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Current Perspective

Towards a pan-European consensus on the treatment of patients with colorectal liver metastases

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ABSTRACT

Colorectal cancer (CRC) caused nearly 204,000 deaths in Europe in 2004. Despite recent advances in the treatment of advanced disease, which include the incorporation of two new cytotoxic agents irinotecan and oxaliplatin into first-line regimens, the concept of planned sequential therapy involving three active agents during the course of a patient's treatment and the integrated use of targeted monoclonal antibodies, the 5-year survival rates for patients with advanced CRC remain unacceptably low. For patients with colorectal liver metastases, liver resection offers the only potential for cure. This review, based on the outcomes of a meeting of European experts (surgeons and medical oncologists), considers the current treatment strategies available to patients with CRC liver metastases, the criteria for the selection of those patients most likely to benefit and suggests where future progress may occur.

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1. Introduction

Colorectal cancer (CRC) is fourth in the league of cancer deaths worldwide with nearly 204,000 deaths in Europe alone each year.[1] Approximately 25% of CRC patients present with overt metastases, and an additional 25–35% of patients will develop metastases during the course of their disease.[2] Significantly between 20% and 30% of patients with advanced CRC have liver only metastases,[3] while approximately 50% of recurrences following resection of the primary tumour are confined to the liver.[4]

Despite the recent advances in first-line chemotherapy strategies for the treatment of patients with advanced CRC,[5–9] liver resection offers the only chance of cure for patients with colorectal liver metastases.[10] Five-year survival rates following resection range between 25% and 40% compared with between 0% and 5% for patients from the same institute who did not undergo liver resection,[4,10–15] and are consistent with the 5-year survivals reported for most large series where liver resection has been performed.[16–19] However, approximately 85% of patients with stage IV CRC, referred to specialist centres, have metastatic liver disease which is considered to be unresectable at presentation.[20]

Over the last five years, there has been a recognition that the improved combination chemotherapy regimens, namely 5-fluorouracil/folinic acid (5-FU/FA) in combination with either irinotecan or oxaliplatin,[5–9] routinely used in the treatment of patients with advanced CRC, can facilitate the downsizing of colorectal liver metastases and render initially unresectable metastases resectable.[18,20–23] Consequently, the percentage of patients potentially eligible for curative liver resection is increasing. Significantly also, the long-term survival rates for those patients with initially unresectable metastases treated with chemotherapy prior to surgery[18] are similar to those of patients whose metastases were considered to be resectable (Fig. 1).[13,17,19,24] The results of a recent study, however, suggest that the recurrence rate may be quite high for these patients.[25]

However, despite these advances the selection criteria for the resection of CRC liver metastases are not well documented. Consequently, the possibility of resection of CRC liver metastases is often underestimated, and currently even in Europe, we have the situation where away from specialist centres, many patients with liver metastases are considered to be incurable and many patients with curable liver metastases are never referred to a surgeon.[26] Conversely, in centres that specialise in liver resection we can have the situation where some patients who are incurable undergo resection.

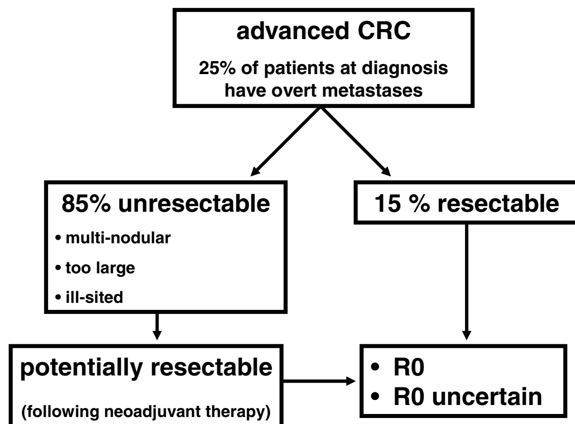

Fig. 1 – Treatment schema for patients with advanced CRC.

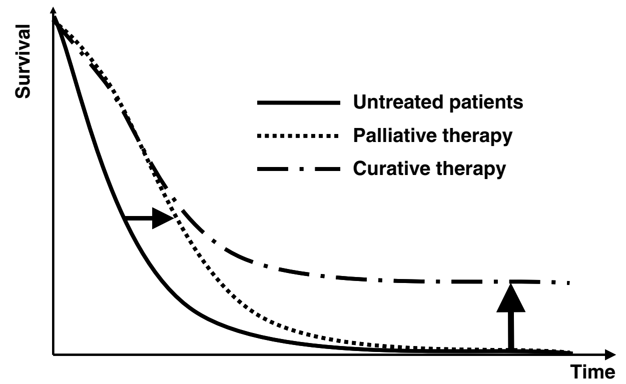

Fig. 2 – Effective curatively intentioned therapy displaces the survival curve in time, and also alters its shape, reflecting a degree of long-term survival (reproduced with the kind permission of Professor C.-H. Kohne).

The goal of a multidisciplinary treatment approach in this context is to increase cost-effectively the number of patients with long-term survival by increasing the number of patients undergoing potentially curative liver resections (Fig. 2). The first question that we need to address is: 'How do we establish guidelines that will facilitate this process and that can be readily adopted by the surgeons and medical oncologists, across Europe, working both inside and outside of specialist centres?' Specifically, how do we prepare generally applicable guidelines to optimise the chances of survival of CRC patients with liver metastases?

2. Current status

Although there are several published clinical scoring systems,[15,19,24,27–30] the French recommendations for clinical practice with regard to the 'Therapeutic management of liver metastases from colorectal cancer' published in March 2003,[31] are by far the most comprehensive. Already in 2005–2006 we have moved on from the French recommendations,[31] in terms not only of what is considered to be surgically resectable disease but also in terms of the recognition of the potential efficacy of planned, preoperative (neoadjuvant) chemotherapy, in selected patients, in facilitating an increase in the number of patients who can undergo liver resection.[23]

Based on the considerable evidence that liver resection either alone or in conjunction with preoperative chemotherapy in selected patients offers a chance for long-term survival,[10,12,13,15,17–19] the aim of this review is to outline the new areas of consensus among European surgeons and medical oncologists in the treatment of patients with colorectal liver metastases, achieved at a meeting of the European Colorectal Metastases Treatment Group held in Paris, November 2005, and identify the emerging areas for discussion.

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