Longitudinal analysis of head and neck cancer-specific immunity in patients treated with (salvage) surgery

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Aim of studyTo investigate whether patients with disease eligible for (salvage) surgery would potentially benefit from immunotherapy, we want to study the anti-tumor reactivity of T cells that have infiltrated the tumor. Infiltration of T cells in...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms benign
Study type	Observational invasive

Summary

ID

NL-OMON42765

Source
ToetsingOnline

Brief title
Tumor-specific immunity in HNSCC treated with surgery

Condition

- Miscellaneous and site unspecified neoplasms benign
- Head and neck therapeutic procedures

Synonym
head and neck cancer, squamous cell carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: private funding

Intervention

Keyword: HNSCC, surgery, T-cell

Outcome measures

Primary outcome

a. To assess the presence and functionality of tumor-specific T cells as

potential target for immunotherapy.

b. To find potential predictive and/or prognostic markers in biopsied tumor

material and peripheral blood.

c. To study the kinetics of tumor-specific T cell populations in the tumor and

blood over time, and the effect of treatment on that.

Secondary outcome

na

Study description

Background summary

Longitudinal analysis of head and neck cancer-specific immunity in patients treated with (salvage) surgery.

A vast majority of head and neck squamous cell carcinoma (HNSCC) patients presents with advanced disease treated by either extensive surgery and / or cisplatin chemoradiation (CRT). Despite these intensive treatment regimens the overall survival of these patients is limited to 40-50% at 5 years, without reliable predictive or prognostic biomarker.

Especially in case of surgically treated patients with advanced HPV negative disease of the oral cavity, overall survival is limited to 30%-40% at 5 years, while in case of salvage surgery after (C)RT radical excision is one of the main concerns and clinical outcome may be maximum 10-20%. Moreover, these patients suffer significantly impaired quality of the rest of their life due to fistulas and mutilation of the face and dysfunction of the upper aerodigestive

tract. This specific patient population did not experience any improvement in survival rates for the past 30-40 years despite advances in reconstruction surgery and the addition of cisplatin to RT in adjuvant setting.

Recently, immunotherapy has shown its effect in patients with a broad range of tumor types, including advanced melanoma and non-small cell lung carcinoma. Tumors with a high mutational load have shown increased immunogenicity and are therefore more likely to benefit from immunotherapy. Especially tumors of patients with HPV negative HNSCC (as tumors of oral cavity) are characterized by a substantial mutational load. Furthermore, promising results concerning immunotherapy for HNSCC patients were presented at ASCO 2015, as pembrolizumab has indeed shown partial response in 25% of recurrent or metastasized patients with either HPV positive or negative disease and independent of PD1 expression. In this study, 132 HNSCC -originating from various anatomical sites- patients were included with recurrent and metastatic disease in a palliative setting.

However, a longitudinal analysis of tumor-specific T cells in patients with HNSCC eligible for (salvage) surgery in a curative setting has not been performed. We wish to study tumor-specific T-cells in RT and chemotherapy naïve patients with SCC of the oral cavity submitted to major surgery (+- (C)RT) with curative intent OR patients eligible for curative salvage surgery (after (C)RT). The results of our study will provide us with a rationale for further study and for the potential usage of immunotherapies (neo)adjuvant to surgical intervention in this specific patient subgroup with an urgent need for improved clinical outcome.

Study objective

Aim of study
To investigate whether patients with disease eligible for (salvage) surgery would potentially benefit from immunotherapy, we want to study the anti-tumor reactivity of T cells that have infiltrated the tumor. Infiltration of T cells in the tumors will be analyzed by using immunohistochemistry. Furthermore, immune infiltrates will be isolated from tumor biopsies taken of the tumor to study the functionality and anti-tumor reactivity of the T cells in the tumor. Transcriptional profiling will be done on T cells from the tumor in collaboration with an international collaborator.

In addition, T cell populations in the peripheral blood will be analyzed for the presence of tumor specific T cells as well to study the kinetics of a possible tumor specific T cell population in blood over time. For this, blood samples taken before and after treatment are required from patients participating in this study. If necessary, T cells from peripheral blood will be used for anti-tumor reactivity assays if the T cell infiltrate from the tumor is not sufficient for performing these assays.

Thirdly, the mutational load in the tumor will be investigated in order to find

predictive or prognostic markers for the response to immunotherapy. DNA and RNA from the tumor will be used for sequencing to determine somatic mutations in the tumor.

Analyses of the tumor biopsies and blood samples will either be done in house or in collaboration with third parties outside the NKI-AVL.

Study design

Patients will be enrolled in this study only after signing of the ICF.

First tumor tissue will be taken during curative surgery.

Blood will be taken:
1. within 2 weeks prior to surgery (during last routine appointment before surgery)
2: within 1 week post surgery, and week 4-5 after surgery (during first routine appointment after surgery or at start (C)RT)
3: every 3 months after surgery, either with or without adjuvant (C)RT, the remaining 1st year of FU after treatment
4. every 4 months during the 2nd year of FU.
Together, this is 500 mL blood in 2 year time FU, in case of complete remission of the tumor.

In case of disease progression within 2 year FU time, the above scheme will be left alone, and blood samples will be taken every 3 months 50mL, for a maximum of 9 months, therefore in total 3 times an extra blood sample per patient.

In case of disease progression after the 2 years FU, extra blood will be taken every 3 months 50 mL, maximum 9 months, thus maximum 3 times per patient.

In case of disease progression within 2-3 years extra tumor tissue will be taken during routine diagnostic work-up

Study burden and risks

No toxicity is expected from drawing blood samples. As tumor biopsies are taken during curative surgical excision of the tumor, no extra burden will be implied on the patients. Tumor biopsies will not interfere with a proper diagnostic pathology report after surgery. In case of disease progression or relapse of tumor within the follow-up of 2-3 years, tumor tissue samples will be obtained, only when easily accessible and limited complication risks; for example easily accessible lymph nodes, primary tumors, subcutaneous or other distant metastases.

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

a. Histologically proven HPV positive or negative HNSCC with an indication for (salvage) surgery with/without adjuvant (C)RT in a curative setting
b. Tumor site: oral cavity, and in case of salvage surgery: all sites
c. Age above 18 years
d. Performance score WHO 0,1 or 2 at time of study entry
e. Written ICF

Exclusion criteria

a. The use of immunosuppressive drugs at start of the treatment
b. Anemia < 6.0 mmol/L

c. In case of disease relapse or progression: Any bleeding disorder or anti-coagulation therapy, that cannot be discontinued or corrected, that significantly increases the risk of a bleeding due to the biopsy.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-04-2016
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Date:	20-11-2015
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

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	NL54413.031.15