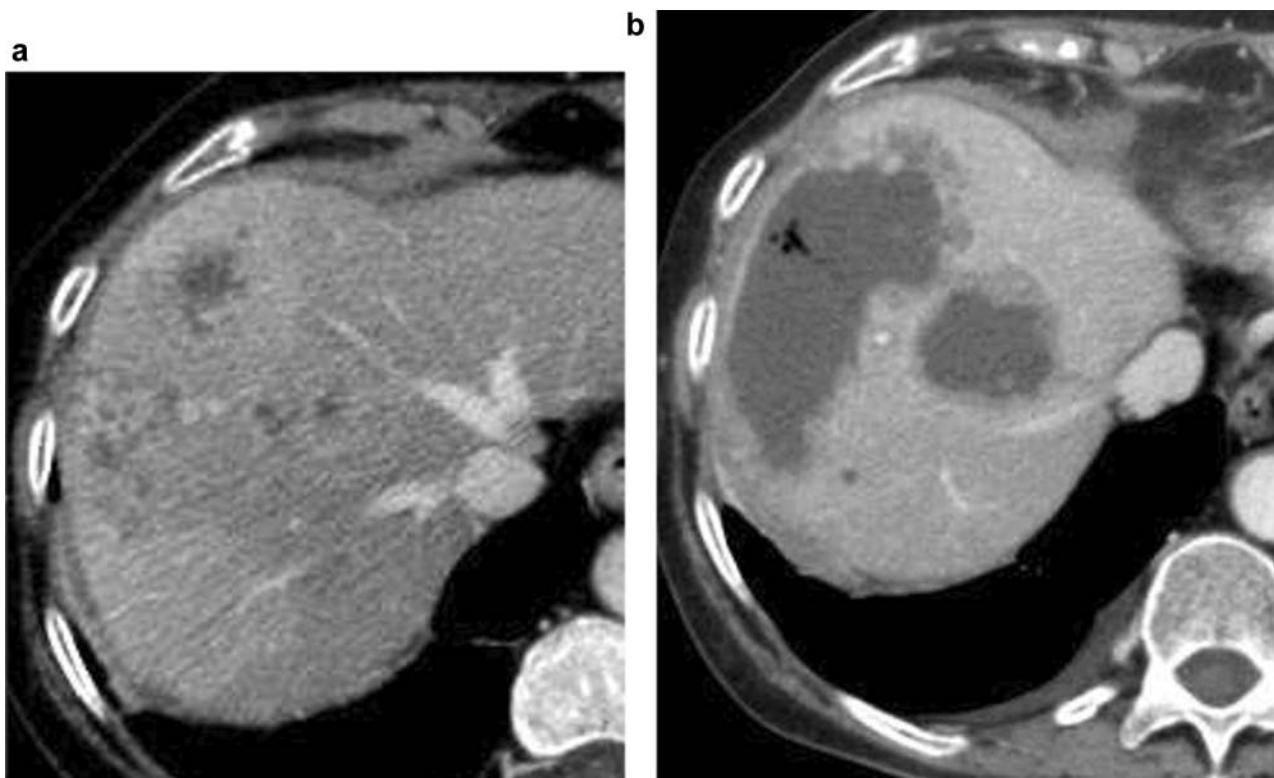


Figure 1. a) CT scan before TACE. Note the metastatic lesions in the right lobe with intense contrast enhancement. b) CT scan 24 hours after TACE. Note the disappearance of contrast enhancement in the metastatic lesions.

of 40% (20-70%). They had prior chemotherapy for metastatic CRC; eight patients progressed after infusion of fluorouracil, leucovorin and oxaliplatin and two after fluorouracil, leucovorin and irinotecan. A total of 18 individual chemoembolizations were valuable for toxicity. All the patients experienced RUQP and shoulder pain, requiring analgesic therapy. Other adverse events observed were vomiting (eight out of 10 patients) and alopecia (seven out of 10 patients). Furthermore, most patients (8 out of 10) developed mild (grade 1-2) asthenia. There was no serious hematological toxicity. One patient developed liver abscess requiring antibiotic therapy. The median duration of hospitalization was 3 days (1-10). In all patients a clear reduction of CEA >50% (range 50%-90%) was documented. Within 1 month after treatment, the CT scan showed a significant reduction of metastatic contrast enhancement in all the patients (Figure 1). In seven out of 10 patients an objective tumor regression was observed.

## Discussion

At present, systemic chemotherapy is the only established treatment in patients with liver metastases from CRC, who are not eligible for surgery. Irinotecan is an active drug against

colorectal cancer, with response rates of 13-27% observed in phase II studies of both chemo-naive and 5-FU-pretreated patients using a weekly or 3-weekly i.v. schedule. A phase III study comparing irinotecan to best supportive care in 5-FU refractory patients showed a survival benefit of 2.7 months. In patients with liver dominant metastases from CRC, studies have been performed using regional chemotherapy. Although high response rates are observed, the results of hepatic arterial 5-FU or FUDR infusion are inconclusive with respect to survival. Phase I and II studies showed that irinotecan infusion is well accepted by the patients, it seems to have less drug effects in the systemic circulation and in liver metastases from CRC it can rescue systemically pre-treated patients (7-9).

The present study examined TACE of irinotecan eluting beads in patients with liver metastases from CRC. The goal of TACE is to deliver large amounts of chemotherapeutic agents to the tumor with the use of the artery as a conduit to the tumor and reduce systemic levels (10-11). Embolic particles are used to reduce arterial inflow and drug wash-out and maximize contact time between the drugs and the tumor cells (12). In our preliminary experience TACE with irinotecan eluting beads (DC Bead™) was feasible, active and well tolerated, although the follow-up was too short to define more detailed conclusions.

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