Early detection of head and neck cancer relapse by expression profiling of blood platelets and/or ctDNA analysis in plasma and oral rinses

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Accuracy of early detection of recurrent/metastatic disease in HNSCC patients treated for cure, and the median and range of time intervals between relapse and presence of ctDNA in plasma and oral rinses as well as TEPs.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON49182

Source
ToetsingOnline

Brief title
Early detection of head and neck cancer relapse

Condition

- Other condition

Synonym
head and neck cancer, Squamous Cell Carcinoma of Head and Neck

Health condition

Hoofd-hals neoplasmata maligne

Research involving

Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: KWF kankerbestrijding

Intervention

Keyword: 1. Circulating tumor DNA, 2. Squamous Cell Carcinoma of Head and Neck, 3. Recurrence

Outcome measures

Primary outcome

Endpoints of the study are the accuracy of early detection of relapse by ctDNA

and/or TEP analyses in head and neck cancer patients during follow-up.

Secondary outcome

- The median time frame of a positive test and the diagnosis of relapse

- The presence of ctDNA in persurgery wound rinses as risk factor for relapse

- Association of mutations in ctDNA with primary tumor and relapse

- The role of intratumor genetic heterogeneity between primary tumor and

relapse in relation to ctDNA detection

Study description

Background summary

Head and neck squamous cell carcinomas (HNSCC) arise in the mucosal lining of the upper aerodigestive tract and are caused by smoking and alcohol consumption or human papillomavirus (HPV) infection. Most HNSCC patients present with advanced stage of disease. Tumors are treated by radiotherapy, chemoradiotherapy, the combination of cisplatin with concomitant radiotherapy, or surgery with or without postoperative (chemo)radiotherapy. Locoregional recurrences occur in 30-40% of advanced stage patients and are difficult to manage as these are mostly detected late. When detected early, re-irradiation

and particularly salvage surgery are curative treatment options, but at present only a minority of patients qualify for salvage surgery. Most reliable methods for diagnosing recurrent disease are FDG-PET and examination under general anesthesia with biopsy, but both are unsuited for screening in routine. Other imaging modalities are too insensitive. Biomarkers for early detection in body fluids as a screening assay for early diagnosis of relapse would be a major improvement in the early detection and management of recurrent disease. Liquid biopsy may guide FDG-PET imaging and/or examination under general anesthesia, and lead to earlier detection of recurrent disease and consequently improved clinical management survival of patients. In this study we focus on detection of circulating tumor DNA (ctDNA) in plasma and oral rinses as well as tumor-educated platelets (TEPs).

Tumor DNA circulates in the bloodstream and can be detected in plasma by DNA sequencing. Both copy number alteration (CNA) profiling as well as ultradeep target enrichment sequencing for mutations have been employed in preliminary studies. We have combined low coverage whole genome sequencing for copy number changes and HPV presence, with high coverage target-enrichment sequencing for mutations in a single assay. We have analyzed ctDNA of 40 HNSCC patients and 20 controls, and ctDNA was found in 78% of patients irrespective of HPV status, and not in controls.

A second potential screenings assay is the detection of tumor-educated platelets (TEPs). Blood platelets circulate through the body including the tumor and take up exosomes from the tumor, which educates them to TEPs. It has been shown that the RNA profiles of these TEPs can be used to detect the presence of a tumor. In a small pilot study, we have shown that this is also the case for head and neck squamous cell carcinoma (HNSCC). In this pre-study, analyses of 45 samples from HNSCC patients showed that HNSCC could be detected with an accuracy of 91%, and in more recent analyses this improved to 98%.

Study objective

Accuracy of early detection of recurrent/metastatic disease in HNSCC patients treated for cure, and the median and range of time intervals between relapse and presence of ctDNA in plasma and oral rinses as well as TEPs.

Study design

This is a prospective observational cohort study. Tumor material, plasma and oral rinses will be collected at baseline and during follow-up of enrolled patients. In this study we will assess the accuracy of ctDNA detection in oral rinses and blood and TEP profiles for early detection of relapsed disease.

Study burden and risks

Under general anesthesia 1-3 extra biopsies next to the standard biopsy will be taken of primary tumor and relapse, and blood and an oral rinse will be collected. For surgically treated patients we will also collect the persurgical rinse fluid in addition. Risk and discomfort will be minimal. At all scheduled follow-up visits (on average 10x) additional blood samples and oral rinses will be collected, which is of low risk and limited burden. Adverse events from extra biopsies or blood withdrawal are not expected. The tests are still experimental, and positive findings have formally no scientific meaning. However, the mutations in the tumor are known and when mutations disappear and reappear in the blood, we will report this to the treating physician and discuss it in the multidisciplinary team that might decide on examination under general anesthesia. This will not influence the main endpoint of the study: early detection of relapse. We will record changes in routine clinical management.

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

Patients must have an HNSCC, sufficient knowledge of the Dutch language to understand the meaning of the study as described in the patient information, signed informed consent for the study, be 18 years of age or older

Exclusion criteria

Patiets who are scheduled for palliative treatment

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	06-05-2021
Enrollment:	94
Type:	Actual

Ethics review

Approved WMO

Date:	20-11-2020
Application type:	First submission
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

ID: 29189
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL72940.029.20
OMON	NL-OMON29189