Personalized follow-up in HPV-related oropharyngeal cancer patients using liquid biopsies

Published: 04-09-2024
Last updated: 07-03-2025

The aim of the proposed study is to investigate the accuracy of a liquid biopsy test using ddPCR for HPV DNA in a standardized follow-up setting for the detection of residual disease and/or (early) tumor recurrence in HPV-related oropharyngeal...

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

Summary

ID

NL-OMON56995

Source
ToetsingOnline

Brief title
Follow-up of HPV+ oropharyngeal cancer patients using liquid biopsies

Condition

- Other condition

Synonym
Oropharyngeal cancer, throat cancer

Health condition

Hoofd-hals oncologie

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Follow-up, Human Papillomavirus, Liquid biopsies, Oropharyngeal cancer

Outcome measures

Primary outcome

of HPV DNA detection in blood plasma compared to standard clinical follow-up (including physical examination, usually with imaging) at 3-4 months post-treatment for the identification of residual tumor and/or tumor recurrences.

Secondary outcome

As a secondary parameter, we will evaluate the accuracy of multiple liquid biopsies over a 2-year follow-up period and assess the correlation between plasma HPV DNA levels and the development of tumor recurrences over time. In addition, we will determine the most accurate timing and frequency of blood collection moments in terms of recurrence prediction. Moreover, we will assess cost-effectiveness of liquid biopsies as a follow-up strategy. Patient characteristics that could correlate to HPV DNA plasma levels and may be a confounder for study results will also be collected, including; plasma HPV DNA levels at baseline (before treatment), gender, age, comorbidities, smoking status, alcohol consumption, HPV type, physical status, viral load, and clinical and pathological tumor characteristics.

Study description

Background summary

The incidence of human papillomavirus (HPV)-related head and neck cancer is increasing worldwide and is expected to rise in coming decades. Typically, this tumor type is located in the oropharynx. In the Netherlands, the portion of HPV-related oropharyngeal tumors increased from 5% in 1990 to up to 50% in recent years. After treatment with (chemo)radiotherapy, follow- up visits are scheduled to detect possible recurrences in an early stage. Although HPV-related oropharyngeal cancer generally has a good prognosis, 10-20% of patients will develop recurrent tumors, mainly within the first 2 years after treatment. Despite this variation in risk of recurrence and treatment-related side effects, the current follow-up in The Netherlands is organized according to a *one-size-fits-all* protocol, consisting of 17 hospital visits, including physical examination, within the first 5 years. In most centres, response evaluation is performed using MRI or PET-CT three to four months after the end of treatment. Recent Dutch studies show that this follow-up shows a 67% sensitivity and a positive predictive value of 20%, meaning that not all recurrences are identified and only 1 in 5 suspected recurrences turn out to be a true relapse. Therefore, this strategy does not seem to be cost-effective, nor does it fit with the understandings of good quality of care, in which personal care, adapted to individual needs, preferences, and values is highly important. Liquid biopsies have emerged as an innovative and promising diagnostic approach for the surveillance of oncological patients. For HPV-related oropharyngeal cancer, circulating HPV DNA has shown to be a very accurate biomarker for residual tumor and (early) recurrences. We expect that liquid biopsy-based testing will enable earlier and more accurate detection of recurrent tumors, resulting in improved survival and increased quality of life for patients.

Study objective

The aim of the proposed study is to investigate the accuracy of a liquid biopsy test using ddPCR for HPV DNA in a standardized follow-up setting for the detection of residual disease and/or (early) tumor recurrence in HPV-related oropharyngeal cancer patients. The accuracy of our liquid biopsy test will be compared to the current standard follow-up, consisting of hospital visits and physical examinations. Validation of our liquid biopsy test, using standardized blood collection moments, is an essential step towards implementation in clinical practice.

Study design

We propose to conduct a prospective, multicenter study, including patients that

are treated for HPV-related oropharyngeal cancer one of the participating NWHHT centers. A single-arm study design is chosen, directly comparing the accuracy of the liquid biopsy test to standard follow-up. Blood samples will be collected once before start of treatment and at every routine follow-up visit (every 2-3 months) for the first 2 years after the end of treatment. This follow-up period is chosen because the vast majority of recurrences present during the first 2 years after the end of treatment. Blood samples from inclusion centers will be shipped to the UMCU and MUMC+, where DNA will be isolated from blood plasma and HPV DNA will be detected using digital droplet PCR (ddPCR). This is a very sensitive method, which is able to quantify the presence of HPV DNA, and is already applied for diagnostic purposes in molecular diagnostics, validated under ISO15189 standards.

Study burden and risks

In the context of this study, participants will undergo a total of 11 blood collection moments; once before treatment and 10 times during a 2-year follow-up period after the end of treatment. These blood collection moments are timed with hospital visits for standard follow-up, so extra hospital visits are not necessary. Per blood sampling, 30 ml peripheral blood will be drawn following standard procedures. Participation will have minimal risks for patients. The withdrawal of venous blood (30 ml) is a regular diagnostic procedure and will be performed by qualified and experienced doctors and/or nurses in compliance with the safety guidelines of both hospitals. Blood collection could causing local pain and bruising. However, this is mostly harmless and recovers within a few days. Therefore, participation in this study will lead to minimal time investment without important risks for the health of the subjects.

Contacts

Public
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584CX
NL
Scientific
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584CX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
- Any age 18 years or older;
- Confirmed diagnosis of HPV-positive squamous cell carcinoma in the oropharynx (positive for p16 and/or HPV DNA);
- Undergoing curative treatment and follow-up in one of the participating centers;
- Being able to provide written informed consent;

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- The presence of distant metastases at diagnosis, except for regional (cervical) lymph node metastases;
- Any other known HPV-related malignancies (e.g. uterine cervix, anal, penile carcinomas);
- Unable to provide written informed consent;

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):	21-10-2024
Enrollment:	278
Type:	Actual

Ethics review

Approved WMO Date:	04-09-2024
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	13-02-2025
Application type:	Amendment
Review commission:	METC NedMec

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	NL83769.041.23