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

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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.

Ethische beoordeling	Niet van toepassing
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON22916

Bron
Nationaal Trial Register

Verkorte titel
preRADAR

Aandoening

rectal cancer

Ondersteuning

Primaire sponsor: UMC Utrecht
Overige ondersteuning: UMC Utrecht

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

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.

Onderzoeksproduct en/of interventie

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.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- 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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- 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.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Anders
Toewijzing:	Niet-gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-11-2021
Aantal proefpersonen:	45
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

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

Ethische beoordeling

Niet van toepassing

Soort:	Niet van toepassing

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 51912
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

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

Resultaten