HIV Rebound and Immune Dynamics at ATI Differ by Global Region and Control Status

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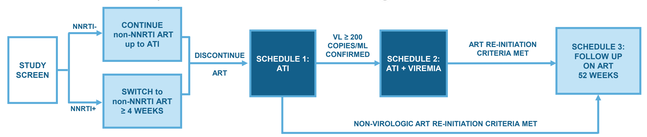
BACKGROUND

Post-treatment ART-free HIV control (PTC) is uncommon. Viral and immune dynamics in analytical treatment interruption (ATI) inform HIV cure strategies and may vary across populations, yet women and MSM in the global South are underrepresented in ATIs. The AMP ATIs (see schema below) help address these gaps.



For example, in a recent ATI meta-analysis[1] in which 91% of the population included in the analysis was male, 75% was white, and almost all were in the global North in an area of largely clade B HIV, VL<50 was observed in 44% of people with HIV (PWH) at D14 and in 4% at D84 of ATI. The authors note that their meta-analysis "leaves behind over half the population of PWH globally." See *Results* for our observations in our cohorts of African women and Peruvian men and trans individuals.

METHODS

The Antibody Mediated Prevention (AMP) ATIs enrolled women in Southern Africa (HVTN 805/HPTN 093/A5393) and MSM in Peru (HVTN 804/HPTN 095/A5390). Participants (ppts) received VRC01 or placebo within 8 weeks of estimated HIV acquisition, initiated ART early and were virally suppressed on ART for ≥1 year before ATI. ART was restarted for VL>1000 for 4wks without 0.5log decline or for ppt/clinician choice. Rebound dynamics were assessed with a nonlinear mixed-effects model including fixed effects for HIV control status, VRC01 vs placebo and global region, and a ppt-level random effect. Longitudinal HIV-specific CD8+ T cell responses were assessed by ICS; autologous neutralizing antibody (anAb) responses against transmitted/founder (TF) and rebound viruses were assessed by TZM-bl after ART-DEX to clear residual ART.

HIV viral rebound patterns vary across global populations. Engagement of diverse populations most impacted by HIV can enhance understanding of & inform global HIV remission & cure strategies and can expedite efforts to advance an HIV cure.

RESULTS

Eleven women and 16 MSM initiated ATI; at day 14 (day 84) of ATI, 91% (28%) of women and 80% (0%) of MSM had VL<40 copies/mL. One woman restarted ART while VL<40. Of ten women in Africa and 16 MSM in Peru who rebounded on ATI, two women and no MSM controlled HIV (≥24 weeks of VL<200 off ART). See Figure 1. Rebound slope was 35-fold lower for controllers vs non-controllers (p<0.001) in Africa and 2-fold lower for African women vs Peruvian MSM (p=0.025) and did not differ by VRC01 vs placebo overall or within each region. See Figure 2. In non-controllers, CD8+ T cell response magnitudes increased from baseline after viral rebound, whereas in controllers, they increased before rebound. AnAb responses were heterogeneous. In Africa, 7/10 ppts' baseline anAb titers were higher against rebound viruses than TFs; anAb titers increased with rebound in 10/10; after ART restart, 8/10 ppts' anAbs were higher against TFs than rebound viruses.

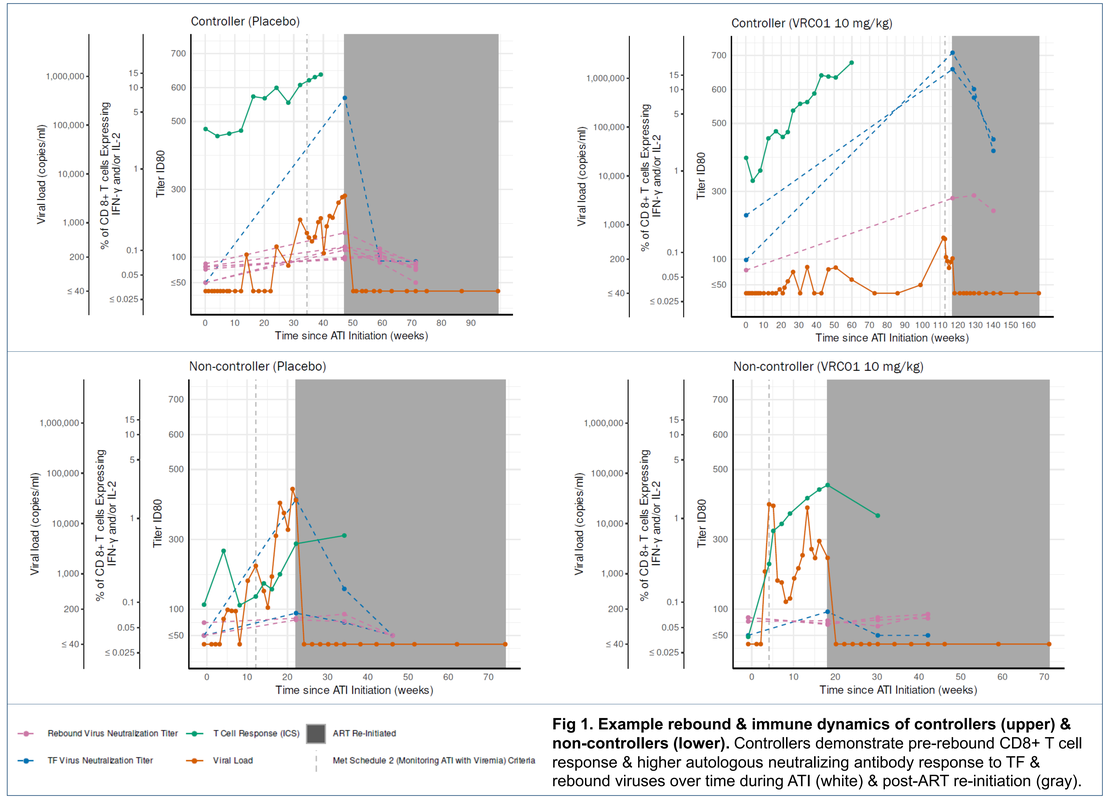


Fig 1. Example rebound & immune dynamics of controllers (upper) & non-controllers (lower). Controllers demonstrate pre-rebound CD8+ T cell response & higher autologous neutralizing antibody response to TF & rebound viruses over time during ATI (white) & post-ART re-initiation (gray).

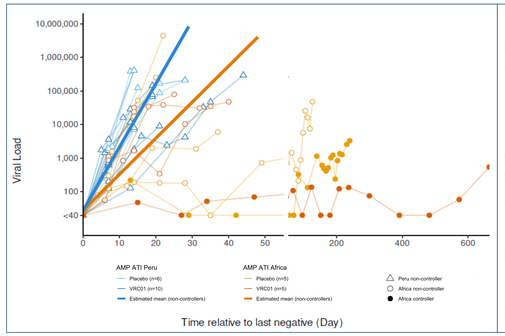


Fig 2. AMP ATI-Africa & AMP ATI-Peru participant rebound kinetics. Viral load (VL) slope from the last ART-free negative VL to the ART-free VL peak is 2-fold lower for African women than for Peruvian MSM & trans individuals (p=0.025).

CONCLUSIONS

Rebound patterns vary across global populations. In the AMP ATIs, African women exhibited more frequent post-treatment control and lower rebound slopes than Peruvian MSM & trans individuals. In African women, viral rebound boosted anAb responses against TFs, suggesting early antigenic imprinting. Controllers also had markedly lower rebound slopes and CD8+ T cell responses that preceded rebound, suggesting a cellular contribution to control. Our data from the global South informs global cure efforts.

REFERENCE:

1. Gunst, J.D., Gohil, J., Li, J.Z. et al. Time to HIV viral rebound and frequency of post-treatment control after analytical interruption of antiretroviral therapy: an individual data-based meta-analysis of 24 prospective studies. Nat Commun 16, 906 (2025).

ACKNOWLEDGEMENTS:

Our thanks first & foremost to the AMP ATI clinical trial participants– the women in Africa and the men and trans individuals in Peru– and their families & communities for contributing to & supporting this research, including interrupting their HIV treatment in an ATI within just a few years of their diagnosis with HIV and after they had already contributed substantially to HIV research by participating in the Antibody Mediated HIV Prevention (AMP) studies. When this pandemic ends, it will end in part because of the contributions of out clinical trial participants.

We also thank the HIV Vaccine Trials Network (HVTN), HIV Prevention Trials Network (HPTN), and the AIDS Clinical Trials Group/Advancing Clinical Therapeutics Globally (ACTG) Network for their support of this trial.

PLAIN LANGUAGE SUMMARY

Our research advances knowledge about how people with HIV may control HIV without ART, including how early ART initiation and broadly neutralizing antibodies (bnAbs) around the time of HIV acquisition might impact later ART-free control. We also describe rates of ART-free control of HIV that vary in different populations around the world, including women in Africa & MSM & trans individuals in Peru.