A phase III, double-blind, randomized, controlled study to evaluate the safety, immunogenicity and efficacy of GlaxoSmithKline Biologicals* HPV 16/18 L1/AS04 vaccine administered intramuscularly according to a three-dose schedule (0, 1, 6 month) in healthy adult female subjects aged 26 years and above.

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* To demonstrate efficacy of the candidate vaccine in the prevention of (1) persistent infection (6-month definition) with HPV-16 or HPV-18 (by polymerase chain reaction [PCR]) and/or (2) histopathologically-confirmed CIN1+ associated with HPV-16 or...

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

Summary

ID

NL-OMON38271

Source
ToetsingOnline

Brief title
Evaluation of HPV-vaccine efficacy in healthy women of 26 years or above

Condition

- Viral infectious disorders
- Reproductive neoplasms female malignant and unspecified
- Cervix disorders (excl infections and inflammations)

Synonym
Cervical cancer, Human Papillomavirus vaccination

Research involving
Human

Sponsors and support

Primary sponsor: GlaxoSmithKline
Source(s) of monetary or material Support: farmaceutische industrie

Intervention

Keyword: adult female, Cervical cancer, HPV vaccine, prevention

Outcome measures

Primary outcome

Co-primary endpoints:

* Persistent infection (6-month definition) with HPV-16 or HPV 18 (by PCR)

and/or histopathologically-confirmed CIN1+ associated with HPV-16 or HPV-18

cervical infection detected within the lesional component of the cervical

tissue specimen (by PCR) (combined endpoint), overall and stratified according

to initial (Month 0) HPV-16 or HPV-18 serostatus (by ELISA).

* Persistent infection (6-month definition) with HPV-16 or HPV 18 (by PCR)

and/or histopathologically-confirmed CIN1+ associated with HPV-16 or HPV-18

cervical infection detected using the HPV TAA, overall and stratified according

to initial (Month 0) HPV-16 or HPV-18 serostatus (by ELISA).

Secondary outcome

Virological endpoints:

* Persistent infection (6-month definition) with HPV-16 or HPV-18 (by PCR), overall and stratified according to initial (Month 0) HPV-16 or HPV-18 serostatus (by ELISA).
* Persistent infection (12-month definition) with HPV-16 or HPV-18 (by PCR), overall and stratified according to initial (Month 0) HPV-16 or HPV-18 serostatus (by ELISA).
* Persistent infection (6-month definition) with oncogenic HPV types (e.g. HPV-16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68, by PCR), individually or in combinations, in subjects HPV DNA negative for the type considered, regardless of initial serostatus.
* Persistent infection (12-month definition) with oncogenic HPV types (e.g. HPV-16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68, by PCR), individually or in combinations, in subjects HPV DNA negative for the type considered, regardless of initial serostatus.

Also several histopathological, cytological, immunogenicity and safety secondary endpoints (see protocol page 125-129).

Study description

Background summary

Human papillomavirus (HPV) infection has been clearly established as the central cause of cervical cancer. GlaxoSmithKline Biologicals has developed a virus-like particle (VLP) vaccine against the high-risk types HPV-16 and HPV-18 formulated with the adjuvant AS04. AS04 is comprised of aluminium salts and

3-deacylated monophosphoryl lipid A (MPL®). In phase II studies, this vaccine has been shown to be safe, immunogenic and efficacious in the prevention of incident and persistent HPV-16/18 infections and associated cytological abnormalities. Although prophylactic vaccination primarily targets adolescents and young adults, vaccination should also be made available to older women who may be (re-) exposed to the virus and may not have generated protective immunity.

Study objective

* To demonstrate efficacy of the candidate vaccine in the prevention of (1) persistent infection (6-month definition) with HPV-16 or HPV-18 (by polymerase chain reaction [PCR]) and/or (2) histopathologically-confirmed CIN1+ associated with HPV-16 or HPV-18 cervical infection detected within the lesional component of the cervical tissue specimen (by PCR), overall and stratified according to initial (Month 0) HPV-16 or HPV-18 serostatus (by enzyme-linked immunosorbent assay [ELISA]).

If efficacy is demonstrated, the following objective will be assessed sequentially:
- To demonstrate efficacy of the candidate vaccine compared with control in the prevention of (1) persistent infection (6-month definition) with HPV-16 or HPV-18 (by PCR) and/or (2) histopathologically-confirmed CIN1+ associated with HPV-16 or HPV-18 cervical infection detected using the HPV TAA, overall and stratified according to initial (Month 0) HPV-16 or HPV-18 serostatus (by ELISA).

Study design

A phase III, double blind, controlled, multicentre study in Asia Pacific, Europe, Latin America and North America, with two parallel groups of 2700 subjects each:
- HPV vaccine group (receiving HPV-16/18 L1/AS04)
- control group (receiving Al(OH)3)
Treatment will be allocated by randomization (1:1). Enrollment will be stratified per region by age and previous HPV history. Three doses of vaccine/control will be administered intramuscularly according to a 0, 1, 6-month schedule. The duration of the study will be 84 months for each subject. There will be seventeen scheduled visits per subject: at Month 0, 1, 6, 7, 12, 18, 24, 30, 36, 42, 48, 54, 60, 66, 72, 78 and 84.

Intervention

One group will receive three HPV (HPV-16/18 L1/AS04) vaccinations (0.5ml, intramuscular) at month 0, 1 en 6
One group will receive three control (Al(OH)3 vaccin) vaccinations (0.5ml,

intramuscular) at month 0, 1 en 6

Study burden and risks

Risks and burden are linked to the protocol procedures, such as vaccination, blood sampling, gynaecological examination, cervical cytology and colposcopy. Although these are routine procedures, carried out by medically qualified personnel, they may cause side effects or discomfort to the volunteers. However, it is expected that these procedures will generally be well-tolerated. Previous studies with the investigational vaccine in approximately 700 healthy adult women showed that most side effects observed (pain, redness and swelling at the vaccination site, tiredness, gastro-intestinal complaints, fever, itching, flu-like symptoms, sore throat) were usually mild, lasting 3-4 days, did not require medical intervention and did not hamper the normal daily activities. No serious, vaccine related adverse events have been reported so far.

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

- A women of at least 26 years of age at the time of the first vaccination
- Free of obvious health problems as established by medical history and clinical examination before entering into the study
- Subject must have intact cervix (e.g. no history of cauterization or surgical treatment involving damage to the transformation zone of the cervix).

Exclusion criteria

See page 58-60 of the study protocol for a complete list of the in- and exclusion criteria.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-03-2006
Enrollment:	360
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cervarix

Ethics review

Approved WMO Date:	27-01-2006
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	16-07-2010
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	03-08-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	25-07-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	10-01-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	25-10-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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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	EUCTR2005-002546-20-NL
ClinicalTrials.gov	NCT00294047
CCMO	NL32795.098.10