Feasibility study of external beam radiation therapy followed by high-dose rate endorectal brachytherapy (HDRBT) in inoperable rectal cancer patients

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-To determine the feasibility and the maximum tolerated radiation dose in HDRBT of the rectum after EBRT in rectal cancer patients who are unfit for surgery or refuse surgery-To determine the incidence and severity of acute and late toxicity of EBRT...

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

Summary

ID

NL-OMON30965

Source
ToetsingOnline

Brief title
Feasibility of brachytherapy in rectal cancer

Condition

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

Synonym
rectal cancer ;bowel cancer

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Brachytherapy, Inoperable, Radiotherapy, Rectal Cancer

Outcome measures

Primary outcome

To determine the feasibility and the maximum tolerated radiation dose in HDRBT

of the rectum after EBRT in rectal cancer patients who are unfit for surgery or

refuse surgery

Secondary outcome

*To determine the incidence and severity of acute and late toxicity of EBRT

followed by HDRBT

*To determine the patient*s sphincter function

*To determine the clinical tumor response of EBRT followed by HDRBT

*To correlate the isodose lines of the irradiated tumor and normal tissue

volumes with toxicity (HDRBT)

Study description

Background summary

In newly diagnosed rectal cancer patients who are unfit for surgery, there is no defined radiotherapy schedule. The treatment can vary from wait-and-see, to schedules ranging from 8 Gy in 1 or 2 fractions to 50 Gy in 25 fractions. The most applied radiation therapy scheme is 45 Gy in 25 fractions. So far, radiotherapy alone could only cure rectal cancer if endocavitary irradiation is used either alone in T1N0 tumors or combined with external beam radiotherapy in patients with superficial T2-3 tumors. In previous studies, the radiation dose

has been specified on the tumor surface or at 0.5 or 1 cm from the surface. Therefore, it was only applied in superficial rectal tumors.
Based on the above mentioned literature, the use of high dose rate brachytherapy (HDRBRT) with the flexible, multichannel applicator is promising. However, the use of HDRBT has only been studied in neoadjuvant treatment of rectal cancer patients, and it has not yet been studied in inoperable rectal cancer patients. The major difference with neoadjuvant treatment is the fact that resection of the irradiated tissue will not take place. With the use of this applicator the prescription of the radiation dose will be at the tumor radial margins instead of more superficial, resulting in potentially high doses at the normal rectal wall. Therefore, the aim of our study is to investigate the feasibility and efficacy of HDRBT in rectal cancer patients who will not undergo surgery. By using HDRBT, we will optimize the dose to the tumor (and tumorpositive perirectal lymph nodes), while limiting the dose to the adjacent tissues to reduce toxicity.

Study objective

-To determine the feasibility and the maximum tolerated radiation dose in HDRBT of the rectum after EBRT in rectal cancer patients who are unfit for surgery or refuse surgery
-To determine the incidence and severity of acute and late toxicity of EBRT followed by HDRBT
-To determine the patient*s sphincter function
-To determine the clinical tumor response of EBRT followed by HDRBT

Study design

Feasibility study, phase I design, multicenter study with a planned sample size of 30 patients
Patients will be treated with external beam raditherapy, followed after 4-6 weeks by brachytherapy in the form of 3 applications with an flexible multichannel catheter.

Brachytherapy
The following rules will be followed for the dose escalation. A dose limiting toxicity is defined as proctitis >= grade 3 according to CTCAE version 3.0.

If 0/6 or 1/6 patient exhibit dose limiting toxicity:
- Dose escalation to the next dose level
If 2/6 patients exhibit dose limiting toxicity:
- Expand dose level to a total of 9 patients
- If no further DLT events seen, dose escalation to the next dose level
- If 1 or more further DLT events are seen (i.e. 3 or more of 9 patients), this dose level will be considered the maximum delivered dose

If > 2/6 patients exhibit dose limiting toxicity:
- This dose level will be considered the maximum delivered dose and 3 extra patients will be included one level below the maximum delivered dose-level

The maximum delivered dose is the dose in which >= 3/6 or >= 3/9 patients experience dose limiting toxicity. One dose level below the maximum delivered dose will be considered the recommended phase II dose.
Dose level Dose per fraction HDRBT Minimum number of patients
-1 3x4 Gy (12 Gy total) 0
1 (starting) 3x5 Gy (15 Gy total) 6
2 3x6 Gy (18 Gy total) 6
3 3x7 Gy (21 Gy total) 6
4 3x8 Gy (24 Gy total) 6

Intervention

External beam raditoherapy
39 Gy will be given in 13 fractions of 3 Gy in 21 days
After 6 weeks a MRI will be performed and if the tumor thickness is:
* tumor <= 2 cm, patients will be treated with brachytherapy; dosespecification at the deepest point of the tumor
* tumor > 2 cm, patients will be treated with brachytherapy, but the dose will be specified at 2 cm

This will be followed by high dose rate brachytherapy according to the schedule as given in the study design.

Study burden and risks

Patients will undergo 3 fractions of high dose rate brachytherapy in addition to external beam irradiation. This treatment has an increased risk of acute signs of proctitis, which usually resides in 1-2 months. However, there is a risk of chronic proctitis, with possible mucus and blood loss per anum.
The benefit for the patients is that a more radical treatment of their rectal tumor is given, with an considerable greater change of reaching a complete response of the tumor.

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

-Histologically verified adenocarcinoma of the rectum within 15 cm of the anal verge, <= 2/3 of the rectal circumferential diameter
-cT2-4N0-1M0-1; in patients with M1 disease, life expectancy is >= 6 months
-Patients who are unfit for surgical treatment, due to co-morbidity, or patients who refuse surgery
-WHO <= 2

Exclusion criteria

-Pregnant women
-Patients with any psychological, familial, sociological or geographical condition potentially 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
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-06-2007
Enrollment:	20
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
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	NL17037.031.07