The feasibility of preparing untreated esophageal adenocarcinoma endoscopic biopsies towards DNA/RNA samples suitable for next-generation sequencing.

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Observational invasive

Summary

ID

NL-OMON42638

Source
ToetsingOnline

Brief title
DNA/RNA from esophagealcarcinoma biopsies suitable for sequencing.

Condition

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

Synonym
esophageal cancer, esophageal carcinoma

Research involving
Human

Sponsors and support

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

Intervention

Keyword: DNA/RNA samples, Esophageal adenocarcinoma, Next generation sequencing, Respons neoajduvant therapy, Untreated biopsies

Outcome measures

Primary outcome

The number of DNA and RNA samples suitable for next-generation sequencing.

To assess this number, the following criteria have to be determined:

- The amount of tumorsamples directly frozen after biopsy

- The percentage of tumorcells in the biopsies

- The amount of DNA in the biopsies

- The amount of RNA in the biopsies

Secondary outcome

not applicable

Study description

Background summary

Esophageal carcinoma is the fastest growing malignancy in the gastrointestinal tract in the Netherlands. In 2014, 2549 patients were diagnosed consisting in 68% of adenocarcinoma and 32% of squamous cell carcinoma. Neoadjuvant chemoradiation combined with radical surgical resection is the standard of treatment in the Netherlands and offers the best chance of cure. Chemoradiation results in a complete tumor response in 25%, partial response in 35% and no response in 40% of the patients (non-responders). Patients with squamous cell carcinoma have a higher reponse rate to chemoradiation compared to patients with adenocarcinoma. Chemoradiation is associated with toxicity, including leukopenia, thrombocytopenia, fatigue, nausea and anorexia. It is of high

clinical importance to identify the non-responders to further refine the treatment regimen, and to apply more selective treatment options. This group of patients suffer from the potential adverse effects without clinical benefit and have surgical delay of 3 months.
As yet, there are no methods available for response prediction to neoadjuvant therapy. Preliminary studies from our research group with tissue microarrays showed an association of the expression of different biomarkers and survival of patients with esophageal adenocarcinoma. The results indicate that expression analysis of many more genes in combination is required for accurate classification.
Next generation sequencing (NGS) can lresult in the identification of expression profiles for predicting the repsonse to neoadjuvant chemoradiation. This will ultimately lead to optimal individualized tailored treatment of patients with esophageal adenocarcinoma. Non-responders will not be exposed to this toxic, ineffective therapies but can be treated directly by surgical resection.
In order to be able to apply NGS, good quality DNA or RNA samples are necessary. The aim of this pilot study will be to determine the feasibility of preparing DNA/RNA samples from untreated esophageal adenocarcinoma biopsies suitable for next-generation sequencing..

Study objective

The feasibility of preparing untreated esophageal adenocarcinoma endoscopic biopsies towards DNA/RNA samples suitable for next-generation sequencing.

Study design

- Patients are selected by the treating physician and informed about the study. If the patient is interested, information about the study is given.
- After at least 24 hours, informed consent is written during the next policlinic visit.
- On the day of the standard endoscopic ultrasonography, the gastroenterologist will take four extra tumor biopsies.
- The PhD candidate will ensure that all biopsies are directly fresh frozen and stored at -80ºC in the tissue biobank. The laboratory manual sampling instructions for sequencing is used for the collecting, processing, storing and shipping of the samples.
- The department of pathology will confirm the diagnosis of esophageal adenocarcinoma and the tumor percentage and evaluate the representativeness of the biopsies.
- Only biopsies with >30% tumor percentage will be used for DNA/RNA extraction.
- DNA or RNA will be extracted from every sample using the automatic setup of QiaSymphony by Hartwig Medical Foundation.
- All biopsy samples with a tumor percentage of at least 30%, a minimum of 500ng DNA, and a minimum of 1 µg RNA can be sequenced under supervision of

prof. Cuppen by Hartwig Medical Foundation. Whole exome sequencing can be applied to analyze DNA with the Agilent SureSelect enrichment followed by Illumina NextSequencing. For RNA sequencing, samples can be prepared with the Illumina Neoprep microfluidics system and sequenced on Illumina Nextsequencing.
- After sequencing, data analysis and interpretation can be performed with the standard CPCT pipelines using BWA and GATK best practice.
- The clinical, surgical and pathological variables of enrolled patients will be kept in our electronic database.

Study burden and risks

Standard endoscopic ultrasonography with taking of biopsies is performed to determine the diagnosis and to make a treatmentplan. Only in rare cases (<1%), a tear or hole (perforation) or bleeding in the esophagus wall can be caused. The taking of additional biopsies is associated with the same risk.

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

Studypopulation: patients who are diagnosed with esophageal adenocarcinoma and who undergo endoscopic ultrasonography.
Inclusion criteria: written informed consent, patients fit for CROSS therapy and surgical resection.

Exclusion criteria

Exclusion criteria: incompetent, <18 year,.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	20
Type:	Anticipated

Ethics review

Approved WMO

Date:	27-10-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Approved WMO

Date:	12-01-2016
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
CCMO	NL54312.041.15