Wetenschappelijk onderzoek naar de veiligheid van HPV-DNA vaccinatie en reactie van het afweersysteem op deze vaccinatie bij patiënten met een HPV16-positieve afwijking aan de schaamlippen.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON29038

Source
Nationaal Trial Register

Brief title
NS16SIG

Health condition

DNA tattoo vaccination; uVIN; usual vulvar intraepithelial neoplasia; HPV16; sig-HELP-E6SH/E7SH-kdel; vulvaire intraepitheliale neoplasie; HPV vaccinatie

Sponsors and support

Primary sponsor: NKI-AVL
Source(s) of monetary or material Support: NKI-AVL

Intervention

Outcome measures

Primary outcome

Primary objectives:

• To study the systemic HPV-specific immune response of two naked DNA vaccines encoding sig-HELP-kdel and shuffled HPV16 E6 or E7 gene products (sig-HELPE6SH/E7SH-kdel).

Secondary outcome

Secondary objective:

• To study the safety of sig-HELP-E6SH/E7SH-kdel.

• To study the clinical response to vaccination of sig-HELP-E6SH/E7SH-kdel.

Exploratory objectives:

• To study the migratory capacity of HPV16-specific T cells by analysis of their presence in vaccine sites.

• The effect of vaccination on the immune infiltrate in VIN lesion microenvironment will be determined by multicolour fluorescent immunohistochemistry.

Study description

Background summary

This is a phase I/II trial to evaluate the toxicity, immunogenicity and clinical response of two novel HPV DNA vaccines (sig-HELP-E6SH-kdel and sig-HELPE7SH-kdel), applied by DNA tattoo vaccination, in uVIN patients. This study will allow us to define the optimal dosis and value of these HPV DNA vaccines for the treatment of HPV16+ (pre)malignancies. The first cohort of patients (n=5) will be vaccinated with 2 mg of sig-HELP-E6SH/E7SH-kdel on days 0, 14, 28 and 42. Just before administration, 1 mg of sig-HELP-E6SH-kdel will be mixed with 1 mg of sig-HELP-E7SH-kdel to have 2 mg of the combined E6SH/E7SH. After all 5 patients received all vaccination, we will perform an interim analysis by flow cytometry. There are 2 possible scenarios after the interim analysis:

1. Acceptable immune response

2. Non acceptable immune response

Depending on the outcome of the interim analysis we will continue with the second cohort of patients.

1. Additional cohort of 9 patients

2. Termination of the trial

Study objective

This study will allow us to define the optimal dosis and value of these HPV DNA vaccines for the treatment of HPV16+ (pre)malignancies.

Study design

Day -30 to 1: screening. Day 0: vaccination, PBMCs. Day 14: vaccination. Day 28: vaccination, PBMCs. Day 42: vaccination. Day 56: follow-uw, PBMC. Day 84: follow-up, PBMC. Month 3: follow-up, biopsy uVIN. Month 6: follow-up. Month 9: follow-up. Month 12: follow-up.

Intervention

This is a phase I/II trial to evaluate the toxicity, immunogenicity and clinical response of two novel HPV DNA vaccines (sig-HELP-E6SH-kdel and sig-HELPE7SH-kdel), applied by DNA tattoo vaccination, in uVIN patients. This study will allow us to define the optimal dosis and value of these HPV DNA vaccines for the treatment of HPV16+ (pre)malignancies. The first cohort of patients (n=5) will be vaccinated with 2 mg of sig-HELP-E6SH/E7SH-kdel on days 0, 14, 28 and 42. Just before administration, 1 mg of sig-HELP-E6SH-kdel will be mixed with 1 mg of sig-HELP-E7SH-kdel to have 2 mg of the combined E6SH/E7SH. After all 5 patients received all vaccination, we will perform an interim analysis by flow cytometry. There are 2 possible scenarios after the interim analysis:

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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 uVIN lesion (histology ≤3 months prior to enrolment and at least 6 weeks after last treatment)

• HPV16-positive VIN lesion (to be determined on archival tumour tissue (≤10 years old); if not available a new biopsy will be required)

• No indication of an active infectious disease: HIV, HCV and HBV negative

• No history of autoimmune disease or systematic undercurrent disease which might affect immunocompetence

• Adequate bone marrow (WBC > 3.0/nL, platelets > 100/nL), renal function (creatinine

clearance > 40 mL/min), and liver function (bilirubin < 1.5 x ULN, normal blood coagulation)

Exclusion criteria

• Prior treatment with anti-HPV agents

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

• Severe cardiac, respiratory, or metabolic disease

• Use of systemic steroids or other immunosuppressive drugs

• Use of oral anticoagulant drugs (except ascal)

• Severe infections requiring antibiotics

• Any treatment for the uVIN lesion within 6 weeks prior to the enrolment (including imiquimod)

• Lactation or pregnancy (if applicable)

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

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	05-01-2017

Enrollment:	0
Type:	Anticipated

Ethics review

Positive opinion Date:	21-06-2018
Application type:	First submission

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
NTR-new	NL7139
NTR-old	NTR7337
Other	HPV16 E6-E7 : N16SIG

Study results