Safety and immunogenicity of month 30 boost of ALVAC + gp120/MF59 preventive HIV vaccines

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BACKGROUND

HVTN 100 Part A:

- Phase 1-2 preventive HIV vaccine trial in South Africa
- ALVAC-HIV (vCP2438) at months 0 and 1, plus ALVAC-HIV with Bivalent subtype C gp120/MF59 at months 3, 6 and 12.
- IgG binding antibody and T-cell responses at month 12.5 were similar or greater compared to month 6.5, then waned by month 18.

Aim of this study, HVTN 100 Part B:
Assess safety and immune responses after the month 30 boost, which was either ALVAC+gp120/MF59 or gp120/MF59 alone.

METHODS

From September 2017 to August 2018, vaccinations were administered to eligible Part A participants: ALVAC-HIV plus gp120/MF59 (n=32), or gp120/MF59 alone (n=31), and placebo group re-administered placebo (n=7).

MEASUREMENT	TEST		
Safety	Reactogenicity	Adverse events	Laboratory tests
Binding antibodies	Binding antibody multiplex assay (BAMA)		
HIV-specific CD4+ T-cell responses	Intracellular cytokine staining assay		
Neutralization ID50 titers	Reductions in Tat-regulated luciferase reporter gene expression in TZM-bl cells		

HVTN 100 Part B Findings: month 30 booster vaccine

✓ Positive Outcomes

- Acceptable safety profile
- Restored binding antibodies
- Restored CD4+ T cells

X Challenges

- No tier 2 neutralizing antibodies
- Regimen has no prevention efficacy (HVTN 702)
- No differences between vaccine groups

RESULTS

- Both vaccine groups had acceptable safety profiles
- No statistically significant differences in IgG binding antibody response rates or magnitudes between the two vaccine groups for any gp120, gp140, or V1V2 antigens at any timepoint.
- The vaccine groups had positive IgG responses to all V1V2 (n=27), gp120 (n=11) and gp140 antigens (n=9) at all timepoints but were more common for gp120 and gp140 antigens and highest at month 30.5 (Fig 1).
- Magnitude-breadth IgG BAMA response to V1V2 antigens were restored, by a booster vaccination after an 18-month interval, at month 30.5 but rapidly waned by month 36 with median area under the curves (AUCs) for combined vaccine groups 0.13, 2.55 and 0.40 for months 30, 30.5 and 36, respectively (Fig 2).
- CD4+ IFN-γ and/or IL-2 and/or CD40L T-cell responses to vaccine-matched Env antigens were seen at month 30, boosted at month 30.5, waned by month 36, with no significant differences between vaccine groups (Fig 3).

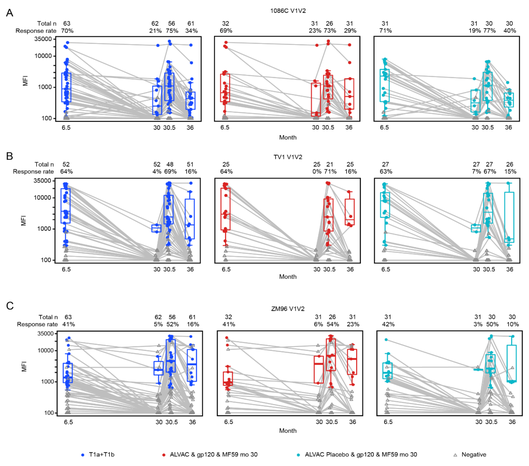

Fig 1. IgG binding antibody responses to the V1V2 vaccine strain antigens 1086, TV1, ZM96. Response rates and magnitudes of IgG binding antibodies to the V1V2 vaccine strain antigens: 1086 (A), TV1 (B) and ZM 96 (C) among per-protocol vaccine recipients of HVTN 100 Part B. Boxplots show magnitude as mean fluorescent intensity (MFI) responses to individual V1V2 antigens and are based on positive responders, shown as solid circles.

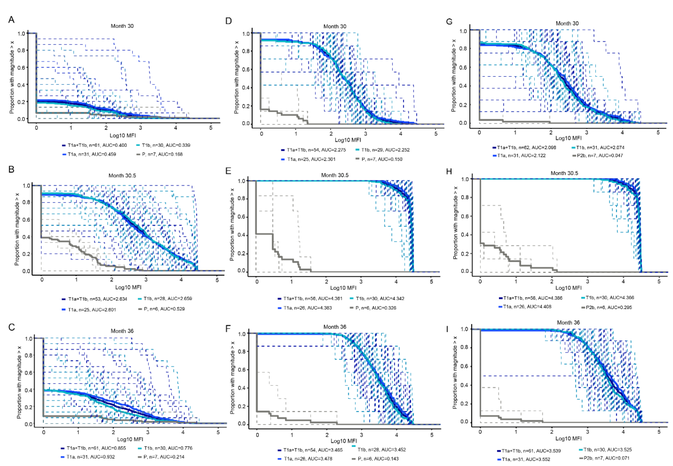

Fig 2. Magnitude-breadth of IgG binding antibody responses to subtype C Env V1V2 (A-C), gp120 (D-F) and gp140 (G-I) antigens among participants in the cohort for Part B at the Month 30 vaccination timepoint (A,D,G), 2 weeks after the Month 30 vaccination (Month 30.5) (B,E,H), and at Month 36 (C,F,I). Panel size is 15 (A-C), 7 (D,F), 6 (E), and 8 (G-I). AUC= area under curve, T=treatment, P=placebo, MFI=mean fluorescence intensity.

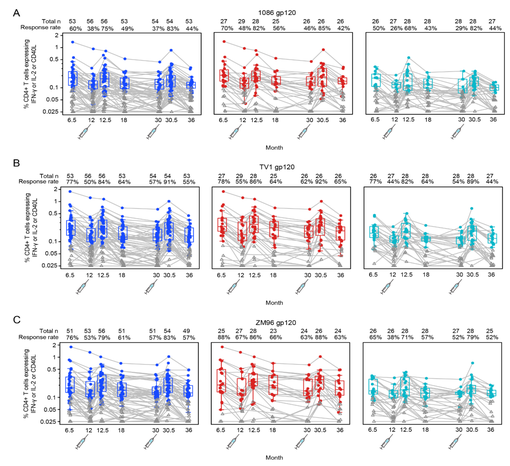

Fig 3. Summary of the response rates and magnitudes of CD4+ T cell responses. Boxplots show response magnitude in the percent expression of IFN-γ and/or IL-2 and/or CD40L T-cell responses to Env 1086 (A), TV1 (B) and ZM96.C (C) gp120 and are based on positive responders, shown as solid circles, and negative responders are shown as grey triangles. Syringes denote timepoint of vaccination series beginning at month 12 (5th vaccination of Part A).

ADDITIONAL KEY INFORMATION

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