RandomizEd Controlled Trial for pre-operAtive dose-escaLation BOOST in locally advanced rectal cancer.

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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-OMON44829

Source
ToetsingOnline

Brief title
RECTAL BOOST study

Condition

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

Synonym
rectal cancer., rectal carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Boost radiotherapy, Pre-operative, Randomized Controlled Trial, Rectal cancer

Outcome measures

Primary outcome

The primary endpoint is complete response either defined as pathological complete response (pCR) in patients who undergo surgery, assessed by standardized pathologic examination of the surgical specimen, or 2-years local recurrence-free survival (LFRS) after chemoradiation in patients who opted for a wait and see approach.

Secondary outcome

Secondary outcomes are treatment acute, perioperative and late toxicity, tumor response assessed with MRI, patient-reported quality of life and workability, local recurrence and (disease-specific) survival.

Study description

Background summary

The current treatment for locally advanced rectal cancer consists of pre-operative chemoradiation treatment (CRT) (50 Gy in 25 fractions) followed by surgical resection. After this neo-adjuvant treatment approximately 15% of patients show pathological complete response (pCR), i.e. no residual tumor in the resected specimen on pathologic examination. Patients with pCR have a lower risk of local and distant recurrences and significantly longer disease-free and overall survival. Furthermore, in these patients surgery could possibly have been omitted. Selected patients with a clinical complete response (cCR), defined prior to surgery by rectoscopy, rectal examination and MRI, may opt for an organ-preserving therapy, a so called wait and see approach.
Response to chemoradiation occurs in a dose dependent fashion. Therefore, recent trials aimed to improve prognosis by radiation dose-escalation that resulted in improved pCR rates. Toxicity rates associated with radiation doses above 60 Gy are manageable and differ between studies; from increased to

comparable or even lower toxicity. Moreover, dose escalation may increase the proportion of patients eligible for organ-preserving therapy.

Study objective

We study whether addition of a radiation boost to standard chemoradiation in patients with locally advanced rectal cancer increases the complete response rate defined as pathological complete response in those who undergo surgery, or 2-years local recurrence-free survival (2y-LRFS), in those who opted for a wait and see approach. Secondary objectives are adverse events due to chemoradiation (acute, perioperative and late toxicity), tumor response assessed with MRI, the impact of the boost on local and distant recurrence and survival as well as patient-reported quality of life and workability.

Study design

Multicenter Randomized Controlled Trial, nested within a prospective cohort according to the *cohort multiple randomized controlled trial* (cmRCT) design.

Intervention

An irradiation boost of 15 Gy delivered to the gross tumor volume (GTV) in 5 fractions in addition to the standard chemoradiation treatment of 50 Gy. Thereby increasing the total GTV dose to 65 Gy.

Study burden and risks

The study will be conducted according to the cohort multiple Randomized Controlled Trial (cmRCT) design. Within our cohort (PLCRC Project), we will identify all patients who are eligible for inclusion in the current study and who have given informed consent to be invited for future experimental interventions. From this subcohort, we offer the boost to a randomly selected group of sixty patients. Randomly selected patients who refuse to undergo the additional boost, will receive standard treatment. Eligible patients who were not randomly selected will undergo standard treatment without further notification.
Patients who accept the experimental intervention will receive an additional five radiation fractions of a total of 15 Gy on the tumor (GTV) in addition to the standard treatment. This requires five additional hospital visits. Patients who participate in the intervention or control group are temporarily excluded from other studies within the PLCRC project that use the same endpoint, of which they are informed in the (initial PLCRC) patient-information letter.
Risks for patients in the intervention arm include higher toxicity, which, based on previous studies, is rather unlikely. Benefits for patients in the intervention arm may include higher probability of complete tumor response and reduced risk of recurrent disease.

Patients in the experimental arm who receive chemoradiation in the UMC Utrecht will undergo one additional MRI to assess tumor response, which will take place during one of the standard radiotherapy visits. Patients in the experimental arm who receive treatment in the MAASTRO clinic will undergo a PET-CT for treatment planning. Both imaging procedures include minimal risks.
Since these patients are participants in the PLCRC cohort, and have also already given informed consent to fill out questionnaires on Patient Reported Outcomes, this is not an additional burden to the patient.

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

* Participant in the PLCRC project (METC 12-510).
* Informed consent obtained for being offered experimental interventions within the PLCRC

project.
* Informed consent obtained for questionnaires on patient reported outcomes within the PLCRC project.
* WHO: 0-2.
* T3+ (circumferential resection margin (CRM) positive) T4N0-1 or N2 M0-1 (if resectable liver and/or lung metastases).
* Referred for chemoradiation.
* No contra-indication for MRI.
* Tumor distance from ano-rectal transition *10cm.

Exclusion criteria

* T3 (limited volume / CRM negative).
* Inflammatory bowel disease.
* Prior pelvic radiotherapy.
* At least one contra-indication for capecitabine administration (based on DPD-deficiency, blood count, liver malfunction, renal failure (Creatinine clearance <30ml/min, medical history such as recent cardiac events).
* Recent pregnancy *1 year ago.
* Inadequate understanding of the Dutch language in speech and/or writing.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-09-2014
Enrollment:	142
Type:	Actual

Ethics review

Approved WMO Date:	20-06-2014
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	01-04-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-06-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-12-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-03-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-03-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-01-2018
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
ClinicalTrials.gov	NCT01951521
CCMO	NL46051.041.13