0283

Post-hoc Comparison of AS01B, MF59 and Alum Adjuvants Across 4 HIV Vaccine Trials

Ferdinando L. Menezes[1], Shiyu Chen[2], Nicole Grunenberg[2], Mookho Malahleha[3], Kathy Mngadi[4], Monde Muyoyeta[5], Fatima Laher[6], Zvavahera M. Chirenje[7,8], Linda-Gail Bekker[3], Paul Goepfert[9], Glenda E. Gray[2,6,10], Georgia Tomaras[11], M Juliana McElrath[2,12], Esper Kallas[1], Alison C. Roxby[2], Zoe Moodie[2], On behalf of the HVTN 100, 107, 120 and 702 Protocol Teams[2].

[1]University of São Paulo, Brazil, [2]Fred Hutchinson Cancer Center, Seattle, WA, USA [3]University of Cape Town, South Africa, [4]Aurum Institute, Tembisa, South Africa, [5]Centre for Infectious Diseases Research, Livingstone, Zambia, [6]University of the Witwatersrand, South Africa, [7]University of California, San Francisco, USA, [8]University of Zimbabwe, Zimbabwe, [9]University of Alabama at Birmingham, USA, [10]South African Medical Research Council, Cape Town, South Africa [11]Duke University School of Medicine, Durham, USA [12]Cape Town HVTN Immunology Laboratory, South Africa

BACKGROUND

$AS01_B$, MF59, and Alum are widely used adjuvants with distinct mechanisms of action, yet direct comparisons of their immunogenicity and reactogenicity when formulated with the same antigen are limited. HIV vaccine trials using the same immunogen and schedule allow a direct comparison of immune responses and reactogenicity across different adjuvants.

METHODS

- Cross-protocol post-hoc analysis of four randomized, double-blind ALVAC-HIV trials (HVTN 100, 107, 120, 702)
- ALVAC-HIV prime with gp120 boost (MF59, Aluminum Hydroxide, or $AS01_B$);immunogenicity at month 6.5 (BAMA, ICS)
- Response rates and magnitudes compared using Barnard's and Wilcoxon tests (FDR-adjusted)

$AS01_B$ adjuvanted vaccine generated stronger HIV specific immune responses than MF59- or alum-adjuvanted formulations
with acceptable but higher short term side effects.

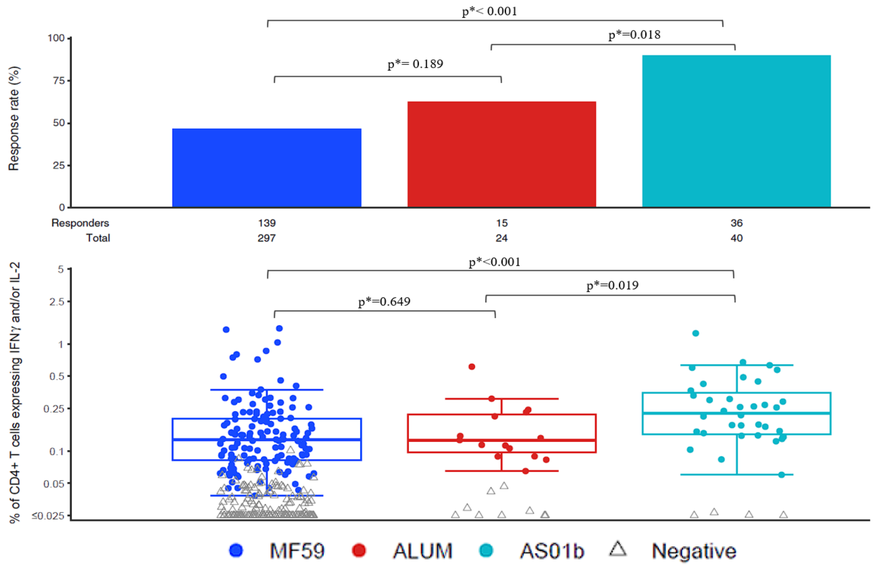


Figure 1: Intracellular cytokine staining (ICS)T-cell assays: Response rates and magnitudes of CD4+ IFNy and/or IL-2 Expression in response to 1086 gp120.

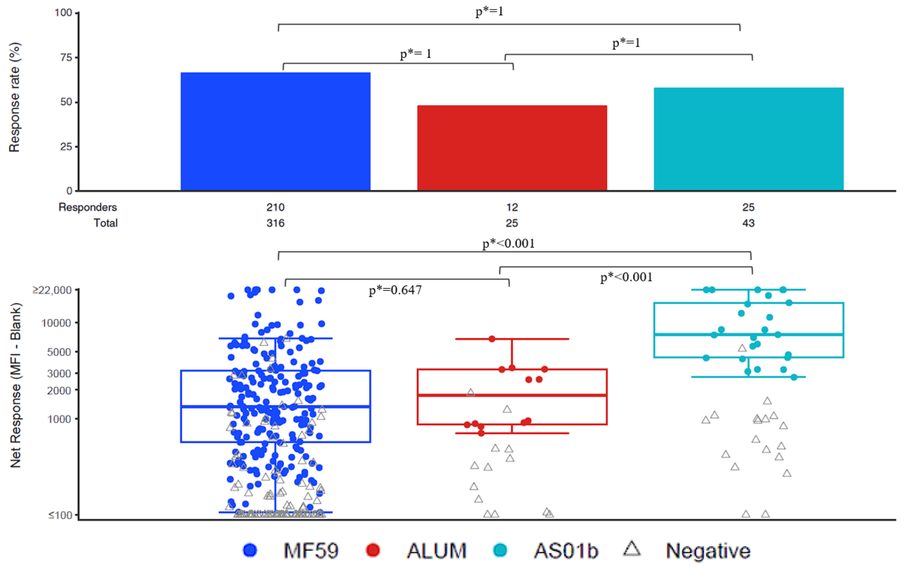


Figure 2: IgG Binding Antibody Response rates and magnitudes to C.1086C_V1_V2 Tags (Dilution 1:50).

RESULTS

- Aggregated participants across studies: MF59 (n=3000), Alum (n=36) and $AS01_B$ (n=50).
- Immunogenicity evaluated in 393 participants (MF59 n=320; Alum n=27; $AS01_B$ n=46).
- Antigen-specific antibody response rates similar across adjuvants; $AS01_B$ induced higher IgG magnitudes (not IgG3). $AS01_B$ elicited higher ag-specific $CD4^+$ T-cell response rates and greater IFN-γ/IL-2 expression
- Reactogenicity acceptable for all adjuvants; systemic symptoms more frequent with $AS01_B$

CONCLUSIONS

$AS01_B$ formulations demonstrated superior immunogenicity, eliciting higher response rates and magnitudes for both antigen-specific IgG and CD4+ T-cell responses when compared to MF59 and Alum-formulations. While $AS01_B$ adjuvanted vaccine was associated with increased reactogenicity, its safety profile remained acceptable. No significant immunogenicity differences were observed between MF59 and Alum-adjuvanted vaccines. These findings support $AS01_B$ as a promising adjuvant for HIV vaccine development and justify its continued use in HIV vaccine development.

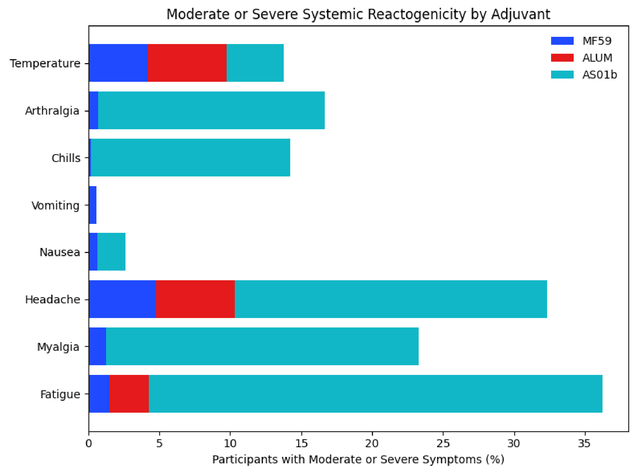


Figure 3: Descriptive analysis of reactions; no formal statistical comparisons.

ACKNOWLEDGMENTS

The authors acknowledge the study participants, community advisory boards, protocol teams, and site staff involved in these trials. We also acknowledge support from the HIV Vaccine Trials Network and funding from the U.S. National Institutes of Health. GSK is acknowledged for financial support, including support for vaccine-related activities and provision of pre-exposure prophylaxis to trial participants.