Rectal preserving treatment for early rectal cancer. A multi-centred, partially randomised patient preference trial of radical surgery versus adjuvant chemoradiotherapy after local excision for early rectal cancers.

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This study has been transitioned to CTIS with ID 2024-517410-15-01 check the CTIS register for the current data. The aim of this study is to determine the oncological safety, treatment related morbidity, and the functional outcome of local excision...

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

Summary

ID

NL-OMON50184

Source
ToetsingOnline

Brief title
TESAR Trial

Condition

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

Synonym
Rectal cancer

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC, locatie VUmc
Source(s) of monetary or material Support: KWF

Intervention

Keyword: Local excision, Organ preserving therapy, Rectal cancer, TEM

Outcome measures

Primary outcome

The primary outcome of the study is local recurrence after 3 year follow-up.

Secondary outcome

Secondary mortality, morbidity, stoma rate, long term interventions, functional

outcomes, health related quality of life (HRQoL) and

costs.

Study description

Background summary

Colorectal cancer is the third most common cancer and second cause of cancer related death in the Netherlands with 13,500 new cases each year. Due to the introduction of the bowel cancer screening a shift is expected towards more early cancers being detected. Current therapy for early colorectal cancer is radical Total Mesorectal Excision (TME). Colorectal surgical resections are accompanied with high morbidity of up to 33% and 90 days mortality of up to 9% in the fragile elderly patients as is seen in the results of the Dutch Surgical Colorectal Audit (DSCA) of 2013. Additionally, rectal cancer surgery is associated with substantial loss of health related quality of life due to defecation disorders, incontinence, sexual dysfunction and stoma related morbidity. These disadvantages are acceptable when radical surgery is the only option for cure. Advances in technology enabled the development of local excision of early rectal cancer with precise endoluminal microsurgery or local endoscopic excision, resulting in a significant decrease in short- and long

term morbidity. However current evidence is of inadequate quality to conclude on the oncologic safety of local treatment for early rectal cancer. Imaging can predict outcome and tailors treatment in more advanced cancer but fails in early cancer. Pathological assessment of the excised tumor tissue provides the optimal information on tumor stage, tumor characteristics and tumor differentiation It thereby enables the prediction of the risk of recurrence after local treatment alone. For early rectal cancers, with a low risk on recurrence based on favourable tumor characteristics, local excision is seen as safe and these patients do not require an additional treatment. However, for patients with early rectal cancer with a higher risk on recurrence based on tumor characteristics there is no consensus on the additional treatment after local excision. According to the National guideline, these patients receive a TME procedure. However, for this subgroup of patients local treatment followed by chemoradiotherapy might also be oncological safe. Current evidence is of inadequate quality to be conclusive. For this subgroup of patients with early rectal cancer with high risk tumor characteristics the TESAR trial is designed.

Study objective

This study has been transitioned to CTIS with ID 2024-517410-15-01 check the CTIS register for the current data.

The aim of this study is to determine the oncological safety, treatment related morbidity, and the functional outcome of local excision followed by adjuvant chemo-radiotherapy compared to local excision followed by completion radical resection of intermediate risk early rectal cancer.

Study design

In this international multicentre, partially randomised patient preference trial, patients with complete excision of intermediate risk T1-2 rectal cancer by transanal endoscopic surgery (TEM/TAMIS) or endoscopic excision (snare polypectomy/EMR/ESD/Endoscopic intramuscular dissection(EID)) will be randomised between organ preserving adjuvant chemoradiotherapy or completion TME surgery. If patients are unwilling to be randomised, they will have the option to choose between completion surgery and adjuvant chemoradiotherapy. Patients who decline further treatment after local excision will be invited to join the registration cohort.

Intervention

The study treatment consists of adjuvant chemo-radiotherapy (25x1.8 Gy) limited to the mesorectum with concurrent capecitabine (825 mg/m2). To monitor the risk of recurrence, there will be additional follow up with frequent MRI and endoscopy in the experimental arm. For a period of 5 weeks patients will

receive the treatment, only during weekdays.

Study burden and risks

The study compares two accepted treatment strategies for rectal carcinoma, aiming to demonstrate reduced treatment-related morbidity in the intervention group. The intervention arm involves an existing treatment for rectal carcinoma with relatively low morbidity. Patients in the intervention group will undergo a 5-week course of radiation therapy, which may impose some burden on them. Any risks associated with chemoradiation, such as enteritis, diarrhea, mild neurotoxicity, and impaired wound healing, will be closely monitored and documented using the comprehensive complication index and the NCI toxicity score. In contrast, the control group will undergo a major radical resection procedure, accompanied by associated hospitalizations, morbidity, and mortality.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Patient has had an endoluminal local excision (by TEM, TAMIS, TSPM, EMR/ESD/endoscopic intramuscular dissection or polypectomy) of an early rectal cancer without carcinoma in the resection plane.
2. Patients without carcinoma in the resection plane or in case of unreliable resection planes (EMR/ESD) no macroscopic residual tumour confirmed by endoscopy are eligible for randomisation.
3. Only lesions for which TME surgery is indicated can be included (If a partial mesorectal excision (PME) is indicated the patient should be excluded).
4. Pathological confirmation of the rectal adenocarcinoma fulfilling the following criteria: T1 with size 3-5 cm of carcinoma or pT1, maximum size of carcinoma of 3 cm, with at least poor differentiation, Haggit 4 and/or sm3, tumour budding, lymphatic and/or venous invasion.
5. Pathological confirmation of the rectal adenocarcinoma fulfilling the following criteria: pT2, maximum size of carcinoma of 3 cm, well/moderate differentiated and without tumour budding or lymphatic or venous invasion.
6. Complete colonoscopy, without synchronous colorectal cancer
7. cN0 stage based on pelvic MRI; lymph nodes smaller than 10 mm will be considered as benign, independent of morphologic features. Staging done within 6 weeks before randomisation.
8. Adequate distant staging (X-thorax or CT-thorax and CT-abdomen) without signs of distant metastasis (cM0)
9. Male or female, Age > 18 years.
10. Life expectancy of at least 12 months.
11. Medically fit (WHO 0-2) to undergo radical surgery and/or radiation.
12. No contraindications to chemotherapy, including adequate blood counts;
- white blood count >= 4.0 x 10 9/l
- platelet count >=100 x 109/l
- clinical acceptable haemoglobin levels
- bilirubin < 35 umol/l
- creatinine levels indicating renal clearance of >=50 ml/min
13. The patient is willing and able to comply with the protocol for the duration of the study, and scheduled follow-up visits and examinations.
14. Written (signed and dated) informed consent and be capable of co-operating with protocol.

Exclusion criteria

1. Incomplete or inconclusive resection margin with macroscopic residual tumour.
2. T1 tumour with carcinoma < 3 cm, moderate/well differentiated, without sm3/Haggit 4,tumour budding, venous or lymphatic invasion.

3. T1 tumour with carcinoma of >5 cm and T2 tumour with carcinoma of > 3 cm.
4. Presence of metastatic disease or recurrent rectal tumour.
5. Previous pelvic radiation.
6. Treatment with any other investigational agent, or participation in another clinical trial that interferes with the outcomes within 28 days prior to enrolment.
7. Concomitant malignancies, except for adequately treated basocellular carcinoma of the skin or in situ carcinoma of the cervix uteri. Subjects with prior malignancies must be disease-free for at least 5 years.
8. Pregnancy, breast-feeding or fertile women without active birth control
9. Clinically significant (i.e. active) cardiovascular disease for example cerebro vascular accidents (<6 months prior to randomization), myocardial infarction (<6 months prior to randomization), unstable angina, New York Heart Association (NYHA) grade II or higher, congestive heart failure, serious cardiac arrhythmia requiring medication.
10. Patients who are known to be serologically positive for Hepatitis B, Hepatitis C or HIV.
11. History of severe and unexpected reactions to fluoropyrimidine therapy.
12. Hypersensitivity to capecitabine.
13. Patients with severe hepatic impairment.
14. Medical or psychiatric conditions that compromise the patient's ability to give informed consent.
15. Patients known with dihydropyrimidine dehydrogenase deficiency.
16. Any contra-indications to undergo MRI imaging.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL
Recruitment status: Recruiting

Start date (anticipated):	11-11-2015
Enrollment:	315
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	Xeloda
Generic name:	Capecitabine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	23-06-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-09-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-10-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-10-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-01-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-02-2016

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-05-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-06-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-06-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-07-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-10-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-01-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-01-2017

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-03-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-07-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-09-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-11-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-11-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-12-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-12-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-01-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-01-2018

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-02-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-05-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-05-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-07-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-10-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
EU-CTR	CTIS2024-517410-15-01
EudraCT	EUCTR2015-000689-79-NL
CCMO	NL50364.029.15