

Safety and immunogenicity of an HIV-1 DNA plasmid vaccine boosted with HIV-1 MVA among Police Officers (PO's) in Dar es Salaam, Tanzania (HIVIS03).

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**Presentation to the AIDS Vaccine 2008 Conference,
Cape Town, South Africa. 13th – 16th October 2008**

Objectives

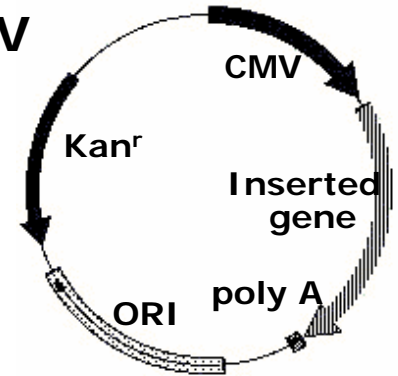
- **To assess the safety and immunogenicity of a plasmid DNA-MVA prime boost HIV-1 vaccine candidate***
- **To build expertise and capacity in evaluating HIV vaccine candidates in Tanzania.**

***Previously tested in Sweden with Excellent results.**

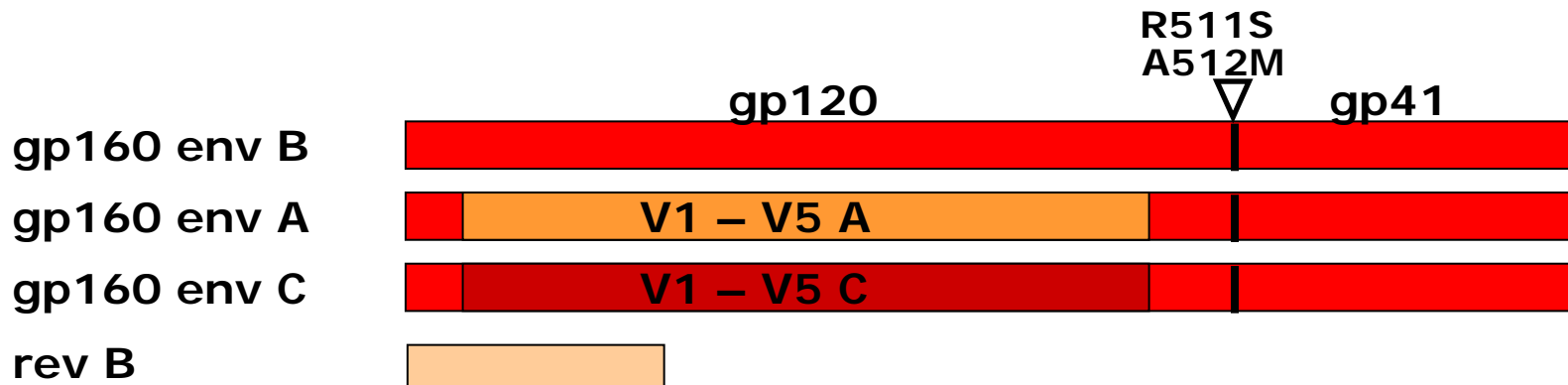
JID 2008, Nov 15.

7 plasmid HIV-1 DNA multigene/multiclade vaccine

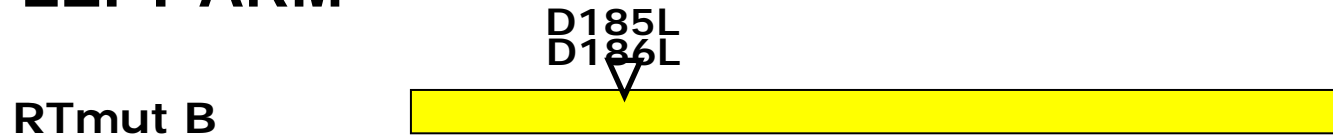
pKCMV



Developed by B Wahren, Dept virology, SMI, Karolinska Inst
Produced by Vecura



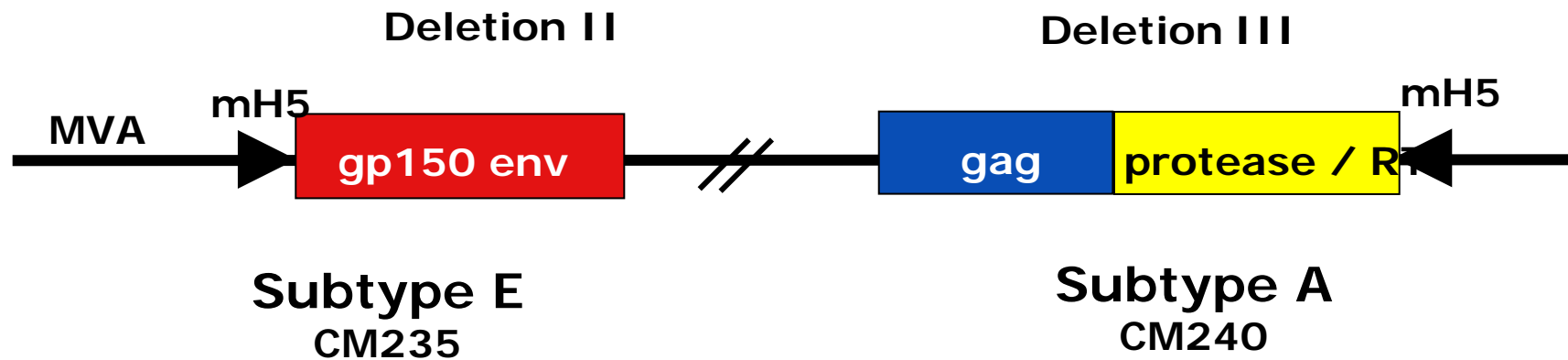
LEFT ARM



RIGHT ARM

MVA* / CMDR boost

Developed by P Earl and B Moss, Laboratory of Viral Diseases, NIAID, NIH
Produced by Walter Reed Army Institute of Research



*Modified Vaccinia Ankara

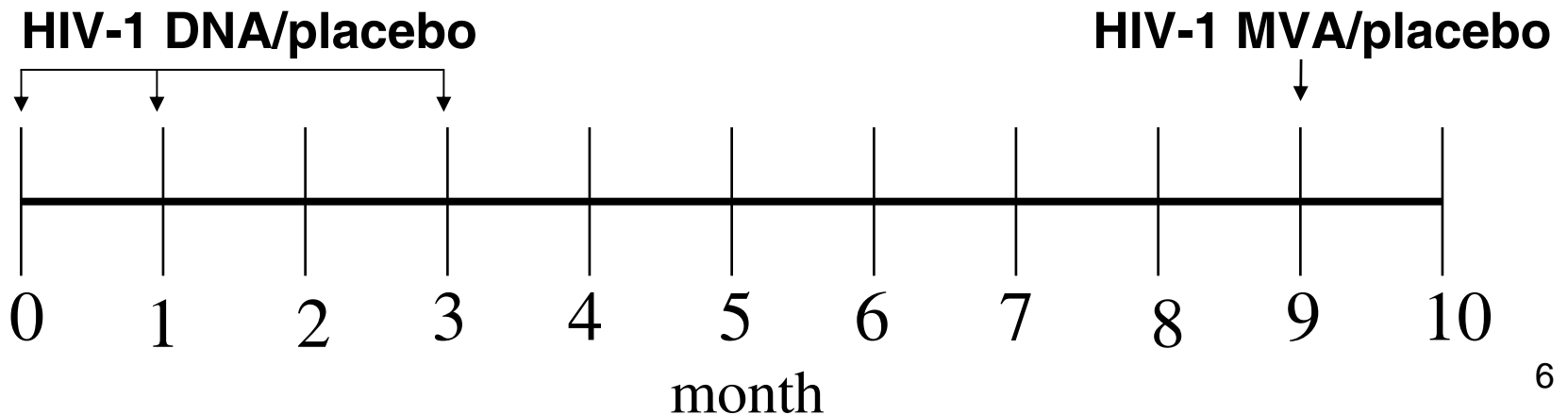
Inclusion Criteria

- Voluntary Informed Consent
- Age <40 years
- HIV negative by Ag-Ab ELISA
- Healthy by Clinical and Laboratory Evaluation

Study Design

Randomized, Double Blind, Placebo controlled

Arm	Number	DNA immunization	MVA boost
I	20	DNA IM by Biojector	MVA 10 ⁸ pfu IM
II	20	DNA ID by Biojector	MVA 10 ⁸ pfu IM
IIIa	10	Saline IM by Biojector	Saline IM
IIIb	10	Saline ID by Biojector	Saline IM



Methods

- IFN- γ ELISpot (*Mabtech, Nacka, Sweden*) responses measured on fresh cells (within 6 hours of collection) stimulated with peptide pools representing HIV-1 p17B, p24A, p55A, gp120A/B, gp120 B, gp41B, gp160E and PolA.
 - Pre-immunization
 - 2 weeks after the third HIV-1 DNA/placebo immunization
 - At the time of HIV-1 MVA/placebo immunization
 - 2 weeks after HIV-1 MVA/placebo immunization
- The criteria for positive ELISpot responses were >55 spots/ 10^6 PBMCs and 4 times the medium background and the baseline value.

Recruitment and Enrolment

By 30th September 2008,

- 162/177 Clinic Attendees were Screened.
- 60 have been enrolled.

Gender	DNA/Placebo Vaccinations			MVA/Placebo Vaccinations	
	1st	2nd	3rd	1st	2nd
Male	45	45	44	41	0
Female	15	15	15	9	0
Total	60	60	59	50	0

So far, Excellent adherence to scheduled visits by the Enrolled

Results, Safety

- **Safety profile has been excellent to date**
 - **400 events reported in total**
 - **Most were of less than grade 3 severity:**
 - **Others (175)**
 - **Headache (20)**
 - **Pain at vaccination site (20)**
 - **Malaise (20)**
 - **None was of grade 4 (extreme) severity**
 - **There were six (6) Grade 3, Severe Adverse Events, none of which was related to vaccination.**

HIV-specific IFN- γ ELISpot Responses

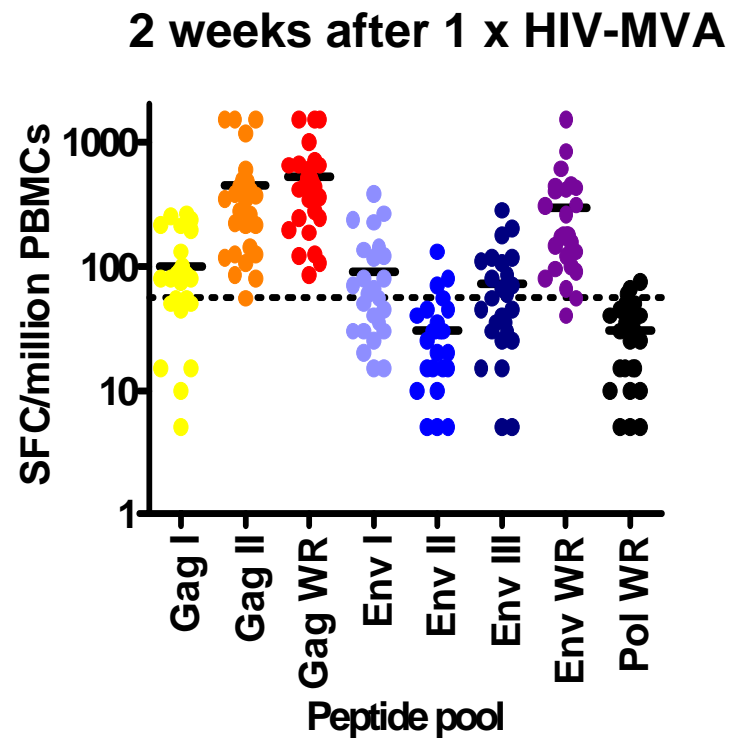
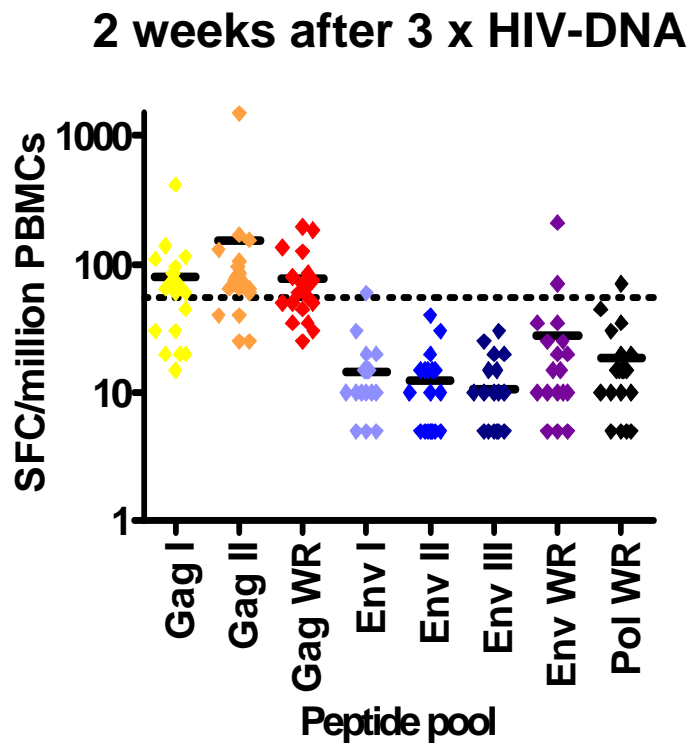
- 23/59 (39%) individuals had a positive IFN- γ ELISpot response after the third HIV-DNA/placebo vaccination.
(excluding 1/3 placebo 23/40=58%)
- 26/37 (70%) had a positive IFN- γ ELISpot response after the HIV-MVA/placebo boost.
(excluding 1/3 placebo approximately 100%)

IFN- γ ELISpot reactivity to peptide pools in 26 responders 2 weeks after HIV-1 MVA boost

- Any Gag 25
- Any Env 20
- Gag and Env 19
- Gag or Env 26

IFN- γ ELISpot reactivity in

23/59 responders 2 weeks after 3 x HIV-DNA and
26/37 responders 2 weeks after HIV-MVA



CD8 + and CD4+ T-cell IFN- γ ELISpot reactivity two weeks after HIV-MVA boost in 13 tested vaccinees*

- Responses to Gag

<u>CD8+</u>	<u>CD4+</u>
9/13	13/13

- Responses to Env

<u>CD8+</u>	<u>CD4+</u>
3/11	11/11

* Determined by IFN- γ ELISpot testing before and after CD8 T-cell depletion

Conclusions

- **The HIVIS DNA-MVA Vaccine has so far:**
 - **Demonstrated an excellent safety profile, and**
 - **Is highly immunogenic**
- **Capacity built through HIVIS03 paved the way for EDCTP-funded TaMoVaC Project aimed at Optimizing DNA vaccine delivery**

Acknowledgements

- **Police Volunteers**
- **EU and Sida/SAREC**
- **Swedish Embassy, Tanzania**
- **WHO and AAVP**
- **Investigators, collaborators and support staff in:**
 - Tanzania; at MUHAS, MNH, Tanzania Police Force
 - Sweden; at Karolinska Institute, Swedish Institute for Infectious Disease Control, Southern Hospital
 - United States of America; at WRAIR and LVD/NIH
- **Tanzania Government, in particular the MoH&SW through its NACP**