Multicentre, open-label, randomised, controlled, parallel arms clinical trial of induction chemotherapy followed by chemoradiotherapy versus chemoradiotherapy alone as neoadjuvant treatment for locally recurrent rectal cancer

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON21546

Source
NTR

Brief title
PelvEx II

Health condition

Locally Recurrent Rectal Cancer (LRRC)

Sponsors and support

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

Intervention

Outcome measures

Primary outcome

To compare the rate of resections with clear resection margins between both arms.

Secondary outcome

- To compare the local re-recurrence free survival between both arms.
- To compare the progression free survival between both arms.
- To compare the metastasis free survival between both arms.
- To compare the disease free survival between both arms.
- To compare the overall survival between both arms.
- To determine the pathologic response and compare this between both arms.
- To assess the objective radiological response to the neoadjuvant treatment.
- To determine the toxicity related to the administration of induction chemotherapy in the experimental arm.
- To determine the compliance to induction chemotherapy in the experimental arm.
- To compare the toxicity related to the administration of chemoradiotherapy between both arms.
- To compare the compliance to chemoradiotherapy between both arms.
- To compare the number of patients undergoing surgery between both arms.
- To compare surgical characteristics between both arms.
- To compare the rate of major surgical complications between both arms.
- To compare the quality of life between both arms.
- To determine the cost-effectiveness and –utility.
- To systematically collect blood and tissue samples from enrolled patients for future translational research.

Study description

Background summary

Rationale: The overall survival of patients undergoing curative multimodality treatment for locally recurrent rectal cancer (LRRC) remains poor, with a 5-year overall survival of approximately 30%. The most important prognostic factor for survival is a clear resection margin (R0 resection). Neoadjuvant chemoradiotherapy aims at downstaging local disease, thus facilitating radical resection. However, even with neoadjuvant chemoradiotherapy, radical resections are achieved in only ±60% of patients. The addition of induction chemotherapy prior to neoadjuvant chemoradiotherapy may improve downstaging of the tumour and thereby result in more R0 resections. Subsequently, increasing the rate of R0

resections should decrease local re-recurrence and thereby improve quality of life and overall survival in patients with LRRC.
Objective: The primary objective of this study is to determine the rate of resections with clear resection margins after treatment with induction chemotherapy followed by neoadjuvant chemoradiotherapy and surgery compared to treatment with neoadjuvant chemoradiotherapy and surgery alone. The secondary objectives are to determine the local re-recurrence free survival, progression free survival, metastasis free survival, disease free survival, overall survival, radiological response, pathologic response, toxicity, surgical complications, quality of life and costs for both arms.
Study design: This is a multicentre, open-label, phase III, parallel arms, randomised controlled trial that randomises eligible patients in a 1:1 ratio to receive induction chemotherapy followed by neoadjuvant chemoradiotherapy and surgery (experimental arm) or neoadjuvant chemoradiotherapy and surgery alone (control arm).
Study population: Patients diagnosed with locally recurrent rectal cancer who previously underwent a partial or total mesorectal excision for rectal cancer with or without (chemo)radiation, without distant metastases or contraindications for the planned intervention are eligible for inclusion.
Intervention: Patients allocated to the experimental arm will receive induction chemotherapy which consists of three 3-weekly courses CAPOX or four 2-weekly courses FOLFOX/FOLFIRI, followed by restaging with pelvic MRI and thoracoabdominal CT-scan. In case of distant metastases or progressive unresectable local disease, palliative treatment will be offered. In case of progressive but resectable local disease, patients will start chemoradiotherapy within 3-5 weeks. In case of responsive or stable disease, one additional 3-weekly course CAPOX or two additional 2-weekly courses FOLFOX/FOLFIRI will be administered. Subsequently, but not earlier than 3 weeks after the first day of the last cycle of induction chemotherapy, chemoradiotherapy will be administered. Chemoradiotherapy will be administered according to standard of care. The radiotherapy dose will be either 30 or 50 Gy, depending on whether the patient received previous radiotherapy. After restaging with MRI and CT-scan, surgery will be performed 10-14 weeks after the last day of chemoradiotherapy. If deemed necessary and feasible, intra-operative radiotherapy will be administered. Patients allocated to the control arm receive chemoradiotherapy alone followed by surgery.
Main study parameters/endpoints: The primary endpoint of the study is the rate of clear resection margins after surgery. Secondary endpoints are local re-recurrence free survival, progression free survival, distant metastasis free survival, disease free survival, overall survival, pathologic response, radiological response, systemic therapy related toxicity (NCI-CTCAE v5.0 grade ≥3), the number of patients completing neoadjuvant treatment, surgical characteristics, major postoperative complications (Clavien-Dindo ≥3) up to 90-days postoperatively, quality of life and cost-effectiveness.

Study objective

The hypothesize is, that treatment with induction chemotherapy will lead to a 15% increase of the R0 resection rate compared to treatment with neoadjuvant chemoradiotherapy and surgery alone.

Study design

4 years of inclusion, 5 years of follow-up

Intervention

Induction chemotherapy

Contacts

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Eligibility criteria

Inclusion criteria

- 18 years or older
- Confirmed locally recurrent rectal cancer after total or partial mesorectal resection for rectal cancer either by histopathology ór clinically proven (evidence on imaging in combination with clinical findings, with consensus in MDT)
- Resectable disease determined by magnetic resonance imaging (MRI) or deemed resectable after neoadjuvant treatment with chemoradiotherapy.
- Expected gross incomplete resection with overt tumour remaining in the patient after resection, tumour invasion in the neuroforamina, encasement of the ischiadic nerve and invasion of the cortex from S3 and upwards are considered not resectable
- WHO performance score 0-1
- Written informed consent

Exclusion criteria

- Radiological evidence of metastatic disease (e.g. liver, lung) at time of randomisation or in the six months prior to randomisation. Patients with enlarged iliac lymph nodes, enlarged inguinal lymph nodes and aspecific lung noduli are not excluded from inclusion.

- Homozygous DPD deficiency (if known in advance).
- Any chemotherapy in the past 6 months.
- Radiotherapy in the past 6 months for primary rectal cancer.□ Any contraindication for the planned chemotherapy (e.g. severe allergy, pregnancy, kidney dysfunction, thrombocytopenia), as determined by the medical oncologist.
- Any contraindication for the planned chemoradiotherapy (e.g. severe allergy to chemotherapy agent, no possibility for radiotherapy due to previous radiotherapy), as determined by the medical oncologist and/or radiation oncologist.
- Any contraindication for surgery, as determined by the surgeon and/or anaesthesiologist.
- Concurrent malignancies that interfere with the planned study treatment or the prognosis of resected LRRC.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	13-11-2020
Enrollment:	364
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	12-10-2021
Application type:	First submission

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
NTR-new	NL9785
Other	MEC-U Nieuwegein : METC100

Study results

Summary results
- PelvEx Collaborative. Induction chemotherapy followed by chemoradiotherapy versus chemoradiotherapy alone as neoadjuvant treatment for locally recurrent rectal cancer: study protocol of a multicentre, open-label, parallel-arms, randomized controlled study (PelvEx II). BJS Open. 2021