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

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Peritoneal and retroperitoneal conditions
Study type	Interventional

Summary

ID

NL-OMON50387

Source
ToetsingOnline

Brief title
INTERACT

Condition

- Peritoneal and retroperitoneal conditions
- Metastases
- Gastrointestinal therapeutic procedures

Synonym
Colon Cancer with metastasis in the peritoneum, Peritoneal carcinomatosis of colorectal origin

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Stichting Coolsingel

Intervention

Keyword: Dose-escalation study, Intraperitoneal chemotherapy, Peritoneal Carcinomatosis, Systemic chemotherapy

Outcome measures

Primary outcome

Primary outcome is the MTD and recommended phase II dose of intraperitoneal

irinotecan

Secondary outcome

Secundary outcomes are the safety and feasibility of this treatment and to

establish the pharmacokinetic profile of intraperitoneal administered

irinotecan

Study description

Background summary

Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) has become standard of care for patients with peritoneal carcinomatosis (PC) of colorectal origin with a low/moderate abdominal disease load. In case of a Peritoneal Carcinomatosis Index (PCI) >20, CRS-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 shows 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 PC, intraperitoneal chemotherapy may be superior to intravenous chemotherapy. The addition of intraperitoneal to systemic chemotherapy in patients with PC of ovarian and gastric origin showed promising results. As of yet, there are no studies investigating intraperitoneal chemotherapy for PC of colorectal origin in this

specific patient population

Study objective

Main objective of this project is to establish the maximum tolerable dose (MTD) and recommended phase II dose of intraperitoneal irinotecan in patients with PC of colorectal origin, added to standard of care systemic chemotherapy. Other endpoints are to explore the safety and feasibility of this treatment and to establish the pharmacokinetic profile of intraperitoneal administered irinotecan. During this study we will systematically collect and store ascites for translational research purposes.

Study design

This study is a classic phase I *3+3* dose-escalation study, which will be conducted in the Erasmus MC, Rotterdam and Catharina Hospital, Eindhoven.

Intervention

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

Study burden and risks

The intervention comes in addition to the standard of care. In participating patients a peritoneal access port will be surgically implanted. Patients will receive intraperitoneal chemotherapy through this port. This happens at the same time as the treatment with systemic chemotherapy. According to Dutch guidelines, patients will receive chemotherapy every 2 weeks, for a maximum of 12 cycles. Participating patients will have additional outpatient hospital visits and have to undergo some extra invasive procedures, like venapunction of intravenous catheter. The risks of these procedures are limited.
The addition of intraperitoneral chemotherapy to systemic chemotherapy forms an increased risk for toxicity. That is why this is subject of our study. Previous clinical studies in patients with ovarian and gastic cancer showed that the administration of intraperitoneal chemotherapy in combination to systemic chemotherapy is safe and feasible.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

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 protocol)

* 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
therap

Exclusion criteria

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 6 weeks 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
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Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-11-2018
Enrollment:	33
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	5-FU
Generic name:	5-flourouracil
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Avastin
Generic name:	Bevacizumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Irinotecan
Generic name:	Irinotecan
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	13-03-2018

Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-04-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-12-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-01-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-05-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-06-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR 2018-000479-3-NL
CCMO	NL63809.078.18