Population-Specific T-Cell Responses and Virologic Control After Analytical Treatment Interruption

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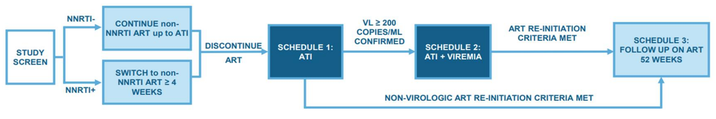
BACKGROUND

- ART prevents and treats but does not cure HIV.
- Early ART initiation and broadly neutralizing anti-HIV antibodies (bnAbs) have been associated with later ART-free HIV control, with more frequent post-intervention control reported for African women with clade C than for men with clade B virus.
- T cells have been identified as key potential mediators of virus control, though data among women are sparse.

METHODS

- After HIV acquisition within ~8wks of VRC01 bnAb or placebo receipt in the HIV prevention efficacy AMP Study, followed by early ART initiation and ≥1 year of viral suppression, women in southern Africa (n=11) and MSM+TG in Peru (n=17) stopped ART and underwent frequent safety, immunologic and virologic monitoring on ATI (Figure 1).
- ART was reinitiated for CD4<250, VL>1,000 for 4wks without 0.5log decline, or participant/clinician request.
- HIV-specific T cell responses (IFN-γ and/or IL-2 expression) were assessed by intracellular cytokine staining following stimulation with peptide pools to all HIV proteins; total response was the sum across responses to each protein.

Figure 1. AMP ATI schema and key design elements



ART RE-INITIATION CRITERIA

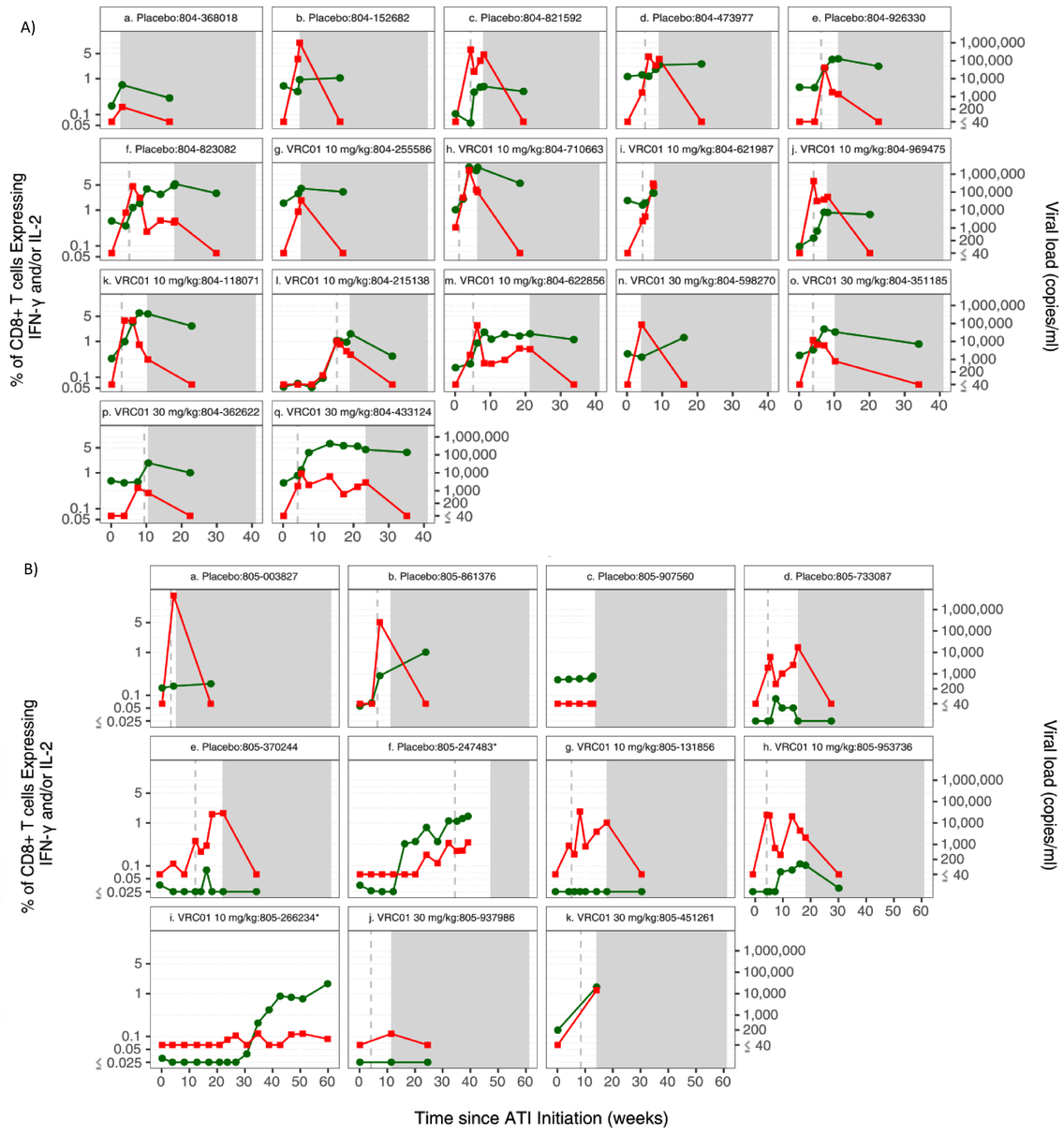
- VL ≥ 1,000 copies/mL for ≥ 4 consecutive weeks, & not declining 0.5 log from the previous week; OR
- CD4⁺ T cell count < 350 cells/mm³, confirmed on a second sample; OR
- Any HIV-related syndrome (eg, acute retroviral syndrome, opportunistic infection); OR
- Participant or provider wish to re-initiate ART.

ADDITIONAL KEY DESIGN ELEMENTS

- Robust informed consent process, including video, assessment of understanding & decision aids
- Facilitated decision-making & psychological assessments periodically throughout the study
- STI testing every 3 months & as indicated
- Weekly counseling on HIV transmission risk reduction and facilitated HIV testing and PrEP for sexual partners

CD8+ (but not CD4+) responses differed in controllers by fold-change from baseline; frequency to Env, Pol and Gag epitopes; and timing, preceding rebound among controllers only.

Figure 2. Longitudinal summaries of ICS response magnitude and viral load - CD8+T cells expressing IFN-γ and/or IL-2 in response to Any Env. A) AMP ATI Peru B) AMP ATI Africa



RESULTS

- In women, median time to confirmed VL>200 was 5.4wks (range 2.3-112); in men it was 4.3wks (0.1-18).
- Maximum HIV-specific CD8+ & CD4+ T-cell responses during ATI did not differ by AMP treatment in either cohort but among women, the increase in CD8+ from baseline was significantly greater for Gag (10-fold; p=0.024) and Vif (4.6-fold; p=0.024) among those who received VRC01 in AMP.
- HIV-specific CD4+ responses were low (max <0.5%) compared to CD8+ responses (mainly 1-5%, max 15%) on ATI.
- No significant correlation was seen between time to ART reinitiation & CD8+ (Spearman r=0.5; p=0.18) or CD4+ (r=0.45; p=0.23) responses.
- Two women maintained VL<200 off ART for ≥32 weeks ("controllers"); no MSM+TG exhibited control on ATI.
- Both controllers had higher frequency CD8+ responses than non-controllers to Env (≥0.8% of CD8+ cells) and Pol (≥10%) and, for the VRC01-recipient controller, also to Gag (4%).
- Both controllers' HIV-specific CD8+ responses preceded viral rebound; non-controllers' CD8+ responses followed rebound (Figure 2).
- Controllers & non-controllers both had HLA alleles associated with protection &/or susceptibility.

CONCLUSIONS

- Rates of control differed by AMP ATI cohort (MSM+TG Peru 0%; women Africa 18%). CD8+ (but not CD4+) responses differed in controllers by fold-change from baseline; frequency to Env, Pol and Gag epitopes; and timing, preceding rebound among controllers only.

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