Preoperative short-term radiotherapy for primary resectable rectal cancer: Accelerated once daily (5x5Gy) versus accelerated hyperfractionated twice daily (12x2,5Gy b.i.d.) (ONCE-TWICE trial) A phase II single-blinded multi-institutional randomised study

Published: 12-09-2006
Last updated: 14-05-2024

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Ethical review	Approved WMO
Status	Pending
Health condition type	Gastrointestinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON29980

Source
ToetsingOnline

Brief title
ONCE-TWICE trial

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
bowel cancer, rectal cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: bowel toxicity, preoperative radiotherapy, resectable rectal cancer

Outcome measures

Primary outcome

CTCAE v3.0 - anal incontinence Grade 2 or higher at one year post treatment (or

at 18 months in case of late closure of a stoma).

Secondary outcome

All at one year post treatment (or at 18 months in case of late closure of a

stoma) and also three and five years post treatment:

1. MSKCC Bowel Function Instrument

2. Local control

3. Disease free survival

4. Overall survival

5. Quality of life (assessed by the EORTC QLQ-C30)

Study description

Background summary

The standard management of primary resectable rectal cancer in the Netherlands and other European countries is preoperative short-term radiotherapy (5 x 5 Gy = 25 Gy within one week) followed by curative surgery.
However, in spite of extensive testing of this regimen in large scale randomised phase III studies, discussion remains about possible and, more recently, demonstrated long term impairment of bowel-function due to this radiotherapy regimen.
Furthermore, an effective but little toxic radiotherapy regimen in order to improve local control may be needed in the foreseeable future, so that full-dose preoperative chemotherapy can be administered after short-term preoperative radiotherapy in high-risk tumours instead of the concomitant preoperative long-term radiochemotherapy regimens presently used.

Study objective

The objective of this prospective randomised trial is to test the hypothesis that hyperfractionated short course preoperative radiotherapy (12 x 2.5 Gy twice daily) leads to less radiation-induced bowel toxicity compared to the standard fractionation schedule of 5 x 5 Gy.

Study design

Prospective randomised single-blinded multi-institutional phase II study.

Intervention

Arm A: 5 x 5 Gy preoperative pelvic radiotherapy (standard)
Arm B: 12 x 2,5 Gy preoperative pelvic radiotherapy (experimental arm)
Comment: On the basis of the most accepted radiobiological modelling (the linear-quadratic model), the two arms are equivalent with respect to tumour-effects (intended prevention of local recurrence), but the experimental arm is less toxic for normal tissue.

Study burden and risks

All available evidence taken together, the experimental arm is likely to be less toxic than the standard treatment. The purpose of this study is to see whether this is also clinically relevant.

Contacts

Public
Universitair Medisch Centrum Groningen

Postbus 30.001
9700 RB Groningen
Nederland
Scientific
Universitair Medisch Centrum Groningen

Postbus 30.001
9700 RB Groningen
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Primary resectable rectal cancer. All patients with primary resectable rectal cancer are eligible for the study, regardless whether a low anterior resection with primary anastomosis or an abdominoperineal resection is planned.
- Histologically proven adenocarcinoma
- No distant metastases
- No prior radiotherapy to the pelvis or abdomen
- Age >18 years
- WHO performance score 0-2
- Patients at reproductive age must agree to practice an effective contraceptive method
- Written informed consent

Exclusion criteria

- Non-resectable rectal cancer (or resectability uncertain)
- Histology other than adenocarcinoma
- Distant metastases
- Pregnancy or lactation
- Psychological, familial, sociological or geographical reasons hampering compliance with the study protocol and follow-up schedule; those conditions should be discussed with the patient before registration in the trial

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-08-2006
Enrollment:	210
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL11561.042.06