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Targeting the liver: Insights from a tertiary center on post-operative hepatic arterial oxaliplatin for metastatic colorectal cancer

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ABSTRACT

Background: As the liver is the most common site of metastasis in colorectal cancer (CRC), and metastatic recurrence frequently occurs after resection of colorectal liver metastases (CRLM), hepatic arterial infusion chemotherapy (HAIC) has emerged as a promising treatment approach. This study investigates the feasibility, safety, and efficacy of postoperative HAIC with oxaliplatin following curative-intent resection of CRLM.

Methods: A retrospective analysis was conducted on all patients with resected CRLM who received postoperative HAIC with oxaliplatin between 2008 and 2022 at a tertiary cancer center. The primary study endpoint were disease-free-survival (DFS) and overall survival (OS).

Results: Overall, 119 patients (median age, 56 years; synchronous metastatic disease, 82%) received post-operative HAIC with oxaliplatin after complete resection of their CRLM (median number of metastases resected, 7). They received a median number of 6 HAIC cycles (range, 1–12), mostly combined with intravenous chemotherapy with 5-fluorouracil/leucovorin (n = 118, 99%) and irinotecan (n = 41, 34%). The median DFS was 10.2 months (95% CI 9–12.4) and the median intrahepatic DFS was 18.4 months (95% CI 12.4–29.7,12 months DFS rate, 60%). The median OS reached 55.5 months (95% CI, 50.0–86.6; 5-year OS rate, 46%). Grade 3–4 toxicities occurred in 45% of patients (neutropenia, 38%; peripheral neuropathy, 9%); 54% of patients experienced pain (mostly mild to moderate) during oxaliplatin infusion. HAI catheter-related complications included extrahepatic perfusion (30%) and catheter occlusion (11%).

Conclusions: HAIC with oxaliplatin is an effective, safe and feasible treatment option after resection/ablation of CRLM. These findings support the therapeutic relevance of postoperative HAIC in liver-limited metastatic CRC.

1. Introduction

Colorectal cancer (CRC) is the third leading cause of cancer-related mortality worldwide, with an estimated 1.8 million new cases diagnosed annually [1]. The liver represents the most frequent metastatic site; 40–60% of patients will develop colorectal liver metastases (CRLM) either at diagnosis or during disease progression. However, only 25% of these patients have resectable CLRM at the time of diagnosis [2]. Complete surgical resection, including liver transplantation, or ablation of CRLM remains the only potentially curative approach, offering a

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10-year survival rate of approximately 24% [3] and a 5-year survival rate of 57 % in patients undergoing liver transplantation [4]. Achieving an R0/R1 resection (or potentially R0/R1 ablation) is a key prognostic factor in metastatic CRC and a determinant of long-term survival [5–7]. This highlights the critical need for optimizing perioperative strategies to enhance disease control following CRLM resection.

Hepatic arterial infusion (HAI) chemotherapy (HAIC) delivers chemotherapy directly into the hepatic artery, achieving high intratumoral drug concentrations while minimizing systemic toxicity [8–10]. Given that liver tumors derive most of their blood supply from the hepatic artery, while normal hepatocytes are predominantly perfused via the portal vein, HAIC offers selective tumor targeting.

The randomized phase II PACHA-01 trial demonstrated the efficacy of HAIC in the postoperative setting, reporting significantly improved hepatic recurrence-free survival (median 25 vs. 12 months; HR = 0.598, [95%CI 0.379-0.944] p = 0.027) in patients with high risk of relapse (≥ 4 CRLM resected/ablated) treated with HAI oxaliplatin compared to those receiving intravenous oxaliplatin [11]. The study also suggested a potential OS benefit (median, 74 vs. 54 months; HR = 0.551 [0.299-1.015], p = 0.056). Despite these promising results, the trial was prematurely terminated due to slow accrual, leaving several questions unanswered. Thus, further evidence is crucial to further evaluate the feasibility, safety and clinical impact of HAIC after resection/ablation of CRLM.

This retrospective study aims to assess the efficacy, safety, and feasibility of adjuvant HAIC with oxaliplatin following curative-intent resection/ablation of CRLM in a high-volume cancer center.

2. Materials and methods

2.1. Study design and patient selection

Patients who received at least one cycle of postoperative HAIC after complete resection or ablation of CRLM at Gustave Roussy Cancer Center between 2008 and 2022 were eligible for this study. The HAIC regimen consisted of HAI oxaliplatin combined with systemic chemotherapy, with or without biologics (anti-EGFR or anti-angiogenic antibodies). HAIC eligibility was determined by a multidisciplinary tumor board including oncologists, gastroenterologists, liver surgeons, and diagnostic and interventional radiologists; potential benefits, constraints and risks were subsequently discussed with the patient.

The presence of initially unresectable and limited extrahepatic disease did not exclude patients from HAIC, and local treatments for extrahepatic metastases could be administered either before or after HAIC, if appropriate. Prior local treatments for hepatic or extrahepatic disease were permitted. All patients were evaluated by liver MRI to optimize lesion detection and surgical planning.

Clinical, radiological, biological, and histopathological data were gathered from electronic medical records and managed through the REDcap electronic database hosted at Gustave Roussy.

2.2. Treatment

Intra-arterial catheters were placed either surgically at the time of hepatic resection, percutaneously by interventional radiology or through a hybrid approach combining arterial pedicle preparation during surgery followed by percutaneous implantation. Proper catheter function and liver perfusion were verified by digital subtraction angiography (DSA) + computed tomography (CT) or cone-beam CT with contrast injection before treatment initiation, and DSA alone every two cycles thereafter, to rule out extrahepatic perfusion. Additional imaging or gastroscopy was performed in the event of persistent abdominal pain or suspected extrahepatic distribution.

The chemotherapy regimen included HAI oxaliplatin at 100 mg/m^2 infused over 2 h on day one, followed by systemic chemotherapy with leucovorin and bolus/infusional 5-fluorouracil (5FU) (modified LV5FU2 regimen) plus or minus irinotecan (FOLFIRI regimen), administered every two weeks. The addition of irinotecan and/or biologic agents was based on RAS/BRAF mutation status and initially unresectable CRLM; continuation of biologic agents in the postoperative setting was not uniform and left to the discretion of the treating physician, taking into account extrahepatic disease, treatment-related toxicity, and postoperative complications. When biologics were incorporated, the following dosages were used: cetuximab 500 mg/m^2, panitumumab 6 mg/kg, or bevacizumab 5 mg/kg, every two weeks, based on tumor *RAS/BRAF* mutational status. In cases of chemotherapy or HAIC-related adverse events, drug dose reduction or interruption or HAIC cycle delays were implemented. The infusion duration was extended in case of infusion-related pain and according to any findings during DSA checks, especially when arterial branches with extrahepatic destinations were detected during high-flow injections but not visible during soft injection. Postoperative chemotherapy continued until the planned number of cycles was completed or until the occurrence of unacceptable toxicity or disease progression.

2.3. Monitoring and safety assessment

Patients were evaluated before each chemotherapy cycle for adverse events and by physical examination and laboratory testing (including complete blood cell count and liver function tests). Systemic toxicities were graded according to the version of the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) in use at the time of the patient's treatment.

HAIC catheter-related complications were categorized as follows: Grade 0 (none), Grade 1 (mild, no intervention required), Grade 2 (moderate, requiring intervention to maintain HAIC), Grade 3 (severe, inability to continue HAIC despite intervention or definitive contraindication), Grade 4 (life-threatening), and Grade 5 (fatal). Similarly, HAIC-related systemic toxicities were classified as: Grade 0 (absent), Grade 1 (mild, not clinically relevant, with no need to delay HAIC), Grade 2 (moderate, reversible with HAIC delay but not requiring treatment discontinuation), Grade 3 (severe, non-reversible with HAIC delay and/or requiring permanent treatment cessation), Grade 4 (life-threatening), and Grade 5 (fatal). Safety assessments included all adverse events related to HAIC or intra-arterial catheter, along with systemic chemotherapy-related toxicities.

2.4. Follow-up

Tumor recurrences were assessed radiologically using CT or magnetic resonance imaging according to the Response Evaluation Criteria in Solid Tumors in use at the time of the patient's treatment (RECIST 1.0 or 1.1). Positron emission tomography was also used when appropriate. Clinical examination for tumor recurrence, blood tumor markers and thoraco-abdomino-pelvic imaging were assessed every 3 months during HAIC and at standard intervals (usually every 3 to 6 months) thereafter.

2.5. Statistical analysis

Descriptive statistics were used to summarize patient characteristics. Categorical variables were compared using Chi-square test or Fisher's exact test. Rank-Wilcoxon's test was used for continuous variables. Disease-free survival (DFS), the study primary endpoint, was defined as the time from the first HAIC cycle to documented disease progression or death for any reason. Overall survival was defined as the time from resection to death from any cause. Survival outcomes were estimated using the Kaplan-Meier method and compared using log-rank tests. All statistical calculations were performed using R version 4.3.0, with two-sided p-values <0.05 considered statistically significant.

3. Results

3.1. Patient characteristics

Between 2008 and 2022, 119 patients who received at least one cycle of postoperative HAI oxaliplatin following CRLM resection were included in the study. Baseline patient demographics and disease characteristics are provided in Table 1.

The median age was 56 years (range, 28-77). At diagnosis, 91 patients (82%) presented with synchronous metastatic disease. Twenty-one patients (19%) exhibited limited extrahepatic disease, mostly lung metastases (11 patients). Ten patients had concomitant ovarian metastasis and/or peritoneal carcinomatosis.

Left colon was the most frequent primary location (65 patients, 55%) followed by right colon (28 patients, 24%) and rectum (25 patients, 21%).

The median number of initial CRLM was 7 (range 1-25), with a bilobar distribution in most patients (86%). Initial surgical assessment classified CRLM as resectable in 23 patients (19%), potentially resectable in 77 (65%), and initially unresectable in 18 (15%).

Preoperative chemotherapy was administered as part of a first-line treatment in 87 patients (74%), a second-line treatment in 23 patients (19%) and a third-line or beyond in 8 patients (7%). The median number of preoperative oxaliplatin cycles administered was 6 (range, 0-22). Most patients (76 patients, 64%) did not experience residual oxaliplatin-related neurotoxicity, while grade 1 and 2 neurotoxicity were experienced in respectively 31 (26%) and 11 (9%) patients.

Disease control (i.e. stable disease or objective response) with preoperative chemotherapy was mandatory for patients' eligibility to resection/ablation of CRLM. Missing metastases after preoperative chemotherapy were not a contraindication to surgery.

Table 1
Patient baseline characteristics (the sum of percentages may exceed 100% because of rounding).

Characteristics	Patients (n = 119)
Gender	
Male	62 (56%)
Female	49 (44%)
Age at diagnosis (median, range)	56 (28-77)
Primary tumor location	
Left colon	65 (55%)
Right colon	28 (24%)
Rectum	25 (21%)
Unspecified	1 (1%)
Metastatic disease pattern	
Synchronous	91 (82%)
Asynchronous	19 (17%)
Unspecified	1 (1%)
Initial multidisciplinary team assessment	
Potentially resectable	77 (65%)
Resectable	23 (19%)
Unresectable	18 (15%)
Metastatic sites at diagnosis	
Liver	86 (77%)
Lungs	11 (9%)
Peritoneum	5 (5%)
Ovaries	5 (5%)
Others	1 (1%)
Unspecified	13 (12%)
KRAS status	
Wild-type	63 (53%)
Mutant	43 (36%)
Unknown	13 (11%)
Number of preoperative chemotherapy lines	
1	87 (74%)
2	23 (19%)
3	6 (5%)
4	1 (1%)
Unknown	1 (1%)
Median number of preoperative oxaliplatin cycles (range)	6 (0-22)

The median number of resected CRLM was 7 (range, 1-37), with 90 patients (80%) having ≥4 resected CRLM and 46 patients (41%) having ≥8. Thirty-three (29%) underwent major hepatectomy (4 or more segments resected). Thermal ablation was performed in 75 patients (68%), with a median number of ablated lesions of 4 (range, 1-36).

3.2. Treatment characteristics

Treatments characteristics are reported in Table 2. HAI catheters were implanted surgically in 59 (50%) patients, percutaneously in 43 (36%), and via a combined approach in 17 patients (14%).

The median number of postoperative HAIC cycles administered was 6 (range, 1–12). Dose reductions were required in 83 patients (70%), affecting either the intra-arterial chemotherapy (54%) or the intravenous chemotherapy (55%). These adjustments were primarily due to hematologic toxicity (40%), non-hematologic toxicity (39%), or a combination of both (20%). HAIC was discontinued prematurely in 21 patients (18%), most commonly due to progressive disease (11 patients, 10%) or catheter-related complications (7 patients, 6%). Only 3 patients discontinued HAIC due to toxicity that could not be managed with dose adjustment.

To the exclusion of one patient who received Tomudex, all patients received concomitant intravenous LV5FU2. Additionally, 41 patients (34%) received intravenous irinotecan, and 48 (40%) received concomitant Bevacizumab (30 patients, 25%) or anti-EGFR agents (cetuximab or panitumumab: 18 patients, 15%) as continuation of their preoperative chemotherapy regimen. In the majority of cases (75%), the use of biotherapies reflected more aggressive treatment approaches for patients with initially unresectable or borderline resectable colorectal liver metastases (CRLM). Among patients who received irinotecan in addition to LV5FU2, a greater proportion had undergone more than one line of preoperative chemotherapy compared to those treated with LV5FU2 alone (33% vs. 20%), suggesting more treatment-resistant or advanced disease. Patients receiving irinotecan were younger (median age 53 vs. 58 years), potentially reflecting a clinical preference for intensified regimens in younger, more fit individuals.

3.3. Toxicity

Overall, 50 patients (45%) experienced grade 3-4 adverse events

Table 2
Treatment characteristics (the sum of percentages may exceed 100% because of rounding).

Characteristics	Patients (n = 119)
Median number of postoperative HAI + IV cycles (range)	6 (1-12)
Concomitant IV chemotherapy	
LV5FU2	118 (99%)
Irinotecan	41 (34%)
Bevacizumab	30 (25%)
Anti-EGFR	18 (15%)
HAI catheter placement	
Surgical	59 (50%)
Radiological	43 (36%)
Combined	17 (14%)
Posology adjustment	
Patients requiring HAI Dose reduction	64 (54%)
Patients requiring IV dose reduction	65 (55%)
Patients requiring HAI and IV dose reduction	83 (70%)
Reason for posology adjustment	
Hematologic toxicity	48 (40%)
Non-hematologic toxicity	46 (39%)
Both	24 (20%)
Reason HAI cessation	
Catheter dysfunction	7 (6%)
Progressive disease	11 (10%)
Toxicity	3 (3%)
Surveillance/end of preplanned number of cycles	94 (82%)
Unknown	4

Table 3
Systemic adverse events. Adverse events are ranked by grade 3-4 frequency.

Adverse events	Patients (n = 119)	
	Grade 1-2	Grade 3-4
Neutropenia	34 (32%)	44 (38%)
Peripheral neuropathy	100 (86%)	11 (9%)
Abdominal pain	46 (48%)	5 (6%)
Thrombocytopenia	40 (35%)	3 (4%)
Mucositis oral	36 (32%)	3 (3%)
Nausea/vomiting	85 (74%)	2 (2%)
Diarrhea	57 (53%)	2 (2%)
Duodenal ulcer	3 (3%)	1 (1%)
Anemia	52 (61%)	-
Alopecia	19 (17%)	-
Extrahepatic perfusion	33 (30%)	-
Catheter obstruction	12 (11%)	-
Arterial thrombosis	5 (5%)	-
Local infection	5 (4%)	-
Drug extravasation	3 (3%)	-
Ischemic cholangitis	3 (3%)	-
Local hematoma	2 (2%)	-

(Table 3), most often neutropenia (n = 44, 38%) and peripheral neuropathy (n = 11, 9%). Fifty-one patients (54%) had pain during HAIC, mostly of mild-to-moderate intensity (grade 1-2, 46/51 [90%]) and easily managed with analgesics and longer infusion times.

The most frequent intra-arterial catheter-related vascular complication was extrahepatic perfusion (33 patients, 30%), responsible for gastric or duodenal ulcer in 3 patients (3%), requiring inpatient management in one patient. Catheter obstruction (12 patients, 11%), arterial thrombosis (5 patients, 5%) or dissection (2 patients) and drug extravasation (3 patients, 3%) were less frequent. HAI port-related complications were rare, including local infection (5 patients, 4%) and hematoma (2 patients, 2%). Three patients (3%) experienced grade 1-2 ischemic cholangitis; no case of biliary stenosis occurred. Overall, HAI catheter revision was required in 44 patients (36%), most often by embolization (20/44 patients) or catheter replacement (6/44 patients).

3.4. Survival

The median DFS was 10.2 months (95% CI 9–12.4), with a 1-, 2- and 3-year DFS rate of 42%, 24% and 15% (Fig. 1A). The median intrahepatic DFS was 18.4 months (95% CI 12.4–29.7), with 12- and 24-month intrahepatic DFS rates of 60% and 46%, respectively. The median extrahepatic DFS was 19.5 months (95% CI 14.1–30.2), with 12- and 24-month extrahepatic DFS rates of 62% and 47%, respectively. The median OS was 55.5 months (95% CI 50.0–86.6), with a 3-year and 5-year OS rate of 68% and 45%.

No significant difference was observed between patients with or without extrahepatic metastasis regarding DFS (median, 10.6 and 10.2 months, respectively, p = 0.52) or OS (median, 54,1 and 56,3 months, respectively, p = 0.71) (Fig. 1B).

The number of resected CRLM had no significant impact on DFS (median, 9.1 months [95% CI 8.0–19.5] if < 4 vs. 10.6 months [95% CI 9.2–17.1] if ≥ 4, p = 0.12). However, patients with fewer than 4 resected CRLM had inferior OS (median, 35.2 months; 95% CI 28.9–NA) compared to those with ≥4 resected CRLM (median, 59.0 months; 95% CI 51–99.6). Only 20 patients had fewer than 4 CRLM resected. Among them, one had concomitant peritoneal carcinomatosis treated with peritonectomy and hyperthermic intraperitoneal chemotherapy. Additionally, among those patients, 7 patients (44%) had received two or more preoperative systemic treatment lines, and 6 patients (35%) had already undergone one or two prior surgical interventions for metastases—compared to 22% in the ≥4 CRLM subgroup who had received more than one line of chemotherapy or previous metastasis surgery.

Patients treated with HAIC as part of first-line treatment showed a trend towards superior DFS (median, 10.9 [95% CI 9,37–17,1] vs. 8.52 months [95% CI 7.7–31.3], p = 0.05) and OS compared to those who received more than one preoperative line (median, 59.4 months [95% CI 51–97.9] vs. 48.3 months [95% CI 32.9–NA), p = 0.1), though not statistically significant. (Fig. 1C). HAIC administered as part of first-line therapy was associated with significantly better extrahepatic DFS (median, 24.9 [95% CI 17.1–33.9] vs. 12.3 months [95% CI 7.7–31.3], p = 0.04).

Overall, patients receiving concomitant targeted therapy experienced worse outcomes in terms of both DFS (mDFS 13.2 [9.17 – 21.7] without targeted therapy vs. 9.2 months [8 – 11.9] with targeted therapy [p = 0.012]). Median OS was 86.6 months [53.2 - NA] without targeted therapy vs. 48.3 months [32.9– 73.3] with targeted therapy [p = 0.0059]) (Fig. 1D).

The addition of intravenous irinotecan to intravenous LV5FU2 to postoperative HAI oxaliplatin did not significantly impact outcomes, yielding mDFS of 9.1 months (95% CI [8.0– 11.5]) and mOS of 53.2 months (95% CI [32,7– 92,6]) compared to respectively 13 months (95% CI [9.2– 18.4]) and 59.4 months (95% CI [51– 99.6]) with LV5FU2 alone (p = 0.08 and 0.269) (Fig. 1E).

4. Discussion

In this study, we analyzed a cohort of 119 patients who received postoperative chemotherapy combining HAI oxaliplatin and 5FU-based systemic chemotherapy after curative-intent resection or ablation of CRLM. To the best of our knowledge, this represents the largest cohort analyzed to date using oxaliplatin-based HAIC within this specific clinical setting.

Our survival analysis yielded encouraging results for HAIC, both in intrahepatic DFS and OS, with 46% of patients alive at 5 years, despite their high risk of recurrence, highlighting the potential long-term benefit of HAIC in the postoperative setting. Our findings are broadly in line with prior studies assessing postoperative HAIC after resection of CRLM, with comparable outcomes despite a higher number of resected CRLM [12,11]. In a recent study aiming at establishing benchmark oncologic outcomes after liver resection for CRLM, benchmark 5-year overall survival was comparable for solitary synchronous liver metastases, while lower benchmark survival expectations were reported for

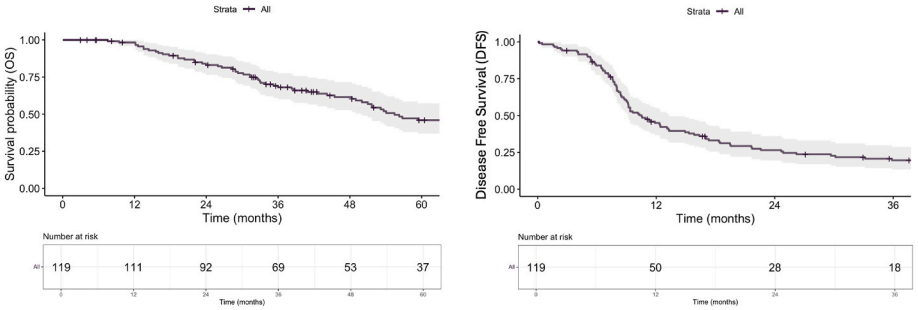

Fig. 1A. Overall survival (OS) and disease-free survival (DFS).

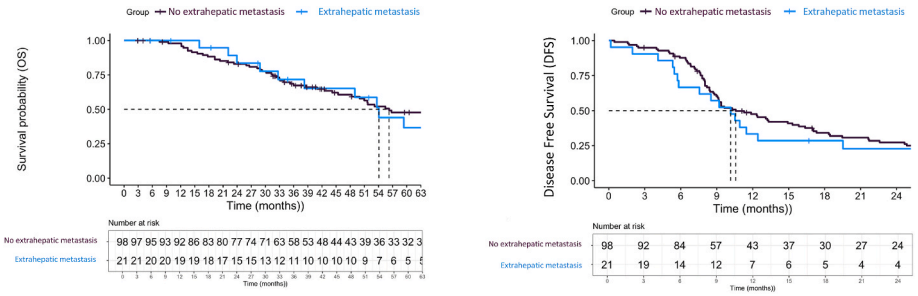

Fig. 1B. Overall survival (OS) and disease-free survival (DFS) according to extrahepatic metastasis.

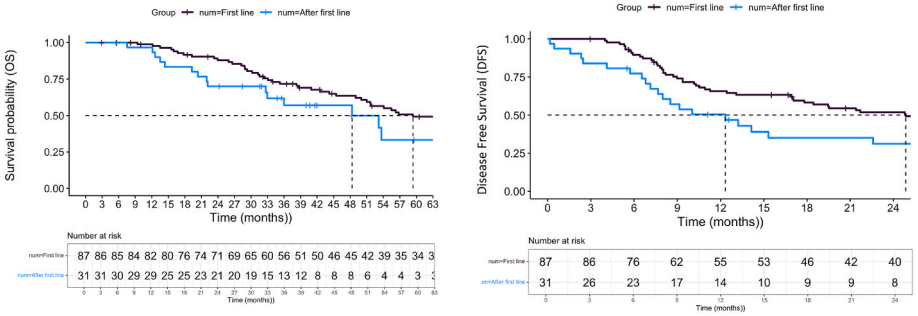

Fig. 1C. Overall survival (OS) and disease-free survival (DFS) according to treatment line.

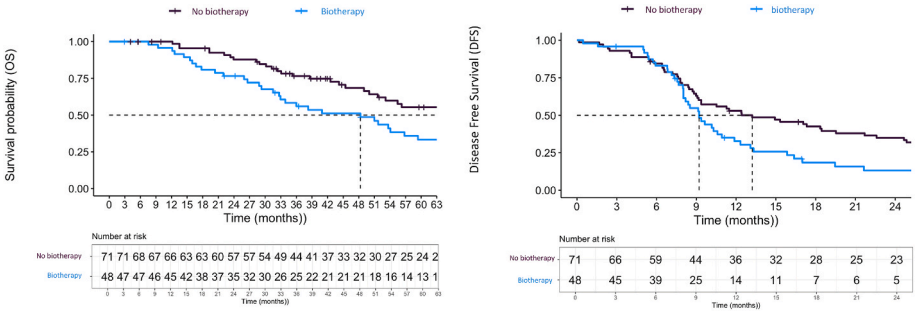

Fig. 1D. OS and DFS according to biotherapy addition.

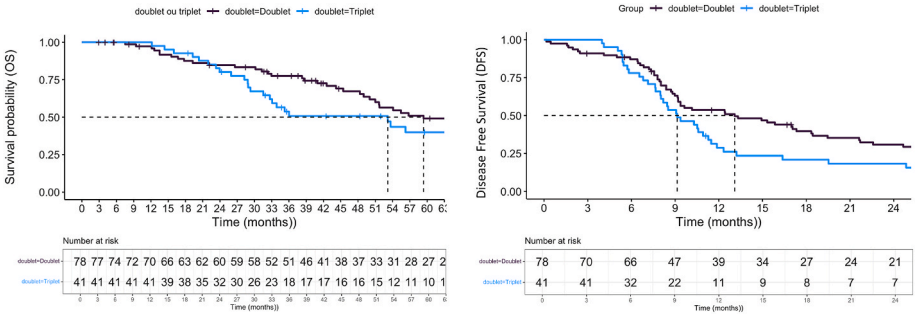

Fig. 1E. OS and DFS according to irinotecan addition.

patients with more than 3 CRLM [13]; in this context, the 5-year overall survival observed in our cohort appears at least comparable and particularly encouraging given the high tumor burden.

Unexpectedly, patients with fewer than four liver metastases had a worse prognosis compared to those with four or more. This counterintuitive result warrants closer scrutiny, as the subgroup with fewer than four resected CRLM was small. In several instances, the number of liver metastases was underestimated by imaging, and more lesions were discovered and resected intraoperatively – potentially limiting the adequacy of preoperative treatment. Importantly, nearly half of the patients in this group had received two or more lines of preoperative systemic therapy, suggesting more aggressive or treatment-resistant disease. These confounding factors likely contributed to the inferior OS in this subgroup.

No significant difference in DFS was observed between patients with and without extrahepatic disease, suggesting that HAI may retain

efficacy in patients with limited extrahepatic involvement managed by local therapies. This potential systemic effect of oxaliplatin-based HAIC is consistent with its partial liver extraction ratio (~50%), unlike floxuridine (FUDR), which undergoes near-complete hepatic metabolism [14,15]. This aligns with the findings of the PACHA-01 trial, which included patients with limited extrahepatic disease encompassing up to four lung metastases [11].

Interestingly, DFS and OS were higher in patients who received HAIC without concomitant biotherapies, with outcomes surpassing those reported in the PACHA trial [11]. This likely reflects differences in baseline disease characteristics rather than a negative effect of biotherapies themselves. In our cohort, anti-VEGF or anti-EGFR agents were mainly administered to patients with initially borderline-resectable or unresectable CRLM, within intensified treatment protocols. Similarly, irinotecan was more frequently used in younger patients and those who had received multiple systemic treatment lines prior to surgery, suggesting a higher disease burden or resistance profile. These findings contrast with those seen in unresectable CRLM, where targeted therapies have yielded more favorable outcomes [16]. Further insight is expected from the ongoing phase III OSCAR trial, which is assessing the role of targeted agents and irinotecan—stratified by RAS status—in combination with intra-arterial oxaliplatin as first-line treatment for patients with unresectable CRLM [17].

In our study, 45% of patients experienced grade 3–4 toxicities, mainly neutropenia and neurotoxicity. These rates are comparable or lower than those in the literature [11] despite the addition of Irinotecan or targeted therapies. However, as a retrospective study, underreporting, particularly of non-hematologic or cumulative toxicities, cannot be excluded. HAI-related abdominal pain, typically grades 1-2, was reported in about half of the patients, in line with previous studies [15,16,18,19].

Abdominal pain associated with HAIC was managed with appropriate pain control measures. Importantly, we observed no significant hepatobiliary toxicity in contrast to what has been reported with HAI FUDR, particularly before routine corticosteroid use [20,21].

Catheter-related complications were mostly addressed percutaneously. Although concerns exist about HAIC feasibility due to catheter malfunction, interventional procedures can often restore function and allow treatment continuation [22]. In our cohort, the most common issue was extra-hepatic perfusion, successfully managed by catheter embolization or replacement, allowing treatment continuation in all but one patient. Recent discontinuation of dedicated HAI devices prompted interventional radiologists to adapt alternative catheters to address this shortage, yielding positive outcomes [23].

Several limitations of our study must be acknowledged. The retrospective design introduces potential biases, including patient selection and data collection. The heterogeneity in treatment regimens, including various combinations of chemotherapy and targeted therapies complicates direct comparisons with other studies. Additionally, subgroup analyses are susceptible to confounding and should be interpreted with caution. Prospective, randomized trials are needed to further clarify the optimal role of HAIC and its integration with systemic therapies for the treatment of CRLM; the PACHA-02 phase III trial will address this critical question [24].

In conclusion, HAIC with oxaliplatin appears to be a feasible and effective postoperative treatment option for patients with CRLM, offering manageable toxicity and catheter-related complications. These findings support the integration of HAIC into multimodal treatment strategies for liver-limited CRLM. Future studies should explore its role in combination with emerging systemic or locoregional therapies and refine patient selection to maximize clinical benefit.

Statement of ethics

This study protocol was reviewed and approved by Gustave Roussy institutional review board.

Author contributions

KS, AB: study conception, acquisition, analysis and interpretation of data, and writing of the manuscript; ID: statistical analysis. All authors reviewed the manuscript and approved the final version.

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Declaration of competing interest

AB: consulting/advisory role, invited lectures and/or travel/accommodation expenses for medical congresses: Ipsen, Merck, Takeda, Servier, Pierre Fabre.

VB: consulting/advisory role, invited lectures and/or travel/accommodation expenses for medical congresses: Amgen, AstraZeneca, Bayer Schering Pharma, Ipsen, Merck Serono, MSD, Roche/Genentech.

MD: consulting/advisory role, invited lectures and/or travel/accommodation expenses for medical congresses: Merck Serono, MSD, Revolution Medicine, AMGEN, Roche, Bayer, Ipsen, Pfizer, Servier, Pierre Fabre, HalioDx, Lilly, Sanofi, BMS.

AEH: consulting/advisory role, invited lectures and/or travel/accommodation expenses for medical congresses: Amgen, AstraZeneca, Debiopharm, Eli Lilly and Company, Incyte Corporation, QED Therapeutics.

DM: Consulting/advisory role: AbbVie, Amgen, AstraZeneca, Bayer, Bionest Partners, BMS, Incyte, Merck Serono, MSD, Pierre Fabre Oncologie, Roche, Sanofi, Simon-Kutcher & Partners, Servier, Taiho. Invited lectures/Medical writing: Amgen, AstraZeneca, Bayer, BMS, Foundation Medicine, Incyte, Leo Pharma, Medscape, Merck Serono, MSD, Pierre Fabre Oncologie, Roche, Sanofi, Servier, Veracyte, Viatris. Travel/accommodation expenses for medical congresses: Amgen, Bayer, BMS, Merck Serono, MSD, Pierre Fabre Oncologie, Roche, Sanofi, Servier, Viatris.

All other authors have no conflicts of interest to declare.

References

[1] Rawla P, Sunkara T, , et alBarsouk A. Epidemiology of colorectal cancer: incidence, mortality, survival, and risk factors. Przegląd Gastroenterol 2019;14(2):89–103. https://doi.org/10.5114/pg.2018.81072.

[2] Adam R, et al. Rescue surgery for unresectable colorectal liver metastases downstaged by chemotherapy: a model to predict long-term survival. Ann Surg oct. 2004;240(4):644–57. https://doi.org/10.1097/01.sla.0000141198.92114.f6. discussion 657-658.

[3] Creasy JM, et al. Actual 10-year survival after hepatic resection of colorectal liver metastases: what factors preclude cure? Surgery juin 2018;163(6):1238–44. https://doi.org/10.1016/j.surg.2018.01.004.

[4] Adam R, et al. Liver transplantation plus chemotherapy versus chemotherapy alone in patients with permanently unresectable colorectal liver metastases (TransMet): results from a multicentre, open-label, prospective, randomised controlled trial. Lancet sept. 2024;404(10458):1107–18. https://doi.org/10.1016/S0140-6736(24)01595-2.

[5] Dhir M, , et alSasson AR. Surgical management of liver metastases from colorectal cancer. J Oncol Pract janv. 2016;12(1):33–9. https://doi.org/10.1200/JOP.2015.009407.

[6] Cummings LC, Payes JD, , et alCooper GS. Survival after hepatic resection in metastatic colorectal cancer: a population-based study. Cancer févr. 2007;109(4):718–26. https://doi.org/10.1002/cncr.22448.

[7] House MG, et al. Survival after hepatic resection for metastatic colorectal cancer: trends in outcomes for 1,600 patients during two decades at a single institution. J Am Coll Surg mai 2010;210(5). https://doi.org/10.1016/j.jamcollsurg.2009.12.040. pp. 744–752, 752-755.

[8] Breedis C, , et alYoung G. The blood supply of neoplasms in the liver. Am J Pathol 1954;30(5):969–77.

[9] Fallik D, et al. Hepatic arterial infusion using pirarubicin combined with systemic chemotherapy: a phase II study in patients with nonresectable liver metastases from colorectal cancer. Ann Oncol Off J Eur Soc Med Oncol juin 2003;14(6):856–63. https://doi.org/10.1093/annonc/mdg247.

[10] Collins JM. Pharmacologic rationale for regional drug delivery. J Clin Oncol Off J Am Soc Clin Oncol mai 1984;2(5):498–504. https://doi.org/10.1200/JCO.1984.2.5.498.

[11] Gelli M, et al. Postoperative hepatic arterial chemotherapy after resection of colorectal liver metastases in patients at high risk of hepatic recurrence: a multicenter randomized phase II trial (PRODIGE 43 - PACHA-01). J Clin Oncol juin 2023;41(16_suppl). https://doi.org/10.1200/JCO.2023.41.16_suppl.3515. pp. 3515–3515.
[12] Groot Koerkamp B, et al. Perioperative hepatic arterial infusion pump chemotherapy is associated with longer survival after resection of colorectal liver metastases: a propensity score analysis. J Clin Oncol juin 2017;35(17):1938–44. https://doi.org/10.1200/JCO.2016.71.8346.
[13] Viganò L, Risi L, Dasari BVM, Marques HP, Giuliante F, Nordin A, et al. Benchmarking oncologic outcomes of liver resection for colorectal metastases: livermetsurvey-based reference values for evaluating alternative treatments. Ann Surg 2025 Nov 1;282(5):876–87.
[14] Ensminger WD, et al. A clinical-pharmacological evaluation of hepatic arterial infusions of 5-fluoro-2'-deoxyuridine and 5-fluorouracil. Cancer Res nov. 1978;38 (11 Pt 1):3784–92.
[15] Guthoff I, et al. Hepatic artery infusion using oxaliplatin in combination with 5-fluorouracil, folinic acid and mitomycin C: oxaliplatin pharmacokinetics and feasibility. Anticancer Res 2003;23(6D):5203–8.
[16] Boilève A, et al. Hepatic arterial infusion of oxaliplatin plus systemic chemotherapy and targeted therapy for unresectable colorectal liver metastases. Eur J Cancer Oxf Engl oct. 2020;138:89–98. https://doi.org/10.1016/j.ejca.2020.07.022. 1990.
[17] Pernot S, et al. Phase III randomized trial comparing systemic versus intra-arterial oxaliplatin, combined with LV5FU2 +/- irinotecan and a targeted therapy, in the first-line treatment of metastatic colorectal cancer restricted to the liver (OSCAR): PRODIGE 49. Dig Liver Dis. 2022 Mar;54(3):324–30.
[18] Lim A, et al. Hepatic arterial infusion chemotherapy for unresectable liver metastases of colorectal cancer: a multicenter retrospective study. Clin Colorectal Cancer déc. 2017;16(4):308–15. https://doi.org/10.1016/j.clcc.2017.03.003.
[19] Malka D, et al. Hepatic arterial oxaliplatin plus intravenous 5-fluorouracil and cetuximab for first-line treatment of colorectal liver metastases: a multicenter phase II trial. Eur J Cancer Oxf Engl déc. 2023;195:113400. https://doi.org/10.1016/j.ejca.2023.113400. 1990.
[20] Hohn DC, Rayner AA, Economou JS, Ignoffo RJ, Lewis BJ, et al. Toxicities and complications of implanted pump hepatic arterial and intravenous floxuridine infusion. Cancer févr. 1986;57(3):465–70. https://doi.org/10.1002/1097-0142(19860201)57:3<465::aid-cncr2820570311>3.0.co;2-s.
[21] Daly JM, Kemeny N, Oderman P, , et alBotet J. Long-term hepatic arterial infusion chemotherapy. Anatomic considerations, operative technique, and treatment morbidity. Arch Surg Chic Ill 1960 août 1984;119(8):936–41. https://doi.org/10.1001/archsurg.1984.01390200054013.
[22] Farouil G, et al. Interventional revisions of malfunctions affecting surgically implanted port-catheters for hepatic artery infusion. Surg Oncol mars 2013;22(1): 48–54. https://doi.org/10.1016/j.suronc.2012.10.002.
[23] Kedra A, et al. Exploring a novel technique to tackle the shortage of devices for hepatic arterial infusion chemotherapy: early results of an alternate approach for percutaneous arterial port catheter placement. Cancers janv. 2023;15(19):19. https://doi.org/10.3390/cancers15194730.
[24] Goéré D, et al. Postoperative hepatic arterial chemotherapy in high-risk patients as adjuvant treatment after resection of colorectal liver metastases - a randomized phase II/III trial - PACHA-01 (NCT02494973). BMC Cancer août 2018;18(1):787. https://doi.org/10.1186/s12885-018-4697-7.