Testing the safety and immune response of HPV-DNA vaccination in patients with a HPV-positive preinvasive lesion of the vulva.

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON27857

Source
NTR

Brief title
SEVEN

Health condition

VIN III lesion, immunotherapy, HPV

VIN III laesie, immuuntherapie, HPV

Sponsors and support

Primary sponsor: NKI-AVL
Source(s) of monetary or material Support: This project has received funding from the European Union’s Seventh Programme for research, technological development and demonstration under grant agreement No 304810.

Intervention

Outcome measures

Primary outcome

* To study the safety and toxicity of two different doses of the naked DNA vaccine encoding the shuffled HPV16 E7 gene products (TTFC-E7SH).

* To study the HPV-specific immune response in two different doses of TTFC-E7SH.

Secondary outcome

* To study the clinical response to vaccination of two different doses of TTFC-E7SH

Exploratory outcomes:

* Local immune response

HPV16-specific proliferative capacity will be tested in triplicate in a 3 day proliferation assay.

* Tumour microenvironment

The effect of vaccination on the tumour microenvironment will be determined by multicolour fluorescent immunohistochemistry.

Study description

Background summary

Human papilloma virus (HPV) infection (genotypes 16 and 18) is strongly associated with the development of squamous cell cancer, such as cancers of the anogenital region and head and neck cancer. HPV16 infection may also cause a chronic skin disorder of the vulva known as vulvar intraepithelial neoplasia (VIN). Patients often have a weak or no spontaneous HPV-specific T-cell response which is thought to be important in the clearance of infection and disease. Because the persistence of oncogenic HPV proteins E6 and E7 is required for carcinogenesis, these viral antigens are exquisite targets for immunotherapeutic interventions.

In this phase I study patients with vulvar intraepithelial neoplasia grade III (VINIII) will be vaccinated with a novel and potent intradermal HPV-DNA vaccination strategy. In preclinical studies this strategy was shown to be much more potent in the induction of (E6 and) E7-specific CD8+ cytotoxic T-cell immunity than existing DNA vaccination strategies, providing a strong rationale for its clinical evaluation.

This study will allow us to define the optimal dosage and value of this novel DNA vaccination strategy for the treatment of HPV16+ (pre)malignancies.

Study objective

HPV16 E7 DNA vaccination may give a HPV-specific T-cell response which is thought to be important in the clearance of infection and disease.

Study design

Vaccination will be on days 0, 3 and 6, and boost vaccination on days 28, 31 and 34.

Anti-HPV T-cell immunity will be evaluated before start of DNA vaccination and at time points 14, 28, 42 and 56 days using peripheral blood mononuclear cells (PBMC).

Lesions will be examined by vulvoscopy, described in detail and measured bi-dimensionally by the same qualified treating physician and a qualified investigator, taking the largest diameters in two dimensions. Drawings will be made on a predesigned vulvoscopy form. In case of multifocality the total lesion size will be determined. Furthermore, monitoring of the lesions by digital photography will take place at time points 0 and 12 weeks after the last vaccination.

Skin biopsies from the vaccination site will be taken at time point t=0 (prior to vaccination), at t=14 and at 42 days.

Biopsies from the VINIII lesion will be taken at time point t=0 and around t=118 days. The effect of vaccination on the VIN lesion microenvironment will be determined.

Intervention

The HPV16 E7 DNA vaccine (TTFC-E7SH) will be injected intradermally on days 0, 3 and 6 using a permanent make-up device, and boost vaccinations after 4 weeks (days 28, 31, and 34) (Derm.MT GmbH, Berlin, Germany). The TTFC-E7SH will be injected at the skin surface area of one of the upper legs, close to the inguinal lymph node area.

Contacts

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Eligibility criteria

Inclusion criteria

* Age above 18 years

* Willing and able to undergo the planned study procedures

* Written informed consent

* Histologically proven visible VINIII lesion (last histology ≤3 months prior to enrolment)

* HPV16+ VINIII lesion (to be determined on archival tumour tissue (≤10 years old); if that is not available a biopsy will be required)

* No indication of an active infectious disease

* No history of autoimmune disease or systemic undercurrent disease which might affect immunocompetence

* Adequate bonemarrow, renal function and liver function

Exclusion criteria

* Prior treatment with anti-HPV agents

* Participation in a study with another investigational drug within 30 days prior to the enrolment in this study

* Severe cardiac, respiratory or metabolic disease

* Use of steroids or other immunosuppressive drugs

* Use of oral anticoagulant drugs

* History of a malignancy except curatively treated low-stage tumour

* Severe infections requiring antibiotic

* Any treatment for the VINIII lesion within 6 weeks prior to enrolment

* Lactation or pregnancy (if applicable)

* Not willing to take adequate contraceptive measures (if applicable)

Study design

Design

Study type:	Interventional
Intervention model:	Other
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-06-2014
Enrollment:	12
Type:	Actual

Ethics review

Positive opinion

Date:	23-05-2014
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 40423
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL4474
NTR-old	NTR4607
CCMO	NL46637.000.13
OMON	NL-OMON40423

Study results