



HIV VACCINE
TRIALS NETWORK

HVTN 204

A phase IIA trial to evaluate a multiclade HIV-1 DNA vaccine followed by a multiclade rAd5 HIV-1 vaccine boost in HIV-1 uninfected adults

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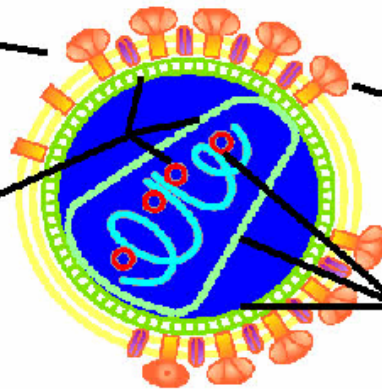
AIDS Vaccine
October 2008



Vaccines

VRC DNA-HIV-1 (4mg)

envelope clade A
envelope clade B
envelope clade C
gag clade B
pol clade B
nef clade B



VRC rAd5 (10¹⁰ PU)

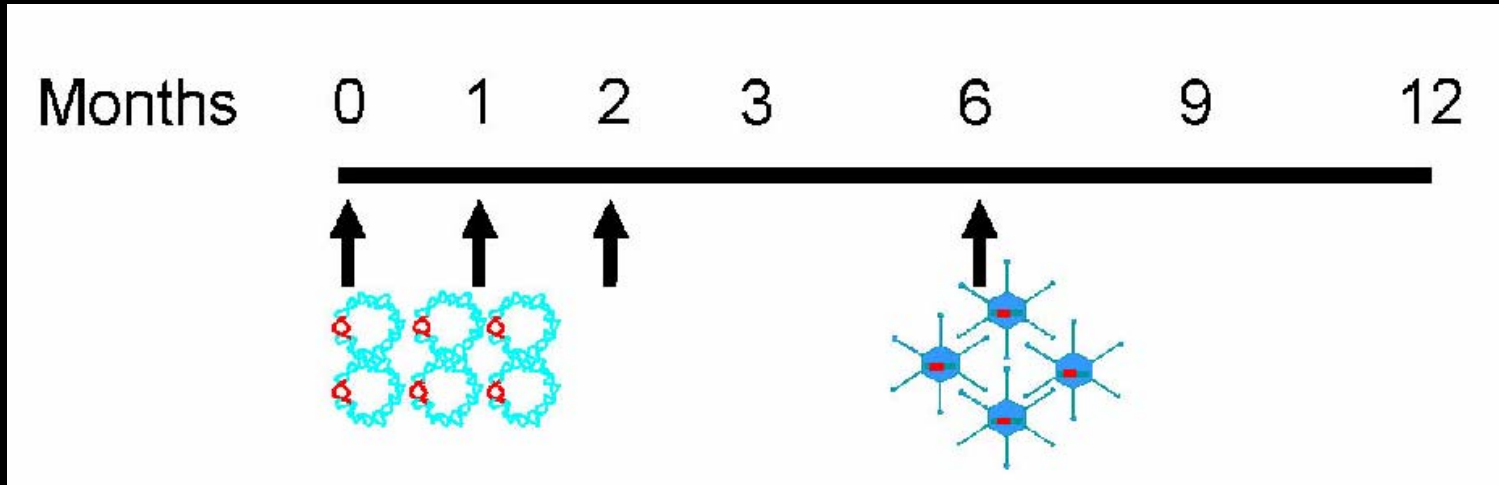
envelope clade A
envelope clade B
envelope clade C
gag/pol clade B

- Placebo

- DNA-HIV placebo: phosphate buffered saline
- Ad5-HIV placebo: adenoviral final formulation buffer



Design



Aim

- To evaluate the safety, tolerability & immunogenicity (cellular & humoral) of HVTN204 vaccine regimen



Immunogenicity assessment

- Cellular (D210, 6 weeks after Ad5 boost)
 - PBMCs were cryopreserved within 12 hours
 - Evaluated by IFN- γ ELISpots and multi-parameter ICS responses to *in vitro* stimulation with
 - *Global Potential T Cell Epitope (PTE) peptides – All*
 - *Clade C PTE peptides – South African participants*
 - A PTE panel consists of 15-mer peptides whose sequences span all possible 10 a.a. T cell epitopes in HIV that occur at a frequency of >15% in the Los Alamos Database
 - Humoral (D196)
- Neutralization screen & anti-env EIA



Results

- **Number enrolled per region**
 - US:180
 - South Africa (SA): 240
 - Jamaica, Haiti & Brazil (Other): 60
- **Race:**
 - White (non-Hispanic)—115 (24%)
 - Black (non-Hispanic)—324 (68%)
 - Hispanic—30 (6%)
 - Asian/other—11 (2%)
- **Age: Mean = 26.0 yrs**

(No difference between vaccine and control groups)



IFN- γ -secreting T cell responses ¹ elicited by the vaccine (ELISpot assay, PTE-G)

Responses (%; 95% CI)

	<u>US sites</u>	<u>SA sites</u>	<u>Other</u>
Placebo	1/74 (1.4%) (0.2 – 7.3)	4/97 (4.1%) (1.6 – 10.1)	0/20 (0.0%) (0.0-16.1)
Vaccinee	55/74 (74.3%) (63.3 – 82.9)	64/93 (68.8%) (58.8 – 77.3)	15/21 (71.4%) (50.0%-86.2%)

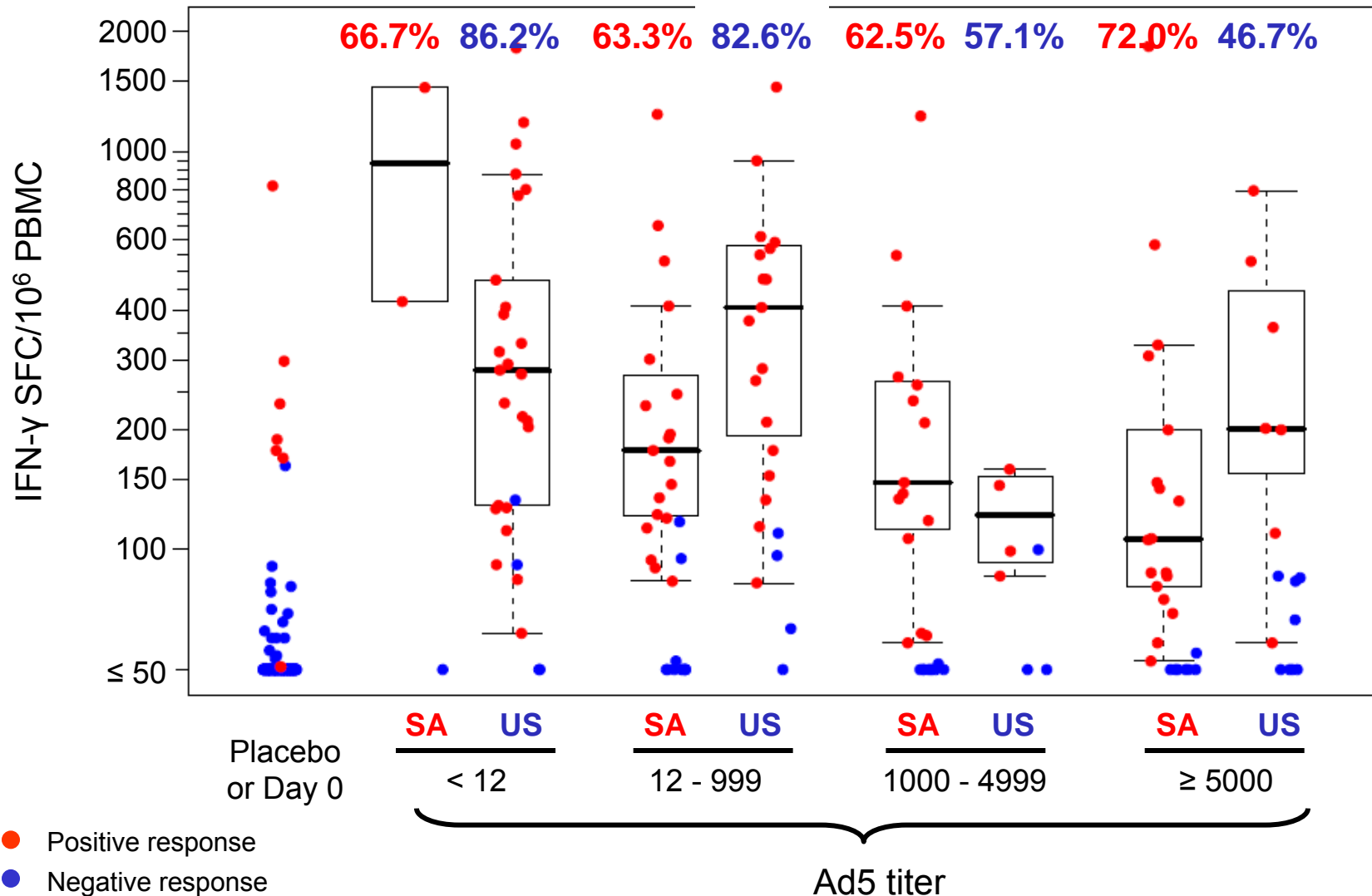
1 = 6 weeks post Ad5-HIV boost

Other = Brazil, Jamaica, Haiti



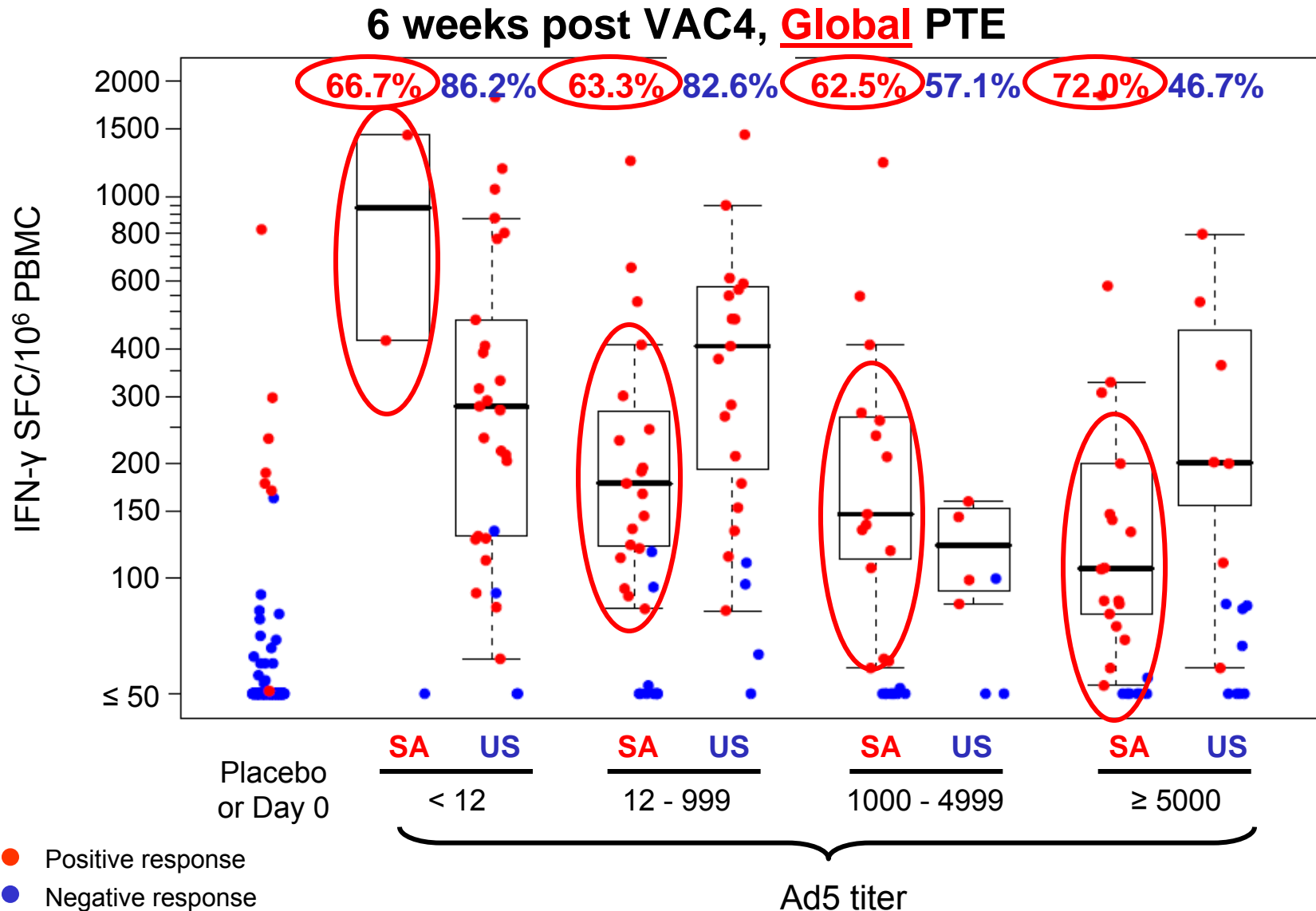
IFN- γ ELISpot Responses to Any Antigen by Region and Ad5 NAb Titer

6 weeks post VAC4, Global PTE



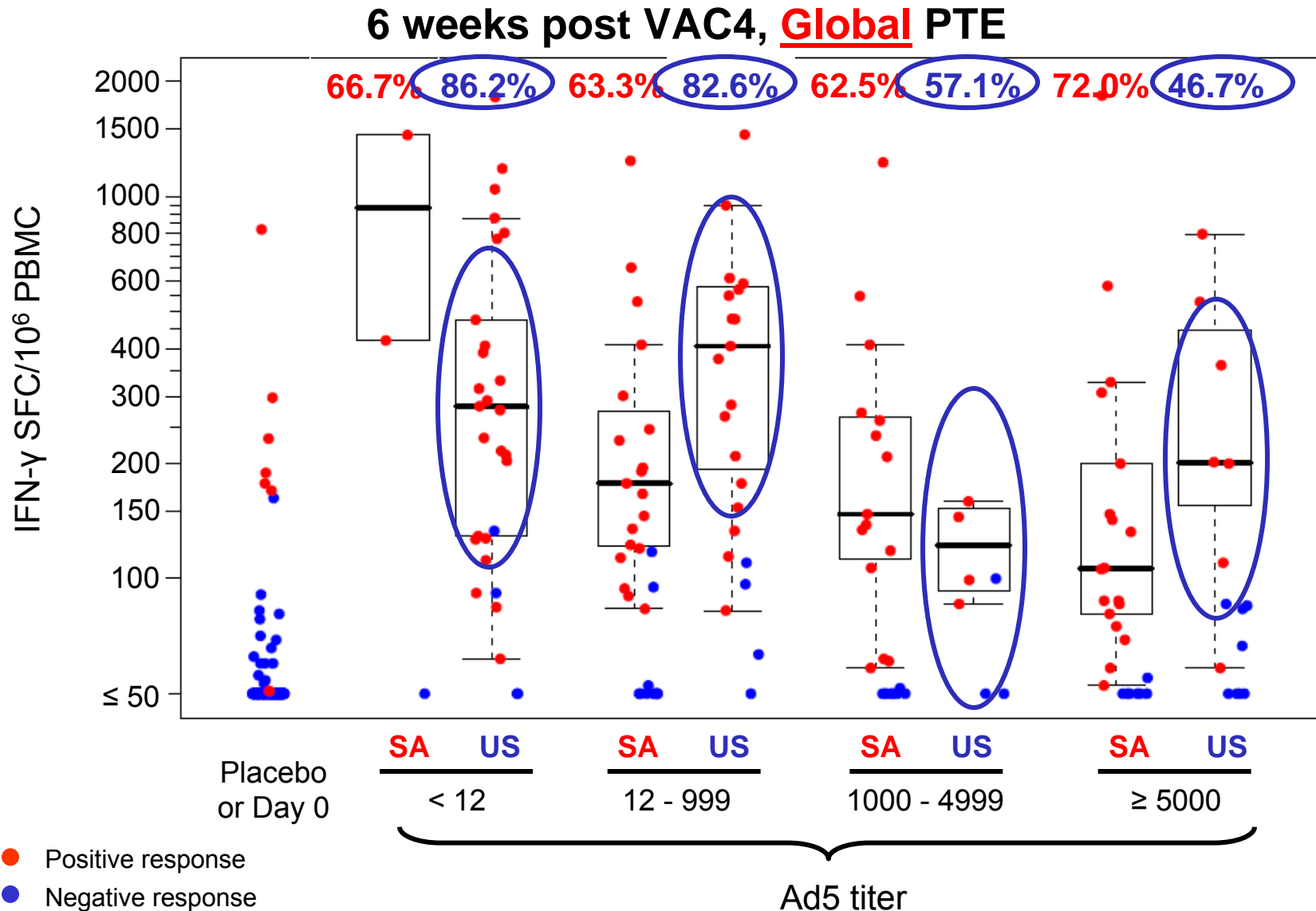


IFN- γ ELISpot Responses to Any Antigen by Region and Ad5 NAb Titer





IFN- γ ELISpot Responses to Any Antigen by Region and Ad5 NAb Titer

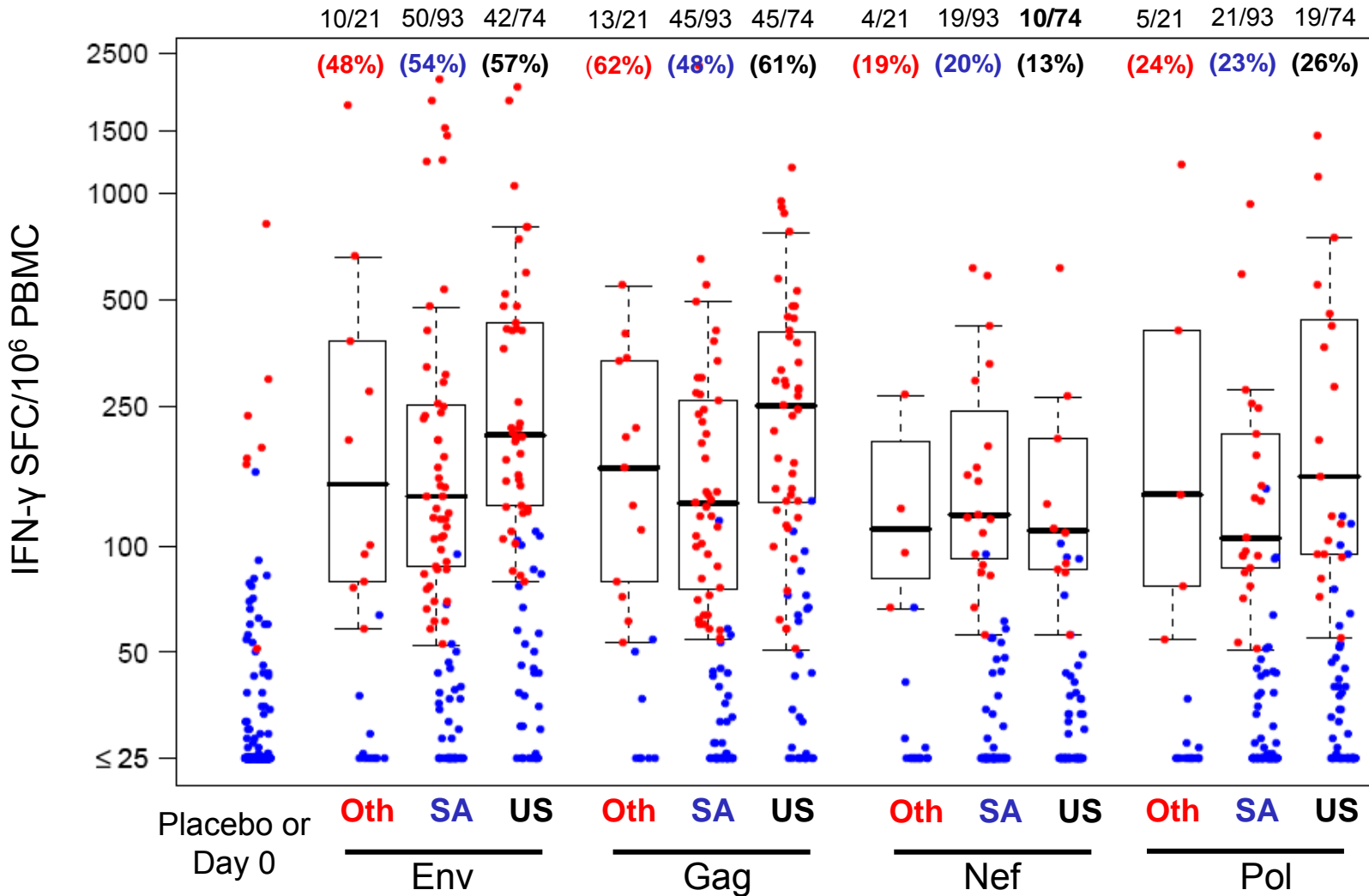




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IFN- γ ELISpot Responses by Antigen and Region

6 weeks post VAC4, **Global** PTE peptides



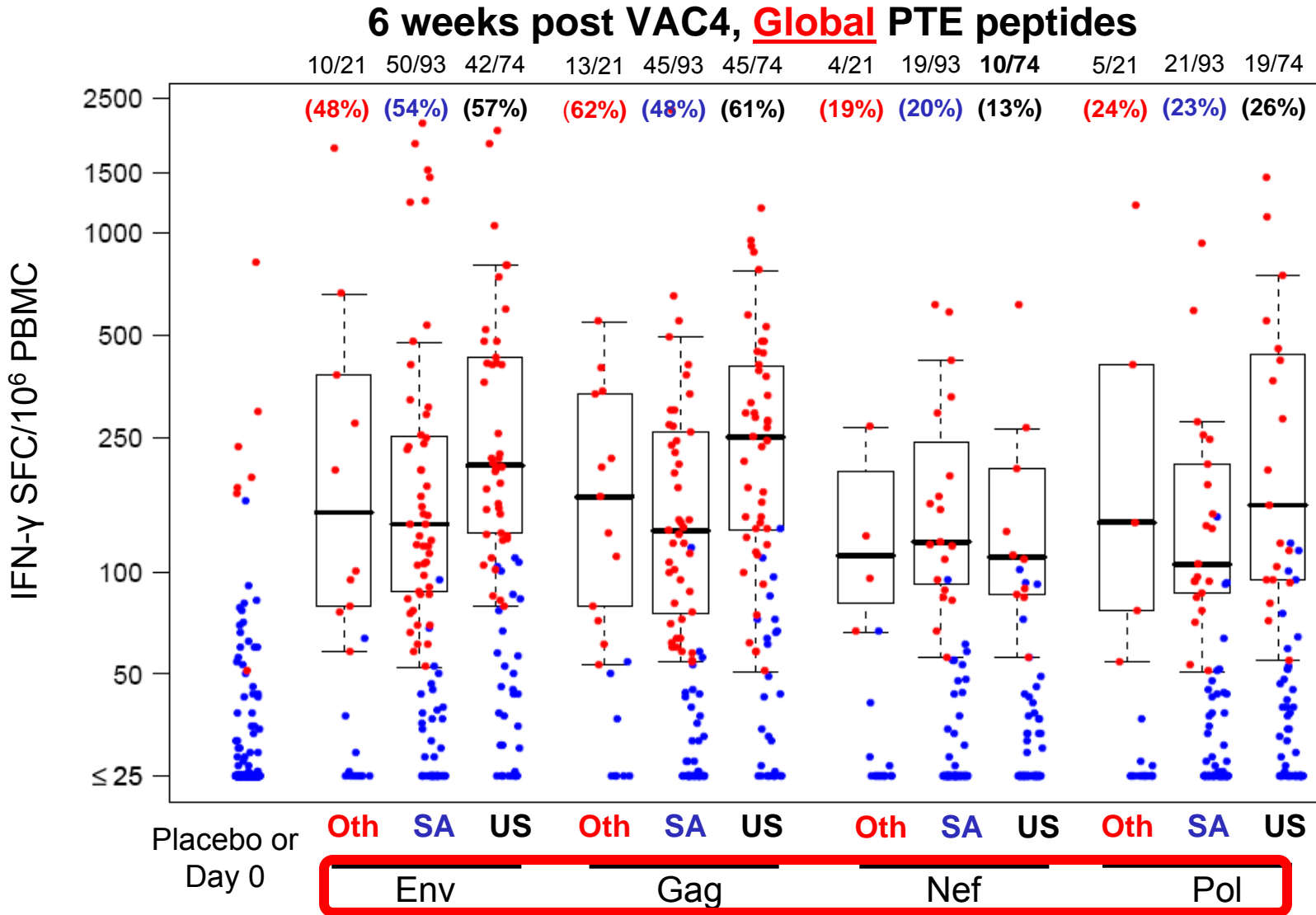
- Positive response
- Negative response

Oth: Brazil, Jamaica, Haiti



HIV VACCINE
T R I

IFN- γ ELISpot Responses by Antigen and Region



- Positive response
- Negative response

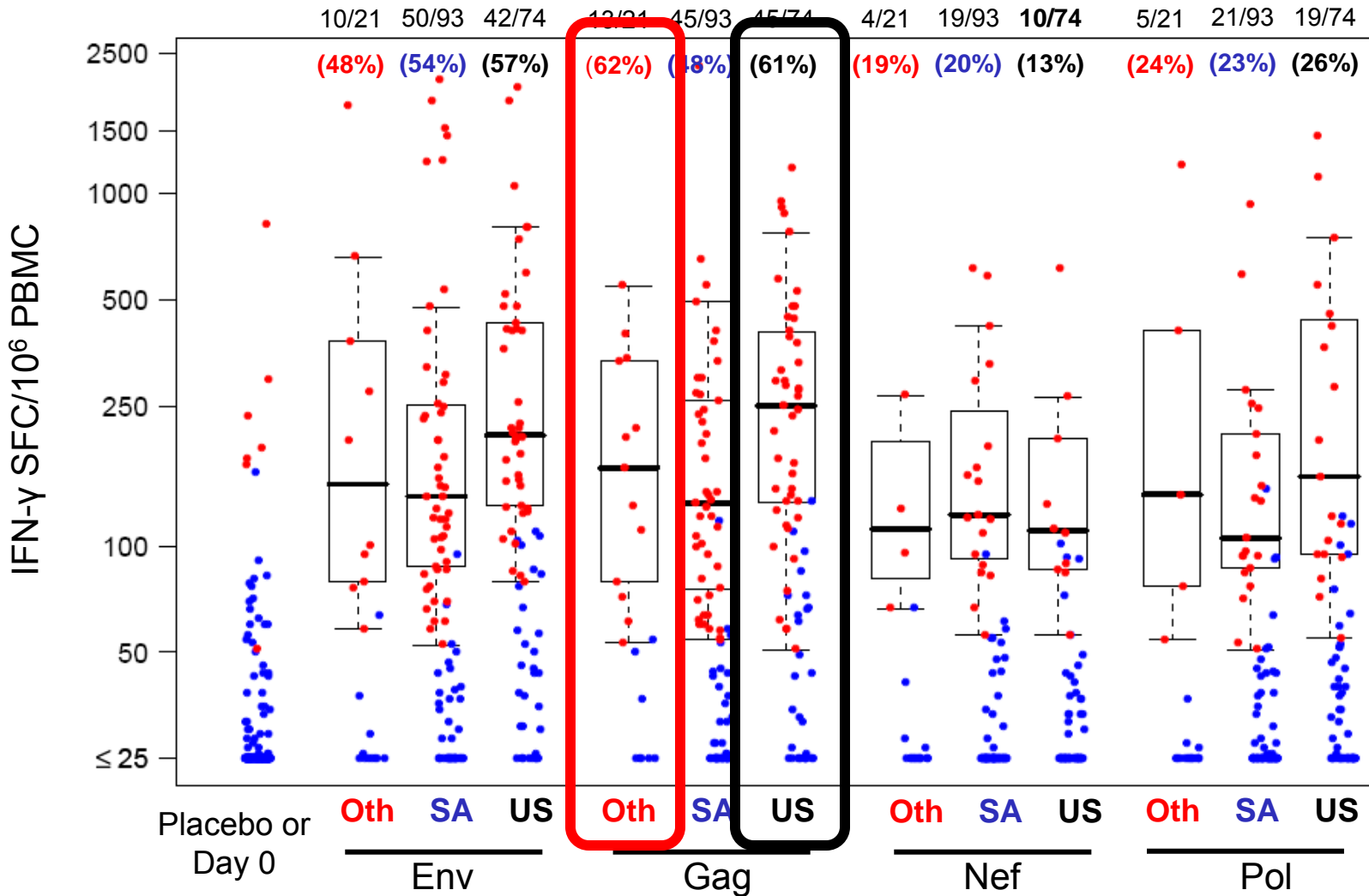
Oth: Brazil, Jamaica, Haiti



HIV VACCINE
T R I

IFN- γ ELISpot Responses by Antigen and Region

6 weeks post VAC4, **Global** PTE peptides



- Positive response
- Negative response

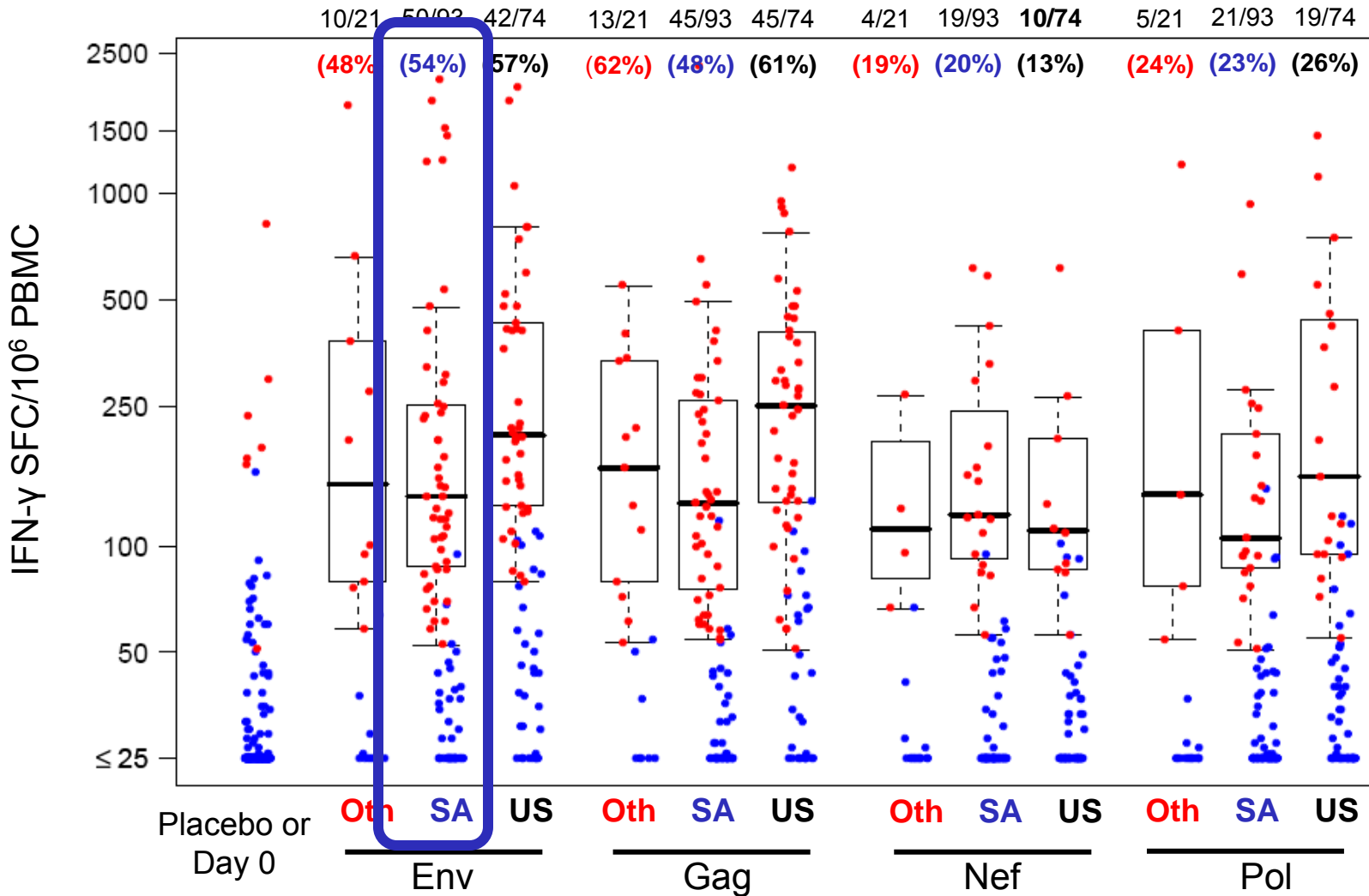
Oth: Brazil, Jamaica, Haiti



HIV VACCINE
T R I

IFN- γ ELISpot Responses by Antigen and Region

6 weeks post VAC4, Global PTE peptides



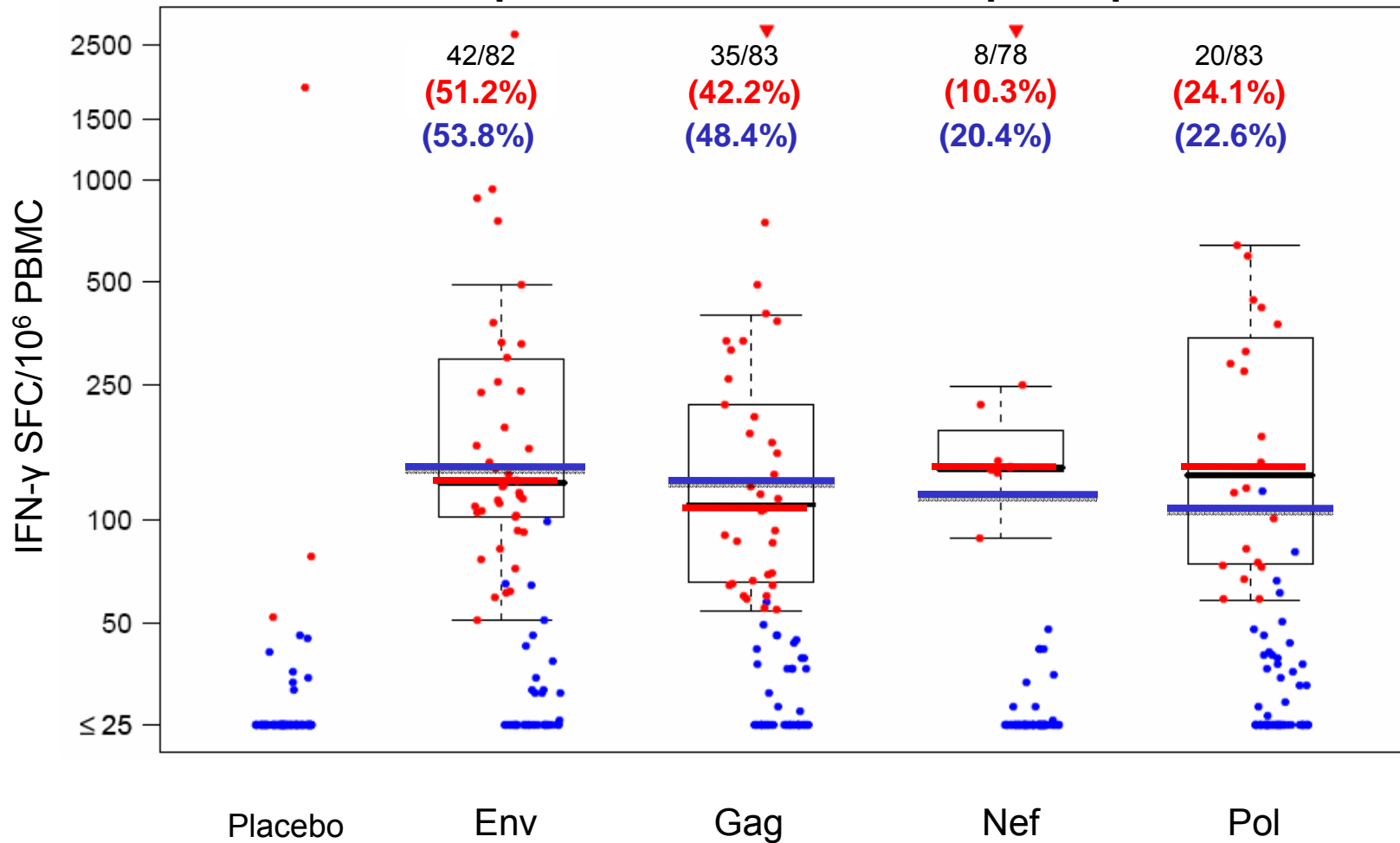
- Positive response
- Negative response

Oth: Brazil, Jamaica, Haiti



IFN- γ ELISpot Responses by Antigen using PTE-C & PTE-G peptides

6 weeks post VAC4, **South Africa** participants



● Positive response
● Negative response

▼ Spot too numerous to count



Frequency of ICS T-Cells responses by region

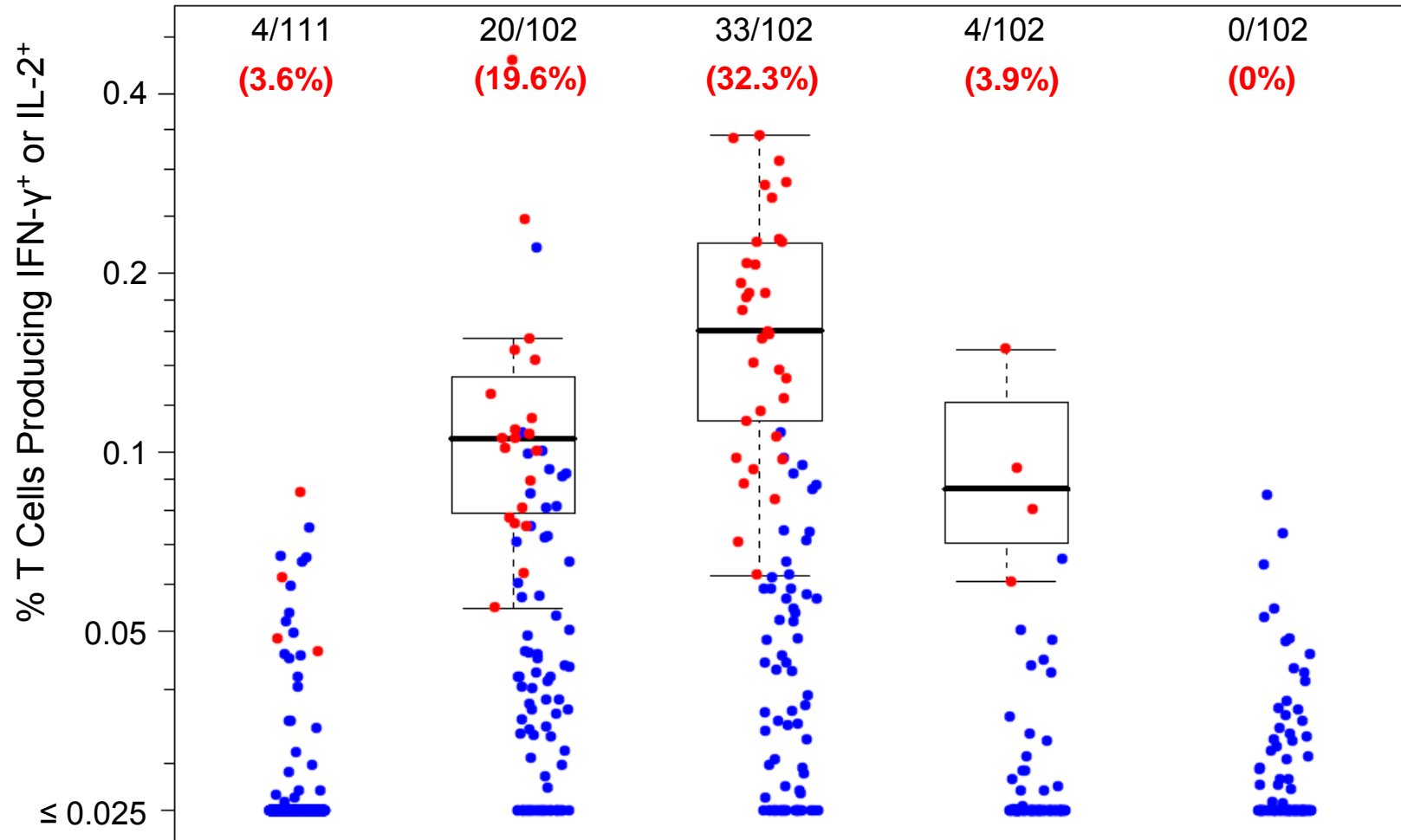
<u>T cell type</u>	<u>T-Cells Responses (%; 95% CI)</u>		
	<u>US Sites</u>	<u>South African Sites</u>	<u>Other*</u>
CD4+	26/57 (45.6%) (33.4-58.4)	5/24 (20.8%) (9.2-40.5)	8/21 (38.1%) (20.8-59.1)
CD8+	30/56 (53.6%) (40.7-66.0)	16/38 (42.1%) (27.9-57.8)	7/22 (31.8%) (16.4-52.7)

* Jamaica, Brazil, and Haiti



CD4+ T-Cell cytokine responses by antigen

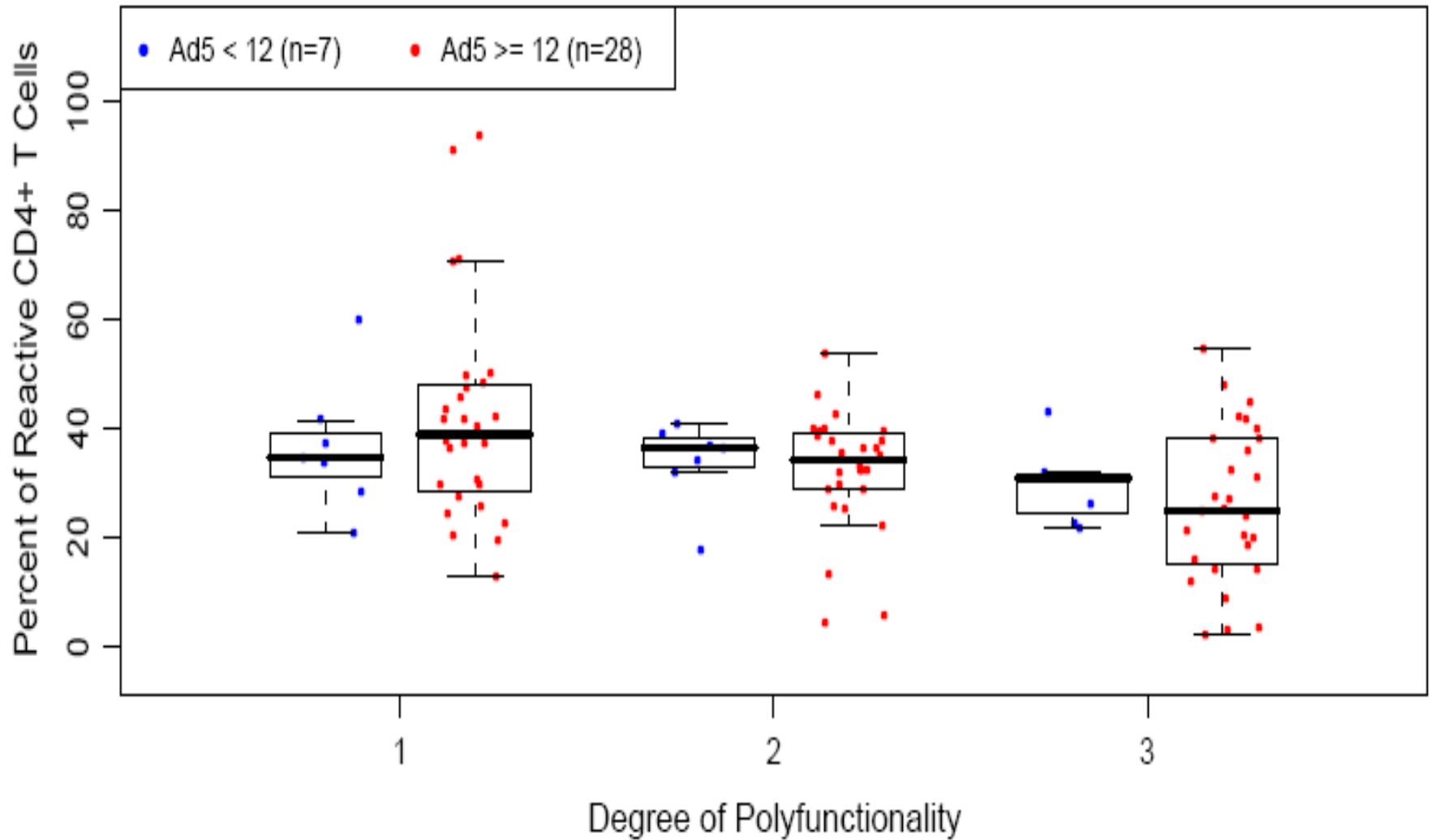
CD4+ T cells, 6 weeks post VAC4



● Positive response
● Negative response



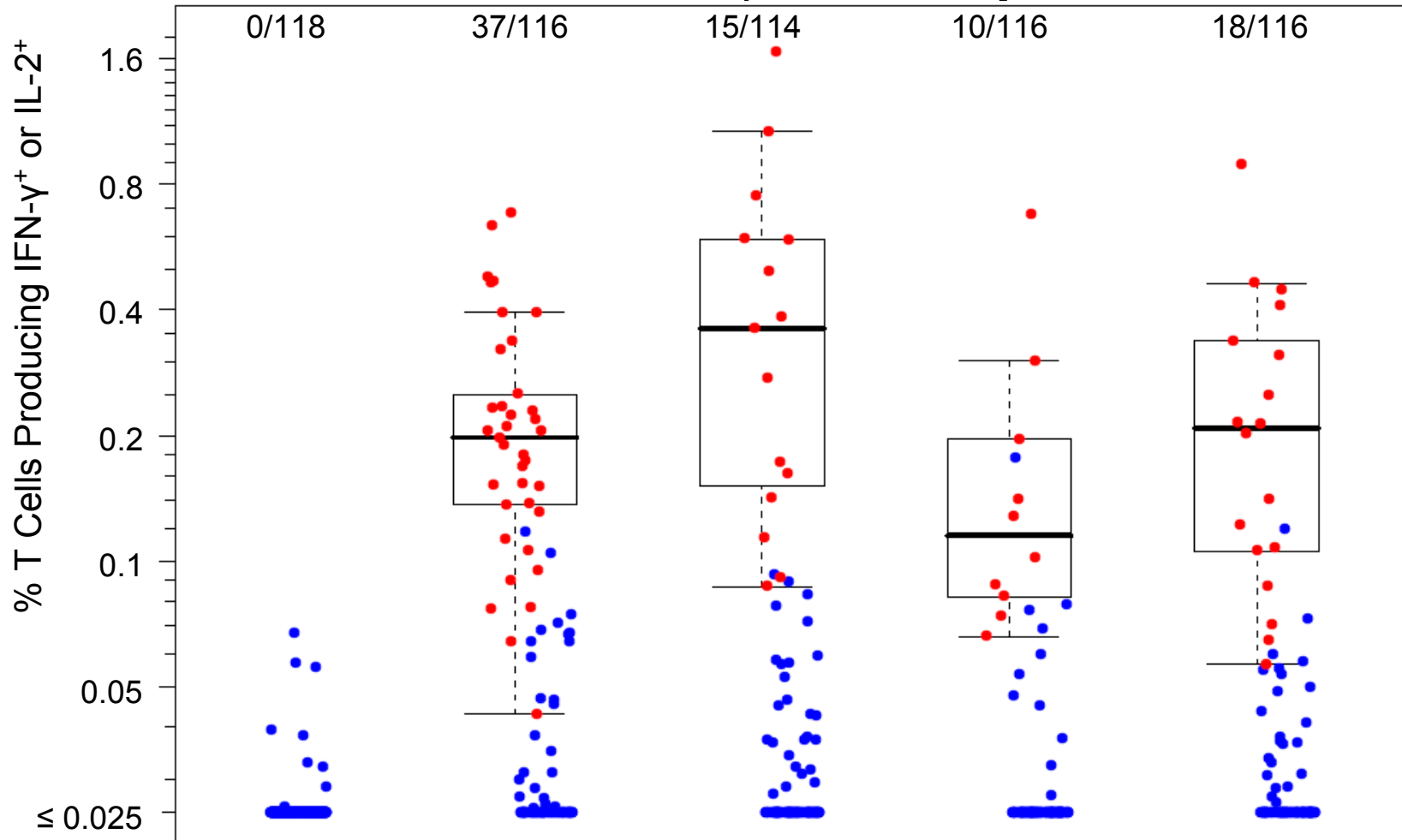
Degree of CD4+ T cell polyfunctionality





CD8+ T cell cytokine responses by Antigen

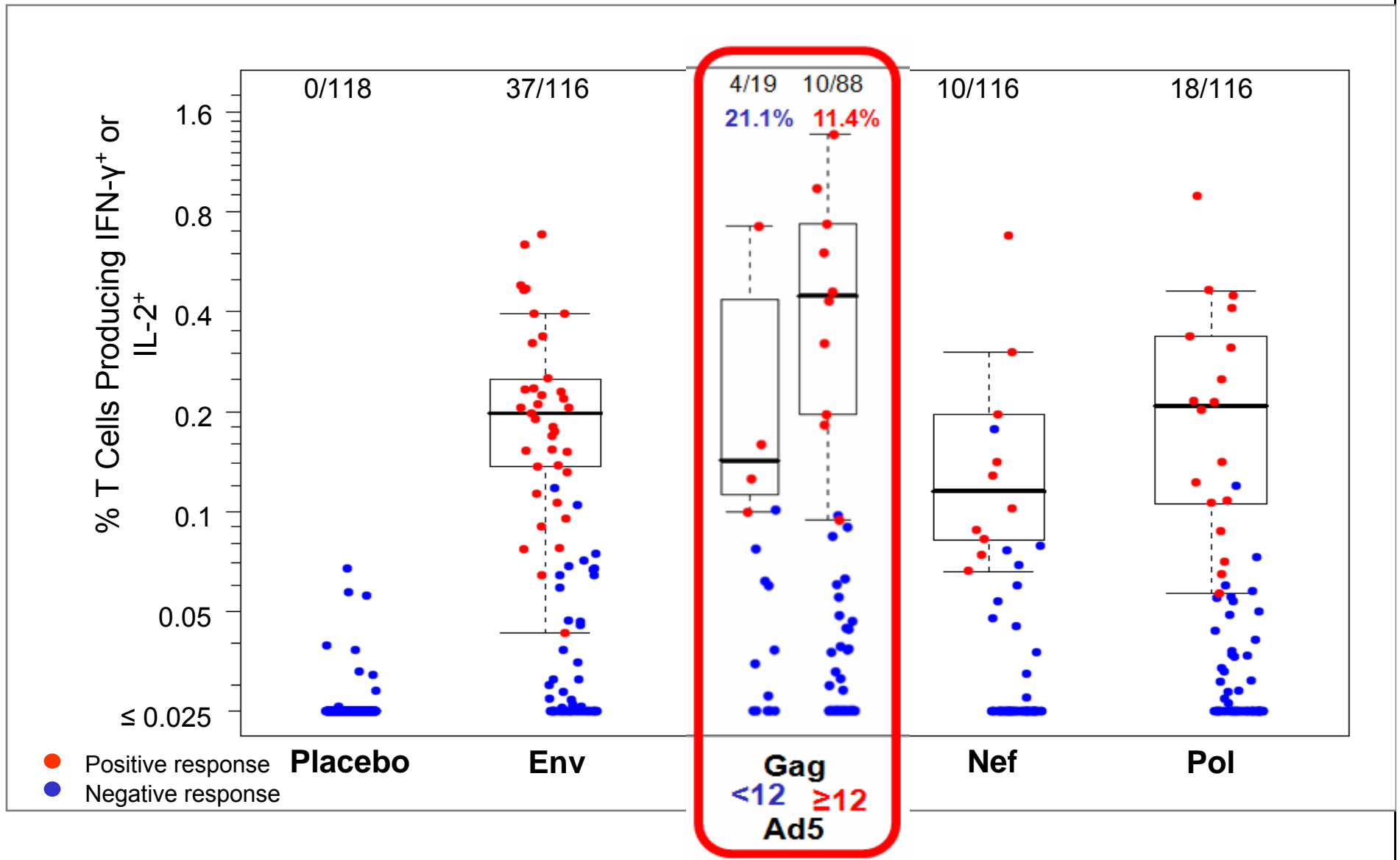
CD8+ T cells, 6 weeks post



- Positive response
- Negative response

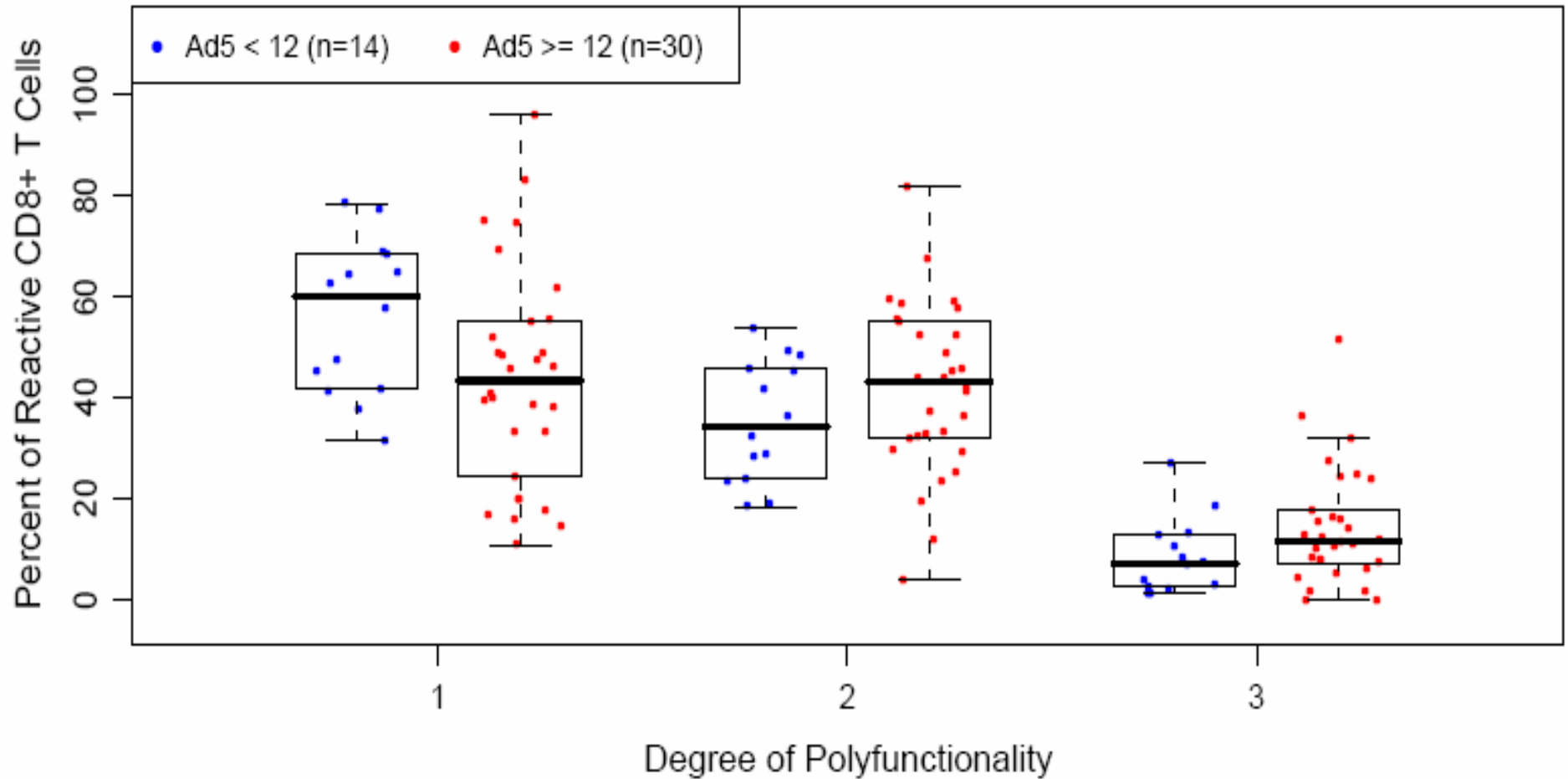


CD8+ T cell cytokine responses by Antigen



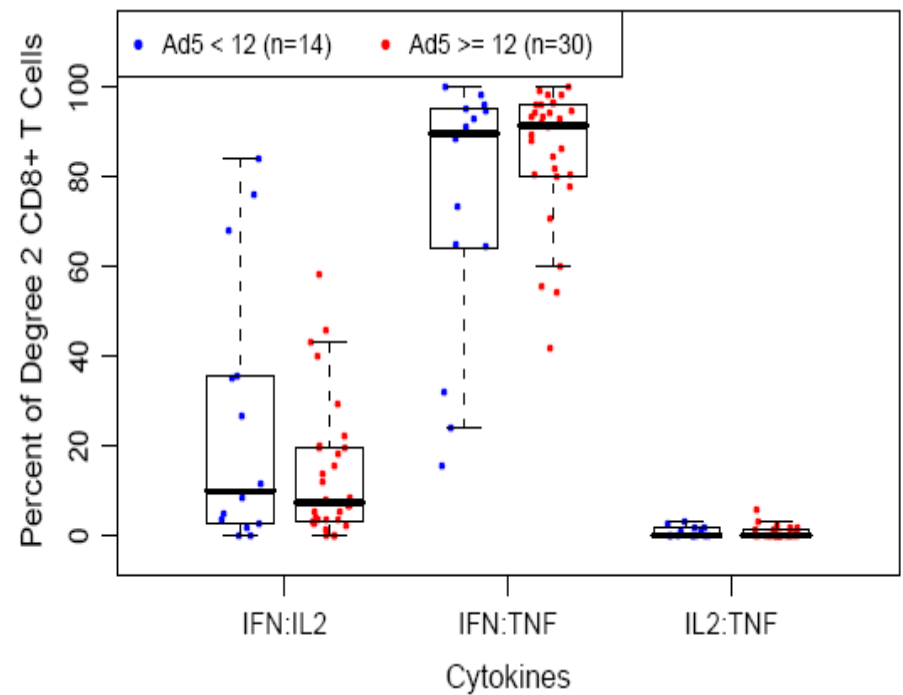
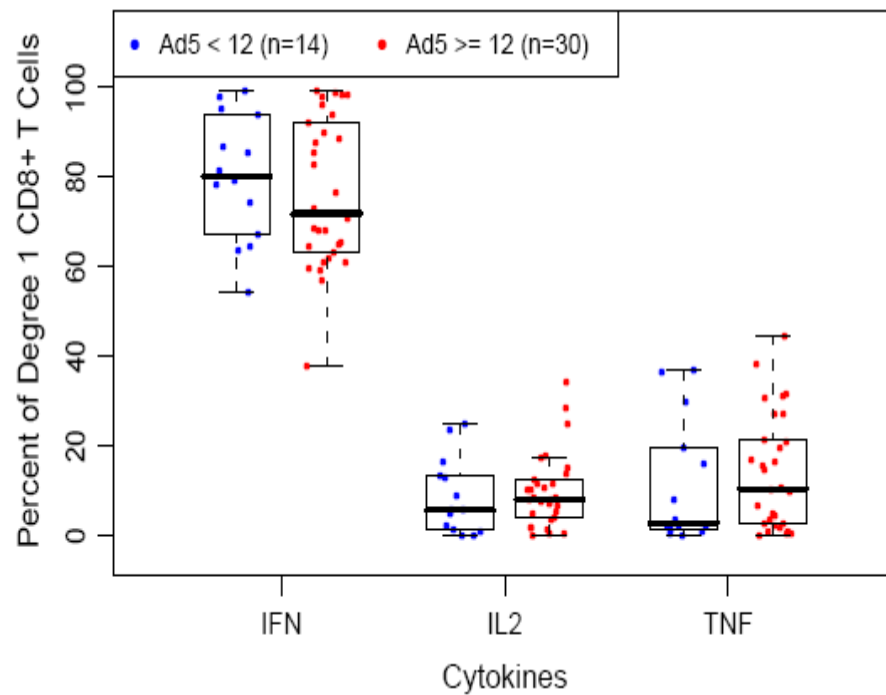


Degree of CD8+ T cell Polyfunctionality





Relative CD8+ T cell cytokine responses





Conclusions

- All vaccine antigens were recognized
- Significant immunogenicity was found using global PTEs
 - Comparison of immune responses between the VRC DNA/rAd5 and the Merck rAD5 (HVTN502/STEP and HVTN503/Phambili trials) vaccine regimens. A Duerr. **Late Breaker Poster (LB-35)**
- In South African participants
 - Pre-existing immunity to Ad5 reduced the magnitude, but not the frequency, of positive responses
 - the frequency & magnitude of IFN- γ ELISpot responses using Global and Clade C PTE peptide pools were similar



Conclusions

- CD4+ reactive T cells were polyfunctional producing 1, 2 or 3 cytokines in similar proportions overall, by Ad5 group and by antigen
- CD8+ reactive T cells were polyfunctional but the proportion producing 1, 2 or 3 cytokines declined with number of functions and was not different by Ad5 group
- Preliminary results support plans for continued evaluation



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All 480 Volunteers!!