Chemoradiation followed by surgery for patients with cT4 oesophageal cancer

Published: 14-11-2011
Last updated: 27-04-2024

The aim of this phase-2-study is to assess the feasibility of surgery following CRT in patients with cT4 oesophageal carcinoma with regard to morbidity, mortality and the possibility to achieve a R0 resection.

Ethical review	-
Status	Recruitment stopped
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Interventional

Summary

ID

NL-OMON38001

Source
ToetsingOnline

Brief title
TOR-study (T4 Oesophagus Resection)

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC
- Gastrointestinal therapeutic procedures

Synonym
oesophageal carcinoma, oesophagus cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: chemoradiation, neoadjuvant, Oesophaguscarcinoma, resection

Outcome measures

Primary outcome

The ability to achieve a radical (R0) resection.

Secondary outcome

• Toxicity profile

• Adequacy of PET-CT and EUS in (re-)staging T4 oesophagus carcinoma

• Peri-operative morbidity and mortality

• Percentage of pathologic complete responses

• Progression free survival at 6 months

Study description

Background summary

Current treatment of cT4 (locally irresectabel) oesophagus carcinoma is subject of debate, but mostly consits of chemoradiation therapy.However, the results of definite CRT in cT4 oesophageal carcinoma remain poor with only 20% of patients alive at 3 years from the start of CRT and a local recurrence rate of up to 60%. The occurrence of a local recurrence has no curative options and prognosis is infaust in the majority of patients within six months after start of therapy. Furthermore local recurrence leads to severe symptoms, mostly caused by perforation or obstruction of the oesophagus, and has a high influence on quality of live.

These poor results lead to the hypothesis that local control and survival might be improved by surgical resection following chemoradiation for CT4 oesophageal cancer. Only small series concerning this topic in patients with a cT4 oesophageal carcinoma exist at present time, suggesting feasibility and improved local control. Previous reports on surgery following CRT for cT3 and cT4 oesophageal carcinoma report of high peri-operative mortality (up to 12,8 % of patients) and morbidity (postoperative complication (major/minor in up to 70% of patients), but none the less a trend toward better cancer-free survival

(64,3% vs. 40,7% progression free survival) and reduced local recurrence rates (66,4 % vs. 57%) in operated patients.

In these series, the high morbidity and mortality of surgery after neoadjuvant teatment, might be contributed to the schedules that were used. These consisted of chemotherapy with cisplatinum and 5-fluorouracil in combination with radiotherapy. More recently, studies with taxanes as concurrently administered cytotoxic drugs show promising results, with acceptable toxicity. A randomized phase III study was conducted in the Netherlands, comparing neoadjuvant chemoradiation followed by surgery versus surgery alone for patients with adenocarcinomas or squamous cell carcinomas of the esophagus. Weekly neoadjuvant carboplatin and paclitaxel with concurrent radiotherapy was demonstrated to be a very tolerable regimen and can be given in an outpatient setting. An interim analysis, after inclusion of 250 patients, revealed a surgical mortality of less than 3%, which was not different between the two study arms (referentie CROSS). Also, in this study a high response rate of neo-adjuvant treatment was observed (pCR rate (32%) in de CROSS studie. , which leads to the hypothesis that resection might be possible, even in advanced tumors.

Study objective

The aim of this phase-2-study is to assess the feasibility of surgery following CRT in patients with cT4 oesophageal carcinoma with regard to morbidity, mortality and the possibility to achieve a R0 resection.

Study design

This is a Phase II, non-randomized trial. Eligible subjects will be treated with the current standard schedule for definite CRT (Weekly carboplatin and paclitaxel with 50.4 Gy radiation therapy in fractions of 1.8 Gy for 5.5 weeks) followed by surgical resection of the esophagus.

Intervention

Chemotherapy regimen: Paclitaxel 50 mg/m2 and Carboplatin AUC = 2 will be given by intravenous infusion on days 1, 8, 15, 22 and 29. This is the standard regimen for definite chemoradiation therapy in our institution and dose adjustments in case of toxicity will follow the regular protocols.

Radiotherapy treatment: A total dose of 50.4 Gy will be given in 28 fractions of 1.8 Gy, 5 fractions per week, starting the first day of the first cycle of chemotherapy. All patients will be radiated by external beam radiation, using 3-D conformal radiation technique. This is the standard treatment protocol for patients with cT4 oesophageal carcinoma in our institution.

Surgery: Surgical procedure will consist of a transthoracic oesophageal resection (open, right thoractomy) with en-bloc two-field lymphadenectomy. If needed, resection of adjacent structures (eg pleura, lung, pericardium, diaphragm) will be conducted. The per-operative need for a tracheobronchial, aortic, cardiac or vertebral resection will be considered a contra-indication for resection. In those cases resection will not be performed and patients will have received the standard treatment for cT4 oesophageal cancer.

A wide local excision including is carried out, including a standard excision of paraoesophageal, subcarinal and celiac lymph nodes. The continuity of the digestive tract will be restored by a gastric tube reconstruction or colonic interposition procedure with an anastomosis in the neck.

Study burden and risks

Risks associated with participation are the risks of standard treatment with chemoradiation, which all patients with cT4 oesophageal carcinoma undergo according to the current protocol.
Furthermore, if the tumour is found to be resectable on restaging modalities, patients will undergo surgical resection which is associated with the risk of developing several complications (eg anastomotic leakage, chylous leakage, pulmonary complications).

Contacts

Public
Academisch Medisch Centrum

Postbus 22700
1100DE Amsterdam
NL
Scientific
Academisch Medisch Centrum

Postbus 22700
1100DE Amsterdam
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Histologically proven squamous cell carcinoma, adenocarcinoma or undifferentiated carcinoma of the intrathoracic esophagus or gastro esophageal junction
Surgical irresectable (T4a and T4b), as determined by Endoscopic Ultra Sound (EUS), CT scan of neck, thorax and abdomen OR Positon Emission Tomography (PET)-scan, without distant metastasis (T4a: ingrowth in pleura, pericardium, diaphragm, or adjacent peritoneum, T4b other adjacent structures,e.g. aorta, vertebral body, trachea)

Exclusion criteria

cT4b oesophageal carcinoma with tracheobronchial involvement, as demonstrated on bronchoscopy after neoadjuvant treatment
Past or current history of malignancy other than entry diagnosis except for non-melanomatous skin cancer, or curatively treated in situ carcinoma of the cervix, or malignancy more than 5 years prior to enrollment
Pregnancy (positive serum pregnancy test) and lactation
Clinically significant cardiovascular disease (including myocardial infarction, unstable angina, symptomatic congestive heart failure, serious uncontrolled cardiac arrhythmia) <= 1 year before enrollment
Active infection or other serious underlying medical condition which would impair the ability of the patient to receive the planned treatment
Dementia or altered mental status that would prohibit the understanding and giving of informed consent
Inadequate caloric- and/or fluid intake
Weight loss > 15%.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-07-2011
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO

Date:	13-06-2012
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
CCMO	NL35439.018.11