PHASE 1/2A TRIAL OF HIV CLADE C DNA WITH MF59- OR AS01$_B$-ADJUVANTED CLADE C PROTEIN (HVTN 108)

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BACKGROUND

- After RV144, the Pox Protein Public Private Partnership initiated multiple trials to evaluate a clade C bivalent protein (TV1.C and 1086.C gp120) vaccine with different adjuvants and priming agents to optimize the design of future vaccine regimens.
- We showed that substituting DNA (DNA-HIV-PT123) for ALVAC can improve immune responses[1].
- The aim of HVTN 108, a phase 1/2a randomized, placebo-controlled trial, was to evaluate the safety and immunogenicity of the DNA vaccine with several protein/MF59/AS01$_B$ adjuvant combinations.

METHODS

- We randomly allocated 334 HIV negative participants from the USA and South Africa to 7 intervention groups or placebo.
- Data from an additional 60 participants who had received the same regimen as groups T1 and T4 in the HVTN 111 trial were also included in the analysis.
- We assessed DNA prime at months (M)0, 1 with DNA/protein/adjuvant boosts at M3 and 6, DNA/protein/adjuvant co-administration at M0, 1 and 6, and only low dose protein/AS01$_B$ at M0, 1 and 6 (**see schema**).
- Protein was either adjuvanted with MF59 or AS01$_B$[#] (GSK).
- Safety was assessed by collecting reactogenicity and adverse events.
- We measured humoral and cellular responses at M6.5 (peak) and M12 (durability) by binding antibody multiplex assay and ex vivo intracellular cytokine staining.

HVTN 108 Study Schema

Group	N	Dose of each protein	Deltoid	Month 0 (Day 0)	Month 1 (Day 28)	Month 3 (Day 84)	Month 6 (Day 168)
T1	30	100mcg	Left	DNA	DNA	DNA	DNA
			Right	Placebo	Placebo	Protein + MF59	Protein + MF59
T2	50	100mcg	Left	DNA	DNA	DNA	DNA
			Right	Placebo	Placebo	Protein + AS01$_B$	Protein + AS01$_B$
T3	50	20mcg	Left	DNA	DNA	DNA	DNA
			Right	Placebo	Placebo	Protein + AS01$_B$	Protein + AS01$_B$
T4	30	100mcg	Left	DNA	DNA	Placebo	DNA
			Right	Protein + MF59	Protein + MF59	Placebo	Protein + MF59
T5	50	100mcg	Left	DNA	DNA	Placebo	DNA
			Right	Protein + AS01$_B$	Protein + AS01$_B$	Placebo	Protein + AS01$_B$
T6	50	20mcg	Left	DNA	DNA	Placebo	DNA
			Right	Protein + AS01$_B$	Protein + AS01$_B$	Placebo	Protein + AS01$_B$
T7	50	20mcg	Left	Placebo	Placebo	Placebo	Placebo
			Right	Protein + AS01$_B$	Protein + AS01$_B$	Placebo	Protein + AS01$_B$
P1	24		Left	Placebo	Placebo	Placebo	Placebo
			Right	Placebo	Placebo	Placebo	Placebo
Total	334 (310 vaccinees; 24 placebo)						

1.Rouphael NG, et al. DNA priming and gp120 boosting induces HIV-specific antibodies in a randomized clinical trial. *J Clin Invest*. 2019 Nov1;129(11):4769-4785.

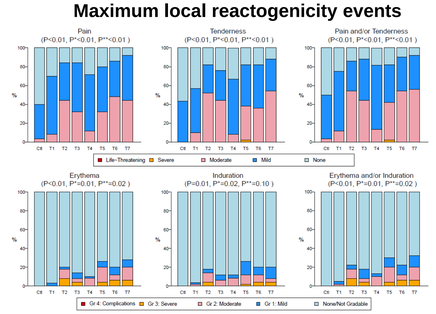
[#]AS01$_B$ is an Adjuvant System containing MPL, liposome (50 µg MPL and 50 µg QS-21) and QS-21 (Quillaja saponaria Molina, fraction 21)(Agenus)

RESULTS

Safety Summary

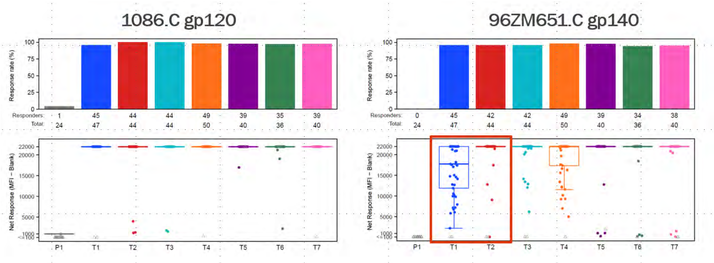
- **Adverse Events:** 4.8% of participants had mild and 1% moderate related AEs, but no related SAEs.
- No clinically significant differences in AEs or SAEs by vaccine group
- **Reactogenicity events:** 48 grade 3 and three grade 4
- 3.6% discontinued vaccinations due to reactogenicity events
- More local reactogenicity events with AS01$_B$ than MF59 regimens

Maximum local reactogenicity events

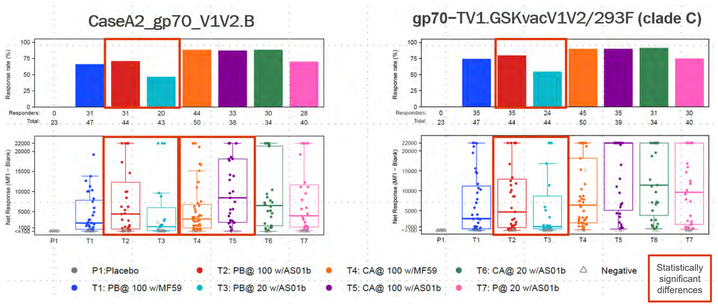


P: Across treatment arms; P*: T1 vs T2/3; P**: T4 vs T5/T6/T7

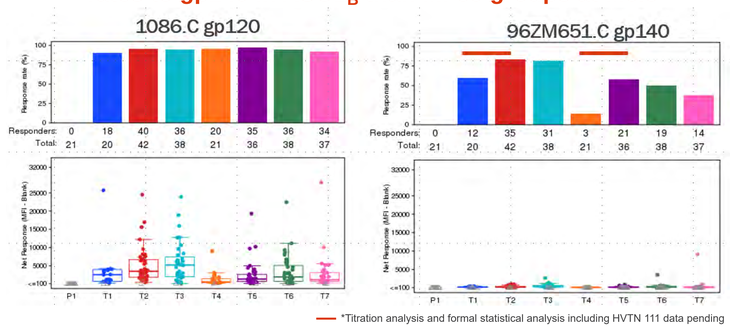
High IgG response rate and magnitude to clade C gp120 and gp140 across groups at M6.5



High response rates to V1V2 antigen (except T3), and highest magnitude in coadministration arms with AS01$_B$ at M6.5



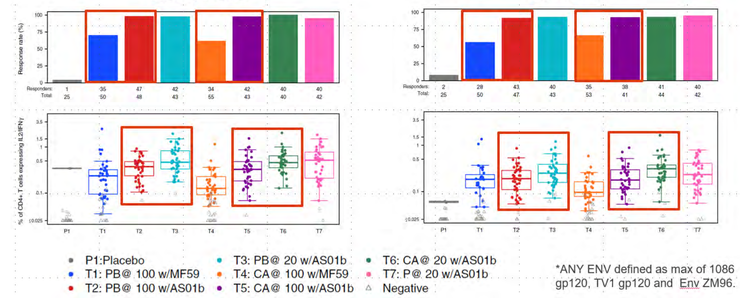
High IgG3 response rates to clade C gp120 and higher response rates to gp140 in ASO1$_B$ than MF59 groups at M6.5*



*Titration analysis and formal statistical analysis including HVTN 111 data pending

CD4+ T-cell response rates and magnitude to Any Env* higher in the AS01$_B$- than MF59-adjuvanted regimens at M6.5 and M12

Low dose protein elicited higher magnitude responses than high dose.



*ANY ENV defined as max of 1086 gp120, TV1 gp120 and Env ZM96.

CONCLUSIONS

- DNA/protein/adjuvant combinations demonstrated acceptable safety profiles, but more reactogenicity events in AS01$_B$ groups.
- All groups showed high IgG response rates to gp120 and gp140, and robust responses to Env V1V2 (except DNA prime with low dose protein and AS01$_B$ boost)
- AS01$_B$ adjuvanted groups showed higher CD4+ T cell responses and responses were durable.
- DNA/protein co-administration with AS01$_B$ may be a promising vaccine strategy for future trials.

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