

Advanced Colorectal Cancer

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Curable Metastatic Colorectal Cancer

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Colon cancer, though already metastatic, may still be curable through multi-modality approaches, which require combined planning between medical and surgical oncologists. Retrospective surgical series have historically shown 5-year survival or “cures” for 30% to 50% of patients with solitary or a few resectable liver metastases. The role of adjuvant chemotherapy in this setting has been poorly defined. A recent European Organization for Research and Treatment of Cancer (EORTC) study randomized 364 patients with solitary resectable liver metastases to surgery alone vs. perioperative chemotherapy with FOLFOX (6 cycles preoperatively and 6 cycles postoperatively).¹ Patients were required to have no more than four resectable, liver-only metastases. Ninety-three percent (93%) of patients randomized to undergo surgery were actually operated compared with 87% for the perioperative chemotherapy group. Three-year disease-free survival (DFS) for the actual eligible group (n=342) was 36% vs. 28% (HR = 0.77, *P* = 0.04). For those actually resected (n= 304), the results were slightly better (HR 0.73). This result (8% actual improvement in 3-yr DFS) compares favorably with the benefit of FOLFOX in patients with stage III resected CRC.

Additional attention has been paid to those patients who have liver-only disease but borderline resectable disease. Current thinking does not define resectability by number of lesions or extent of resection, but by extent of remaining liver, which should be 25% to 30%. Limiting factors for resection include proximity to vital structures and need for negative margins. Strategies for improving resection rates include staged surgery, portal vein embolization, and preoperative (neoadjuvant) chemotherapy. A long experience with oxaliplatin-based therapy showed that patients considered surgically unresectable but treated initially with chemotherapy had 5-year survival similar to that of patients treated with initial surgery.² This approach is supported by the EORTC study, showing a 30% average shrinkage in tumor diameter. The addition of targeted therapies could increase conversion rates further; data on cetuximab have shown a 10% surgical

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resection rate compared with 5% for those treated with FOLFIRI alone (not selected for K-ras wild-type).³ In the NO16966 study of FOLFOX or CapeOX ± bevacizumab,⁴ resection rates for those with liver-only disease were 19% vs. 12% with the use of bevacizumab. Toxicities of chemotherapy used in the perioperative setting include hepatic steatosis (5-fluorouracil), steatohepatitis (irinotecan), and sinusoidal scarring (oxaliplatin). The use of irinotecan is associated with increased surgical complications and mortality in a dose-dependent manner.⁵ Multimodality planning with a defined number of preoperative cycles is essential in the approach to the patient with potentially resectable liver metastases.

References:

1. Nordlinger B, Sorbye H, Glimelius B, et al: Perioperative chemotherapy with FOLFOX4 and surgery versus surgery alone for resectable liver metastases from colorectal cancer (EORTC Intergroup trial 40983): a randomised controlled trial. *Lancet* 2008 Mar 22;371(9617):1007-16.
2. Bismuth H, Adam R, Lévi F, et al: Resection of nonresectable liver metastases from colorectal cancer after neoadjuvant chemotherapy. *Ann Surg* 1996 Oct;224(4):509-20; discussion 520-2.
3. Van Cutsem E, Köhne CH, Hitre E, et al: Cetuximab and chemotherapy as initial treatment for metastatic colorectal cancer. *N Engl J Med* 2009 Apr 2;360(14):1408-17.
4. Saltz LB, Clarke S, Díaz-Rubio E, et al: Bevacizumab in combination with oxaliplatin-based chemotherapy as first-line therapy in metastatic colorectal cancer: a randomized phase III study. *J Clin Oncol* 2008 Apr 20;26(12):2013-9.
5. Vauthey JN, Pawlik TM, Ribero D, et al: Chemotherapy regimen predicts steatohepatitis and an increase in 90-day mortality after surgery for hepatic colorectal metastases. *J Clin Oncol* 2006 May 1;24(13):2065-72.