A phase II, double blind randomized study to evaluate the efficacy of the therapeutic HIV-1 vaccine NYVAC-B versus placebo in chronic HIV-1 infected patients successfully treated with HAART (TheraVac-03)

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON31815

Source
ToetsingOnline

Brief title
TheraVac-03

Condition

- Viral infectious disorders

Synonym
HIV, HIV-1 infection

Research involving

Human

Sponsors and support

Primary sponsor: EuroVacc Foundation
Source(s) of monetary or material Support: subsidie Europese Unie

Intervention

Keyword: HIV-1 infection, vaccination, vaccinia

Outcome measures

Primary outcome

Primary endpoint (outcome measure) is the difference in plasma HIV-1 RNA between the study arms during the 28 weeks after the first vaccination.

Secondary outcome

The difference in the percentage of patients with un undetectable plasma HIV-1 RNA (using an ultrasensitive assay with a lower limit of detection of 5 copies/mL) between patients who received two vaccinations with either the HIV-1 specific recombinant vaccinia vaccine NYVAC-B or a placebo vaccine; the changes in the plasma HIV-1 RNA (using an ultrasensitive assay with a lower limit of dectection of 5 copies/mL) in patients who received two vaccinations with the NYVAC-B vaccine compared to the patients who received a placebo vaccine, in HIV-1 infected patients during concomitant successful antiretroviral therapy; the changes of the cell-associated HIV-1 DNA in PBMC (using an ultrasensitive assay) in patients who received two vaccinations with the NYVAC-B vaccine compared to the patients who received a placebo vaccine, in HIV-1 infected patients during concomitant successful antiretroviral therapy; the changes from baseline in the numbers of HIV-specific PBMC producing IFN-g measured using an

ELISpot assay in patients who received two vaccinations with the NYVAC-B vaccine compared to the patients who received a placebo vaccine, in HIV-1 infected patients during concomitant successful antiretroviral therapy; the characteristics of the HIV-1 specific T cell responses generated by the vaccine (multifunctional and differentiation characteristics, breadth of HIV-1 specific CD4+ and CD8+ T cells); safety parameters (measured as standard safety parameters ([targeted] physical examination, clinical symptoms, laboratory hematology and biochemistry, specific clinical signs and symptoms of vaccination [e.g. injection site reactions]) up to 12 and 28 weeks after the first vaccination.

Study description

Background summary

Because of the drawbacks of the current antiretroviral treatment (side effects, inconvenience, emergence of resistance and costs), possibilities to enable the (temporary) interruption of antiretroviral treatment, for example by boosting the HIV-1 specific immunity by a vaccine prior to the interruption of the antiretroviral treatment. One possibility is vaccination with a viral vector containing HIV-genes. The viral vector in this study is New York Vaccinia (NYVAC), containing the HIV-1 genes Bx08gp120 and IIIB gag-pol-nef.

Study objective

Primary objective is to evaluate the HIV-1 specific immunity after two vaccinations with the HIV-1 specific recombinant vaccinia vaccine NYVAC-B, compared to placebo. Secondary objectives are the evaluate of the change in plasma HIV-1 RNA in patients previously vaccinated twice with the HIV-1 specific recombinant vaccinia vaccine NYVAC-B or a placebo vaccine, in HIV-1 infected patients during concomitant successful antiretroviral therapy; to evaluate the safety of NYVAC-B, up to 40 weeks after he first vaccination.

Study design

This is an international multi centre, two-armed phase II study, in which patients will be vaccinated twice with the HIV-1 subtype-B specific vaccine NYVAC-B at week 0 and week 4. Vaccination is followed by one hour of clinical observation. Study duration is 28 weeks, with visits on week -4 (screening), week 0 (vaccination 1), 4 (vaccination 2), 12 and 28. During the visits, blood will be drawn for standard safety laboratory examinations, plasma HIV-1 RNA en CD4+/CD8+ T cel l count, HIV 1 specific immunity. Furthermore, physical examination will be performed, as well as follow-up on (vaccine-related) signs and symptoms.

Intervention

Participants will be vaccinated twice via I.M. injection with 10E7.4 pfu of the HIV-1 subtype-B specific vaccine NYVAC-B at week 0 and week 4.

Study burden and risks

The vaccine that will be used in this study, NYVAC-B, was found to be well tolerated in an earlier phase I study. The injection itself may be painful. The first days after vaccination mild symptoms may occur on the injection site (pain, redness, swelling), or systemic (malaise, fever, tiredness). The frequent blood draws can be inconvenient. Finally, in total there are 5 study visits, which take the participant quite some time.

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

1. Patient is >= 18 years of age;
2. Voluntarily signed informed consent;
3. Patient is male, or female with negative pregnancy test prior to enrolment;
4. Patient has a proven HIV-1 infection (with positive antibodies against HIV-1 and a detectable plasma HIV-1 RNA, measured for the first time at least 6 months prior to inclusion);
5. Patient must be on stable treatment with HAART for at least 6 months (HAART is defined as an antiretroviral regimen consisting of at least three registered antiretroviral agents*; changes within the same class of drugs only for toxicity or simplification reasons are allowed, at least 3 months for inclusion);
6. Mean of all measured CD4+ T cell counts during the 6 months prior to the start of HAART is above or equal to 200 cells/ mm3;
7. Plasma HIV-1 RNA must be below 50 copies/ mL at screening and during at least 3 months prior to inclusion, during at least two measurements (occasional so called *blips* up to 200 copies/mL are permitted, but not at screening),
8. HIV-1 subtype is proven to be clade B; if subtype is unknown, subtype should determined in stored samples with detectable plasma HIV-1 OR in HIV-1 DNA isolated from PBMCs at screening;
9. Patient is one of the following:
- the patient is a heterosexually active female, agreeing to use condoms with her partner from 14 days prior to the first vaccination until 4 months after the last, even though using another method of contraception, and willing to undergo pregnancy tests at screening and prior to each vaccination, OR
- the patient is male and agreeing to use condoms with his partner from the day of the first vaccination until 4 months after the last vaccination, OR
- none of these apply.

Exclusion criteria

1. History of a CDC class C event (see Appendix I, page 46);
2. Infection with a non-B HIV-1 subtype;

3. Interruption of HAART during the course of the study which is expected at the time of inclusion;
4. History of exposure < 20 years ago to any poxvirus based vaccine;
5. Previous exposure to any HIV experimental vaccine;
6. Patient is female and is breast-feeding or has a positive pregnancy test or the wish of pregnancy;
7. Any active infection or any serious disease such as cancer, hepatitis, severe liver, renal or cardiovascular diseases or dysfunctions;
8. Current or previous antiretroviral treatment with CCR5-blockers (i.e. maraviroc), integrase inhibitors (i.e. raltegravir) or etravirine (TMC125);
9. Therapy with immunomodulatory agents, including cytokines (e.g. IL2) and gamma globulin, or cytostatic chemotherapy within 90 days prior to screening visit;
10. History of egg-allergy;
11. Use of anti-coagulant medication;
12. Use of any investigational drug or vaccine during the 90 days prior to study entry;
13. Patient received a *live* attenuated vaccine within the last 30 days;
14. Any other condition which, in the opinion of the investigator, may interfere with the evaluation of the study objectives.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Start date (anticipated):	01-10-2008
Enrollment:	15
Type:	Anticipated

Ethics review

Approved WMO Date:	28-08-2008
Application type:	First submission
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	EUCTR2007-001627-35-NL
CCMO	NL17204.000.08