Immune modulating effects and safety of Vvax001, a therapeutic Semliki Forest Virus based cancer vaccine, in patients with a history of (pre) malignant cervical lesions.

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The objective of this trial is to assess the immunological activity of Vvax001 by monitoring HPV-16 specific immune responses in order to determine the optimal dose inducing the highest immune responses.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hepatobiliary neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON43094

Source
ToetsingOnline

Brief title
Vvax001 cancer vaccine in (pre) malignant cervical lesions

Condition

- Hepatobiliary neoplasms malignant and unspecified
- Reproductive neoplasms female malignant and unspecified

Synonym
cervical neoplasia/cervical cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: KWF subsidie en ViciniVax (spin-off van UMCG),ViciniVax (spin-off UMCG)

Intervention

Keyword: Cervical neoplasia, Phase 1, Therapeutic immunization

Outcome measures

Primary outcome

The main study endpoint is the immunogenicity of Vvax001. By monitoring HPV-16 E6,7-specific T-cell immune responses, the optimal dose inducing the highest immune responses will be determined.

Secondary outcome

The secondary parameters are side effects/ adverse events related to Vvax001. Toxicity will be graded according to the NCI Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0.

The injection sites will be screened for local transformation by means of inspection and palpation. If indicated, imaging (e.g. ultrasound) and/or biopsy will be performed. Screening of the injection sites will be performed during visit 3, 5 and 6.

Study description

Background summary

HPV infection is an important cause of premalignant genital and oropharyngeal lesions, cervical cancer, vulvar cancer, anal cancer, and penile cancer.

HPV-induced cancer is the second largest cause of cancer deaths in women worldwide. Current treatment for premalignant HPV-induced genital lesions primarily relies on surgery, which is highly discomforting and carries a risk of complications like bleeding, stenosis and/or cervical incompetence which may lead to infertility. Above all, it does not eradicate the underlying HPV infection.
Therapeutic immunization is an attractive alternative to the current options for treating precancerous lesions and (invasive) cancer. The immune cells induced by cancer immunotherapy can target the tumor cells and kill them. When long-lasting immunity is induced the immunotherapy may prevent recurrence of the disease. Hence, the approach taken in this study, is to immunize with a replication-incompetent Semliki Forest Virus (SFV) vector encoding HPV-related tumor antigens. Intramuscular immunization with these replication-incompetent SFV particles (Vvax001) is aimed at eliciting a therapeutic anti-tumor response.

Study objective

The objective of this trial is to assess the immunological activity of Vvax001 by monitoring HPV-16 specific immune responses in order to determine the optimal dose inducing the highest immune responses.

Study design

In this phase I immunization study, four dose levels of Vvax001 will be tested; 5x10^5, 5x10^6, 5x10^7 and 2,5x10^8 Infectious Particles (IP) Vvax001. Patients will receive three consecutive doses, with an interval of 3 weeks. Each dose is administered intramuscularly bilaterally and consists of two injections of 1 ml each (total 2 ml). Cohorts of 3 patients will be treated per dose level.
Although no limiting toxicities are anticipated based on previous experience with similar viral vector vaccines, enrollment of subsequent patients will proceed with an interval of 48 hours.
Participants will be observed for 4 hours at the treatment site (1hr after 2nd and 3rd vaccination) and will be contacted by telephone 6-8 hours after immunization in order to obviate any adverse events (AEs).

Intervention

Patients will receive three intramuscular immunizations with a 3-week interval. Patient evaluation will be performed before, immunization including history, physical examination, full blood count, urea, electrolytes and liver function tests and a pregnancy test. Participants will be observed for 4 hours at the treatment site (1hr after 2nd and 3rd vaccination) and will be contacted by telephone 6-8 hours after immunization in order to obviate any adverse events (AEs).
Peripheral blood mononuclear cells (PBMC) will be collected at baseline, 7-10

days after the second immunization, and 7-10 days after the third immunization to monitor HPV-specific immune responses.

Study burden and risks

The burden in this phase I trial is relatively low. The study procedures require 6 visits to the hospital. Immunization by intramuscular injection is performed three times. Six venepunctions will be performed for PBMC collection and biochemistry.
Toxicity will be graded according to the NCI Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0. Given the design of the Vvax001 vaccine, the results of preclinical animal studies, and previous clinical experience with similar viral vector vaccines, little toxicity is anticipated from intramuscular administration of Vvax001.

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

Patients with a history of cervical intraepithelial neoplasia (CIN) II and III and patients with a history of cervical cancer, both minimally 12 weeks after completion of treatment.

Exclusion criteria

- Prior treatment with immunotherapeutic agents against HPV
- History of an autoimmune disease or other systemic intercurrent disease that might affect the immunocompetence of the patient, or current or prior use (4 weeks before start of the study) of high dose immunosuppressive therapy.
- History of a second malignancy except curatively treated low-stage tumors with a histology that can be differentiated from the cervical cancer type
- Participation in a study with another investigational drug within 30 days prior to the enrolment in this study
- Any condition that in the opinion of the investigator could interfere with the conduct of the study
- Pregnancy

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-01-2017
Enrollment:	24
Type:	Actual

Ethics review

Approved WMO Date:	04-07-2016
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	02-09-2016
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	29-11-2016
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	19-12-2016
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	EUCTR2015-004979-74-NL
CCMO	NL56680.000.16