The MIRACLE study

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Determination of preoperative cell-free DNA and circulating tumor cells alone or in combination with each other in peripheral blood of patients with colorectal liver metastases can discriminate between patients who have a recurrence of metastatic...

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON21289

Bron
Nationaal Trial Register

Verkorte titel
MIRACLE

Aandoening

Colorectal Cancer Liver Metastases

Ondersteuning

Primaire sponsor: Prof. Dr. C. Verhoef Erasmus, Head of department of Surgical Oncology, MC Cancer Institute Groene Hilledijk 301, 3075 EA, Rotterdam
Overige ondersteuning: Dutch Cancer Society, (KWF Kankerbestrijding)

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Recurrence of disease after hepatic resection for colorectal cancer liver metastases within one year after resection

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale:
For colorectal cancer (CRC) patients presenting with isolated liver metastases, a treatment comprising a liver metastasectomy is the only potentially curative option. However, a substantial number of patients shows a relapse following this procedure underlining the need for prognostic factors. Such prognostic factors allow a more personalized treatment strategy; more intensified treatments for those with a high risk for relapse and maybe less intensified approaches for those with a low risk. In recent years, several pre-operative prognostic factors in patients with isolated colorectal liver metastases have been revealed for the risk of relapse after a metastasectomy including the number and size of metastases, synchronicity and CEA serum levels. Although this type of clinical risk scoring is well-validated and able to distinguish between high-risk and low-risk patients, further fine-tuning is desperately needed. Clinically low-risk patients may experience relapse rates of 40% at 1 year, whereas clinically high-risk patients may show a 5-year survival rate of 20-40%. This underlines the importance of novel pre-clinical and biological prognostic factors. Relevant prognostic and predictive factors are required to determine the most effective combination of treatments for each individual patient with metastatic CRC.

Objective:
To establish (i) whether or not pre-operative determination of cell-free DNA (cfDNA) and circulating tumor cells (CTC), alone or in combination with each other, in peripheral blood of CRC patients with isolated colorectal liver metastases (CRLM) undergoing hepatic resection determined before and/or after resection with or without pre-operative chemotherapy, can discriminate between patients showing a recurrence within 1 year from those who do not, and (ii) whether or not these novel factors significantly add to the current known prognostic factors.

Study design:
Prospective observational cohort study

In summary:
1. In total, 240 colorectal cancer patients with isolated liver metastases undergoing a potentially curative hepatic resection will be studied.
2. Known pre-operative prognostic factors nowadays used in the prognostic clinical scoring systems (including number and size of liver metastases, the time interval from primary tumor to metastases, CEA levels, free resection margins) will be established.
3. Peripheral blood samples for quantitative determination of cfDNA levels and enumeration of CTCs will be drawn from all participating patients: before and after the start of neoadjuvant chemotherapy, and before and after hepatic resection.
4. Patients will be monitored for recurrence of disease with traditional imaging techniques such as ultrasound, CT-, MRI- and PET-scans, according to the National guidelines.
5. Assessment whether or not determination of cfDNA, CTC, alone or in combination with each other, improves the prognostic value of currently known prognostic models to predict

early recurrence in colorectal cancer patients with isolated liver metastases undergoing a potentially curative hepatic resection.
6. Assessment whether or not determination of cfDNA, CTC, alone or in combination with each other, have predictive value with respect to the outcome of neoadjuvant chemotherapy.
7. Exploratory analyses will be done using targeted next-generation sequencing of a panel of genes thought to be involved in the outcome of colorectal cancer to establish whether or not the genomic constitution of cfDNA taken at different time points relative to treatment is associated with outcome.
Study population: Patients ≥ 18 years of age with liver metastases of histologically confirmed primary colorectal carcinoma. Metastasis in other sites than the liver are excluded. Liver metastases must be deemed resectable.

Main study parameters/endpoints:
Primary endpoint
Our primary endpoint is recurrence of disease after hepatic resection for colorectal liver metastases within one year after resection.

Secondary endpoints
- Improve the selection of patients who respond to neoadjuvant chemotherapy.
- Improve the selection of patients who will have a complete response after neoadjuvant chemotherapy.
- To identify tumor-specific characteristics of CTC and cfDNA at the molecular level, and to correlate these parameters with the response on chemotherapy and the recurrence rate within 1 year.
- To objectify whether serial measurements of cfDNA and CTCs will provide more adequate information than single point measurement prior to therapy.
- To address whether or not (serial) assessments of tumor-specific characteristics of CTC and DNA at the molecular level add to the current known prognostic factors in overall survival.

Doel van het onderzoek

Determination of preoperative cell-free DNA and circulating tumor cells alone or in combination with each other in peripheral blood of patients with colorectal liver metastases can discriminate between patients who have a recurrence of metastatic disease within 1 year and those who do not.

Onderzoeksopzet

Preoperative, postoperative: day 1, 5, and 21

Onderzoeksproduct en/of interventie

Venous blood samples (60 ml per sample) at 4 time points: preoperative on the day of surgery and postoperative day: 1, 5, and 21

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Age ≥ 18 years.
Histologically confirmed primary colorectal carcinoma.
Radiological confirmed and resectable liver metastasis of colorectal cancer, planned to undergo resection with or without neo-adjuvant chemotherapy.
Before patient registration, written informed consent must be given according to ICH/GCP, and national/local regulations.

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.
Second primary malignancy within the past 5 years with the exception of adequately treated in situ carcinoma of any organ or basal cell carcinoma of the skin.
Presence of extrahepatic disease. Patients with small (≤1 cm) extrahepatic lesions that are not clearly suspicious of metastases are eligible.
Females with a positive pregnancy test (within 14 days before treatment start).
History of psychiatric disability judged by the investigator to be clinically significant, precluding informed consent.

Current or recent 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 study.

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	21-10-2015
Aantal proefpersonen:	240
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	26-01-2021
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL9227
Ander register	METC EMC : MEC-2015-289

Resultaten