The effect of HPV16 peptide vaccination on the local immune response in woman with high grade HPV16+ pre-malignant disorders of the uterine cervix, a placebo controlled phase II study

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This study aims to reveal whether vaccination of women with HPV 16+ cervical intraepithelial neoplasia not only results in a strong systemic T-cell response, but also endows these T-cells with the capacity to infiltrate HPV16-induced lesions....

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cervix disorders (excl infections and inflammations)
Study type	Interventional

Summary

ID

NL-OMON31758

Source
ToetsingOnline

Brief title
Immunotherapy in CIN II-III

Condition

- Cervix disorders (excl infections and inflammations)

Synonym
Cervical Intraepithelial Neoplasia, cervix lesion

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: KWF kankerbestrijding

Intervention

Keyword: CIN, HPV, immunity, vaccination

Outcome measures

Primary outcome

Before first vaccination and 4 weeks after second vaccination (week 7),

histological material will be tested for the quantity of different infiltrating

immune cells.

Secondary outcome

Characterisation of the HPV16-specific infiltrating T-cells; cytokine milieu

and presence of HPV16.

Study description

Background summary

Patients with (pre-) malignant cervical lesions often have a weak or absent spontaneous HPV-specific T-cell response thought to be important in the clearance of infection and disease. Vaccination with HPV 16 E6 and E7 long peptides is known to give a strong systemic HPV16-specific type 1 T-cell response and seems excellently suited to overcome these deficits. For the rational design of potentially successful vaccine candidates it is important to determine if vaccine-regimens succeed in driving the migration of HPV16+ T-cells into the HPV16+ lesions and to establish whether the presence of such immune cells is related to clearance of HPV16.

Study objective

This study aims to reveal whether vaccination of women with HPV 16+ cervical intraepithelial neoplasia not only results in a strong systemic T-cell response, but also endows these T-cells with the capacity to infiltrate

HPV16-induced lesions. Furthermore it will evaluate the systemic HPV16 E6 and E7 specific T cell immune response and the clearance of the HPV infection in response to vaccination.

Study design

This is a placebo-controlled randomised clinical study.

Intervention

Half of the patients will be vaccinated twice with a mix of HPV E6 and E7 long peptides at a dose of 300µg/peptide, the other half will be vaccinated with a matching placebo.

Study burden and risks

From each study patient, at baseline, cervical swaps and small biopsies will be taken as part of the routine diagnosis of CIN. 4 weeks after second vaccination histological material will be obtained by surgical excision of the cervical lesion. 2-4 weeks after surgery, patients will undergo a skin test. At three occasions during the study 70 mL of peripheral blood will be obtained via venapuncture. At least 4 visits to the LUMC clinics are needed. As compared to the routine treatment of CIN patients, only the vaccinations, the blood draws and the skin testing are extra procedures for this study. The risks for and burden to patients will be minimal considering previous experiences with the same vaccination. The skin testing and vaccinating will be performed under close medical supervision at the gynaecology department*s day care unit at the LUMC.

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

- patients of 18 years and older
- willing and able to comply with the protocol, and provide informed consent in accordance with institutional and regulatory guidelines
- histological evidence of CIN, grade II or III, HPV16 positive
- performance status 1 or 2 at the WHO scale, or 60 on the Karnofsky scale
- baseline laboratory findings; white blood cells (WBC) > 3,000 x 10 9/l, lymphocytes >1,000 x 10 9/l, platelets > 100 x 10 9/l, and hematocrit > 30%, HIV- and HBV-negative
- patients of child-bearing potential should test negative using a pregnancy test and agree to utilize effective contraception or remain abstinent during the entire treatment period of the study

Exclusion criteria

- indication of a current active infectious disease other than HPV16,
- history of an autoimmune disease or other systemic intercurrent disease that might affect patient*s immunocompetence
- history of a second malignancy except curatively treated low-stage tumours with a histology that can be differentiated from the vulvar/cervical cancer type
- radiotherapy, chemotherapy or other potentially immunosuppressive therapy administered within 4 weeks prior to the colposcopy visit

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-12-2006
Enrollment:	34
Type:	Anticipated

Ethics review

Approved WMO Date:	15-12-2006
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-10-2007
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-05-2008
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-10-2009

Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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
EudraCT	EUCTR2006-004443-30-NL
CCMO	NL14015.000.06