



Original Research

# Resection of colorectal liver metastases after second-line chemotherapy: is it worthwhile? A LiverMetSurvey analysis of 6415 patients



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**KEYWORDS**

Colorectal cancer;  
Liver metastasis;  
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Second line;  
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**Abstract Purpose:** Patient outcome after resection of colorectal liver metastases (CLM) following second-line preoperative chemotherapy (PCT) performed for insufficient response or toxicity of the first-line, is little known and has here been compared to the outcome following first-line.

**Patients and methods:** From January 2005 to June 2013, 5624 and 791 consecutive patients of a prospective international cohort received 1 and 2 PCT lines before CLM resection (group 1 and 2, respectively). Survival and prognostic factors were analysed.

**Results:** After a mean follow-up of 30.1 months, there was no difference in survival from CLM diagnosis (median, 3-, and 5-year overall survival [OS]: 58.6 months, 76% and 49% in group 2 versus 58.9 months, 71% and 49% in group 1, respectively,  $P = 0.32$ ). After hepatectomy, disease-free survival (DFS) was however shorter in group 2: 17.2 months, 27% and 15% versus 19.4 months, 32% and 23%, respectively ( $P = 0.001$ ). Among the initially unresectable patients of group 1 and 2, no statistical difference in OS or DFS was observed. Independent predictors of worse OS in group 2 were positive primary lymph nodes, extrahepatic disease, tumour progression on second line, R2 resection and number of hepatectomies/year <50. Positive primary nodes, synchronous and bilateral metastases were predictors of shorter DFS. Initial unresectability did not impact OS or DFS in group 2.

**Conclusion:** CLM resection following second-line PCT, after oncosurgically favourable selection, could bring similar OS compared to what observed after first-line. For initially unresectable patients, OS or DFS is comparable between first- and second-line PCT. Surgery should not be denied after the failure of first-line chemotherapy.

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## 1. Introduction

Liver resection is the only treatment that currently offers a chance of long-term survival to patients with colorectal liver metastases (CLM). For patients with primarily resectable CLM, especially those with advanced, multiple or borderline resectable disease, perioperative systemic chemotherapy has been given to increase their long-term survival by reducing the risk of recurrence after resection. However, the majority of patients with CLM are not initial candidates for hepatic resection. Without conversion chemotherapy, surgical resection is not possible for 70%–80% of those patients. Encouragingly, the combination of systemic chemotherapy and liver surgery could switch a significant proportion of patients from a palliative to a potentially curative situation, with a reported postoperative 5-year survival of 33% after rescue surgery [1–3]. Recently, an international panel of multidisciplinary experts developed recommendations for the management of patients with CLM, indicating that preoperative treatment to induce resectability should be as short as possible, and that postoperative chemotherapy (POCT) should continue with the same protocol when preoperatively effective [4].

Failure to respond to first-line therapy has frequently predicted poor response rates of subsequent lines of therapy [5–7]. For patients where disease control is the goal, patients should proceed to second-line therapy when there is evidence of disease progression, or toxicity of the first-line [8]. However, the combination of second-line systemic chemotherapy (for neoadjuvant or conversion purpose) with CLM resection has been

scarcely described. Its impact on survival is not yet demonstrated, and what kind of patients can really benefit from the resection is so far unknown. In this study, we aimed to analyse the impact of the CLM resection after second-line treatment, in terms of overall survival (OS) and disease-free survival (DFS) in a large international dataset, and to find out the predictive factors of outcomes for such patients. The survival data were also compared to that of the CLM resection following first-line chemotherapy, in the same oncosurgical teams, although the two cohorts were not rigorously comparable.

## 2. Patients and methods

### 2.1. Patient selection

LiverMetSurvey is a prospective international internet-based registry, collecting and regularly updating clinical data from all consecutive patients undergoing surgery for CLM, and was designed to assess the efficacy of multimodality treatment of CLM [3]. It accounted on 25th December 2015, with 243 individual patients from 313 institutions worldwide (70 countries). In this study, the data of 6415 consecutive patients were retrospectively analysed. Between January 2005 and June 2013, 5624 patients underwent resection after first-line chemotherapy (group 1) and 791 patients following second-line chemotherapy (group 2), respectively.

Patient eligibility criteria included the completion of hepatic resection with intent to resect all the metastases, irrespective of the initial resectability of CLM and of the

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