Towards Response guided ADAptive Radiotherapy for organ preserving treatment of intermediate risk rectal cancer: a phase I dose finding trial

No registrations found.

Ethical review	Not applicable
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON22916

Source
Nationaal Trial Register

Brief title
preRADAR

Health condition

rectal cancer

Sponsors and support

Primary sponsor: UMC Utrecht
Source(s) of monetary or material Support: UMC Utrecht

Intervention

Outcome measures

Primary outcome

Maximum tolerated dose based on the incidence of dose limiting toxicity, a composite of (1)

radiation toxicity grade ≥4 according to Common Toxicity Criteria for Adverse Events (CTCAE) version 5.0 occurring within 20 weeks after start of radiotherapy and before surgery, (2) radiation toxicity grade 3 persisting > 12 weeks after start of radiotherapy, (3) postponing of surgery > 16 weeks due to any grade of radiation toxicity and (4) post-operative complications Clavien-Dindo IIIb-IV in case of residual disease and indication for surgery.

Secondary outcome

Eligibility of patients, intervention acceptance rate, GTV coverage of the boost fractions, non-dose limiting radiation toxicity and postoperative complications, organ preservation rate, locoregional control, disease free survival, overall survival, late radiation toxicity, quality of life (EORTC QLQ-C30 and CR-29) and functional outcome (LARS score).

Study description

Background summary

Rationale: Since recently, non-operative management is considered a possible treatment option for patients with rectal cancer who reach a clinical complete response (cCR) after neoadjuvant (chemo)radiotherapy. The chance of reaching cCR is dependent on the neoadjuvant treatment schedule. For patients with intermediate risk rectal cancer this schedule is short course radiotherapy (SCRT). This scheme consists of 5 fractions of 5 Gy on the rectal tumor, pathological lymph nodes and elective lymph node regions. Unfortunately, cCR rates after SCRT seem to be only around 10%. As response after radiotherapy is thought to be dose dependent, increasing the radiotherapy dose with SCRT potentially will lead to more cCR and thereby more organ preservation opportunities for these patients. However, there is only very limited experience with dose escalation after 5x5 Gy and the safety of clinically significant dose escalation is unclear.

Objective: The main objective is to determine the maximum tolerated dose (MTD) that will be the recommended radiation dose for the phase 2 study, using a MR-guided boost after SCRT in patients with intermediate risk rectal cancer. Secondary objectives are to determine the feasibility, non-dose limiting toxicity, organ preservation rate, oncological outcome and functional outcome, and to explore variables for early response evaluation.

Study design: 6+3 dose-escalation design with 4 radiotherapy dose levels.

Study population: patients with intermediate risk rectal cancer; referred for short-course radiotherapy and delayed surgery.

Intervention: 2, 3, 4, or 5 sequential, homogenous boost fractions of 5 Gy on the gross tumor volume (GTV) in the week following SCRT using MR-guided online adaptive radiotherapy on the MR-linac.

Main study parameters/endpoints: primary endpoint is the incidence of dose limiting toxicity,

a composite endpoint of (1) radiation toxicity grade ≥4 according to Common Toxicity Criteria for Adverse Events (CTCAE) version 5.0 occurring within 20 weeks after start of radiotherapy and before surgery, (2) radiation toxicity grade 3 persisting > 12 weeks after start of radiotherapy, (3) postponing of surgery > 16 weeks due to any grade of radiation toxicity and (4) post-operative complications Clavien-Dindo IIIb-IV in case of residual disease and indication for surgery. Secondary endpoints are eligibility of patients, intervention acceptance rate, GTV coverage of the boost fractions, non-dose limiting radiation toxicity and postoperative complications, organ preservation rate, locoregional control, disease free survival, overall survival, late radiation toxicity, quality of life (EORTC QLQ-C30 and CR-29) and functional outcome (LARS score).

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Benefits for patients may include higher probability of complete tumor response that creates the opportunity for a watchful waiting strategy instead of surgical resection. Watchful waiting is expected to result in a higher quality of life. Compared to standard treatment, the SCRT regimen including the sequential boost will take 2 to 5 days extra in the week following SCRT. Possible risks include higher radiation toxicity and surgical complication rates.

Study objective

We hypothesize that a boost on the Gross Tumor Volume (of 3x5, 4x5 or 5x5Gy) in the week following SCRT using MR-guided online adaptive radiotherapy can be safely administered on the MR-Linac.

Study design

The incidence of DLT will be assessed at 20 weeks after start radiotherapy in case of a complete response, or at 30 days after completion surgery in case of residual disease and indication for surgery at the 1st or 2nd clinical response assessment.
All participants will be followed up for at least 24 months to evaluate the secondary endpoints.

Intervention

2, 3, 4, or 5 sequential, homogenous boost fractions of 5 Gy on the gross tumor volume (GTV) in the week following SCRT using MR-guided online adaptive radiotherapy on the MR-linac.

Contacts

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Eligibility criteria

Inclusion criteria

- Age ≥18;
- Biopsy proven rectal adenocarcinoma;
- Intermediate risk tumor, based on TNM (AJCC 8th edition) stage (T3c-d (MRF-) N0M0 or cT1-3 (MRF-) N1M0)
- Mid-rectal or distal rectal tumor: lower border anteriorly not above peritoneal fold, upper border below sigmoid take-off;
- Indication for neoadjuvant short course radiotherapy as judged by multidisciplinary tumor board discussion;
- Fit for multimodal treatment, as judged by multidisciplinary tumor board discussion;
- Written informed consent.

Exclusion criteria

- Mucinous tumor or neuro-endocrine tumor, as defined on MRI and/or histopathology;
- No residual luminal tumor after local excision;
- Recurrent tumor or regrowth after previous treatment;
- Extra-mesorectal pathological lymph nodes;
- Planned systemic therapy (either with curative or palliative intent);
- History of inflammatory bowel disease;
- Prior pelvic radiotherapy;
- Contraindications for MRI at 1.5T;
- Orthopedic hip implants;
- Pregnancy.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-11-2021
Enrollment:	45
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Plan description
Sharing of data with other researchers is possible, if consent of both PIs is obtained for the specific research purposes.

Ethics review

Not applicable

Application type:	Not applicable

Study registrations

Followed up by the following (possibly more current) registration

ID: 51912
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL8997
CCMO	NL75671.041.21
OMON	NL-OMON51912

Study results