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# HIVIS07: A phase I trial to assess the safety and immunogenicity of a plasmid DNA-MVA prime boost HIV-1 vaccine candidate administered together with dermal electroporation among volunteers in Stockholm, Sweden

**Submission date**
01/06/2010

**Registration date**
06/09/2010

**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

**Study website**
http://www.sodersjukhuset.se/hivis

## Contact information

**Type(s)**
Scientific

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## Additional identifiers

**EudraCT/CTIS number**

### IRAS number

### ClinicalTrials.gov number

### Secondary identifying numbers
2009-011478-13

# Study information

### Scientific Title
A phase I, double-blind, randomised, placebo-controlled trial to assess the safety and feasibility of administering plasmid DNA carrying multiple HIV-1 genes together with dermal electroporation

### Acronym
HIVIS DNA 7

### Study objectives
Primary:
Is it safe and tolerable to immunize with seven or eleven DNA plasmids carrying HIV-1 genes with electroporation?
Secondary:
1. Is it possible to increase immunogenicity of a DNA vaccine delivered intradermally and to reduce the number of injections needed by using electroporation?
2. Will electroporation improve/alter the quality of the immune responses induced by the HIV-1 DNA plasmids?
3. Is it possible to obtain similar immune reactivity by replacing two intramuscular boosts using Modified Vaccinia-Virus Ankara (MVA) with two intradermal injections of HIV-1 DNA plasmids together with electroporation?
4. Can electroporation increase immunogenicity of all included DNA plasmids to permit mixing of all vaccine plasmids instead of delivering them as two different entities?
5. Will additional DNA plasmids broaden the anti-HIV-1 immune response?

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
The Regional Ethical Review Board Stockholm Sweden, 18/02/2009, ref: 2008/2:2

### Study design
Randomised double-blind placebo-controlled trial

### Primary study design
Interventional

### Secondary study design
Randomised controlled trial

### Study setting(s)
Hospital

## Study type(s)
Prevention

## Participant information sheet
Not available in web format, please use contact details below to request a patient information sheet [in Swedish]

## Health condition(s) or problem(s) studied
HIV

## Interventions
The clinical staff, volunteers and laboratory staff are all blinded during the study. The volunteers are randomly allocated to four arms (B1 - B4). Priming injections in arms B1 to B3 are conducted with seven plasmids (pKCMVgp160A, pKCMVgp160B, pKCMVgp160C, pKCMVp37A(ba), pKCMVp37B2, pKCMVRTmut, pKCMVrev). In total 0.6 mg DNA is injected intradermally at week 0, 6 and 12 with the ZetJet® device. In groups B2 and B3 injections are combined with dermal electroporation. In arm B4 priming injection is conducted with 11 plasmid (pKCMVgp160A, pKCMVgp160B, pKCMVgp160C, pKCMVcoPR, pKCMVRTmut, pKCMVp37A(ba), pKCMVp37B2, pKCMVp37C(bc), pKCMVrev, pKCMVnef, pKCMVtat). Also in arm B4 the vaccine is administered with the ZetJet® device in combination with electroporation.
Boost injections: Two HIV MVA-CMDR (108 pfu) injections are administered im at weeks 36 and 60 in groups B1, B2 and B4. Arm B3 will receive additional injections with HIV DNA in combination with electroporation, similar to the priming injections.
In all four arms two placebo patients will be injected with saline with or without electroporation.

## Intervention Type
Biological/Vaccine

## Phase
Phase I

## Primary outcome measure
The safety of immunization will be assessed by clinical signs and standard biochemical and haematological laboratory tests where any worsening of the severity grade will be considered for causality with the vaccine. The immunization will be evaluated by assessing local (pain, cutaneous reactions including indurations), general (fever, chills, headache, nausea, vomiting, malaise, myalgia) and other unsolicited adverse events within 28 days. Any grade III or IV event will be taken as an indication that the group of patients tolerate this schedule less well.
The primary safety parameters will be graded:
1. Local adverse event Grade 3 or above (pain, cutaneous reactions including indurations)
2. Systemic adverse event Grade 3 or above (temperature, chills, headache, nausea, vomiting, malaise, or myalgia)
3. Other clinical or laboratory adverse events Grade 3 or above confirmed at examination or on repeat testing
Any event attributable to vaccine leading to discontinuation of the immunisation regimen must be documented. Data on local and systemic events listed above will be solicited with specific questions or using a diary card for 7 days following each immunisation. Data on other clinical events and laboratory events will be collected with an open question at each visit and through routinely scheduled investigations.

### Secondary outcome measures
A qualitative evaluation of cellular responses against peptides representing the different immunogens will be performed primarily by the ELISPOT technique. Additional testing will be performed by intracellular cytokine staining quantifying IFN-γ, IL-2, TNF-α and MIP-1β production by CD4 and CD8 T cells, lymphoproliferation against inactivated HIV using fresh cells and multi-colour intracellular cytokine staining using cryopreserved cells for assessment of multiple T cell effector functions including immunophenotyping of responding cells. Testing for binding antibodies and, if binding antibodies are present, also neutralizing antibodies will be performed. Group B1 will be compared with the ID only group (group A) in the HIVIS study (ISRCTN32604572) for evaluation of the lower dose of HIV DNA (0.6 vs 1.0 mg). Group B2 will be compared with Group B1 for evaluation of the lower dose of HIV DNA with and without electroporation. Group B3 will be compared to the group B2 for the evaluation of HIV DNA as a boost compared to boosting with HIV MVA. Group B4 will be compared to groups B1-B3 to show if priming with additional HIV-related plasmids will increase immunogenicity to any of the included antigens.

### Overall study start date
01/06/2010

### Completion date
01/06/2012

## Eligibility

### Key inclusion criteria
1. Men and women 18 to 40 years of age
2. Negative antibody/antigen test for HIV infection
3. Willing to undergo 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 during 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
6. Willing to undergo a genital infection screening if need arises
7. Participants will agree to practice effective contraception from study entry until 4 months after the last immunization
8. 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. Hb >10.5g/dL
10.2. White blood cell count <13.000/mm3
10.3. Neutrophils >1500/mm3
10.4. Lymphocytes >1.0
10.5. Platelets >120.000/mm3
10.6. CD4 >400/mm3
10.7. Glucose 2.5-7.0 mmol/L
10.8. Bilirubin <1.25xULN
10.9. Aspartate Aminostransferase (AST) <1.25xUNL
10.10. Alanine Aminotransferase (ALT) <1,25xUNL

10.11. Alkaline Phosphatase (ALP) <1.25xUNL
10.12. Creatinine <1.0xUNL
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

## Age group
Adult

## Lower age limit
18 Years

## Sex
Both

## Target number of participants
48

## Key exclusion criteria
1. Have active tuberculosis or other systemic infectious process, such as laboratory detection of tuberculosis bacteria, Hepatitis antigen, acute 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. Have received blood products or immunoglobulin in the past 3 months
6. Are receiving ongoing therapy with immunosuppressive therapy such as systemic corticosteroids or cancer chemotherapy
7. Have used experimental therapeutic agents within 30 days of study entry
8. Have ECG deviations that indicate heart disease or would make interpretation of vaccine induced effect difficult
9. Have received any live, attenuated vaccine within 60 days of study entry (NOTE: Medically indicated subunit or killed vaccines [e.g., Hepatitis or influenza] 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 >= 39.5oC 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 access to the immunogenicity results
13. Unlikely to comply with protocol

**Date of first enrolment**
01/06/2010

**Date of final enrolment**
01/06/2012

# Locations

**Countries of recruitment**
Sweden

**Study participating centre**
**Venhalsan**
Stockholm
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118 83

# Sponsor information

**Organisation**
Swedish Institute for Infectious Disease Control (SMI) (Sweden)

**Sponsor details**
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**Sponsor type**
Research organisation

**Website**
http://www.smittskyddsinstitutet.se/

**ROR**
https://ror.org/05x4m5564

# Funder(s)

**Funder type**
Government

**Funder Name**
Styrelsen för Internationellt Utvecklingssamarbete

**Alternative Name(s)**
Swedish International Development Cooperation Agency, Swedish Development Cooperation, The Swedish International Development Cooperation Agency, Sida

**Funding Body Type**
Private sector organisation

**Funding Body Subtype**
International organizations

**Location**
Sweden

**Funder Name**
European and Developing Countries Clinical Trials Partnership (EDCTP) (Sweden)

**Alternative Name(s)**
Le partenariat Europe-Pays en développement pour les essais cliniques, A Parceria entre a Europa e os Países em Desenvolvimento para a Realização de Ensaios Clínicos, The European & Developing Countries Clinical Trials Partnership, European and Developing Countries Clinical Trials, EDCTP

**Funding Body Type**
Private sector organisation

**Funding Body Subtype**
International organizations

**Location**
Netherlands

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

# Results and Publications

**Publication and dissemination plan**
Not provided at time of registration

## Intention to publish date

## 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 | 29/06/2015 | | Yes | No |