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EV06 Trial: Modulation of the Immunogenicity of the DNA-HIV-PT123 and AIDSVAX®B/E combination HIV vaccine in adult Ugandans by S. mansoni Infection

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Background: The prevalence of *S. mansoni* (SM) in Sub Saharan Africa raises concerns on the worm´s effects on the response to vaccines. We investigated the impact of SM infection on the humoral response to a novel DNA vaccine expressing Clade C Env, Gag and PolNef co-administered with AIDSVAX B/E.
Methods: This randomized double blind trial enrolled 72 male and female Ugandans aged 18-45, 36 infected with *S. mansoni* (SM+) and 36 uninfected (SM-). In each arm 30 received vaccine and 6 placebo at week 0, 4 and 24. Responses were evaluated at week 0, 6, 26 and 36. Humoral responses were measured by binding and neutralization assays. IgG against a panel of HIV-1 envelope glycoproteins were measured by BAMA. Neutralizing antibodies (Nabs) were measured using TZM/bl cells and tier 1 pseudoviruses.
Results: Significant differences in binding IgG response rates were observed against the vaccine matched clade C V1V2 (gp70-96ZM651.02 V1V2) at week 6: 56% among SM+ vaccinated participants compared to 86% among SM- vaccinated participants (P = 0.039). At week 36, response magnitudes were also statistically lower in the SM+ group against the clade C vaccine matched gp120 and gp140 proteins (P = 0.04 for both). Response rates between groups were tested using Fisher's exact test and magnitudes using the Wilcoxon sum-rank test. Furthermore, vaccinated SM+ participants had: 1) significantly lower Nab response rates at week 36 for Clade C MW965.26 and Clade A/E TH023.6 (P < 0.05); 2) significantly lower IC50 titers for MW965.26 and TH023.6 at both weeks 26 and 36; and 3) lower median AUC-MB at each study week, which was statistically significantly different at week 36.
Conclusions: This DNA/gp120 protein vaccine regimen induced strong gp120, gp140 and V1V2 region-focused binding IgG and Nab responses. Preliminary evidence that *S.mansoni* infection may modulate antibody responses induced by vaccination is provided.