Circulating tumor DNA based adjuvant chemotherapy in stage II colon cancer patients: the MEDOCC-CrEATE trial

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Primary objective: to investigate how many patients with detectable ctDNA after surgery start with adjuvant chemotherapySecondary objective: to reduce recurrence rate by ctDNA based adjuvant chemotherapy (ACT) in stage II colon cancer (CC) patients...

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

Summary

ID

NL-OMON54658

Source
ToetsingOnline

Brief title
MEDOCC-CrEATE

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC
- Gastrointestinal neoplasms malignant and unspecified

Synonym
Colon carcinoma, large bowel cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: ZonMW: ¤3.2 miljoen (¤1.4 miljoen cash en

¤1.8 mijoen in kind door PGDx), Personal Genome Diagnostics (PGDx, Baltimore, USA).,Maag-;Lever- Darm stichting: ¤250.000. HealthHolland: ¤4.2 miljoen (¤2.4 miljoen cash en ¤1.8 miljoen in kind door PGDx)

Intervention

Keyword: Adjuvant chemotherapy, Circulating tumor DNA, Colon cancer

Outcome measures

Primary outcome

Proportion of patients with detectable ctDNA in their blood starting with

chemotherapy

Secondary outcome

- Recurrence Rate 2 years after surgery (intention-to-treat analysis)

- 2-year RR in a per-protocol analysis

- 5-year RR (intention-to-treat and per-protocol)

- 2- and 5-year disease free survival (DFS) rate

- disease-related 5- and 7-year overall survival (OS) rate

- quality of life (QoL), RR in patients without detectable ctDNA after surgery

- time-to-recurrence (TTR)

-cost-effectiveness of the ctDNA-based treatment.

Study description

Background summary

Colon cancer (CC) is worldwide a major cause of cancer related mortality. Patients with early stage disease (stage I and II) have a good chance of survival, however 15-20% of patients with stage II CC will experience disease recurrence. Indication for adjuvant chemotherapy (ACT) in stage II CC is not well established. Currently, only stage II patients with a pT4 lesion are recommended to receive ACT, but this biomarker lacks sensitivity and

specificity. Circulating tumor DNA (ctDNA) is an emerging biomarker that recently demonstrated strong prognostic value for disease recurrence in stage II CC. Detection of ctDNA in the postoperative time period identifies patients with the highest risk for disease recurrence. Therefore ctDNA-based adjuvant treatment may lead to a decreased recurrence rate in stage II CC.

Study objective

Primary objective: to investigate how many patients with detectable ctDNA after surgery start with adjuvant chemotherapy
Secondary objective: to reduce recurrence rate by ctDNA based adjuvant chemotherapy (ACT) in stage II colon cancer (CC) patients after primary tumor resection.

Study design

The proposed study is conducted within the cohort study PLCRC and follows the TwiCs design (i.e. a randomized controlled trial within a prospective cohort). Within PLCRC, patients that gave informed consent for additional blood withdrawals (at time of regular withdrawals) are participating in the observational substudy PLCRC-MEDOCC. In this substudy, blood samples are collected before and after surgery in stage II and stage III colon cancer patients for future ctDNA analysis. Patients and doctors are not informed about results in this observational trial. Patients with a histologically confirmed stage II colon cancer that are not considered for adjuvant chemotherapy, will be included in the MEDOCC-CrEATE study. Patients included in MEDOCC-CrEATE will be randomized 1:1 to the intervention versus control group. Intervention group : Patients will be asked informed consent (IC) for immediate testing of ctDNA after surgery. Patients with detectable ctDNA (estimated proportion ~5%) are considered high risk and will be offered ACT and can subsequently decide whether they are willing to receive this adjuvant treatment with CAPOX. Control group : Patients have given IC for randomization to a control group within PLCRC and participate in PLCRC-MEDOCC. They will get the treatment and follow-up according to current standard of care and will not get extra information about this trial (no consequences for this group). At all follow-up time points in the first 3 years after surgery, blood will be collected for ctDNA analysis in the observational PLCRC-MEDOCC study. This analysis will be performed after completion of accrual or during the trial with an interval of at least 12 weeks after surgery.

Intervention

Patients will be asked informed consent to immediately analyse their post-surgery sample for ctDNA. Patients with detectable ctDNA are seen as high risk and will be offered adjuvant chemotherapy.

Adjuvant chemotherapy is not part of the intervention, but preferably consists of four 3-weekly cycles with capecitabine and oxaliplatin (CAPOX) for a total treatment duration of 12 weeks (3 months).

Study burden and risks

Participation in the MEDOCC-CrEATE study (intervention group) will not pose a risk to the majority of patients (no detectable ctDNA), but in the small group (~5% of 660 patients in the intervention group, therefore ~30 patients) with detectable ctDNA after surgery the expected high risk of disease recurrence will be communicated by the treating physician and counselling will take place about adjuvant chemotherapy. The combination chemotherapy schedule of a fluoropyrimidine and oxaliplatin is part of the standard of care in the adjuvant colon cancer setting since the beginning of this century. Therefore the risks and toxicity of the used ACT are well-known. The majority of side-effects are manageable and transient.
The risk of the withdrawal of extra tubes of blood during regular blood withdrawal in all study participants is negligible.

Contacts

Public
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3508 GA
NL
Scientific
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3508 GA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Age >= 18 years
- Informed consent for PLCRC with specific consent for additional blood withdrawals, collection of tissue and being informed about future experimental research
- Histological confirmed stage II colon cancer
- Fit for combination chemotherapy (fluoropyrimidin and oxaliplatin) according to the treating physician

Exclusion criteria

- Indication for adjuvant chemotherapy according to treating physician
- Another malignancy in previous 5 years, except carcinoma in situ or skin cancer other than melanoma
- Incomplete tumor resection (R1 or R2 resection)
- Contra-indications for fluoropyrimidines or oxaliplatin
- Pregnancy

Study design

Design

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

Primary purpose: Diagnostic

Recruitment

NL
Recruitment status: Recruiting

Start date (anticipated):	28-08-2020
Enrollment:	1320
Type:	Actual

Ethics review

Approved WMO Date:	05-03-2020
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	16-06-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-06-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-07-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-08-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-09-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-10-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-11-2020

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-01-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-03-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-04-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-06-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-07-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-09-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-11-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	17-03-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-05-2022

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-02-2023
Application type:	Amendment
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Approved WMO Date:	09-03-2023
Application type:	Amendment
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Approved WMO Date:	28-03-2023
Application type:	Amendment
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Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-08-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	08-05-2024
Application type:	Amendment
Review commission:	METC NedMec

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
CCMO	NL71881.041.19