Randomized multicentre phase III study of short course radiation therapy followed by prolonged pre-operative chemotherapy and surgery in patients with high risk primary rectal cancer compared to standard preoperative chemoradiotherapy, surgery and optional adjuvant chemotherapy.

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Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON24092

Bron
Nationaal Trial Register

Verkorte titel
RAPIDO

Aandoening

Primary rectal cancer with high risk of failing locally and/or systemically.

Keywords: rectal cancer, neoadjuvant chemotherapy, short course radiotherapy

Ondersteuning

Primaire sponsor: University Medical Center Groningen, PO BOX 3001 , 9700 RB , Groningen , The Netherlands
Overige ondersteuning: Dutch Cancer Society and Swedisch Cancer Society

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Disease related Treatment Failure (3-years after surgery)

Toelichting onderzoek

Achtergrond van het onderzoek

Currently the 3-year disease free survival of patients with locally advanced rectal cancer is about 50%. Current standard treatment for patients at high risk of failing locally includes pre-operative long course radiotherapy (5 weeks) in combination with chemotherapy (so called neoadjuvant chemoradiotherapy). The neoadjuvant chemoradiotherapy has been demonstrated to improve local control, but had no effect on the overall survival. Different studies in patients with rectal cancer studying the effect of adjuvant post operative chemotherapy did not result in an improved survival. This may be due the fact that rectal cancer surgery (TME) is associated with a high complication rate so substantial proportion of patients cannot receive chemotherapy postoperatively. An alternative approach is to administer the systemic therapy preoperative. To guarantee control of the rectum tumor short-course radiotherapy (5 days) is given, as different studies showed local control of the tumor for a long time. During this waiting period the patient is in a good condition to receive an optimal dose of chemotherapy. We hypothesize that with this proposed protocol both the local tumour and possible micrometastases are effectively treated and that this will result in an increased survival.
We will compare this with the standard treatment of neoadjuvant chemoradiation followed by TME surgery and adjuvant chemotherapy.

Doel van het onderzoek

Currently the 3-year disease free survival of patients with locally advanced rectal cancer is about 50%. Current standard treatment for patients at high risk of failing locally and/or systemically includes pre-operative long course radiotherapy (5 weeks) in combination with chemotherapy (so called neoadjuvant chemoradiotherapy). The neoadjuvant chemoradiotherapy has been demonstrated to improve local control, but had no effect on the

overall survival. Different studies in patients with rectal cancer studying the effect of adjuvant post operative chemotherapy did not result in an improved survival. This may be due the fact that rectal cancer surgery (TME) is associated with a high complication rate so substantial proportion of patients cannot receive chemotherapy postoperatively. An alternative approach is to administer the systemic therapy preoperative. To guarantee control of the rectum tumor short-course radiotherapy (5 days) is given, as different studies showed local control of the tumor for a long time. During this waiting period the patient is in a good condition to receive an optimal dose of chemotherapy. We hypothesize that with this proposed protocol both the local tumour and possible micrometastases are effectively treated and that this will result in an increased survival.
We will compare this with the standard treatment of neoadjuvant chemoradiation followed by TME surgery and optional adjuvant chemotherapy.

Onderzoeksopzet

The primary endpoint will be analyzed two years after the last patient was included. At this time point median follow up is three years.

Duration of the study: Four year inclusion, two year follow up after inclusion of the last patient. Estimated duration of the study is six year.

Onderzoeksproduct en/of interventie

Patients will be randomized between an experimental group in which short course 5 x 5 Gy radiation scheme is followed by six cycles of combination chemotherapy (capecitabine and oxaliplatin) and surgery and a control group with long course chemoradiotherapy followed by surgery. Optional adjuvant chemotherapy is allowed in the control group.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Primary tumour characteristics:

1. Histological proof of newly diagnosed primary adenocarcinoma of the rectum;

2. Locally advanced tumour fulfilling at least one of the following criteria on pelvic MRI indicating high risk of failing locally and/or systemically (T4a, i.e. overgrowth to an adjacent organ or structure
like the prostate, urinary bladder, uterus, sacrum, pelvic floor or side wall (according to TNM version 5), cT4b, i.e. peritoneal involvement, extramural vascular invasion (EMVI+). N2, i.e. four or
more lymph nodes in the mesorectum showing morphological signs on MRI indicating metastatic disease. Four or more nodes, whether
enlarged or not, with a rounded, homogeneous appearance is thus not sufficient. Positive MRF (previously named CRM), i.e. tumor or
lymph node < 1 mm from the mesorectal fascia. Enlarged lateral nodes, > 1 cm (lat LN+).

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Extensive growth into cranial part of the sacrum (above S3) or the lumbosacral nerve roots indicating that surgery will never be possible even if substantial tumour down-sizing is seen;

2. Presence of metastatic disease or recurrent rectal tumour;

3. Familial Adenomatosis Polyposis coli (FAP), Hereditary Non-Polyposis Colorectal Cancer (HNPCC), active Crohn's disease or active ulcerative Colitis;

4. Concomitant malignancies, except for adequately treated basocellular carcinoma of the skin or in situ carcinoma of the cervix uteri. Subjects with prior malignancies must be disease-free for at least 5 years;

5. Known DPD deficiency;

6. Any contraindications to MRI (e.g. patients with pacemakers);

7. Medical or psychiatric conditions that compromise the patient's ability to give informed consent;

8. Concurrent uncontrolled medical conditions;

9. Any investigational treatment for rectal cancer within the past month;

10. Pregnancy or breast feeding;

11. Patients with known malabsorption syndromes or a lack of physical integrity of the upper gastrointestinal tract;

12. Clinically significant (i.e. active) cardiac disease (e.g. congestive heart failure, symptomatic coronary artery disease and cardiac dysrhythmia, e.g. atrial fibrillation, even if controlled with medication) or myocardial infarction within the past 12 months;

13. Patients with symptoms or history of peripheral neuropathy.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Actieve controle groep

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	21-06-2011
Aantal proefpersonen:	885
Type:	Werkelijke startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Ja

Ethische beoordeling

Positief advies

Datum:	11-01-2012
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL3082
NTR-old	NTR3230
Ander register	EudraCT number : 2010-023957-12
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A