Concomitant intraperitoneal and systemic chemotherapy in patients with extensive peritoneal carcinomatosis of colorectal origin

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Hyperthermic intraperitoneal chemotherapy (HIPEC) has become standard of care for patients with peritoneal carcinomatosis of colorectal origin with a low/moderate abdominal disease load. In case of a peritoneal cancer index (PCI) above 20, a HIPEC-...

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

Samenvatting

ID

NL-OMON23907

Bron
NTR

Verkorte titel
INTERACT

Aandoening

Peritoneal carcinomatosis
Colorectal cancer
Intraperitoneal chemotherapy

Ondersteuning

Primaire sponsor: Erasmus Medical Center Rotterdam
Overige ondersteuning: Stichting Coolsingel

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

This project will establish the maximum tolerable dose and recommended phase II dose of intraperitoneal irinotecan added to systemic FOLFOX + bevacizumab.

Toelichting onderzoek

Achtergrond van het onderzoek

The INTERACT trial is a multicenter, fase I dose-escalation study, that will be performed by two centers in the Netherlands; the Erasmus MC Cancer Institute in Rotterdam and the Catharina Hospital in Eindhoven. The main goal of this study is to determine the maximum tolerated dose of intraperitoneal irinotecan, added to standard of care systemic chemotherapy (FOLFOX + bevacizumab) in patients with peritoneal carcinomatosis of colorectal origin. This study is the first step in the establishment of a line of research, investigating the value of (life prolonging) intraperitoneal chemotherapy in colorectal cancer.

Doel van het onderzoek

Hyperthermic intraperitoneal chemotherapy (HIPEC) has become standard of care for patients with peritoneal carcinomatosis of colorectal origin with a low/moderate abdominal disease load. In case of a peritoneal cancer index (PCI) above 20, a HIPEC-procedure is not considered to be beneficial. Patients who have undergone an open-close procedure are offered palliative/life prolonging systemic chemotherapy. Previous research suggests that systemic chemotherapy is less effective against peritoneal carcinomatosis than it is against hematogeneous spread of colorectal cancer.

Several studies suggested that in patients with peritoneal carcinomatosis, intraperitoneal chemotherapy may be superior to intravenous chemotherapy. Higher concentrations of chemotherapy may persist for a longer period intraperitoneally, resulting in an increased area under the curve (AUC).
In this study we will establish the maximum tolerated dose (MTD) of intraperitoneal administration of irinotecan, added to standard of care systemic chemotherapy (fluorouracil/oxaliplatin (FOLFOX) + bevacizumab) in patients with peritoneal carcinomatosis of colorectal origin. This may be the first step towards a more effective, life prolonging and possible curative treatment for this patient group.

Onderzoeksopzet

The end of the study is defined as the last patient’s last visit.

Onderzoeksproduct en/of interventie

According to standard work-up for HIPEC-procedure, patients will undergo a planned diagnostic laparoscopy to score the PCI. In case of a PCI >20, a peritoneal access port will be placed in the abdomen of the patient. Through this port we will administer intraperitoneal irinotecan (according to dose-escalation schedule), in combination with standard of care chemotherapy: systemic FOLFOX + bevacizumab.

Contactpersonen

Publiek

Erasmus MC Kanker Instituut
drs. Nadine de Boer
Erasmus MC
Department of Surgical Oncology

Rotterdam
The Netherlands
+31 107042125

Wetenschappelijk

Erasmus MC Kanker Instituut
drs. Nadine de Boer
Erasmus MC
Department of Surgical Oncology

Rotterdam
The Netherlands
+31 107042125

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

In order to be eligible to participate in this study, a subject must meet all of the following

criteria:

• Patients with a histologically confirmed diagnosis of colorectal cancer

• Radiologically or clinically confirmed diagnosis of peritoneal carcinomatosis

• Age ≥ 18 years old

• Written informed consent according to the ICH-GCP and national/local regulations

• Unknown PCI for which a DLS is planned in the work-up for a HIPEC-procedure OR known PCI >20 evaluated by laparoscopy or laparotomy before inclusion in this trial

• Patients must be ambulatory, WHO performance status 0 or 1 (Appendix A)

• Life expectancy of at least 3 months

• Ability to return to the Erasmus MC/Catharina Hospital for adequate follow-up as required by this protocol

• Patients must have normal organ function and adequate bone marrow reserve as assessed by the following laboratory requirements:

o absolute neutrophil count >1.5 * 10^9/l

o platelet count >100*10^9/l

o Hb>6.0mmol/l

o Bilirubin < 1.5x upper limit of normal (ULN)

o Serum AST and ALT < 2.5 x ULN

o GFR>45 and Creatinine clearance <2 x ULN

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

A potential subject who meets any of the following criteria will be excluded from participation in this study:

• Extra-abdominal disease/metastatic disease established by preoperative CT-scan of thorax-

abdomen and/or PET-scan. Imaging not older than one months at time of surgery

• Prior cytoreductive surgery

• Prior treatment with systemic chemotherapy for (metastatic) colorectal cancer within the last 6 months

• Medical or psychological impediment to probable compliance with the protocol

• Serious concomitant disease or active infections

• History of auto-immune disease or organ allografts, or with active or chronic infection, including HIV and viral hepatitis

• Serious intercurrent chronic or acute illness such as pulmonary (COPD or asthma) or cardiac (NYHA class III or IV) or hepatic disease or other illness considered by the study coordinator to constitute an unwarranted high risk for participation in this study

• Homozygous UGT1A1*28 genotype

• Homozygous or (compound) heterozygous DPYD genotype (tested for *2A, *13, 2846A>T, and 1236G>A)

• Current use of strong CYP3A4-inhibitors or inducers. If patients use this CYP3A4-modulating medication, it is allowed to stop it within 14 days of start of treatment

• Pregnant or lactating women

• Concomitant participation in another competing clinical study

• Absence of assurance of compliance with the protocol

• An organic brain syndrome or other significant psychiatric abnormality which would comprise the ability to give informed consent, and preclude participation in the full protocol and follow-up

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
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:	01-05-2018
Aantal proefpersonen:	33
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:	26-04-2018
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	NL6988
NTR-old	NTR7177

Register	ID
Ander register	NL63809.078.18 : MEC-2018-059

Resultaten

Samenvatting resultaten

de Boer NL, Brandt-Kerkhof ARM, de High IHJT, Mathijssen AHJ, van Meerten E, Creemers GJ, Verhoef C, Burger JWA. Gelijktijdige intraperitoneale en systemische chemotherapie voor patiënten met uitgebreide peritonitis carcinomatosa van colorectale origine: de INTERACT-trial. Nederlands Tijdschrift voor Oncologie, november 2019.