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

Published: 13-01-2022
Last updated: 14-09-2024

This study has been transitioned to CTIS with ID 2024-516265-37-00 check the CTIS register for the current data. The primary goal of the study is to establish the maximum tolerated dose (MTD) of intraperitoneal administration of irinotecan, added to...

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

Summary

ID

NL-OMON51789

Source
ToetsingOnline

Brief title
INTERACT stomach

Condition

- Peritoneal and retroperitoneal conditions
- Metastases
- Gastrointestinal therapeutic procedures

Synonym
Peritoneal carcinomatosis of gastric origin, Stomach Cancer with metastasis in the peritoneum

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Afdeling oncologie en chirurgie Erasmus MC en Catharina Ziekenhuis

Intervention

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

Outcome measures

Primary outcome

The aim of this study is to establish the maximum tolerable dose and recommended phase II dose of intraperitoneal irinotecan added to systemic chemotherapy (capecitabine/oxaliplatin) in patients with peritoneal metastasis of gastric origin.

Secondary outcome

Secondary 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 also collect and store ascites for (future) translational research purposes and we will investigate the value of the 68Ga-FAPI PET/CT for peritoneal response evaluation.

Study description

Background summary

Gastric cancer with peritoneal carcinomatosis has a poor prognosis, with little treatment options available. The current treatment strategy consists of palliative systemic chemotherapy. However, previous research suggests that systemic chemotherapy is less effective against peritoneal carcinomatosis than against metastases that spread hematogeneously. Several studies suggested that

in patients with peritoneal carcinomatosis, intraperitoneal chemotherapy may be superior compared to intravenous chemotherapy. Intraperitoneal chemotherapy could lead to higher concentrations of chemotherapy in the peritoneal cavity for a longer period of time, resulting in an increased cumulative exposure to the peritoneal metastases. A few Asian studies have shown promising results with intraperitoneal chemotherapy in patients with peritoneal carcinomatosis of gastric origin. However, intraperitoneal chemotherapy combined with systemic chemotherapy has not been investigated in Western patients with peritoneal carcinomatosis of gastric origin yet.

Study objective

This study has been transitioned to CTIS with ID 2024-516265-37-00 check the CTIS register for the current data.

The primary goal of the study is to establish the maximum tolerated dose (MTD) of intraperitoneal administration of irinotecan, added to systemic capecitabine/oxaliplatin (CAPOX) in patients with peritoneal carcinomatosis of gastric origin. Secondary goals are to investigate the safety en feasibility of this treatment, en to further investigate the pharmacokinetic profile of intraperitoneal irinotecan. During this study, ascites will also be collected systemically for further translational research and the value of FAPI PET/CT will be evaluated for peritoneal response evaluation.

Study design

This study will be a phase I '3+3+3' dose-escalation study, performed in the Erasmus MC, Rotterdam & Catharina Hospital, Eindhoven.

Intervention

Patients are first discussed in a multi-disciplinary tumor board for eligibility for this study, that is macroscopic peritoneal metastases and no other regular treatment options available. Patients will then be informed about this study and after signing informed consent, a peritoneal access port will be placed during a DLS in the abdomen of the patient. Through this port intraperitoneal irinotecan will be administered (according to dose-escalation schedule), in combination with systemic CAPOX. During the study, patients will undergo 2 68Ga-FAPI-46 PET/CT scans; one prior to therapy initiation and one after completion of the 6 cycles; these scans will be used to evaluate peritoneal response.

Study burden and risks

The intervention will be an addition upon the regular systemic treatment. Patients have to undergo extra outpatient visits for this study and extra

procedures for this trial, like placement of a peritoneal access port and intravenous catheter. Risks are limited for these invasive procedures. The extra intravenous catheter is necessary to establish the pharmacokinetic profile of intraperitoneally administered irinotecan. The intraperitoneal access port is necessary for the administration of intraperitoneal irinotecan and for the collection of intraperitoneal fluid samples/ascites. Placement of the intraperitoneal port will be performed according to standard procedures during the planned diagnostic laparoscopy under general anesthesia. There is a limited risk for complications, like infection. The administration of intraperitoneal chemotherapy is a potential risk for treatment related toxicities. This risk should be weighed against the potential survival benefit of the treatment. Previous clinical studies showed that administration of intraperitoneal irinotecan was feasible and overall well tolerated. Additionally, patients will undergo FAPI PET/CT scans twice; the estimated radiation dose from adding the FAPI PET is 0.82 mSv (compared to the 4.0 mSv from the CT scan). We believe this slight increase is justified by the potential for better assessment of peritoneal lesions through the FAPI PET/CT scan.

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

• Patients with a histologically confirmed diagnosis of HER2-negative gastric cancer.
• A histologically confirmed diagnosis of macroscopic peritoneal carcinomatosis (PCI >=1).
• Age >= 18 years old.
• Written informed consent according to the ICH-GCP and national/local regulations.
• 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 or 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.

Exclusion criteria

• Medical or psychological impediment to probable compliance with the protocol.
• Serious concomitant disease or active infections.
• Distant metastasis other than peritoneal metastasis or metastatic lymph nodes.
• No sufficient oral food intake.
• Polyneuropathy grade 2 or worse according to CTCAE version 5.0.
• 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 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 a 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.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	25-05-2022
Enrollment:	54
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	[68Ga]Gallium (S)-2,2',2''-(10-(2-(4-(3-((4- (2-(2-cyano-4,4-difluoropyrrolidin-1-yl)-2- oxoethylcar
Generic name:	[68Ga]FAPI-46
Product type:	Medicine
Brand name:	Irinotecan
Generic name:	Irinotecan
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	13-01-2022
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-03-2022
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-11-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-03-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-05-2024
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
EU-CTR	CTIS2024-516265-37-00
EudraCT	EUCTR2021-005907-11-NL
ClinicalTrials.gov	NCT05379790
CCMO	NL79619.078.21