

# Chemotherapy followed by versus surgery alone in high-risk patients with colorectal liver metastases

No registrations found.

<b>Ethical review</b>	Positive opinion
<b>Status</b>	Pending
<b>Health condition type</b>	-
<b>Study type</b>	Interventional

## Summary

### ID

NL-OMON27498

### Source

Nationaal Trial Register

### Brief title

CHARISMA

### Health condition

Colorectal liver metastases, clinical risk score, high risk patients, colorectale levermetastasen, klinische risico score, hoog risico patienten

## Sponsors and support

**Primary sponsor:** Prof. Dr. C. Verhoef

Erasmus MC Cancer Institute

**Source(s) of monetary or material Support:** Dutch Cancer Society

## Intervention

## Outcome measures

### Primary outcome

Overall Survival (OS)

## Secondary outcome

Progression free survival (PFS), quality of life, treatment response on chemotherapy, morbidity of resection, predictive value of carcinoembryonic antigen (CEA) for treatment response, PFS and OS

## Study description

### Background summary

Efforts to improve the outcome of liver surgery by combining the resection with chemotherapy have failed to demonstrate overall survival (OS) benefit. This may partly be due to the fact that these studies often involve strict study protocol inclusion criteria. Consequently, patients with a high Clinical Risk Score (CRS) - who might benefit the most from chemotherapy - are often underrepresented in these studies. Since genuine survival benefit has not yet been demonstrated, could this low impact of chemotherapy on survival then be explained by the relatively low risk of the patients in these trials? In view of the retrospective observations that pre-selection of patients by using prognostic characteristics may define the patient population most likely to benefit from chemotherapy, it was decided to take CRS stratification as the base for a randomized controlled trial in resectable patients. This study will therefore evaluate the impact of neo-adjuvant chemotherapy in patients with high-risk (CRS 3-5) resectable colorectal liver metastases (CRLM) without extrahepatic disease. Our hypothesis is that adding neo-adjuvant chemotherapy to surgery will provide an improvement in OS in this high-risk patient group.

### Study objective

Our hypothesis is that adding neo-adjuvant chemotherapy to surgery will provide an improvement in overall survival in this high-risk patient group.

### Study design

Estimated inclusion: 4 years.

Follow-up: 5 years.

### Intervention

Arm A: Surgery

Arm B: 6 cycles chemotherapy (XELOX), followed by surgery

## Contacts

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## Eligibility criteria

### Inclusion criteria

- Age  $\geq$  18 years
- ECOG performance status 0 or 1
- Histologically confirmed primary colorectal carcinoma. Primary colorectal carcinomas to be included are:
  - \* Previously resected histologically proven colorectal carcinoma
  - \* Colonic carcinoma still in situ, deemed suitable for resection at the time of liver surgery
  - \* Rectal carcinoma still in situ, requiring no neo-adjuvant radiotherapy, deemed suitable for resection at the time of liver surgery
  - \* Rectal carcinoma still in situ, requiring short-course neo-adjuvant radiotherapy, deemed suitable for resection at the time of liver surgery
  - \* Radiologically confirmed and resectable liver metastasis of colorectal cancer after surgery.
- Clinical risk score (Fong) of 3-5
- Adequate bone marrow, liver and renal function as assessed by the following laboratory requirements to be conducted within 15 days prior to randomization: absolute neutrophil count (ANC)  $\geq 1.5 \times 10^9/L$ , platelets  $\geq 100 \times 10^9/L$ , HB  $\geq 5.5$  mmol/L, total bilirubin  $\leq 1.5$  UNL,

ASAT  $\leq 5 \times \text{UNL}$ ,  
ALAT  $\leq 5 \times \text{UNL}$ , alkaline phosphatase  $\leq 5 \times \text{UNL}$ ,  
creatinin clearance  $>30 \text{ ml/min}$ .

## Exclusion criteria

- Prior adjuvant chemotherapy for the primary colorectal carcinoma given  $<6$  months prior to detection of the liver metastases.
- Prior non colorectal malignancies, except for patients with basal or squamous cell carcinoma of the skin, or patients with carcinoma in situ of the cervix.
- Presence of extrahepatic disease
- Locally advanced rectal cancer in situ requiring long-course pre-operative chemoradiotherapy
- Major surgical procedure  $<4$  weeks prior to randomization.
- Females with a positive pregnancy test (within 14 days before treatment start).
- Lactating women.
- History of psychiatric disability judged by the investigator to be clinically significant, precluding informed consent or interfering with compliance for oral drug intake.
- Clinically significant (i.e. active) cardiovascular disease e.g. cerebrovascular accidents ( $\leq 6$  months prior to randomization), myocardial infarction ( $\leq 1$  year prior to randomization), uncontrolled hypertension while receiving chronic medication, unstable angina, New York Heart Association (NYHA) Grade II or greater congestive heart failure, or serious cardiac arrhythmia requiring medication.
- Lack of physical integrity of the upper gastro-intestinal tract, malabsorption syndrome, or inability to take oral medication.
- Known peripheral neuropathy, including oxaliplatin induced neuropathy  $>$  grade 1. Absence of deep tendon reflexes as the sole neurological abnormality does not render the patient ineligible.
- Organ allografts requiring immunosuppressive therapy.
- Serious, non-healing wound, ulcer, or bone fracture.
- Current or recent (within 10 days prior to randomization) use of full-dose oral anticoagulants or thrombolytic agents for therapeutic purposes. Patients can be rendered eligible by

changing the treatment to low molecular weight heparines.

- Chronic treatment with corticosteroids (dose of  $\geq 10$  mg/day methylprednisolone equivalent excluding inhaled steroids).

- Serious intercurrent infections (uncontrolled or requiring treatment).

- Current or recent (within the 28 days prior to randomization) treatment with another investigational drug or participation in another investigational study.

- 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

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

### Recruitment

NL	
Recruitment status:	Pending
Start date (anticipated):	22-10-2014
Enrollment:	224
Type:	Anticipated

## Ethics review

Positive opinion	
Date:	11-11-2014
Application type:	First submission

## Study registrations

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

ID: 44796

Bron: ToetsingOnline

Titel:

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

No registrations found.

### In other registers

Register	ID
NTR-new	NL4688
NTR-old	NTR4893
CCMO	NL47227.078.14
OMON	NL-OMON44796

## Study results