Bidirectional treatment consisting of repetitive laparoscopic electrostatic pressurized intraperitoneal aerosol chemotherapy with oxaliplatin (ePIPAC-OX) and systemic intravenous chemotherapy for isolated unresectable colorectal peritoneal metastases: feasibility, safety, tolerability, and preliminary efficacy.

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To determine the safety, feasibility, and tolerability of adding PIPAC with oxaliplatin (92 mg/m2) to systemic chemotherapy in patients with isolated PM from CRC.

Ethical review	Approved WMO
Status	Completed
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Interventional

Summary

ID

NL-OMON50015

Source
ToetsingOnline

Brief title
CRC-PIPAC-II

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC

- Metastases
- Gastrointestinal therapeutic procedures

Synonym
Colorectal Cancer with Metastases in the Peritoneum, Colorectal Peritoneal Carcinomatosis

Research involving
Human

Sponsors and support

Primary sponsor: Catharina-ziekenhuis
Source(s) of monetary or material Support: Catharina Ziekenhuis en St. Antonius Ziekenhuis

Intervention

Keyword: Colorectal Cancer, Intraperitoneal Chemotherapy, Oxaliplatin, Peritoneal Metastases

Outcome measures

Primary outcome

Major toxicity, defined as grade >2 according to the Common Terminology

Criteria for Adverse Events v4.0, and measured up to four weeks after the last

PIPAC procedure.

Secondary outcome

- Mild to moderate toxicity, defined as grade 1-2 according to the Common

Terminology Criteria for Adverse Events v4.0, and measured up to four weeks

after the last PIPAC procedure.

- The completed amount of cycles of bi-directional therapy with PIPAC and

systemic chemotherapy

- The completed amount of cycles of systemic chemotherapy; the amount dose

reductions, and reasons for dose reductions.

- Intra operative characteristics of PIPAC with oxaliplatin (e.g. laparoscopic

access rate, ascites volume, blood loss)

- Intra operative complications during PIPAC with oxaliplatin (e.g. bowel perforation, bleeding)

- Length of hospital stay during bi-directional therapy with PIPAC and systemic chemotherapy

- Readmission rate during bi-directional therapy with PIPAC and systemic chemotherapy

- To determine nephrotoxicity, hepatotoxicity, and haematological toxicity of bi-directional therapy with PIPAC and systemic chemotherapy

- To determine tumour markers (CEA) during bi-directional therapy with PIPAC and systemic chemotherapy

- To determine macroscopic tumour respons during bi-directional therapy with PIPAC and systemic chemotherapy

- To determine histopathological tumour resonse of tumour tissue and ascites collected during second and third PIPAC

- To determine quality of life during bi-directional therapy with PIPAC and systemic chemotherapy

- To determine intraperitoneal and systemic progression free survival after bi-directional therapy with PIPAC and systemic chemotherapy

- To determine overall survival after bi-directional therapy with PIPAC and systemic chemotherapy

- To collect blood and frozen tissue for translational research

- To determine the systemic pharmacokinetics of oxaliplatin after one cycle of

systemic chemotherapy and one PIPAC.

Study description

Background summary

The majority of patients with isolated peritoneal metastases (PM) from colorectal cancer (CRC) do not qualify for curative intent treatment with cytoreductive surgery and HIPEC (CRS/HIPEC), mostly due to extensive intraperitoneal disease. In this particular group, the limited efficacy of palliative systemic chemotherapy has encouraged the development of intraperitoneal palliative therapies with a similar or increased efficacy and low side effects.
Pressurized IntraPeritoneal Aerosol Chemotherapy (PIPAC) is such an innovative therapy that carries a significant potential due to its minimally invasive character, limited systemic toxicity, and encouraging preliminary efficacy and quality of life outcomes. The addition of PIPAC to treatment with systemic chemotherapy will hopefully result in long-term intraperitoneal disease control without resulting in increased toxicity, thus preserving quality of life. The PIPAC-I trial was the first Dutch study to investigate the safety, feasibility and tolerability of PIPAC-monotherapy in patients with PM from CRC, showing that PIPAC monotherapy is safe and well tolerated by patients. Yet there is no experience in the Netherlands with adding the PIPAC-surgery to systemic chemoteherapy. Therefore, this studie investigates the feasibility, safety, tolerability and efficacy of bidirectional therapy consisting of PIPAC and systemic chemotherapy.

Study objective

To determine the safety, feasibility, and tolerability of adding PIPAC with oxaliplatin (92 mg/m2) to systemic chemotherapy in patients with isolated PM from CRC.

Study design

This is a prospective, multi centre, single arm, phase II feasibility study.

Intervention

Besides regular treatment with palliative systemic chemotherapy, patients will also receive three PIPAC-surgeries with oxaliplatin during a 9 week interval. Each 0 week interval starts with 2-3 cycles of systemic chemotherapy and is followed by a PIPAC surgery. After this, the next interval starts.

Study burden and risks

The most important risks associated with participation are toxicity related to and inefficacy of PIPAC.

Patients that do not participate to the study, will only receive palliative systemic chemotherapy, instead of bi-directional therapy consisting of systemic chemotherapy and PIPAC. We expect that the addition of PIPAC will result in only low systemic side effects, as shown in the PIPAC-I study and other international studies (section 1.5 of the protocol).
Patients that participate in the trial will receive both the experimental treatment (PIPAC) and the regular treatment (systemic chemotherapy). They receive an extra treatment, possibly leading to increased intraperitoneal disease control.

Therefore, the addition of PIPAC to regular systemic chemotherapy is considered justified by the investigators, since the potential benefits (possible longer term intraperitoneal disease control) overrule the potential harms (low risk of toxicity)

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

- 18 years or older
- Histologically confirmed PM from a colorectal (including appendiceal) carcinoma that are not amenable for complete cytoreductive surgery, as determined by laparotomy, laparoscopy or radiology.
- WHO performance score of 0-1
- Written informed consent

Exclusion criteria

- Radiological evidence of systemic metastatic disease (e.g. liver, lung);
- Symptomatic presentation (e.g. non-deviated obstructive symptoms);
- Histologically confirmed PM from a low grade appendiceal carcinoma (Disseminated Peritoneal Adeno-Mucinosis / Low-grade Appendiceal Mucinous Neoplasm);
- Inadequate organ functions, defined as an Hb of <5.0 mmol/L, an absolute neutrophil count of <1.5 x 10^9/L, platelet count of <100 x 10^9/L, serum creatinine of >1.5 x ULN, creatinine clearance (Cockroft formula) of <30 ml/min, and liver transaminases of >5 x ULN;
- Any contraindication for the planned chemotherapy (e.g. severe allergy, pregnancy, uncompensated cardiac disease, coagulopathy, serious active infections), as determined by the medical oncologist;
- Any contraindication for a laparoscopy, as determined by the surgeon and/or anesthesiologist;
- Previous PIPAC-procedures;
- Previous treatment with palliative systemic chemotherapy (Note: this criterium does not include patients that received systemic chemotherapy in a (neo-)adjuvant setting. Patients treated with (neo-)adjuvant chemotherapy are able to enrol in the study if this treatment was finished >6 months before trial enrolment).

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	05-02-2020
Enrollment:	20
Type:	Actual

Medical products/devices used

Generic name:	Micropump
Registration:	Yes - CE intended use
Product type:	Medicine
Brand name:	Oxaliplatin
Generic name:	Oxaliplatin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	08-10-2019
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	08-01-2020
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	25-03-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-04-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-06-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-12-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 28502
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2019-002290-63-NL
CCMO	NL70298.100.19
OMON	NL-OMON28502