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

Published: 29-03-2021
Last updated: 19-03-2025

The main objective is to determine the maximum tolerated dose (MTD) that will be the recommended radiation dose for the phase 2 study, in which we intend on using a MR-guided boost after SCRT in patients with intermediate risk rectal cancer to...

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

Summary

ID

NL-OMON51912

Source
ToetsingOnline

Brief title
preRADAR

Condition

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

Synonym
rectal cancer, rectal carcinoma

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Organ preservation, Phase I, Radiotherapy dose-escalation, Rectal carcinoma

Outcome measures

Primary outcome

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 > 20 weeks after start of radiotherapy due to any grade of radiation toxicity and (4) post-operative complications Clavien-Dindo IIIb-IV in residual disease requiring surgery.

Secondary outcome

Secondary endpoints are technical feasibility of boost delivery, 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, MFSQ, UDI-6 en IIQ, IIEF)

Study description

Background summary

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, among others, 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.

Study objective

The main objective is to determine the maximum tolerated dose (MTD) that will be the recommended radiation dose for the phase 2 study, in which we intend on using a MR-guided boost after SCRT in patients with intermediate risk rectal cancer to increase the chance for cCR. 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.

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.

Study burden and risks

Benefits for patients may include higher probability of complete tumor response that creates the opportunity for a watchful waiting strategy instead of 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.

Contacts

Public
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584 CX
NL
Scientific
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584 CX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

primary intermediate risk rectal adenocarcinoma, fit for multimodal treatment

Exclusion criteria

contra-indication for magnetic resonance-guided treatment or for pelvic radiotherapy (such as inflammatory bowel disease, prior pelvic radiotherapy, pregnancy, hip implants)

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	08-11-2021
Enrollment:	45
Type:	Actual

Ethics review

Approved WMO Date:	29-03-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	04-10-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-03-2022
Application type:	Amendment
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

ID: 22916
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL75671.041.21
Other	NL8997
OMON	NL-OMON22916

Study results

Date completed: 23-09-2024

Summary results
Trial ended prematurely