Second and third look laparoscopy in pT4 colon cancer patients for early detection of peritoneal metastases; the COLOPEC 2 randomized multicentre trial.

Published: 02-10-2017
Last updated: 19-04-2025

The primary aim of this study is to determine the added value of third look DLS to detect PM at a clinically occult stage following a negative second look DLS.

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

Summary

ID

NL-OMON53004

Source
ToetsingOnline

Brief title
COLOPEC 2

Condition

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

Synonym
metastasis to the peritoneum, peritoneal carcinomatosis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: KWF Kankerbestrijding

Intervention

Keyword: colon cancer, peritoneal metastases, second look laparoscopy, third look laparoscopy

Outcome measures

Primary outcome

The primary endpoint of the study is the proportion of PM detected after

negative second look DLS. The primary endpoint will be determined at 20 months.

Secondary outcome

Secondary endpoints are the incidence of PM, incidence of PM in patients who

did or did not undergo adjuvant chemotherapy, clinical manifestation of PM

within 6 months of second look DLS, sensitivity of CT imaging to detect PM,

proportion of detected PM eligible for curative intent CRS+HIPEC, 30-day

morbidity related to second/third look DLS, extent of adhesiolysis required at

second/third look DLS, sequence of developing peritoneal and other distant

metastases, 5-year disease-free and overall survival and quality of life.

Study description

Background summary

In 2015, the incidence of colorectal cancer was 15.500 in the Netherlands. A common place for recurrence is the peritoneum, which is the sole site of metastasis in up to 25%. Peritoneal metastases (PM) were traditionally associated with dismal prognosis. Modern systemic chemotherapy prolonged median survival to a maximum of 24 months, but long-term survival remains limited. The only curative option is cytoreductive surgery (CRS) followed by hyperthermic

intraperitoneal chemotherapy (HIPEC), but the efficacy highly depends on the extent of peritoneal involvement. The availabilty of an effective therapy and the fact that CRS+HIPEC yields better survival rates and lower postoperative morbidity when the extent of peritoneal disease is more limited underline the importance of detection and treatment of PM in its initial stages. Due to absence of symptoms and restricted accuracy of imaging modalities, PM are often detected at a stage in which only about 25% of patients can be treated with CRS+HIPEC. The only way to diagnose minimal PM at an overt stage is by re-exploration of the abdominal cavity during second look surgery. Since it is an invasive and costly procedure, second look surgery should only be proposed to selected patients at high-risk of developing PM. Peritoneal metastases (PM) can develop in approximately 30% after curative resection of pT4 colon cancer. Restricted sensitivity of imaging modalities in combination with a poor prognosis if PM are detected at a clinically apparent stage underlines the need for early detection and prevention strategies. The COLOPEC trial (NL49960.018.14) randomized 205 patients with T4 colon cancer between adjuvant HIPEC followed by routine systemic chemotherapy and systemic chemotherapy alone between March 2015 and March 2017. Preliminary findings revealed that PM were already detected at intentionally adjuvant hyperthermic intraperitoneal chemotherapy (HIPEC) between 5-8 weeks after resection of the primary tumour in 10% of patients with pT4 colon cancer. Based on these findings and literature, second look diagnostic laparoscopy (DLS) to detect PM when the disease is still potentially curable by cytoreductive surgery (CRS) and HIPEC was considered to be an essential component of follow-up of locally advanced colon cancer. However, some metachronous PM develop later on. For this reason, there might be benefit of a third look DLS after a negative second look DLS to detect occult metachronous PM later on, which is the primary research question of the proposed trial.

Study objective

The primary aim of this study is to determine the added value of third look DLS to detect PM at a clinically occult stage following a negative second look DLS.

Study design

This is a randomised multicentre trial in which eligible patients will have routine CT-abdomen at 6 months postoperative (+3 months for those still treated with adjuvant chemotherapy), followed by second look DLS within 1 month after CT if no PM or other metastases not being eligible for curative intent treatment are detected. Patients without PM found during second look DLS will subsequently be randomised between routine follow-up including CT-abdomen at 18 months in the control arm, or an experimental arm with a third look DLS if no PM or other metastases not being eligible for curative intent treatment are detected at 18 months CT.

Intervention

Third look DLS will be performed between 18 and 20 months after primary tumour resection in patients not already diagnosed with PM and without other metastases that impede curative intent treatment. Access to the abdominal cavity is obtained under general anaesthesia by open introduction away from areas of expected adhesions, followed by adhesiolysis if necessary. Complete staging of the intra-abdominal cavity is performed, with biopsy of any lesion suspicious of PM, and determining the peritoneal cancer index (PCI) for those patients with suspected PM.

Study burden and risks

The burden for the patients is to undergo DLS in outpatient surgery setting. DLS is associated with a risk of wound infection of the trocar sites, bleeding from the abdominal wall or biopsy sites, and bowel injury related to adhesiolysis. Intervention-related morbidity is assumed to be low. With an expected number needed to diagnose clinically occult PM of 10, DLS related morbidity will probably not outweigh the potential survival benefit related to higher proportions of curative intent treatment compared to detection at a clinically apparent stage.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9 Meibergdreef 9
Amsterdam 1105 AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9 Meibergdreef 9
Amsterdam 1105 AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Curative intent resection (R0/R1) of pT4N0-2M0 colon cancer, proximal rectal cancer, or small bowel cancer, with or without adjuvant systemic therapy;
2. Age between 18 and 80 years;
3. Written informed consent.

Exclusion criteria

1. Histological subtype other than (mucinous) adenocarcinoma or signet-ring cell carcinoma;
2. Clinical condition does not allow for second look DLS and subsequent treatment of PM if detected;
3. Second look surgery thought not to be technically possible (i.e. because of extensive abdominal surgery / re-interventions).

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-02-2018
Enrollment:	389
Type:	Actual

Ethics review

Approved WMO Date:	02-10-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-12-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-01-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-11-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-12-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-05-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-06-2019

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-04-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-06-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-07-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-03-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-04-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-06-2022
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
ClinicalTrials.gov	NCT03413254
CCMO	NL61507.018.17