# Adjuvant hepatic arterial infusion pump chemotherapy after repeat hepatectomy for patients with liver confined recurrence of colorectal cancer – a phase II study

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Survival of patients treated with hepatic arterial infusion pump chemotherapy will be superior to that of a historical cohort with similar patient characteristics

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| **Ethical review** | Positive opinion |
| **Status** | Recruiting |
| **Health condition type** | - |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON20478

**Source**
NTR

**Brief title**
PUMP -III

**Health condition**

Colorectal liver metastases, adjuvant, Hepatic Arterial Infusion Pump (HAIP) chemotherap, recuring, repeat hepaticetomy, resectable

### Sponsors and support

**Primary sponsor:** Erasmus Medical Center
**Source(s) of monetary or material Support:** Funding by Erasmus MC (sponsor). No additional funds.

## Intervention

## Outcome measures

### Primary outcome

hepatic progression free survival

### Secondary outcome

Overall survival, progression free survival, postoperative complications, adverse events

# Study description

### Background summary

Colorectal cancer (CRC) is the third most common cancer in the Netherlands. About 50% of patients develop colorectal liver metastasis (CRLM) throughout the course of the disease. Resection and/or ablation of the CRLM is the only curative treatment. Unfortunately, approximately 70% of patients develop recurrence, half of which is still confined within the liver. Repeat hepatectomy has emerged as a viable therapy for recurrent CRLM showing comparable survival and morbidity as resection for index CRLM. Consequently, the number of patients undergoing repeat resections for recurrent CRLM is increasing over the years. This patient group has withstood the test of time for developing extrahepatic recurrences. Currently, no effective adjuvant treatment options are available for this patient population. Even after repeat hepatectomy for recurrent CRLM, half of the recurrences after resection of recurrent CRLM occur in the liver. Therefore optimal disease control within the liver may lead to improved disease-free survival and overall survival. Treatment with hepatic arterial infusion pump (HAIP) chemotherapy allows high dosage chemotherapy to be directed into the liver without the chemotherapy reaching other organs. The drug used, floxuridine (a5-FU analogue), has a 95% first pass effect in the liver. In addition CRLM derive most of their blood supply from the hepatic artery, rather than the portal vein. By administering high dose floxuridine in the liver, lmicroscopic liver metastasis that are invisible during imaging are also tackled, thus preventing growth of these micrometastases at a later stage. Floxuridine is best delivered with a subcutaneous pump that can deliver high dose floxuridine continuously for two weeks and is accessible through the skin. Hepatic arterial infusion pump chemotherapy has been developed and evaluated in Memorial Sloan Kettering Cancer Center (MSKCC) and has been implemented in standard guidelines for treatment for metastatic colorectal cancer confined to the liver. In a recent retrospective study of 2378 patients treated in MSKCC, patients receiving adjuvant HAIP chemotherapy after resection of index CRLM had an Overall survival (OS) benefit of 2 years compared with those that did not receive HAIP chemotherapy. Preliminary results of a retrospective study including 363 patients treated in MSKCC and the Erasmus MC show that patients that have received adjuvant HAIP chemotherapy after repeat

hepatectomy for CRLM had an hepatic disease frees survival (hDFS) of 50 months compared with 18 months in patients that received resection only (p=0.003). This translated to an overall survival (OS) of 89 and 57 months with and without adjuvant HAIP chemotherapy respectively (p=0.01). Due to the retrospective nature of the studies, the results could be subjected to bias. However, such promising results deserve further research with a prospective study design.

### Study objective

Survival of patients treated with hepatic arterial infusion pump chemotherapy will be superior to that of a historical cohort with similar patient characteristics

### Study design

One year after inclusion of the last patient

### Intervention

Adjuvant HAIP chemotherapy with Floxuridine

## Contacts

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## Eligibility criteria

### Inclusion criteria

• Age ≥ 18 years. • ECOG performance status 0 or 1. • Histologically confirmed colorectal cancer (CRC). • Liver only recurrence after previous local treatment of index CRLM • Radiologically confirmed and resectable CRLM. Criteria for resectability are outlined in section 5.1. • Positioning of a catheter for HAIP chemotherapy is technically feasible (see chapter 5)

based on a CT with excellent arterial phase. The default site for the catheter insertion is the gastroduodenal artery (GDA). Accessory or aberrant hepatic arteries are no contraindication for catheter placement. The GDA should have at least one branch to the liver remnant; accessory or aberrant hepatic arteries should be ligated to allow for cross perfusion to the entire liver through intrahepatic shunts. • Adequate bone marrow, liver and renal function as assessed by the following laboratory requirements to be conducted within 15 days prior to inclusion: o Absolute neutrophil count (ANC) ≥1.5 x 109/L o Platelets ≥100 x 109/L o HB ≥ 5.5 mmol/L o Total bilirubin ≤ 1.5 UNL o ASAT ≤ 5 x UNL o ALAT ≤ 5 x UNL o Alkaline phosphatase ≤ 5 x UNL o (Calculated) glomerular filtration rate (GFR) >30 ml/min. • Written informed consent must be given according to ICH/GCP, and national/local regulations.

### Exclusion criteria

• A positive history of extrahepatic disease (including positive portal lymph nodes) at any time since CRC diagnosis. Patients with small (≤ 1 cm) extrahepatic lesions that are too small to characterize are eligible. • Second primary malignancy except in situ carcinoma of the cervix, adequately treated non-melanoma skin cancer, or other malignancy treated at least 5 years previously without evidence of recurrence. • CRLM requiring two-staged liver resections • Recurrence CRLM at same location as previously unsuccessfully (i.e. residual disease) resected/ablated CRLM and <6 months after its resection. • Known DPYD-deficiency. • Pregnant or lactating women. • History of psychiatric disability judged by the investigator to be clinically significant, precluding informed consent or interfering with compliance for HAIP chemotherapy. • Serious concomitant systemic disorders that would compromise the safety of the patient or his/her ability to complete the study, at the discretion of the investigator. • Organ allografts requiring immunosuppressive therapy. • Serious, non-healing wound, ulcer, or bone fracture. • Chronic treatment with corticosteroids (dose of ≥ 10 mg/day methylprednisolone equivalent excluding inhaled steroids). • Serious infections (uncontrolled or requiring treatment). • Inclusion in another interventional clinical study with survival as primary outcome. • Any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule; those conditions should be discussed with the patient before registration in the trial.

## Study design

### Design

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| Study type: | Interventional |
| Intervention model: | Other |
| Allocation: | Non controlled trial |
| Masking: | Open (masking not used) |

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| Control: | N/A , unknown |

### Recruitment

NL

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|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 19-02-2021 |
| Enrollment: | 45 |
| Type: | Anticipated |

### IPD sharing statement

**Plan to share IPD:** Undecided

## Ethics review

Positive opinion

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| Date: | 25-02-2021 |
| Application type: | First submission |

## Study registrations

### Followed up by the following (possibly more current) registration

ID: 50045
Bron: ToetsingOnline
Titel:

### Other (possibly less up-to-date) registrations in this register

No registrations found.

### In other registers

| Register | ID |
|---|---|
| NTR-new | NL9294 |
| CCMO | NL71691.078.19 |
| OMON | NL-OMON50045 |

# Study results

**Summary results**
https://pubmed.ncbi.nlm.nih.gov/32648182/