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HIVIS 01: A phase I trial to assess the safety of different modes of administering plasmid DNA with HIV genes env, rev, gag, and RT, with Amendment 3, HIVIS 02: Assessment of the safety and immunogenicity of administering modified vaccinia Ankara (MVA), carrying HIV-1 genes env, gag, and pol in subjects who have previously received plasmid DNA with analogous HIV-1 genes in HIVIS 01

Submission date
11/02/2008

Registration date
10/03/2008

Last Edited
18/12/2017

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
ver 3.3 and ver 3.42

Study information

Scientific Title
HIVIS 01: A phase I trial to assess the safety of different modes of administering plasmid DNA with HIV genes env, rev, gag, and RT, with Amendment 3, HIVIS 02: Assessment of the safety and immunogenicity of administering modified vaccinia Ankara (MVA), carrying HIV-1 genes env, gag, and pol in subjects who have previously received plasmid DNA with analogous HIV-1 genes in HIVIS 01

Acronym
HIVIS

Study objectives
Delivery of plasmid DNA containing HIV-1 genes boosted with a pox vector with analogous genes is safe and immunogenic.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Karolinska Institute Syd Ethics Review Board (Dnr 484/03)
2. Regional Ethics Review Board (etikprövningskommittén),Stockholm (Dnr 2005/616-32)

Study design
Blinded, randomised controlled trial.

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
HIV type 1

Interventions
The immunological laboratory was blinded during the study. The clinic staff and participants were not blinded, since this was a safety study with different modes of administration without placebo.

Priming injections (HIVIS 01): Four different modes of delivery of seven plasmids containing env subtype A, B and C, gag subtype A and B, RTmut and rev subtype B.

Four different modes of priming with DNA was investigated (HIVIS 01):
Group A: 1 mg DNA intradermally
Group B: 3.8 mg DNA intramuscularly
Group C: 1 mg DNA intradermally with 150 ug sargramostim subcutaneously under the site of DNA injection in the left arm
Group D: 2 mg DNA with 150 ug sargramostim intramuscularly at the site of the DNA injection in the left arm

All injections were administered with the Bioject® device, except the subcutaneous injection of sargramostim in Group C that was given by syringe and needle. The env and rev plasmids were injected in the left deltoid muscle and the gag and RT plasmids in the right deltoid muscle. Injections were given at month 0, 1 and 3.

Boost injections (HIVIS 02): Two different modes of delivery of MVA containing analogous HIV-1 genes from subtype A/E. The HIVIS 01 participants were formally re-recruited and treated with the MVA boost 6 months after the last priming injection. This addendum to the protocol was approved by the ethics/regulatory committees separately.

Participants were block re-randomized to either be boosted with 10^7 plaque forming units (pfu) MVA intradermally or 10^8 pfu intramuscularly in the left deltoid muscle. All injections were performed with needle and syringe 6 months after the last priming DNA injection.

Participants have been followed for 6 months after under the protocol. Approval for an extended follow up has been obtained and all 37 eligible participants have agreed to participate.

Added 06/07/2010:
A second boost with the same MVA as was given before was offered to the remaining 24 participants 3 years after the first MVA boost. The MVA was administered at the dose that seemed optimal after the first MVA, ie 10^8 pfu intramuscularly in the left deltoid muscle with needle and syringe. Follow-up for cellmediated and antibody responses was done at 1 and 6 months with the same methods as before.

This amendment was approved by the Medical Products Agency and Regional Ethics Committee (ref: HIVIS 05).

Intervention Type
Other

Phase
Not Specified

Primary outcome(s)
1. Safety:
1.1. Samples for routine biochemistry and haematology (see inclusion criteria) were obtained at screening, before and 2 weeks after each immunization, and 3 month after the last DNA and MVA immunization
1.2. Creatinine phosphokinase and antinuclear antibodies were determined at baseline and after the last DNA injection
1.3. 12-lead electrocardiograms were performed before and 2 weeks after the MVA injection

1.4. Clinical adverse reactions and vital signs at 10 and 30 minutes, in addition a contact was made by telephone 1-3 days after each injection
1.5. A 7-day diary card (including standardized measurements of body temperature) was filled in and presented at the visit 2 weeks after each injection, when direct questions were asked on the basis of the diary card
2. Specific reactivity to HIV-1 peptides in IFN-gamma Enzyme-linked immunosorbent spot (ELISpot), performed on fresh Peripheral Blood Mononuclear Cell (PBMC) before the first DNA and the MVA immunization and 2 weeks after the last DNA and MVA immunization

Key secondary outcome(s))
The following were performed on fresh Peripheral Blood Mononuclear Cell (PBMC) before the first DNA and the MVA immunization and 2 weeks after the last DNA and MVA immunization:
1. Specific reactivity to HIV-1 peptides in IL-2 ELISpot
2. Lymphoproliferation to inactivated whole HIV-1 virions

Completion date
13/09/2006

Eligibility

Key inclusion criteria
1. Age: Men 18 to 67 years of age or women from one year after menopause (or from 18 with verified infertility) to 67 years of age
2. Negative antibody/antigen test for HIV infection
3. Willing to undergo a HIV testing
4. Residents in Stockholm at low risk of HIV and willing to remain so for the duration of the study
5. Low risk of HIV infection defined as:
5.1. No history of injecting drug use in the previous ten years.
5.2. No gonorrhoea, chlamydia or syphilis in the last six months.
5.3. No high risk partner (e.g. injecting drug use, HIV positive partner) either currently or within the past six months
5.4. No unprotected vaginal and/or anal intercourse outside a relationship with a regular known /presumed HIV negative partner in the last six months
6. Willing to undergo a genital infection screening if need arises
7. If heterosexually active male, using an effective method of contraception with their partner from the first day of vaccination until 4 months after the last vaccination
8. Be willing to practice safer sex for the duration of the study to avoid sexually transmitted infections
9. Good health as determined by medical history, physical examination, and clinical judgment
10. No grade 1 or higher routine laboratory parameters:
10.1. Haemoglobin (Hb) >10.5 g/dL
10.2. White blood cell count <13,000/mm^3
10.3. Neutrophils >1,500/mm^3
10.4. Lymphocytes >1.0
10.5. Platelets >120,000/mm^3
10.6. CD4 >400/mm^3
10.7. Glucose 2.5-7.0 mmol/L
10.8. Bilirubin <1.25 x upper limit of normal (ULN)
10.9. Aspartate aminotransferase (AST) <1.25 x UNL
10.10. Alanine aminotransferase (ALT) <1.25 x UNL
10.11. Alkaline phosphate <1.25 x UNL

10.12. Creatinine <1.0 x UNL
10.13. Complete urinalysis (UA). If microscopic UA confirms evidence of hematuria or proteinuria = 1+, the volunteer is ineligible).
11. Availability for the duration of the study
12. Able to give fully informed consent at screening visits 1 and 2

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Have active tuberculosis or other systemic infectious process by review of systems and physical examination and laboratory detection, such as laboratory detection of hepatitis B antigen or hepatitis C acute or active syphilis
2. Have a history of immunodeficiency, chronic illness requiring continuous or frequent medical intervention, autoimmune disease, severe eczema.
3. Have history of psychiatric, medical and/or substance abuse problems during the past 6 months that the investigator believes would adversely affect the volunteer's ability to participate in the trial
4. History of grand-mal epilepsy, or currently taking anti-epileptics
5. Positive for anti-double strand DNA antibodies and/or ANA
6. Have received blood products or immunoglobulins in the past 3 months
7. Are receiving ongoing therapy with immunosuppressive therapy such as systemic corticosteroids or cancer chemotherapy
8. Have used experimental therapeutic agents within 30 days of study entry
9. Have received any live, attenuated vaccine within 60 days of study entry (NOTE: Medically indicated subunit or killed vaccines [e.g., hepatitis A or hepatitis B] are not exclusionary but should be given at least 2 weeks before or after HIV immunization to avoid potential confusion of adverse reactions)
10. Have previously received an HIV vaccine
11. History of severe local or general reaction to vaccination defined as:
11.1. Local: extensive, indurated redness and swelling involving most of the antero-lateral thigh or the major circumference of the arm, not resolving within 72 hours
11.2. General: fever >= 39.5°C within 48 hours, anaphylaxis, bronchospasm, laryngeal oedema, collapse, convulsions or encephalopathy within 72 hours
12. Are study site employees who are involved in the protocol and may have direct access to the immunogenicity results
13. Unlikely to comply with protocol

Date of first enrolment

10/01/2005

Date of final enrolment
13/09/2006

Locations

Countries of recruitment
Sweden

Study participating centre
Karolinska Institute
Stockholm
Sweden
11883

Sponsor information

Organisation
Swedish Institute for Infectious Disease Control (Sweden)

ROR
https://ror.org/05x4m5564

Funder(s)

Funder type
Government

Funder Name
European Council, Framework 5 Programme (EU)

Funder Name
Swedish International Development Agency, (Sida/SAREC) (Sweden)

Funder Name
Swedish Medical Research Council (Sweden)

Funder Name
Physicians Against AIDS Foundation (Läkare mot AIDS forskningsfond; http://www.aids-fond.se) (Sweden)

Funder Name
MVA was donated by the National Institute of Allergy and Infectious Diseases (NIAID) through Walter Reed Army Institute for Research (WRAIR) (USA)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	15/11/2008		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes