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

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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.

Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON27857

Bron
Nationaal Trial Register

Verkorte titel
SEVEN

Aandoening

VIN III lesion, immunotherapy, HPV

VIN III laesie, immuuntherapie, HPV

Ondersteuning

Primaire sponsor: NKI-AVL
Overige ondersteuning: This project has received funding from the European Union's Seventh Programme for research, technological development and demonstration under grant agreement No 304810.

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

* 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.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

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.

Onderzoeksproduct en/of interventie

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.

Contactpersonen

Publiek

Leiden University Medical Center

Department of Gynaecology
 PO Box 9600
G. Kenter
Albinusdreef 2
Leiden 2300 RC
The Netherlands
+31 (0)71-5263332

Wetenschappelijk

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Department of Gynaecology
 PO Box 9600
G. Kenter
Albinusdreef 2
Leiden 2300 RC
The Netherlands
+31 (0)71-5263332

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

* 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

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

* 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)

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Anders
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	01-06-2014
Aantal proefpersonen:	12
Type:	Werkelijke startdatum

Ethische beoordeling

Positief advies

Datum:	23-05-2014
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 40423
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

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

Resultaten