The state of the (sentinel) lymph node and tumour microenvironment in patients with HPV-positive and HPV-negative cancer of the vulva.

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Reproductive neoplasms female malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON44257

Source
ToetsingOnline

Brief title
Micro environment lymphnodes and tumour vulvar cancer

Condition

- Reproductive neoplasms female malignant and unspecified

Synonym
vulva carcinoma, vulvar cancer

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis

Source(s) of monetary or material Support: KWF-subsidie

Intervention

Keyword: HPV, Lymph nodes, Vulvar cancer

Outcome measures

Primary outcome

Different subsets of the microenvironment in patients with vulvar cancer will be measured by the use of multi-color flow cytometry and/or CyTOF mass cytometry and immunohistochemistry.

Secondary outcome

- to assess the differences of the microenvironment in HPV-positive and HPV-negative (sentinel) lymph nodes.

- to assess the difference of the microenvironment of tumour-negative and metastatic (sentinel) lymph nodes.

- to assess the difference of the microenvironment of sentinel lymph node(s) and non-sentinel lymph nodes.

- to assess the differences of the microenvironment of the (sentinel) lymph nodes and the primary tumour

Study description

Background summary

Vulvar cancer most frequently occurs in women 65 to 75 years of age. Squamous cell cancer of the vulva can be developed in at least two ways. In up to half of all cases, human papilloma virus (HPV) infection appears to have an important role, and are often found along with areas of vulvar intraepithelial neoplasia (VIN). The women who have these cancers tend to be younger and are often smokers.

The second process by which squamous cancer of the vulva might develop does not involve HPV infection and are usually diagnosed in older women (over age 55). These women may have lichen sclerosis and may also have the differentiated type of VIN.
Other types of vulvar cancer comprises adenocarcinoma which may start in the cells of the Bartholin glands or is found in patients with vulvar Paget disease and melanoma of the vulva which develops from cells producing pigment in the skin. This happens usually on sun-exposed areas, but can also start in areas as the vulva or vagina.
Sentinel lymph nodes are the first lymph nodes that are under the influence of tumour-derived factors and in which an immune response can be generated by the activation of naive T and B cells. Thus the state of the sentinel lymph node microenvironment is critical in the initial decision between activation and suppression of the immune system by the primary tumour. A better understanding of the microenvironment of the vulvar sentinel lymph node is therefore critical for the development of new immunotherapeutic strategies. Also non sentinel lymph nodes can be influenced in their microenvironment, due to draining tumour derived factors from the sentinel lymph nodes.

Study objective

The primary objective of this study is to analyse the microenvironment of the tumour, (sentinel) lymph nodes (i.e. various T-cell populations, antigen presenting cells and myeloid-derived suppressor cells) in patients with vulvar carcinoma.
The secondary objectives of this study are to assess the differences of the microenvironment in HPV-positive and HPV-negative (sentinel) lymph nodes; the difference of the microenvironment of tumour-negative and metastatic (sentinel) lymph nodes.
Exploratory objectives of this study are to analyse the difference in microenvironment in (sentinel) lymph nodes; and to analyse the difference in the (sentinel) lymph nodes compared to the primary tumour.

Study design

This is an exploratory study to further delineate the microenvironment of (sentinel) lymph nodes in HPV-positive and HPV-negative vulvar cancer.

Study burden and risks

The isolation of lymph node cell samples via scrapings of the longitudinal cutting edges of lymph nodes that are processed for diagnosis may carry a very small risk for a false-negative diagnosis for the presence of metastases in lymph nodes because a little bit of lymph node material is removed before the lymph node is processed according to standard procedures. Notably, a surgically dissected lymph node is cut through the longitudinal axis as part of the

standard procedures in the department of Pathology. Then the lymph node is paraffin embedded. From each half only one section is taken for diagnosis. The section used for diagnosis follows the cutting of several sections, a procedure which is needed to have an optimal section cut off the embedded lymph node. It should be appreciated that there is always loss of lymph node material before a diagnosis can be made. Also in case of a sentinel node procedure only a few sections are used for diagnosis. This indicates that there will always be a small risk for a false -negative diagnosis. The department of Pathology considers the chance of missing a metastasis in a lymph node by introduction of scraping the cutting edge of the lymph nodes very small, but they cannot exclude it.

Patiënts will be asked to donate 2x 10 ml blood for further analysis (at two different timepoints).

Performing a sentinel node procedure extra (only using patent blue), directly followed by a complete lymph node dissection gives a small chance on an allergic reaction. This procedure gives no benefit for the patient and is to determine the difference in microenvironment between sentinel and non-sentinel lymph nodes.

In case of a lymph node debulking, a small tumour biopsy will be performed on the surgery room. This carries a small risk of infection/bleeding, but as the patient will be hospitalized for a couple of days, this can be adequately monitored and/or treated.

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

Age >= 18 years at start of the study;
Primary carcinoma of the vulva with an indication for sentinel node procedure or inguinofemoral lymphadenectomy;
Operation at the NKI-AVL or AMC/VUmc;
Signed informed consent.

Exclusion criteria

Patiënts < 18 years at start of the study;
Patiënts who had previous therapy for macro invasive vulvar cancer (including sentinel node procedure) will not participate in the sentinel node part of the study.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-06-2018
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO

Date:	16-02-2018
Application type:	First submission
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

ID: 25060
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL61965.031.17
Other	NTRcode volgt