# REBOUND DYNAMICS FOLLOWING IMMUNOTHERAPY WITH AN HIV VACCINE, TLR-9 AGONIST, AND BROADLY NEUTRALIZING ANTIBODIES

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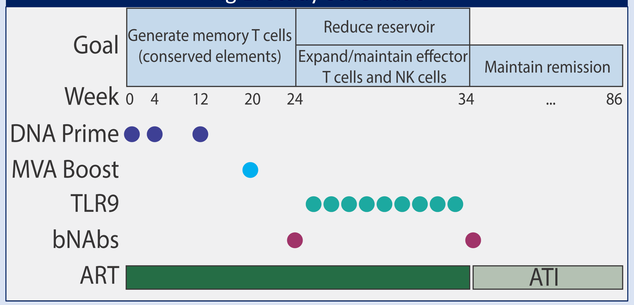
## BACKGROUND

- Various anti-HIV immunotherapy strategies have been associated with ART-free control in non-human primates.[1-3]
- We sought to determine whether a combination of such strategies was safe and could affect virologic control in people with HIV (PWH) after ART discontinuation.

## METHODS

- We performed a single-arm proof-of-concept study to evaluate the efficacy of a combination approach involving (1) Gag conserved element (CE)-targeted DNA+IL-12 prime/MVA boost vaccination, followed by (2) a combination of two broadly neutralizing antibodies (bNAbs; 10-1074, VRC07-523LS) and a TLR-9 agonist (lefitolimod) and then (3) two bNAbs given at the time of ATI.

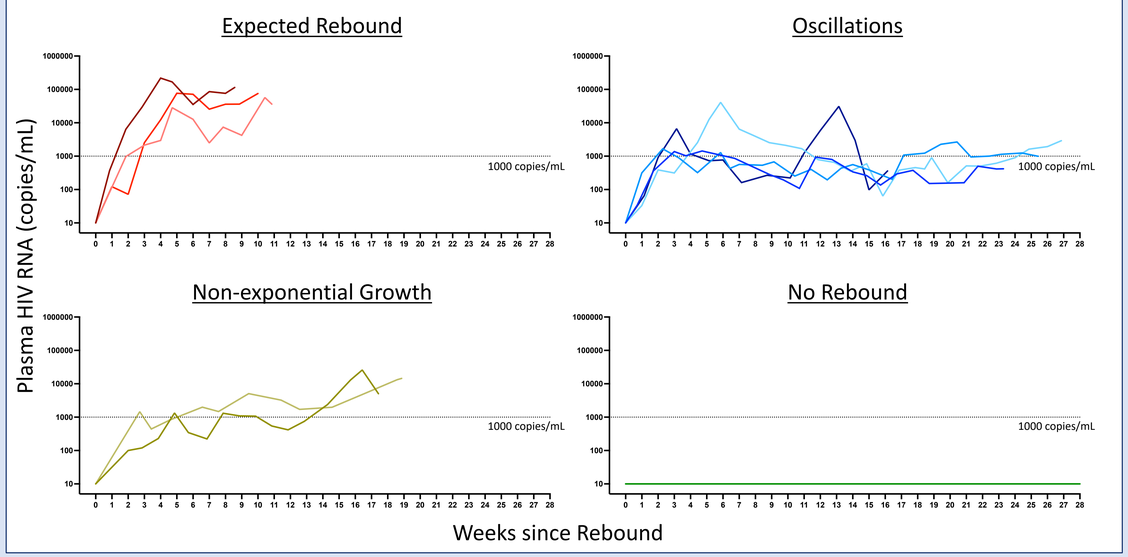
Fig 1. Study Schematic




- ART restart criteria included plasma HIV RNA (copies/mL) >50,000 for 4 weeks, >10,000 for 6 weeks, >2000 for 12 weeks, or >400 for 24 weeks.
- Seven of the 10 participants (9 cisgender men, 1 transgender woman) had initiated ART within 6 months of HIV infection.
- We defined the set point as the median of all values off ART beginning 2 weeks after peak rebound.
- We measured T cell responses prior to enrollment and after the vaccine boost by intracellular cytokine staining and bNAb sensitivity prior to enrollment and during rebound using the PhenoSense assay.

## RESULTS

Fig 2. Rebound Dynamics




- Two participants experienced ALT elevations (Grade 3 and Grade 4) that were considered possibly related to the treatment regimen but ultimately attributed to external causes.
- 7/10 exhibited atypical rebound dynamics characterized by non-exponential growth and/or oscillations; 5/10 had set points < 1000 copies/mL and 7/10 < 5000 copies/mL (Fig 2).
- Viral rebound occurred on average 15 weeks after ART interruption (Fig 3). Median ATI length was 37 weeks.
- One individual did not rebound (18 months off ART), with low levels of non-intact provirus in gut tissue and intermittent detection below the quantification limit of HIV DNA and RNA in PBMCs during the ATI.
- Higher bNAb exposure (AUC) was associated with a later time to rebound (p=0.054 and p=0.052 for VRC07-523LS and 10-1074, respectively), but bNAb levels at rebound were highly variable across participants (1.3-38.3 mcg/mL for 10-1074, 0.2-57.9 mcg/mL for VRC07-523LS).
- The vaccine regimen increased the magnitude of IFNg+ CE-specific CD4+ and CD8+ T cell responses in all 10 participants between pre-vaccination and 2-weeks post-boost (Fig 4; median CD4: 0.030% vs 0.341% [p=0.002]; CD8: 0.026% vs 0.158% [p=0.002]).
- Phenotypic susceptibility to both 10-1074 and VRC07-523LS declined over time (Fig 5).
- Neither antibody levels nor associated susceptibility could completely explain the different post-ART set points between the three non-controllers and the 7 with set points < 5000 copies/mL, suggesting the involvement of other factors.

## RESULTS, continued

Fig 3. Time to Rebound

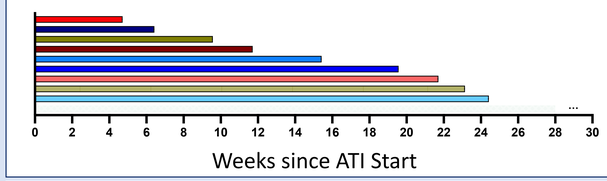



Fig 4. Vaccine-induced T Cell Responses to Conserved Elements

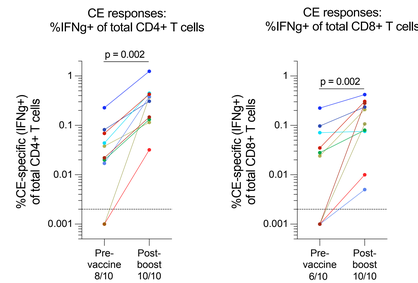
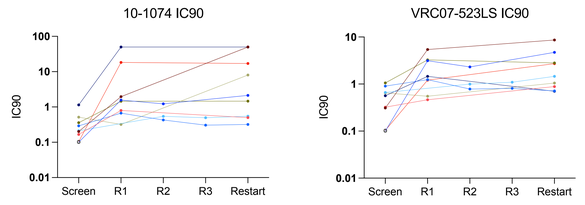



Fig 5. Evolving Phenotypic Susceptibility to bNAbs




## CONCLUSIONS

- Seven of ten individuals exhibited evidence of at least partial virologic control post-ART.
- Treatment-mediated virologic and immunologic factors may have contributed to this outcome.
- Ongoing work is evaluating changes in the characteristics of the reservoir and T cell responses prior to and during the ATI, including assessment of the vaccinal effect.

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