Immune response after Human Papillomavirus vaccination in patients with automimmune disease

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Objective: The primary goal of the current study is to study the immunogenicity and safety of HPV vaccination in patients with an autoimmune disease. Based on retrospective analysis with other vaccines we hypothesize that patients with autoimmune…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Autoimmune disorders
Study type	Observational invasive

Summary

ID

NL-OMON40068

Source
ToetsingOnline

Brief title
HPV study

Condition

- Autoimmune disorders
- Reproductive neoplasms female malignant and unspecified
- Uterine, pelvic and broad ligament disorders

Synonym
JDM, Juvenile Idiopathic Arthritis, SLE

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht

Source(s) of monetary or material Support: Ministerie van OC&W,Universitair Medisch Centrum Utrecht

Intervention

Keyword: autoimmunity, HPV, immune suppression, JIA

Outcome measures

Primary outcome

Primary outcome immunogenicity is defined as the serological immune response measured by antibody levels against HPV serotype 16 & 18. The antibody levels will be measured prior to vaccination, and after 3, 7 and 12 months. Antibody titers over time above the cutoffs 20 and 24 mMU/ml for HPV 16 and 18 or a >=2 fold increase in antibody titers against both serotypes are seen as a positive response and will be analyzed in patients and healthy controls..

Secondary outcome

The secondary outcome is safety of vaccination, measured as activity of the underlying disease. Other secondary outcomes are frequency of common adverse effects, and immunological changes induced by HPV vaccination, such as number and function of cytotoxic T cells and Tregs.

Study description

Background summary

Rationale:
In the Netherlands, the human Papillomavirus (HPV) vaccination will be added to the National Vaccination Program for girls to protect against the development of cervical cancer. The vaccine protects against HPV type 16 & 18, which cause about 75% of cervical cancer. Studies have shown that the vaccine is effective in healthy subjects in preventing infection by HPV 16 & 18. However, no evidence exists on the immunogenicity and safety of HPV vaccination in patients

with an immunesytem disorder, such as autoimmune diseases. Concerns exist that vaccination may cause an aggravation of the underlying disease. In addition, the immune response to vaccination may be diminished due to immunosuppressive therapy or the underlying disease.

Study objective

Objective: The primary goal of the current study is to study the immunogenicity and safety of HPV vaccination in patients with an autoimmune disease. Based on retrospective analysis with other vaccines we hypothesize that patients with autoimmune diseases who are under immunosuppressive medication and patients with a immunesystem disorder are still able to mount a serological response to HPV vaccination (in case of humoral immunodeficiency we assume a protective cellular immune response can be induced); that these HPV antibodies are maintained; and that vaccination is safe. The secondary objective is to study immune regulatory mechanisms induced by vaccination in a subset of patients. We hypothesize HPV-induced regulatory T cells are able to prevent an increase in the activity of an autoimmune disease.

Study design

Study design: multi center prospective observational cohort study.

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:
Burden: included patients will be asked to visit the hospital 4 times in a period of 12 months. During these visits, physical examination will be performed and blood will be obtained for serological and immunological analysis. Most of these visits are combined with routine follow-up and venapunctures of the patients. However, one extra visit to the hospital and vena puncture is expected. 4 ml (extra) blood is obtained four times from all patients for serological analysis. Included healthy controls will have a venapunctures four times during the study, during which 4mL of blood is obtained. In a subset of patients (n=50) and healthy controls (n=15), an additional 18 ml is obtained for immunological analysis.
Risks: participants may experience adverse events of the HPV vaccination.
Benefits: Protection against human Papillomavirusinfection and therefore reduced risk of cervix carcinoma, certainty about protection against HPV 16 & 18 and about safety of HPV vaccination.
Group relatedness: This study can only be done in patients who need this vaccination (i.e. females in the age group 12-17 years) and have an immunesystem disorder, such as JIA, SLE, JDM.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)

Inclusion criteria

Females Who have one of the following immunsystem disorder:
a. Juvenile Idiopathic Arthritis
b. Systemic Lupus Erythematosus
c. Juvenile Dermatomyositis
Current co-medication: all co-medication such as Methotrexate, etanercept, anakinra or infliximab may be continued.
And who are in the following age groups:
a. 12 years (these girls are vaccinated via the National Vaccination Program from September 2009)
b. 13-17 years (these girls are vaccinated during a national vaccination campaign from March-May 2009)

Exclusion criteria

- Refusal to be vaccinated with the HPV vaccine
- Allergic reactions to one of the components of the vaccine.
- Acute, severe disease accompanied with fever. In this case, the moment of vaccination will be postponed for 1 month. A light infection, such as an upper airway infection, is not a reason to postpone the vaccination.
-Proven or suspected cervix carcinoma
-failure to comply

Study design

Design

Study phase:	4
Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-02-2009
Enrollment:	140
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cervarix
Product type:	Medicine
Brand name:	Gardasil/Silgard

Ethics review

Approved WMO Date:	09-02-2009
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	17-02-2009
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	23-06-2009
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-07-2009
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Not approved Date:	08-04-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-06-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	17-06-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO

Date:	07-04-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	02-06-2014
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	14-08-2014
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	EUCTR2008-008169-36-NL
ClinicalTrials.gov	NCT00815282
CCMO	NL26113.000.08