Neo-adjuvant FOLFOXIRI and chemoradiotherapy for high risk (“ugly”) locally advanced rectal cancer.

No registrations found.

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

Summary

ID

NL-OMON28766

Source
NTR

Brief title
MEND-IT

Health condition

Locally advanced rectal cancer

Sponsors and support

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

Intervention

Outcome measures

Primary outcome

The main study parameter is the proportion of patients with a pathological complete response (pCR) and those patients who started a wait and see strategy and have sustained clinical complete response (cCR) at 1 year.

Secondary outcome

Secondary Objective(s):
 To determine the recurrence free survival.
 To determine the distant metastasis free survival.
 To determine the progression-free survival.
 To determine the disease-free survival.
 To determine the overall survival.
 To determine the radiological response after induction chemotherapy.
 To determine the radiological response after induction chemotherapy and chemoradiotherapy.
 To determine the pathological response as determined by Mandard grading system.
 To determine the toxicity related to the administration of induction chemotherapy.
 To determine the compliance related to the administration of induction chemotherapy.
 To determine the toxicity related to the administration of chemoradiotherapy.
 To determine the compliance related to the administration of chemoradiotherapy.
 To determine the number of patients undergoing surgery.
 To determine the type and extent of surgery after neoadjuvant therapy.
 To determine the major surgical complications rate.
 To determine the quality of life.
 To determine the cost-effectiveness and -utility.
 To systemically collect blood and tissue samples for future translational research.

Study description

Background summary

Despite developments in the multidisciplinary treatment of patients with locally advanced rectal cancer (LARC), such as the introduction of total mesorectal excision (TME) by Heald et al. and the shift from adjuvant to neoadjuvant (chemo)radiotherapy ((C)RT), local and distant recurrence rates remain between 5-10% and 25-40% respectively. Several studies established tumour characteristics with particularly bad prognosis; it was demonstrated that the occurrence of mesorectal fascia involvement (MRF+), grade 4 extramural venous invasion (EMVI), tumour deposits (TD) and enlarged lateral lymph nodes (LLN) lead to high local and distant recurrence rates and decreased survival when compared with LARC without these particularly negative prognostic factors. This type of LARC is described as high risk LARC (hr-LARC). Achieving a resection with clear resection margins (R0) is an important prognostic factor for local (LR) and distant recurrence (DM) as well as survival. With the aim to further reduce the risk of recurrent rectal cancer, to diminish distant metastasis and to improve overall survival for patients with LARC, induction chemotherapy (ICT) became a growing area of research. The addition of ICT has the ability to induce more local tumour downstaging, possibly leading to resectability of previously unresectable tumours, more R0 resections and less extensive surgery. In the case of a complete clinical response, surgery may even be omitted. ICT may also have the potential to eradicate micrometastases. Hence,

increased local downstaging and reducing distant metastatic spread may reduce LR and DM rates and improve survival and quality of life. In recent years, the use of ICT was investigated and showed promising results, but little is known about the addition of ICT in patients with high risk LARC. Since these patients have a particularly bad prognosis, both with regard to locoregional and distant failure, a more intensified neoadjuvant treatment with FOLFOXIRI is anticipated to improve short- and long term results.

Study objective

In our sample size estimation a population proportion of 10% pCR (pathological complete response) was assumed after standard chemoradiotherapy. A pCR/sustained cCR (clinical complete response) rate of 20% (reflecting a 100% increase in pCR/cCR) was predicted for in the study population.

Study design

Inclusion: 3 years. Follow-up: 5 years.

Intervention

All patients are treated with neoadjuvant chemotherapy (FOLFOXIRI; 5-fluorouracil, oxaliplatin, leucovorin, irinotecan) followed by chemoradiotherapy.

Contacts

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Eligibility criteria

Inclusion criteria

 18 years or older

 WHO performance score 0-1.
 Fit for (modified dose) triple chemotherapy (FOLFOXIRI)
 Histopathologically confirmed rectal cancer.
 Lower border of the tumour located below the sigmoidal take-off as established on MRI of the pelvis.
 Confirmed high-risk locally advanced rectal cancer, meeting one of the following imaging based criteria:
o Tumour invasion of mesorectal fascia (MRF+)
o The presence of grade 4 extramural venous invasion (mrEMVI)
o The presence of tumour deposits (TD)
o The presence of extramesorectal lymph nodes with a short-axis size ≥ 7mm (LNN)
 Resectable disease as determined on magnetic resonance imaging (MRI) or deemed resectable disease after neoadjuvant treatment.
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
 Written informed consent.

Exclusion criteria

 Evidence of metastatic disease at time of inclusion or within six months prior to inclusion except for patients with enlarged iliac or inguinal lymph nodes and aspecific lung noduli.
 Homozygous DPD deficiency.
 Any chemotherapy within the past 6 months.
o Any contraindication for the planned systemic therapy (e.g. severe allergy, pregnancy, kidney dysfunction and thrombocytopenia), as determined by the medical oncologist.
 Radiotherapy in the pelvic area within the past 6 months.
 Any contraindication for the planned chemoradiotherapy (e.g. severe allergy to the chemotherapy agent or no possibility to receive radiotherapy), as determined by the medical oncologist and/or radiation oncologist. Any contraindication to undergo surgery, as determined by the surgeon and/or anaesthesiologist.
 Concurrent malignancies that interfere with the planned study treatment or the prognosis of the resected tumour.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non controlled trial

Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-06-2021
Enrollment:	128
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Plan description
N/A

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	NL9790

Register ID

Other	Medical Research Ethics Committees United (MEC-U) Nieuwegein : METC100

Study results

Summary results

N/A