Adjuvant vaccination against HPV in surgical treatment of CIN lesions, a Randomised Controlled Trial.

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Evaluate the efficacy of nonavalent HPV vaccination in women with a CIN lesion who will undergo or have undergone a LEEP in preventing recurrent CIN II-III after 24 months.

Ethical review	Approved WMO
Status	Completed
Health condition type	Reproductive neoplasms female malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON54737

Source
ToetsingOnline

Brief title
VACCIN study

Condition

- Reproductive neoplasms female malignant and unspecified

Synonym
cervical intra-epithelial neoplasia, precursor of cervical cancer

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: ZonMW,Merck Sharp & Dohme (MSD)

Intervention

Keyword: CIN, HPV, LEEP, Vaccination

Outcome measures

Primary outcome

Primary outcome

Recurrence of CIN II-III after 24 months

Secondary outcome

Secondary outcome

1 Recurrence of CIN I-II-III at 6 and 24 months

2 The effect of treatments on HPV DNA presence

3 Pap-smear results

4 Number of LEEP

5 Cost-effectiveness analysis

6 Quality of life

7 Side effects and adverse events

Study description

Background summary

Cervical cancer is preceded by precursor stages: Cervical Intraepithelial Neoplasia Neoplasia, (CIN). These CIN abnormalities are caused by the Human Papilloma virus (HPV) and are mostly found in women in their reproductive age. There is an effective prophylactic vaccine against HPV, given since 2009 in the Netherlands to girls of 12 and 13 years old. This vaccine is very effective against the occurrence of CIN abnormalities in this group. Also, in older women who already had an HPV infection, without CIN abnormalities, the vaccine has shown to be effectively for preventing to develop CIN. The current treatment of CIN II-III (moderate to severe precursor stages) is surgical removal of a part of the cervix. This is called a Loop Electrosurgical Excision Procedure (LEEP).

This treatment has a recurrence rate or residual rate up to 17%. A secondary surgical treatment is necessary in these women. Surgical treatments are associated with bleeding, narrowing of the cervix and infection. The biggest problem, with sometimes lifelong consequences, are the obstetric complications, especially premature birth. This becomes more frequent and more serious after repeated surgical intervention. The (repeated) treatment is also a burden of the women and her loved ones.
HPV is also known to cause other forms of cancer later in life(including pubic cancer, vaginal cancer and anus cancer). This chance is reduced when the virus is cleared.

Hypothesis
Vaccination with the HPV vaccine at the time of surgical intervention reduces the risk of recurrent CIN
abnormalities in unvaccinated women, by an enhanced immune response. This will additionally reduce the risk of other HPV-initiated cancers. The treatment of women
with a CIN abnormalities will thus become more effective and cost-efficient.

Study objective

Evaluate the efficacy of nonavalent HPV vaccination in women with a CIN lesion who will undergo or have undergone a LEEP in preventing recurrent CIN II-III after 24 months.

Study design

Randomized, double blinded, placebo controlled trial

Intervention

Intervention: 0.5 ml nonavalent HPV vaccination. Comparator: placebo vaccination.
Dosing scheme: preferable at day of LEEP(or within 4 weeks), at 2 and 6 month follow-up visits.

The syringes of the placebo and the vaccine will be identical. At the day of LEEP or within 4 weeks after the
LEEP the first vaccination should be administered. The HPV vaccine should be administered according a 3-
dose (0,2 and 6 months) schedule. Vaccination is by intramuscular injection in the deltoid region of the
upper arm or in the higher anterolateral area of the thigh. All three doses should be given within a 1-year
period . We choose a placebo as comparator to minimize selection bias.

Study burden and risks

All included patients receive regular treatment according to the latest Dutch guideline. Risk and burden are linked to protocol procedures. These are routine procedures and carried out by medical qualified personnel. Adverse events and symptoms of the vaccination will be evaluated. The vaccinations and/or the placebo injections may cause side effects or discomfort. However, it is expected that these procedures will generally be well tolerated.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

Dr. Molewaterplein 40
Rotterdam 3015 GD
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

Dr. Molewaterplein 40
Rotterdam 3015 GD
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Women 18 years or older

- Histologically proven CIN II or III
- Patients treated with LEEP (inclusion within 4 weeks after LEEP)

Exclusion criteria

- Prior HPV vaccination
- (Micro-) invasive carcinoma
- Immune-compromised patients
- Pregnancy
- Prior treatment for CIN-lesions
- Insufficient understanding of the Dutch language
- Women allergic to vaccine components

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:	Completed
Start date (anticipated):	17-10-2019
Enrollment:	750
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Gardasil 9

Ethics review

Approved WMO Date:	13-02-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-07-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-10-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-10-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-01-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-02-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-04-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 22561
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2018-002764-94-NL
CCMO	NL66775.078.18
OMON	NL-OMON22561