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

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

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON27498

Bron
Nationaal Trial Register

Verkorte titel
CHARISMA

Aandoening

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

Ondersteuning

Primaire sponsor: Prof. Dr. C. Verhoef
Erasmus MC Cancer Institute
Overige ondersteuning: Dutch Cancer Society

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Overall Survival (OS)

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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

Onderzoeksopzet

Estimated inclusion: 4 years.

Follow-up: 5 years.

Onderzoeksproduct en/of interventie

Arm A: Surgery

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

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- Age ≥ 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

* Coloncarcinoma 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) ≥1.5 x 109/L, platelets ≥100 x 109/L, HB ≥ 5.5 mmol/L, total bilirubin ≤ 1.5 UNL, ASAT ≤ 5 x UNL,
ALAT ≤ 5 x UNL, alkaline phosphatase ≤ 5 x UNL,
creatinin clearance >30 ml/min.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- 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 (≤ 6 months prior to randomization), myocardial infarction (≤ 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 arrhytmia 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 ≥ 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

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	22-10-2014
Aantal proefpersonen:	224
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	11-11-2014

Soort: Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 44796
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

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

Resultaten