A prospective, explorative cohort study to identify biomarkers of treatment response in oropharyngeal cancer.

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON27421

Source
NTR

Brief title
BIO-ROC

Health condition

Oropharyngeal cancer

Sponsors and support

Primary sponsor: Erasmus MC
Source(s) of monetary or material Support: Department of Radiotherapy, Erasmus MC

Intervention

Outcome measures

Primary outcome

The main endpoint of this study is establishing the relation between the ex vivo radiosensitivity assay and clinical evaluation by physical examination (and MRI imaging, if indicated), at three months after treatment in the complete group of OPC patients included in

this study.
In the ex vivo radiosensitivity assay, the percentage of surviving tumor cells after irradiation (relative to untreated control) is determined. This continuous variable will be related to a categorical outcome of clinical (and radiological, if indicated) evaluation of tumor response, namely: complete response, residual disease or uncertain.

Secondary outcome

- establishing the above mentioned relation in various treatment groups (radiation only, chemo-radiotherapy, bioradiation with cetuximab, radiotherapy with protons instead of photons);
- determining the effect known prognostic factors for head-and-neck SCC (smoking, HPV-status, age, comorbidities) on the above mentioned relation;
- establishing if the relation of ex vivo radiosensitivity assay with the locoregional tumor control of OPC patients treated with (chemo/bio-)radiotherapy at 2 years after treatment. Clinical evaluation will be performed as described in 5.1.1;
- determining the prognostic value, specificity and sensitivity of ctDNA as biomarkers of treatment response (for the subgroup of patients that also participate in the COMPLETE study protocol);
- building a repository of tumor biopsies and blood samples of OPC patients for future testing and validation of new (combinations of) biomarkers to predict treatment outcomes.

Study description

Background summary

Rationale: Oropharyngeal cancer (OPC) is most commonly primarily treated with radiotherapy, with or without addition of systemic agents. Treatment outcomes are highly variable, with approximately 40% of patients experiencing locoregional recurrence (LRR) within 2 years after treatment. Human papillomavirus (HPV) status of the tumor has emerged as an important prognostic factor for overall survival (OS), highlighting the influence of tumor biological properties on the treatment outcomes. However, to date no assays exists to allow prediction of tumor response to radiotherapy on the individual patient’s level.
We have developed an ex vivo assay for tumor radiosensitivity for head-and-neck squamous cell carcinoma (HNSCC). We hypothesize that this assay is able to predict clinical outcomes of tumor treatment. Furthermore, we hypothesize that by combining ex vivo sensitivity assay with tumor characteristics, such as circulating tumor DNA (ctDNA), new response biomarkers would be identified that could be implemented in clinical practice. For that, a repository of OPC patient samples needs to be established.
Objective: The main objective of this study is to assess the relation between ex vivo tumor radiosensitivity assay and clinical tumor response. Furthermore, we will build a repository of both tumor material and liquid biopsies to allow future identifications of biomarkers of treatment response.
Study design: This study is a prospective explorative cohort study for OPC patients treated

with (chemo-/bio)radiotherapy to assess the correlation between tumor ex vivo radiosensitivity with clinical response and to build a biological database for future biomarker identification.
Study population: All OPC patients >=18 years, who are eligible for curative treatment with radiotherapy with or without the addition of systemic agents.
Intervention (if applicable): All eligible patients will be informed about the study during the first visit at the outpatient clinic of a head-and-neck or maxillofacial surgeon. For patients with OPC accessible during physical examination an additional tumor biopsy will be obtained during their second scheduled visit by a head-an-neck or maxillofacial surgeon. For patients without histology confirmation of OPC and requiring general anaesthesia for tumor approach, an extra biopsy next to the diagnostic one will be obtained during a single procedure. For all patient an additional blood sample will be obtained during their second scheduled visit and during the clinical response evaluation visit. Clinical outcomes will be assessed within the standard follow-up scheme. In case of tumor recurrence, patients will be approached for obtaining additional tumor and blood samples.
Main study parameters/endpoints: The primary study endpoint is establishing the relation of the ex vivo radiosensitivity assay with clinical evaluation of tumor response (physical examination and MRI if indicated) at three months after treatment. The secondary endpoints are: establishing this relation for various treatment groups; describing the effect of known prognostic factors on this relation; establishing the relation between ex vivo radiosensitivity and LRR at two years after treatment; and the predictive value of ctDNA in liquid biopsies of OPC patients.
Nature and extent of the burden and risks associated with participation, benefit and group relatedness: This is an explorative prospective cohort study. The burden and risks associated with participation for the patient include those resulting from tumor biopsy (temporary pain and minor local bleeding) and blood sampling (temporary pain and bruising). No additional appointments will be scheduled. The results will be used for research purposes only and will not affect the treatment choices.

Study objective

We hypothesize that tumor ex vivo radiosensitivity correlates with clinical response to (chemo/bio-)radiotherapy in vivo. The manner of relation will be assessed in this study. Moreover, we postulate that establishing a biobank of OPC tumor and blood samples is crucial for successful biomarker discovery. ctDNA is one of the potential biomarkers and will be investigated in this study. The departments and experts of Erasmus MC involved in this project will furthermore test and validate novel (combinations of) biomarkers to predict and eventually improve treatment outcomes.

Study design

Before start of the treatment, 3 months and 2 years after completion of treatment

Intervention

None

Contacts

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Eligibility criteria

Inclusion criteria

To be eligible participating in this study, patients must meet all the following criteria:
• Clinical diagnosis of squamous cell carcinoma of the oropharynx, with or without histological confirmation
• In case of already histology-confirmed oropharyngeal cancer - primary tumor accessible for re-sampling without general anaesthesia
• Eligible for curative treatment with radiotherapy with or without the addition of systemic agents
• Written informed consent obtained
• Age >= 18 years

Exclusion criteria

The following patients are not eligible for participation in this study:
• Patients with histology-confirmed oropharyngeal cancer, safely accessible for re-sampling only under general anaesthesia
• Patients currently under treatment for other malignant disease (unless basal cell carcinoma of the skin)
• Previous radiotherapy in the head and neck area (with overlapping RT area)
• Recurrent oropharyngeal cancer

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-05-2020
Enrollment:	200
Type:	Anticipated

IPD sharing statement

Plan to share IPD: No

Ethics review

Not applicable

Application type:	Not applicable

Study registrations

Followed up by the following (possibly more current) registration

ID: 52756
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL8450
CCMO	NL73248.078.20
OMON	NL-OMON52756

Study results