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HIVIS 03: A phase I/II trial to assess the safety and immunogenicity of a plasmid DNA-MVA prime boost HIV-1 vaccine candidate among volunteers in Dar es Salaam, Tanzania

Submission date
13/08/2008

Recruitment status
No longer recruiting

Registration date
10/10/2008

Overall study status
Completed

Last Edited
05/03/2019

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
Version 4

Study information

Scientific Title
A phase I/II trial to assess the safety and immunogenicity of a plasmid DNA-MVA prime boost HIV-1 vaccine candidate among volunteers in Dar es Salaam, Tanzania

Acronym
HIVIS 03

Study objectives
Delivery of plasmid DNA containing HIV-1 genes boosted with a pox vector (MVA) with analogous genes is safe and immunogenic among healthy Tanzanian volunteers.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Research and Publications Committee of the Muhimbili University of Health and Allied Sciences (MUHAS). The study was approved on the 26/04/2006 (ref: MU/RP/AEC/Vol.V/76). As of 19/08/2008, the last amendments were approved on 19/06/2008 (ref: MU/DRP/PA/Vol. I/37)
2. National Ethics Committee at the National Institute for Medical Research (NIMR). The study was approved on 30/01/2006 (ref: NIMR/HQ/R.8a Vol.IX/410). As of 19/08/2008, the last amendments were approved on 19/06/2008 (ref: MU/DRP/PA/ Vol.I/37)

Study design
Randomised double-blind placebo-controlled trial

Primary study design
Interventional

Study type(s)
Prevention

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

Interventions
The clinical staff and participants are blinded throughout the trial. The immunological laboratory is blinded during the study.

Priming injections: Injections of seven plasmids containing HIV-1 env subtype A, B and C, gag subtype A and B, RTmut and rev subtype B.

The participants were randomly allocated to the following four arms:
Arm I (n = 20): DNA 3.8 mg (intramuscular [IM])
Arm II (n = 20): DNA 1.0 mg (intradermal [ID])
Arm IIIa (n = 10): saline placebo IM
Arm IIIb (n = 10): saline placebo ID

All injections were administered with the Bioject® device. 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: One MVA-CMDR given as an IM or ID injection (with needle and syringe) at a dose of 10^8 pfu in the left deltoid muscle. The MVA contains analogous HIV-1 genes from subtype A/E. It will be given 6 months after the last DNA/placebo injection.

The second MVA boost is planned to be given at 80 weeks (6 months after the first MVA boost). The participants will be formally re-recruited for the second MVA boost. This phase of study will be funded by the European and Developing Countries Clinical Trials Partnership (EDCTP), under the TAMOVAC-I Project.

Intervention Type
Biological/Vaccine

Phase
Phase I/II

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 immunisation, and 3 month after the last DNA and MVA immunisation
1.2. 12-lead electrocardiograms were performed before and 2 weeks after the MVA injection
1.3. 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
1.4. A 7-day diary card (including standardised 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 immunisation and 2 weeks after the last DNA and MVA immunisation

Key secondary outcome(s))
1. The following will be performed on fresh PBMC before the first DNA and the MVA immunisation and 2 weeks after the last DNA and MVA immunisation:
1.1. Specific reactivity to HIV-1 peptides in IL-2 ELISpot
1.2. Lymphoproliferation to inactivated whole HIV-1 virions
2. A qualitative and quantitative presence of necessary infrastructure and human capacity to conduct HIV-related vaccine studies at MUHAS

Completion date
31/12/2009

Eligibility

Key inclusion criteria
1. Both males and females, age: 18 to 40 years
2. Willing to undergo counselling and HIV testing
3. Have a negative antigen/antibody ELISA for HIV infection
4. Able to give informed consent
5. Literacy corresponding to a minimum of 7 years of primary education
6. Resident in Dar es Salaam, and willing to remain so for the duration of the study
7. At low risk of HIV infection, defined as the absence of an identifiable risk factor/ behaviour:

7.1. Sexual partner with HIV
7.2. Sexual partner with unknown HIV serostatus who is also unwilling to use protective condoms consistently in all sexual relations
7.3. Sexual partner is known to be at high risk for HIV
7.4. More than one sexual partner in the last 6 months
7.5. History of being an alcoholic (as medically defined or more than 35 units /week)
7.6. History of STI within the past 6 months
8. Verbal assurances that adequate birth control measures are used not to conceive/father a child during the study and up to 4 months after the last vaccine injection
9. Have a negative urinary pregnancy test
10. Be willing to practice safe sex for the duration of the study to avoid sexually transmitted infections including HIV.
11. Good health as determined by medical history, physical examination, clinical judgment and by key laboratory parameters (reference ranges are in accordance with data generated at MUHAS for haematology values, and that generated at Mbeya (MMRP) for biochemical parameters. Exclusion by presence of Diabetes mellitus will be based on the WHO cut-off value of a fasting blood glucose <7.8 mmol/l). Hence no grade 1 or higher routine laboratory parameters, defined as:
11.1. Hb >10.5g/dl
11.2. White blood cell count >1,300/mm^3
11.3. Granulocytes >6.4/mm^3
11.4. Lymphocytes >1.0/mm^3
11.5. Platelets >120,000/mm^3
11.6. CD4 >400 cells/mm^3
11.7. Random blood glucose 2.5-7.0 mmol/L; if elevated, then a fasting blood glucose <7.8 mmol /l
11.8. Bilirubin <1.25 x upper limit of normal (ULN)
11.9.ALT <1.25 x ULN
11.10. Creatinine <1.25 x ULN
11.11. Urine dipstick for protein and blood: negative or trace. (If either is >=1+, obtain complete urinalysis (UA). If microscopic UA confirms evidence of haematuria or if proteinuria >=1+, the volunteer is ineligible)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Active tuberculosis or other systemic infectious process elicited by review of systems, physical examination and laboratory detection, such as detection of Hepatitis B surface antigen, or active

syphilis
2. Have a history of immunodeficiency, chronic illness requiring continuous or frequent medical intervention
3. Autoimmune disease by history and physical examination
4. Severe eczema
5. Have a 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.
6. History of grand-mal epilepsy, or currently taking anti-epileptics
7. Have received blood or blood products or immunoglobulins in the past 3 months
8. Are receiving immunosuppressive therapy such as systemic corticosteroids or cancer chemotherapy.
9. Have used experimental therapeutic agents within 30 days of study entry
10. 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 immunisation to avoid potential confusion of adverse reactions)
11. Have previously received an HIV candidate vaccine
12. History of severe local or general reaction to vaccination defined as:
12.1. Local: Extensive, indurated redness and swelling involving most of the major circumference of the arm, not resolving within 72 hours
12.2. General: Fever >=39.5°C within 48 hours, anaphylaxis, bronchospasm, laryngeal oedema, collapse, convulsions or encephalopathy within 72 hours
13. Are lactating mothers
14. Are study site employees who are involved in the protocol and may have direct access to the immunogenicity results
15. Unlikely to comply with protocol as judged by the principal investigator or his designate

Date of first enrolment
20/02/2007

Date of final enrolment
31/12/2009

Locations

Countries of recruitment
Tanzania

Study participating centre
Muhimbili University of Health and Allied Sciences (MUHAS)
Dar es Salaam
Tanzania
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Sponsor information

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

Organisation
Muhimbili University of Health and Allied Sciences (MUHAS) (Tanzania)

Organisation
Public Health Agency of Sweden

ROR
https://ror.org/05x4m5564

Funder(s)

Funder type
Other

Funder Name
European Union (Belgium)

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

Funder Name
Swedish Embassy in Tanzania through the Government of the United Republic of Tanzania (Tanzania)

Funder Name
MVA was donated by the National Institute of Allergy and Infectious Diseases (NIAID) through Walter Reed Army Institute for Research (WRAIR) (USA) to the Swedish Institute for Infectious Diseases Control (SMI) and subsequently made available to the Muhimbili University of Health and Allied Sciences (MUHAS) (Tanzania)

Funder Name

European and Developing Countries Clinical Trials Partnership (EDCTP)

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

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	09/12/2013		Yes	No
Results article	results	14/04/2015		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes