# ANTIBODY RESPONSES IN THE HVTN 073E HIV VACCINE TRIAL

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## Background

The HIV Vaccine Trials Network (HVTN) 073E Phase I trial, led by Prof. Glenda Gray, tested the ability of the South African AIDS vaccine initiative (SAAVI) DNA/MVA vaccines (developed by Prof. Anna-Lise Williamson and Prof. Carolyn Williamson, University of Cape Town) to prime antibody responses following two booster vaccinations containing gp140 protein with MF59 as an adjuvant.[1] This study enrolled HIV uninfected healthy adult participants in South Africa and the United States (US) who previously participated in the HVTN 073/ SAAVI 102 study.

Previous studies have shown that a protein vaccine boost to an HIV vaccine may improve antibody responses.[2] The aim of the trial extension was therefore to explore whether the SAAVI DNA-C2/SAAVI MVA-C vaccine regimen provided a good prime for antibody responses following protein boosting.

## Methods

*Participant cohort*

The study enrolled 27 participants from the US and South Africa. There were 6 participants (5 from the vaccine group and 1 from the placebo group) from the US and 21 participants (17 vaccinees, 4 placebos) from South Africa. All enrolled participants received their first gp140/MF59 vaccination at visit 17 (day 0) and the second at visit 20 (day 84) (table 1). The time lag between the last vaccination in the HVTN073 trial and visit 17 (HVTN073E) was, on average, two years.

*Study schema*

All data are taken from HVTN 073 trial participants who rolled over to the extension study HVTN 073E. Participants received either DNA/MVA with a protein boost (T1/T2), DNA/MVA with a placebo boost (T1/C2), placebo with a protein boost (C1/T2), or double placebo (C1/C2) (table 1).

Table 1: The vaccination regimen for the HVTN 073 trial (visits 2 – 11) and the extension study HVTN 073E (visits 17 and 20).

| **Treatment Group (n=27)** | **HVTN 073** | | | | | **HVTN 073E** | |
|---|---|---|---|---|---|---|---|
| **Visit** | **2 (Day 0)** | **4 (Day 28)** | **6 (Day 56)** | **8 (Day 112)** | **11 (Day 140)** | **17 (Day 0)** | **20 (Day 84)** |
| C1/C2 (n=4) | Placebo | Placebo | Placebo | Placebo | Placebo | Placebo | Placebo |
| C1/T2 (n=1) | Placebo | Placebo | Placebo | Placebo | Placebo | gp140/MF59 | gp140/MF59 |
| T1/C2 (n=6) | DNA-C2 | DNA-C2 | DNA-C2 | MVA-C | MVA-C | Placebo | Placebo |
| T1/T2 (n=16) | DNA-C2 | DNA-C2 | DNA-C2 | MVA-C | MVA-C | gp140/MF59 | gp140/MF59 |

*Neutralization Assays*

Neutralizing antibodies against HIV-1 were measured as a function of the reduction in Tat-regulated luciferase (Luc) reporter gene expression in TZM-bl cells. This assay measures neutralization titers against a panel of heterologous Env-pseudotyped viruses that exhibit either a Tier 1A (Clade B: MN.3, Clade C: MW965.26) or a Tier 2 (Clade C: Du151.2, Clade B: TV1.21) neutralization phenotype in TZM-bl cells. Neutralization assays were performed at baseline (visit 17), 2 weeks after the 1st gp140/MF59 extension vaccination (visit 19), at the primary immunogenicity time point - 2 weeks after the 2nd gp140/MF59 (visit 22) and at 6.5 months after the 2nd protein boost (visit 24).

*Binding Assays*

Binding antibodies to ConS, TV1.21 and Du151 gp140 envelope glycoproteins and p24 Gag protein were assessed by a validated enzyme linked immunosorbent assay (ELISA). The ELISA was performed at the same time points as the neutralization assays.

**Results**

Figure 1 shows the percentage of responders by ELISA in the treatment arm (T1/T2) who received vaccines in both the HVTN 073 and HVTN 073E trials. At day 0 of the study extension, less than 30% of participants had positive responses to all antigens. More than 60% of the participants had binding antibody responses to Con S, TV1.21 and Du151 envelope proteins two weeks after the first gp140 extension boost (not shown) and reached their peak at 100% responders two weeks after the second protein boost (visit 22). As expected, there was a low percentage of responders for antigen p24 (gag) given that the protein boost in this regimen was an envelope protein. There was no positive response in the placebo group at any visit.

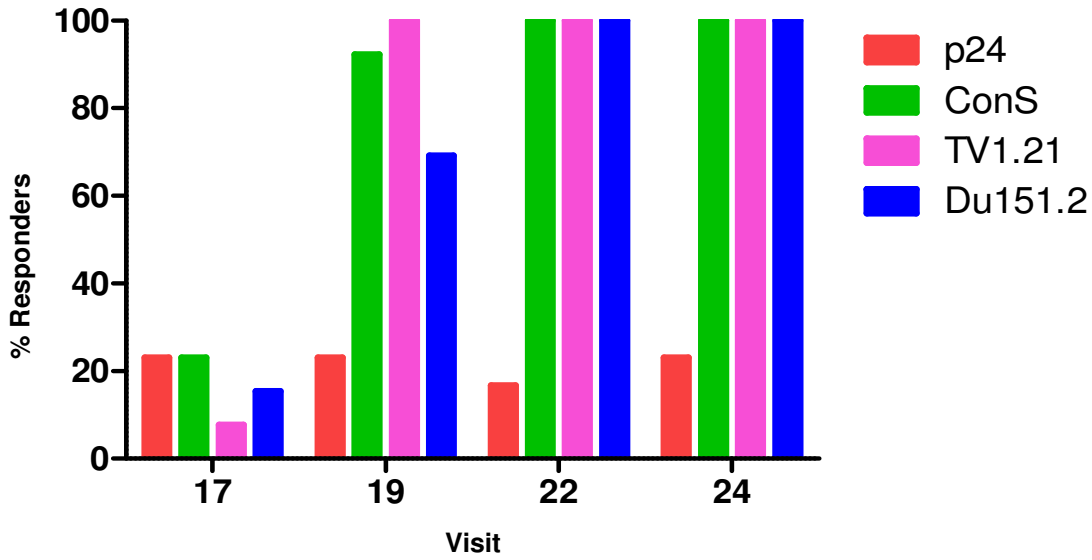


Figure 1: Percentages of individuals in the treatment arm who showed antibody responses to HIV-specific binding antibodies (p24, ConS, TV1.21, Du151.2) by visit in the HVTN073E vaccine trial.

Figure 2 shows the neutralizing antibody titer response rates by virus and visit. At visit 17 (day 0), none of the participants had HIV neutralizing antibodies against the viruses tested in their sera. However, the neutralizing antibody responses peaked at visit 22 (2 weeks after the 2nd protein boost), similar to the binding antibody data. Participants who received the vaccine in both HVTN 073 and HVTN 073E (T1/T2) had higher antibody

responses, in frequency and magnitude, than participants who received the vaccine in HVTN073 but not the protein boost in HVTN073E (T1/C2). However, by visit 24 (day 273), neutralization antibody titers began to wane (data not shown).

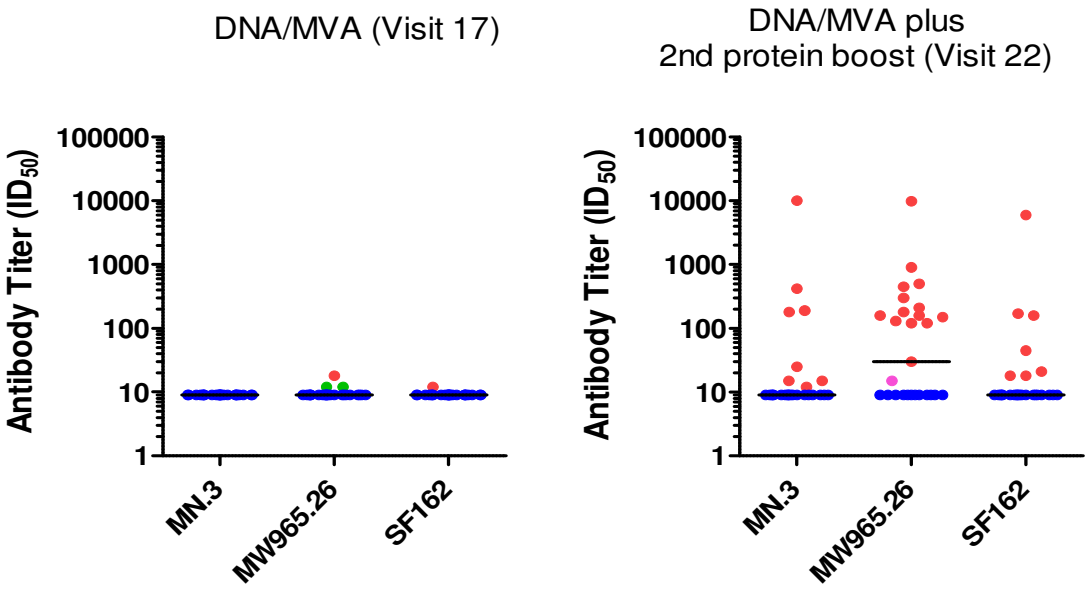


Figure 2: Neutralization of Tier 1 viruses in samples from the HVTN 073E trial. Each dot represents one individual and the black lines represent the median titer for each group. Red circles represent positive responders from the T1/T2 group, green circles represent T1/C2, pink circles represent C1/T2. Negative responders and the placebo group are in blue.

**Conclusion**

The first and second protein boosts elicited HIV-specific binding and neutralizing antibodies. We observed that antibody responses peaked after the second boost with most participants still showing detectable antibody responses 6 months later (visit 24). Responses were consistently stronger in the participants that received the DNA/MVA vaccine with protein boost providing strong evidence for the inclusion of a protein immunogen in the vaccine regimen. This is the first clinical trial of a subtype C vaccine showing measurable antibody responses and it is evident that the protein boost is necessary to elicit these responses. These data will provide a crucial step in the iterative process of developing an AIDS vaccine. Further studies aim to modify the immunogens, dosage, adjuvants and immunization schedules in order to stimulate primary virus (Tier 2) neutralization.

**Acknowledgements**

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**References**

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