Accuracy of detecting residual disease after neoadjuvant chemoradiotherapy for oesophageal cancer (PRESANO trial)

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The aim of this present diagnostic study is to determine the accuracy by which we can detect residual disease after neoadjuvant chemoradiotherapy.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Observational invasive

Summary

ID

NL-OMON43870

Source
ToetsingOnline

Brief title
PRESANO trial

Condition

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

Synonym
carcinoma of the oesophagus, oesophageal cancer

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W,KWF

Kankerbestrijding;Stichting Coolsingel

Intervention

Keyword: esophageal cancer, neoadjuvant chemoradiotherapy, surgery, wait-and-see

Outcome measures

Primary outcome

Primary endpoint

• Correlation between the clinical response during CRE-I and CRE-II (CRE= clinical response evaluation) and the final pathological response in the resection specimen as measured by the modified tumour regression grading system of Chirieac (Cancer 2005).

Secondary outcome

Secondary endpoints

• Serious complications during endoscopic and endosonographic tissue sampling (conventional biopsies and FNA).

• R0-resection rates for all included patients that undergo resection.

Other important measurements that will be registered

Further details per individual diagnostic modality will be registered and correlated with pathological findings in the resection specimen

• Endoscopic examinations

• Endoscopic ultrasonography (EUS) examinations

• PET-CT

• Analysis of (cyto)histological biopsies

Study description

Background summary

CROSS trial
Results from the recently completed CROSS trial show that the addition of neoadjuvant chemoradiation (Carboplatin, Paclitaxel and 41.4 Gy of concurrent radiotherapy) to surgery significantly increases long term survival as compared to surgery alone. Therefore, neoadjuvant chemoradiation plus surgery is now considered the therapy of first choice in The Netherlands for potentially curable oesophageal cancer in patients fit to undergo this treatment.

Pathologically complete response
In subsequent analyses of secondary endpoints of the CROSS trial a striking finding was made. In the neoadjuvant chemoradiotherapy (nCRT) arm 49% of patients with a squamous cell carcinoma and 23% of patients with an adenocarcinoma had a pathologically complete response (pCR) in the resection specimen. Therefore, these results impose an ethical imperative to reconsider and study the necessity of standard oesophagectomy in all patients after application of the CROSS-regimen.

Surgery As Needed for Oesophageal cancer (SANO-)approach
We propose a surgery as needed approach after completion of neoadjuvant chemoradiotherapy for carcinoma of the oesophagus. In this surgery as needed approach, patients will undergo close surveillance after completion of neoadjuvant chemoradiotherapy. Surgical resection would be offered only to those patients in whom a locoregional recurrence is highly suspected or proven, without any signs of distant dissemination. Such an organ-preserving strategy would clearly have great advantages, but only if long term survival would be comparable to that of the trimodality approach comprising neoadjuvant chemoradiotherapy followed by standard surgery.

Feasibility of the SANO-approach
Before a surgery as needed approach can be tested in a (randomised) trial, we aim to determine the feasibility of accurate detection of residual disease after chemoradiotherapy in a preliminary trial (PRESANO trial). The feasibility to accurately detect residual or recurrent disease at an early stage will be essential for the safety of the SANO-approach.

Study objective

The aim of this present diagnostic study is to determine the accuracy by which we can detect residual disease after neoadjuvant chemoradiotherapy.

Study design

This study is set up as a prospective multi-centre feasibility trial, using a single arm.

Study burden and risks

In the current protocol, patients with oesophageal cancer undergo surgical resection 6-8 weeks after neoadjuvant chemoradiotherapy (nCRT), without additional diagnostics in the intervening period.
In the context of this study, patients receive a first clinical response evaluation (CRE-I) 6-8 weeks after the end of nCRT (prior to surgery). This CRE consists of a complete physical examination, endoscopy with biopsies and a radial endoscopic ultrasonography. If residual tumour is demonstrated, these patients are offered immediate surgical resection. These patients will then have little delay compared to the standard protocol. If during CRE-I no tumour is found, surgery is postponed for another 6-8 weeks. Prior to this delayed surgery, patients will undergo a second CRE (CRE-II), which will consist of a PET-CT, followed by endoscopy with biopsies, radial endoscopic ultrasonography and endoscopic linear ultrasonography with fine needle biopsies. In principle, all patients will undergo surgical resection after CRE-II, unless disseminated disease is found.

The burden for the patient can be summarized as:
CRE-I: endoscopy with biopsies and endoscopic ultrasonography. These studies are extra as compared with the standard protocol.
There is a very small risk of bleeding, infection and perforation during endoscopy with biopsies.

CRE-II: again endoscopy with biopsies and endoscopic ultrasonography will be performed. During endoscopic ultrasonography fine-needle aspirations (FNA) of suspected lymph nodes is performed. These studies are extra as compared with the standard protocol.
There is again a very small risk of bleeding, infections and perforations during endoscopy with biopsies and endoscopic ultrasonography with FNA.
PET-CT: This diagnostic is additional to the standard protocol and has a small additional burden for patients. In the standard protocol, a PET-CT scan is already performed pre-treatment. Therefore, in our study protocol a second (additional) PET-CT scan will be performed.

An additional potential risk is the delay in surgery (12-16 weeks after completion of nCRT rather than the standard 6-8 weeks). Possible risks include more (surgical) complications and a lower radical resection rate. However, previous studies from our group and other international groups have shown that delaying surgery after pretreatment does not negatively influence outcome (it might possibly even improve certain outcome parameters). We therefore consider the risk of delayed surgery after pretreatment to be very small. However, we did add the rate of radical resections to the list of stopping-rules in this

protocol.

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

- Planned to undergo neoadjuvant chemoradiotherapy according to CROSS, followed by surgical resection for histologically proven oesophageal squamous cell carcinoma or adenocarcinoma
- Age >= 18
- Written, voluntary informed consent

Exclusion criteria

- Dementia or altered mental status prohibiting the understanding and giving of informed consent

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-07-2013
Enrollment:	215
Type:	Actual

Ethics review

Approved WMO Date:	18-06-2013
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-10-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-07-2015

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-09-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-02-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-03-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL41732.078.13