Quadrivalent HPV vaccination after effective treatment of Anal Intraepithelial Neoplasia in HIV+ men (VACCAIN-P)

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON44810

Source
ToetsingOnline

Brief title
HPV vaccination after treatment of anal intraepithelial neoplasia

Condition

- Viral infectious disorders
- Gastrointestinal neoplasms benign

Synonym
anal intraepithelial neoplasia

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: ZON MW programma Goed Gebruik Geneesmiddelen,Sanofi Pasteur MSD: verstrekt Gardasil vaccins

Intervention

Keyword: anal dysplasia, HIV, HPV, vaccination

Outcome measures

Primary outcome

Screening for AIN will be performed by high-resolution anoscopy (HRA), at inclusion (first vaccination) and at last vaccination (6 months), and repeated at 6 and 12 months after the last vaccination. Safety Monitoring for spontaneous adverse events and injection-site reactions will be performed one week after each vaccination and thereafter every 6 months for a total of 12 months of follow-up.

Primary end point will be the cumulative recurrence of HG AIN at 12 months after the last vaccination, as assessed by HRA (High-Resolution Anoscopy), with biopsies taken of suspect lesions.

Secondary outcome

Secondary outcome measures are toxicity/ safety, recurrence of HG AIN at last vaccination and 6 months afterwards, cumulative occurrence of LG AIN at 12 months after the last vaccination, cumulative occurrence of anogenital warts at 12 months after the last vaccination, causative HPV type in recurrent AIN lesions, as assessed by LCM (Laser Capture Microdissection)/ PCR (polymerase

chain reaction), and HPV type-specific antibody response.

Study description

Background summary

Since the introduction of combination antiretroviral therapy (cART), human immunodeficiency virus (HIV)-related morbidity and mortality have considerably decreased. However, as a result of the significantly prolonged life span, new causes of morbidity and mortality have become evident. In particular, anal cancer incidence has increased dramatically in HIV-positive men. Like cervical cancer, anal cancer is causally linked to infections with high-risk papillomaviruses, and is preceded by precursor lesions: anal intraepithelial neoplasia (AIN). Over 90% of HIV-positive MSM (men who have sex with men) have persisting anal HPV (human papilloma virus) infection, and high-grade (HG) AIN is present in 30% of all HIV+ MSM.
As in cervical intraepithelial neoplasia, early diagnosis and treatment of AIN have been advocated to prevent malignancy. Electrocoagulation/ cauterization is standard of care for intra-anal AIN, but after treatment, recurrence of lesions occurs in approx. 50% of cases. This is a major problem in an effective screening program for AIN.

In a nonconcurrent, nonblinded cohort study qHPV (quadrivalent human papilloma virus) vaccination significantly (HR 0.50) reduced HG AIN recurrence among MSM successfully treated for AIN. This is in accordance with findings in women treated for cervical intraepithelial neoplasia. Previous vaccination with quadrivalent HPV vaccine among women who had surgical treatment for HPV related disease significantly reduced the incidence of subsequent HPV related disease, including high grade disease.

Therefore, a strategy that is worth investigating is vaccination with the qHPV vaccine to prevent recurrences in HIV+ MSM who were successfully treated for HG AIN.

Study objective

The primary objective of the current study is to assess the efficacy of qHPV vaccination in preventing recurrence of high-grade AIN in HIV+ MSM with CD4 counts >350 x 10E6/l who were successfully treated for high-grade intra-anal AIN in the past year.

Study design

A multicentre, randomised, double-blind clinical trial in three hospitals in

the Netherlands.

Patients are randomised for vaccination with the quadrivalent HPV vaccine (Gardasil ®) or vaccination with a matching placebo at months 0, 2 and 6.

Intervention

Patients are randomised for vaccination with the quadrivalent HPV vaccine (Gardasil ®) or vaccination with a matching placebo at months 0, 2 and 6. Randomisation will be stratified for complete response versus partial response (from HG AIN to low-grade (LG) AIN) of the initial HG AIN lesion, and for treatment less than 6 months ago versus treatment more than 6 months ago.

Study burden and risks

HIV+ MSM who were successfully treated for HG AIN are still at a 50% risk for recurrences, with additional treatment sessions needed, and an ongoing risk for malignant degeneration of lesions.
Costs of 3 vaccinations are approx. ¤ 400, but if vaccination reduces recurrence rates by 50%, this will be a highly cost-effective intervention, very likely to be introduced into regular care.
For the study, patients will be vaccinated 3 times with the quadrivalent vaccine Gardasil ® or placebo, and will undergo two extra HRA*s. Clinical trial data show that the most common adverse events of Gardasil ® were mild or moderate, so few risks are associated with study participation.

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

• Written informed consent
• HIV+ males having sex with males (MSM), CD4 count > 350/ul.
• Biopsy-proven intra-anal high-grade AIN successfully treated in the past year with cauterization, cryotherapy, Efudix, imiquimod or another form of local treatment. Lesions with regression from HG to Low grade (LG) AIN will also be eligible.
• Lesion (still) in remission at the moment of first vaccination (a maximum interval of 6 weeks between last HRA and first vaccination is allowed).
• Good performance status (a Karnofsky performance score of >= 60 [on a scale of 0 to 100, with higher scores indicating better performance status])
• Normal pretreatment laboratory blood values

Exclusion criteria

• Immunosuppressive medication or other diseases associated with immunodeficiency
• Life expectancy less than one year
• Previous vaccination with the bivalent or quadrivalent HPV vaccine
• History of anal carcinoma

Study design

Design

Study phase:	4
Study type:	Interventional

Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-04-2014
Enrollment:	125
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Gardasil

Ethics review

Approved WMO Date:	11-09-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-10-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-03-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-07-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO Date:	04-02-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-09-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-09-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-02-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2013-002009-70-NL
CCMO	NL45200.018.13