Adjuvant hyperthermic intraperitoneal chemotherapy in patients with colon cancer at high risk of peritoneal carcinomatosis; the COLOPEC randomized multicenter trial.

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

Summary

ID

NL-OMON47140

Source
ToetsingOnline

Brief title
COLOPEC

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC
- Metastases
- Gastrointestinal therapeutic procedures

Synonym
metastases of peritoneum, peritoneal carcinomatosis

Research involving

Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: ZonMw (CVZ)

Intervention

Keyword: adjuvant intraperitoneal chemotherapy, colon cancer, peritoneal carcinomatosis

Outcome measures

Primary outcome

Primary endpoint is peritoneal recurrence-free survival at 18 months.

Secondary outcome

Secondary endpoints are treatment related toxicity, incidence of PC,

sensitivity of imaging to detect PC during follow-up, differences in patterns

of dissemination (peritoneal plus or minus distant metastases), disease-free

survival, overall survival, quality of life and costs.

Study description

Background summary

The peritoneum is the second most common site of recurrence in patients with colorectal cancer (CRC). Early detection of peritoneal carcinomatosis (PC) by imaging is difficult and adjuvant systemic treatment does not seem to affect peritoneal dissemination in contrast to haematogenous dissemination in the liver or lungs. Of all patients eventually presenting with clinically apparent PC, only a quarter have potentially curable disease. The curative option is cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CR/HIPEC), but the effectiveness depends highly on the extent of disease and is associated with a considerable complication rate. These clinical problems underline the need for effective adjuvant intraperitoneal therapy in high risk colon carcinoom patients in order to prevent the development of PC with treatment at a subclinical stage.

Study objective

The aim is to determine the effectiveness of adjuvant HIPEC using oxaliplatin following a curative resection of a pT4 or intra-abdominally perforated colon cancer in preventing the development of PC in comparison to the standard adjuvant systemic treatment

Study design

This will be a multicentre study in which eligible patients will be randomized to adjuvant HIPEC followed by adjuvant systemic chemotherapy in the experimental arm, or standard adjuvant systemic chemotherapy alone in the control arm. Adjuvant HIPEC will preferably be performed simultaneously with primary tumour resection or within 10 days after resection, either by laparoscopy or open approach, similar to the technique used for resection of the primary tumour. If adjuvant HIPEC cannot be performed within 10 days (i.e. complicated postoperative course), the procedure will be delayed until 5 to 8 weeks postoperatively. Subsequently, patients will receive routine adjuvant chemotherapy (CAPOX) within 3 weeks from HIPEC.

Intervention

Adjuvant HIPEC procedure: re-laparoscopy or re-laparotomy under general anaesthesia, adhesiolysis if necessary, complete staging of the intra-abdominal cavity, positioning of in- and outflow catheters, perfusion with a minimum of 2l isotonic dialysis fluid at a flow rate of 1-2l/min and an inflow temperature of 42-43*C, adding Oxaliplatin (460 mg/m2) after attaining at least 42 degrees, 30 minutes perfusion time. Before the beginning of HIPEC, fluorouracil 400 mg/m2 and leucovorin 20 mg/m2 will be administered intravenously to potentiate oxaliplatin activity.
Diagnostic laparoscopy will be performed routinely after 18 months postoperatively in both arms of the study in patients without evidence of disease based on routine follow-up using CT imaging and CEA. If peritoneal carcinomatosis is found during staging laparoscopy, cytoreductive surgery with HIPEC will be performed in patients with a maximum of 5 involved regions and without evidence of systemic disease.

Study burden and risks

The burden for the patients in the experimental arm are adding HIPEC to the primary tumour resection or undergoing relaparoscopy or relaparotomy with HIPEC, A Dutch pilot study showed no morbidity and no mortality of staged adjuvant laparoscopic HIPEC in 10 patients, with a postoperative stay between 1 and 3 days. Based on literature, adjuvant HIPEC is associated with a slightly increased risk of wound infection, chemical peritonitis, bowel perforation,

abdominal pain, intraabdominal abscess, and ileus.

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

(1) age between 18 and 75 years. (2) adequate clinical condition to undergo re-laparoscopy or re-laparotomy within either 10 days or between week 5-8 from primary resection. (3) written informed consent (4) white blood cell count at least 3000/mm3, platelet count at least 100.000/mm3. (5) no bleeding diathesis or coagulopathy. (6) creatinine normal or creatinine clearance at least 50 ml/min.

Exclusion criteria

(1) postoperative complications that interfere with adjuvant HIPEC within 8 weeks (i.e. persisting intra-abdominal abscess, significant fascial dehiscence, enteric fistula). (2) liver and/or lung metastases. (3) pregnant or lactating women. (4) unstable or uncompensated respiratory or cardiac disease. (5) serious active infections. (6) other concurrent chemotherapy. (7) hypersensitivity for fluorouracil folinic acid (calciumfolinate) or another substance of leucovorin or Oxaliplatin. (8) Stomatitis, ulceration in the mouth or gastrointestinal tract. (9) severe diarrhea (10) severe hepatic and / or renal dysfunction. (11) plasma bilirubin concentrations greater than 85 *mol/l. (12) Pernicious anemia or other anaemias due to vitamin B12 deficiency.(13) peripheral sensory neuropathy with functional impairment.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-03-2015
Enrollment:	185
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Not applicable (Oxaliplatin for infusion, Leucovorin for infusion, 5-fluorouracil infusion)
Generic name:	Oxaliplatin, Leucovorin, 5-fluorouracil
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	01-09-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-12-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-12-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-03-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-04-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-08-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-09-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-11-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-12-2015

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-02-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-03-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-05-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-11-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-08-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-12-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-12-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-02-2019

Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2014-002794-11-NL
ClinicalTrials.gov	NCT02231086
CCMO	NL49960.018.14