The long-term immune response after HPV16 peptide vaccination in woman with low-grade pre-malignant disorders of the uterine cervix, a placebo controlled phase II study

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Evaluation of the capacity of a HPV 16 peptide vaccine to install a long term HPV-specific T cell response, to define the importance of a booster vaccine after 1 year, the induction of Cytotoxic T lymphocyte (CTL) immunity against HPV16E6 and E7 and...

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

Summary

ID

NL-OMON31739

Source
ToetsingOnline

Brief title
Immunotherapy in CINI/ Pap2

Condition

- Cervix disorders (excl infections and inflammations)

Synonym
cervical intraepithelial neoplasia, lesion of the cervix

Research involving
Human

Sponsors and support

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

Intervention

Keyword: HPV, Immunity, Memory, Vaccination

Outcome measures

Primary outcome

By comparing blood drawn at different time points during the study, in vitro analysis will reveal the induction of Cytotoxic T lymphocyte (CTL) immunity against HPV16E6 and E7, induction of HPV16-specific T-helper (Th) type 1 cells to evaluate the capacity of this vaccination strategy to install long term HPV-specific T cell immunity.

Secondary outcome

By comparing the results between the patients receiving a placebo after 1 year and patients boosted with the HPV16 peptides, the capacity of re-vaccination to boost the HPV16-specific response will be evatluated.

Furthermore in vivo analysis via Skin tests will also be used to measure the presence and type of immunity against HPV16 E2, E6- and E7 peptides.

Study description

Background summary

Vaccination with HPV 16 long peptides is known to give a strong systemic HPV16-specific type 1 T-cell response in patients with cervical cancer and VIN. An important factor for a vaccine to be effective is the capacity to create a long term HPV-specific T cell response to provide a long term protective anti tumor effect. The capacity of an HPV 16 long peptide vaccination strategy to

install such a long term immune response and the importance of re-vaccination after one year to boost this response is unknown.

Study objective

Evaluation of the capacity of a HPV 16 peptide vaccine to install a long term HPV-specific T cell response, to define the importance of a booster vaccine after 1 year, the induction of Cytotoxic T lymphocyte (CTL) immunity against HPV16E6 and E7 and the induction of HPV16-specific T-helper (Th) type 1 cells.

Study design

This is a placebo-controlled randomised clinical study.

Intervention

40 Patients will receive two sequential vaccinations containing a dose of 50ug per peptide with a 3-week interval (week 0, 3). After 1 year patients will be randomized to receive a booster vaccine with peptide (n=20) or placebo (n=20). 10 Patients will receive a matching placebo at all three vaccination time points.

Study burden and risks

Blood samples required for in vitro analysis of HPV-specific T cell responses, will be taken at five time points: before the first vaccination (week 0), 4 weeks after the first series of two vaccinations (week 7), before the booster vaccination (week 52), 4 weeks after the booster vaccination (week 56) and 12 months after the booster vaccination (week 104). Skin DTH tests and HPV typing will be performed three times (before the first vaccination, before the boost vaccination and at 2 years). In 2 years 11 visits to the LUMC clinics are needed. 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

- patiënts 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 I or cytological evidence of a persistent PAP II (two consecutive pap II smears with a 6 month interval)
- 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):	31-05-2007
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO Date:	13-12-2006
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	25-10-2007
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	EUCTR2006-004548-22-NL
CCMO	NL14057.000.06