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

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Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON28766

Bron
NTR

Verkorte titel
MEND-IT

Aandoening

Locally advanced rectal cancer

Ondersteuning

Primaire sponsor: Catharina Hospital Eindhoven
Overige ondersteuning: ZonMw

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

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

Onderzoeksproduct en/of interventie

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

Contactpersonen

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

 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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

 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.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-06-2021
Aantal proefpersonen:	128
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Toelichting
N/A

Ethische beoordeling

Positief advies

Datum:	12-10-2021
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL9790
Ander register	Medical Research Ethics Committees United (MEC-U) Nieuwegein : METC100

Resultaten

Samenvatting resultaten
N/A