Frequent anti-V1V2 Responses Induced by HIV-DNA Followed by HIV-MVA with or without CN54rgp140/GLA-AF in Healthy Tanzanian and Mozambican Volunteers

Frank Msafiri[1, 2], Agricola Joachim[1], Raquel Matavele Chissumba[3], Christof Geldmacher[4, 5], Said Aboud[1], Wolfgang Stöhr[6], Edna Viegas[3], Arne Kroidl[4, 5], Patricia M. Munseri[7], Britta Wahren[8], Eric Sandström[9], Merlin L. Robb[10], Sheena McCormack[6], Sarah Joseph[11], Ilesh Jani[3], Guido Ferrari[12], Mangala Rao[13], Gunnel Biberfeld[14], Eligius Lyamuya[1], Charlotta Nilsson[2, 15].

[1] Muhimbili University of Health and Allied Sciences, Department of Microbiology and Immunology, Dar es Salaam, Tanzania. [2] Karolinska Institutet, Department of Laboratory Medicine, Stockholm, Sweden. [3] Instituto Nacional de Saúde, Maputo, Mozambique. [4] Division of Infectious Diseases and Tropical Medicine, Klinikum of the University of Munich (LMU), Munich, Germany. [5] German Centre for Infection Research (DZIF), partner site Munich, Munich, Germany. [6] MRC Clinical Trials Unit at UCL, London, United Kingdom. [7] Muhimbili University of Health and Allied Sciences, Department of Internal Medicine, Dar es Salaam, Tanzania. [8] Karolinska Institutet, Department of Microbiology, Tumor and Cell Biology, Stockholm, Sweden. [9] Karolinska Institutet at Södersjukhuset, Venhälsan, Stockholm, Sweden. [10] The US Military HIV Research Program, the Henry M Jackson Foundation for the Advancement of Military Medicine and Walter Reed Army Institute of Research, Silver Spring, MD, United States. [11] Imperial College London, London, United Kingdom. [12] Department of Surgery and Molecular Genetics and Microbiology, Duke University Medical Center, Durham, North Carolina, USA. [13] United States Military HIV Research Program, Walter Reed Army Institute of Research, Silver Spring, Maryland, USA. [14] Karolinska Institutet, Department of Public Health Sciences, Stockholm, Sweden. [15] Public Health Agency of Sweden, Department of Microbiology, Solna, Sweden.

CONCLUSION

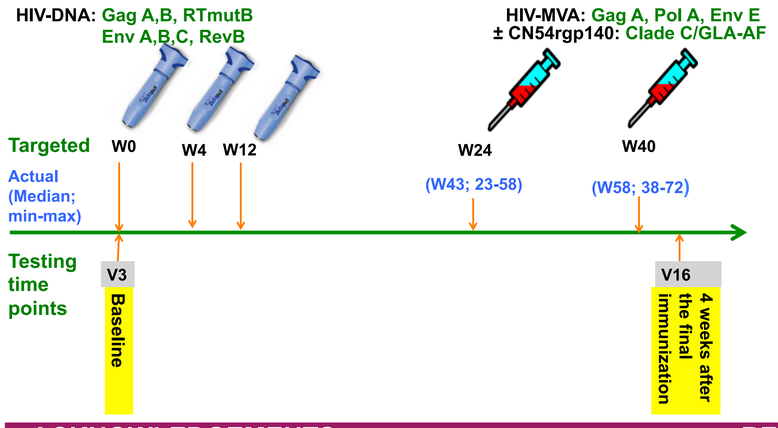
Anti-V1V2 responses were frequently detected after HIV-DNA prime followed by HIV-MVA boosting. Co-administration of CN54rgp140/GLA-AF with HIV-MVA did not increase the frequencies of anti-V1V2 or ADCC-mediating antibodies.

BACKGROUND

We evaluated the impact of co-administration of CN54rgp140/GLA-AF with HIV-MVA after HIV-DNA priming on anti-V1V2 responses and antibody-dependent cellular cytotoxicity (ADCC)-mediating antibodies, shown to be associated with reduced risk of HIV acquisition in the RV144 trial (1).

METHODS

Healthy HIV-uninfected adults (N=191) in the TaMoVaC II phase IIa trial were randomized twice; first to one of three HIV-DNA intradermal priming regimens by needle-free ZetaJet^{TM} device at weeks 0, 4 and 12 (Group I: 2x0.1mL [3mg/mL], Group II: 2x0.1mL [3mg/mL] plus electroporation (EP), Group III: 1x0.1mL [6mg/mL] plus EP). Second the same volunteers received 10^8 pfu HIV-MVA twice, alone or combined with CN54rgp140/GLA-AF, intramuscularly by syringe, 16 weeks apart. Additionally, 20 volunteers received saline placebo (2). Plasma was collected four weeks after the final vaccination (n=145), and a subset (57 vaccinees and 9 placebos) was tested for binding antibodies to gp70V1V2 proteins of CRF01_AE (A244) and subtype C (CN54) using ELISA. ADCC activity was measured in 145 samples using a luciferase assay employing CRF01_AE IMC $_{CM235}$ virus infected target cells (3).

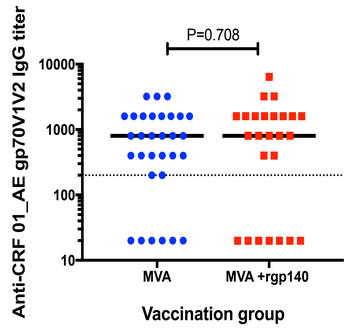


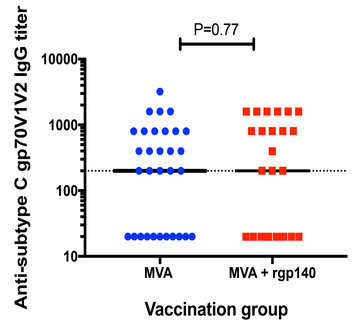
RESULTS

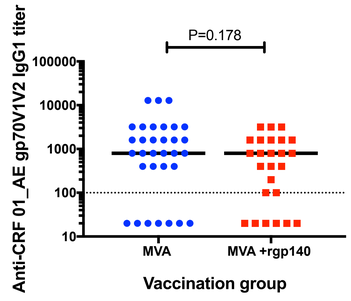
High anti-V1V2 total IgG response rates to A244 and CN54 were detected in both groups of vaccinees; HIV-MVA alone and HIV-MVA +rgp140. Anti-V1V2 A244 responses were predominantly IgG1. Anti-V1V2 IgG3 responses to A244 were more frequent in HIV-MVA than in HIV-MVA+rgp140 recipients. Anti-V1V2 IgG1 and anti-V1V2 IgG3 responses to CN54 were rare. Placebos were negative.

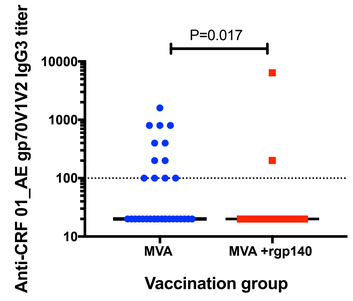
Antibody	Antigen (gp70V1V2)	HIV subtype	Frequency of responses (Four weeks after the final immunization)		
			HIV-MVA	HIV-MVA+rgp140	P value
IgG	A244	CRF01_AE	25/31 (81%)	18/25 (72%)	0.532
IgG	CN54	C	20/31 (65%)	15/25 (60%)	0.786
IgG1	A244	CRF01_AE	25/32 (78%)	19/25 (76%)	1
IgG1	CN54	C	0/32 (0%)	2/25 (8%)	0.188
IgG3	A244	CRF01_AE	12/32 (38%)	2/25 (8%)	**0.013**
IgG3	CN54	C	0/32 (0%)	1/25 (4%)	0.448

The magnitude of anti-V1V2 total IgG and IgG1 responses to A244 and CN54 was not significantly different between the two boost groups.



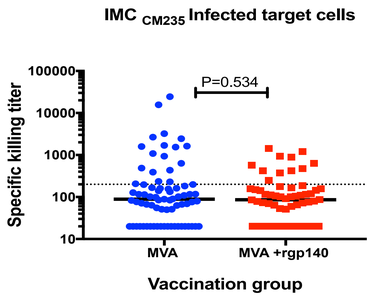






The frequency and magnitude of ADCC mediating antibodies to CM235 CRF01_AE infected cells were not significantly different between the two boost groups.

Vaccination group	Frequency of ADCC mediating antibodies	P value
HIV-MVA	16/76 (21%)	0.393
HIV-MVA + rgp140	10/66 (15%)	



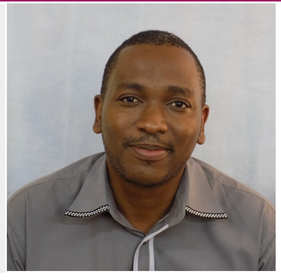
For graphing, plasma samples with no V1V2 IgG1 and V1V2 IgG3 antibody responses at 1:100 dilutions were arbitrarily assigned a value of 20. The dotted line indicates the cut off for positive values.

ACKNOWLEDGEMENTS

This work was supported by the European Union [INCO-DEV A4 ICFP501A4PR03], the Swedish International Development Cooperation Agency (Sida), Swedish Embassy Tanzania, the European Developing Countries Clinical Trials Partnership (EDCTP) [grant CT.2006.33111.007], the Regional HIV/AIDS Team for Africa, the Embassy of Sweden in Lusaka, jointly funded by Sweden and Norway [Sida ID 2150012801], the US Military HIV Research program, Walter Reed Army Institute of Research (WRAIR) and the Division of Intramural Research, National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH). We gratefully acknowledge all the volunteers who participated in this study. We thank all the clinical and laboratory personnel involved in the trial.

REFERENCES

1. Haynes BF, et al. (2012) Immune-correlates analysis of an HIV-1 vaccine efficacy trial. N Engl J Med 366: 1275-1286.
2. Viegas E, et al. (2016) Intradermal electroporation of HIV-DNA vaccine followed by HIV-MVA boost with or without addition of GLA adjuvanted gp140. AIDS Research and Human Retroviruses 2016, 32(S1): PD01.03, p. 109.
3. Joachim A, et al. (2017) Three-Year Durability of Immune Responses Induced by HIV-DNA and HIV-Modified Vaccinia Virus Ankara and Effect of a Late HIV-Modified Vaccinia Virus Ankara Boost in Tanzanian Volunteers. AIDS Res Hum Retroviruses; 33(8): 880-888



Karolinska Institutet
Frank Msafiri
Department: Laboratory Medicine
Email: frank.msafiri@ki.se
fmsafiri82@gmail.com
Telephone: +255768944937

Karolinska Institutet