

Comparing Different Priming Strategies to Optimize HIV Vaccine Antibody Responses: Results from HVTN 096/EV04 (NCT01799954)

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Antibodies directed at conserved regions of the V1V2 loop and antibodies that mediate ADCC to HIV envelope have correlated with decreased HIV infection. In HVTN096, a phase I double blind, placebo controlled clinical trial, we evaluated safety and immunogenicity of co-administration of AIDSVAX B/E gp120 proteins during priming with either NYVAC or DNA candidate vaccines expressing clade C Env, Gag, and Pol-Nef.

96 volunteers were enrolled and randomized to 1 of 4 vaccine groups (T1-T4; n = 80) or placebo (n = 16). T1 received NYVAC prime at Month (M) 0 and 1, then NYVAC/AIDSVAX B/E at M3 and 6; T2 NYVAC/AIDSVAX B/E co-administration at M0, 1, 3 and 6; T3 DNA at M0 and 1, then NYVAC/AIDSVAX at M3 and 6; T4 DNA/AIDSVAX co-administration at M0 and 1, then NYVAC/AIDSVAX at M3 and 6.

Co-administration of gp120 with the priming vaccines (T2 and T4) generated detectable IgG Env binding antibody responses against V1V2 by M 1.5 in all volunteers while these Abs were not detected until M3.5 in the prime-boost strategies (T1 and T3). Furthermore, the area under the IgG V1V2 binding antibody curve over M 0-18 was significantly greater with co-administration ($p < 0.01$, T1 vs. T2 and T3 vs. T4). IgG Env responses to vaccine-matched antigens were enhanced by co-administration of gp120 with DNA primes ($p < 0.01$, T3 vs. T4) but not with NYVAC primes ($p = 0.70$, T1 vs. T2). Rates of CD4 and CD8 T cell responses to vaccine-matched antigens at M 6.5 was not affected by co-administration ($p > 0.15$), but higher response rates were observed in the DNA vs. NYVAC vaccine groups ($p < 0.02$): T3 88.2% CD4 and 41.2% CD8, T4 83.3% CD4 and 36.8% CD8 as compared to T1 47.4% CD4 and 5.3% CD8 and T2 18.8% CD4 and 5.9% CD8. ADCC responses were detected in all groups.

Co-administration of gp120 proteins with DNA or NYVAC during priming resulted in earlier induction and higher magnitude and durability of protective V1V2 antibody responses over 18 months. DNA priming induced more potent T cell responses.