Preoperative Image-guided Identification of Response to Neoadjuvant Chemoradiotherapy in Esophageal cancer

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To develop a model that predicts the probability of pathologic complete response to nCRT in esophageal cancer, by integrating diffusion weighted magnetic resonance imaging (DW-MRI) and dynamic contrast enhanced magnetic resonance imaging (DCE-MRI)…

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

Summary

ID

NL-OMON50293

Source
ToetsingOnline

Brief title
PRIDE study

Condition

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

Synonym
Esophageal cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Koningin Wilhelmina Fonds (KWF)

Kankerbestrijding

Intervention

Keyword: Esophageal cancer, MRI scan, Pathologic complete response, PET scan

Outcome measures

Primary outcome

A multiparametric prediction model that predicts the probability of a pathologic complete response to nCRT in esophageal cancer by integrating DW-MRI and DCE-MRI in conjunction with 18F-FDG PET-CT scans acquired prior to, during and after administration of nCRT, as compared to the pathological specimen as gold standard.

Secondary outcome

• MRI and 18F-FDG PET-CT imaging parameters (including estimated tumor volume, SUVmean, SUVmax, *SUVmean, *SUVmax, ADC, *ADC and Ktrans values) to assess the optimal parameters that correlate best with pathological response.

• The presence of residual disease after nCRT according to a radiological (qualitative) assessment based on T2W-MRI and DW-MRI.

• The estimated post-nCRT T-stage and N-stage, as determined by an expert radiologist blinded to other imaging results, obtained at the MRI images after completion of nCRT (MRIpost), will be compared to the pathological TN-stage.

• The diagnostic accuracy of an additional endoscopy and/or endoscopic ultrasonography (EUS) with biopsies of the primary tumor site, other suspected lesions and suspected locoregional lymph nodes after completion of nCRT, the 18F-FDG PET/CTpost and the MRIpost, and before surgery (in patients that provide informed consent for this additional and optional study procedure).

• MRI and 18F-FDG PET-CT imaging parameters (including estimated tumor volume, SUVmean, SUVmax, *SUVmean, *SUVmax, ADC, *ADC and Ktrans values) to assess whether these parameters correlate with disease-free and overall survival.

• The presence of, and changes in, ctDNA (circulating tumor DNA) in blood samples during nCRT as a biomarker for a patients* response to nCRT, the detection of residual disease after nCRT and disease-free and overall survival

Study description

Background summary

For locally advanced esophageal cancer the standard treatment consists of 5 weeks of neoadjuvant chemoradiotherapy (nCRT) followed by surgery. Surgery is currently performed independent of the response to nCRT and is associated with substantial morbidity. Prior knowledge of the eventual response to nCRT would greatly impact on the optimal care for many esophageal cancer patients for two imperative reasons.
Firstly, it is argued that patients who achieved a pathologic complete response (pCR, 28-34%) may not have benefitted from surgery. Consequently, proper identification of pathological complete responders prior to surgery could yield an organ-preserving regimen avoiding unnecessary toxicity.
Secondly, non-responders are exposed to the side effects of nCRT without showing any tumor regression. Early identification of the non-responders during nCRT would be beneficial for this group as ineffective therapy could be stopped, and for who altered treatment strategies could be explored.

Study objective

To develop a model that predicts the probability of pathologic complete response to nCRT in esophageal cancer, by integrating diffusion weighted magnetic resonance imaging (DW-MRI) and dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) in conjunction with combined 18F-fluorodeoxyglucose positron emission tomography and computed tomography (18F-FDG PET-CT) scans acquired prior to, during and after administration of nCRT.

Study design

Multi-center observational study (n=200).
Intervention: In addition to the standard diagnostic work-up for esophageal

cancer that includes a 18F-FDG PET-CT scan at diagnosis and after nCRT, one 18F-FDG PET-CT scans will be performed during nCRT, as well as three MRI scans (before, during and after nCRT) within fixed time intervals. Furthermore, after response imaging after nCRT has been performed, but prior to surgery, patients will undergo (on an opt-out basis) an endoscopy and/or endoscopic ultrasonography (EUS) with biopsies of the primary tumor site, other suspected lesions and suspected lymph nodes. Furthermore, blood samples will be collected at three time points.

Study burden and risks

For study purposes patients will undergo three MRI scans and one 18F-FDG PET-CT scan, in addition to a pre-nCRT and post-nCRT 18F-FDG PET-CT scan which is standard of care. During the MRI examinations, an intravenous contrast agent is administered to the patient. This can lead to mild side effects of headache, nausea, injection site reaction, disturbed sense of taste and feeling cold. The use of the contrast agent has a very low risk (<1%) of an allergic reaction to the contrast medium. The extra 18F-FDG PET-CT exposes the patient to low radiation dose, which is deemed justified in the study population that receives 41.4 Gy external beam irradiation. Furthermore, on an opt-out basis patients will undergo an endoscopic assessment after nCRT, which carries a very small risk of complications, such as esophageal perforation or bleeding (<0.1-1%). All risks described are considered comparable to the risks associated with these diagnostic procedures during the initial diagnostic pretreatment work-up. The additional examinations will be scheduled in combination with standard diagnostic scans, radiation treatment or standard follow-up appointments. For the patients included in the study, there is no individual benefit. There are no risks specifically related to the blood samples that will be collected at three time points. These will be collected accompanied with regular venipunctures as much as possible, e.g. with chemotherapy administration or accompanied with the intravenous cannulas placed for the PET-CT or MRI scans related to the current study.

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

• Histologically confirmed squamous cell carcinoma or adenocarcinoma of the esophagus or gastroesophageal junction (i.e. tumors involving both cardia and esophagus on endoscopy)
• Potentially resectable locally advanced esophageal tumor (cT1b-4a N0-3 M0): based on standard primary staging by EUS and 18F-FDG PET-CT
• Scheduled to receive neoadjuvant chemoradiotherapy according to the CROSS-regimen: weekly administration of carboplatin and paclitaxel for 5 weeks and concurrent radiotherapy (41.4Gy in 23 fractions, 5 days per week) followed by esophagectomy
• Age > 18 years
• Signed informed consent

Exclusion criteria

• Patients who meet exclusion criteria for MRI
• Patients who meet exclusion criteria for intravenous gadolinium-based contrast:
o Glomerular Filtration Rate (GFR) of <30 mL/min/1.73m2
o Nephrogenic Systemic Fibrosis (strict contra-indication for gadolinium-based contrast)
o Known allergy for gadolinium-based contrast
• Patients with a blood plasma glucose concentration >10 mmol/L or poorly controlled diabetes mellitus

• Irradical endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) of primary tumor prior to start of neoadjuvant chemoradiotherapy
• Pregnant or breast-feeding patients

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-06-2018
Enrollment:	200
Type:	Actual

Ethics review

Approved WMO Date:	06-03-2018
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	02-08-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	17-07-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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
ClinicalTrials.gov	NCT03474341
CCMO	NL62881.041.17