Characterization of HIV Antibodies and p24 Antigen During Analytical Treatment Interruption

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BACKGROUND

- This study explored the role of HIV antibodies (Ab) as indicators of HIV replication during infection and antiretroviral therapy (ART). It aimed to determine if measuring HIV antibodies and antigens (Ag) could detect an immune response before a rebound in plasma viral load (VL) after analytical treatment interruption (ATI). Additionally, it investigated whether long-term p24 antigen/antibody measurements could provide insights into viral replication post-rebound..

METHODS

- Longitudinal plasma samples from 41 ACTG A5345 study participants who started antiretroviral therapy (ART) during chronic or early phase of infection and underwent ATI (88% males, 485 samples; mean 12/participant), previously characterized for plasma VL rebound kinetics and virological correlates of time to rebound, were analyzed using the Ortho Vitros HIV1+2 (p24/env Ab) and Combo (p24 Ag/env Ab) assays, the Sedia Limiting antigen avidity assay and the Bio-Rad BioPlex2200 HIV Ag-Ab (p24 Ag/HIV M/O/2 Ab) which discriminates p24 Ag and Ab signals, with and without a denaturation step to separate p24 Ag-Ab immune complexes (IC).

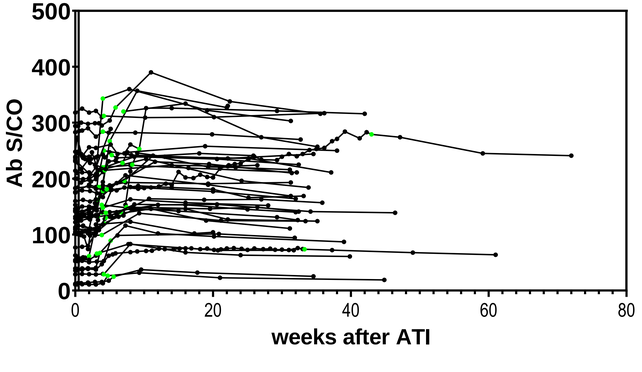
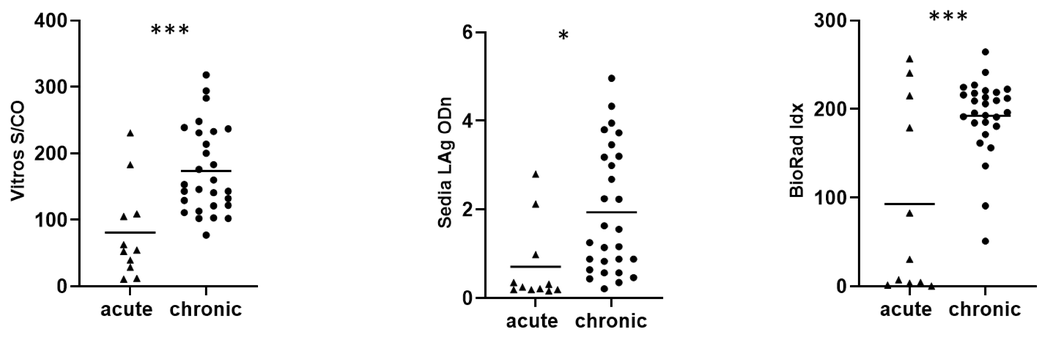


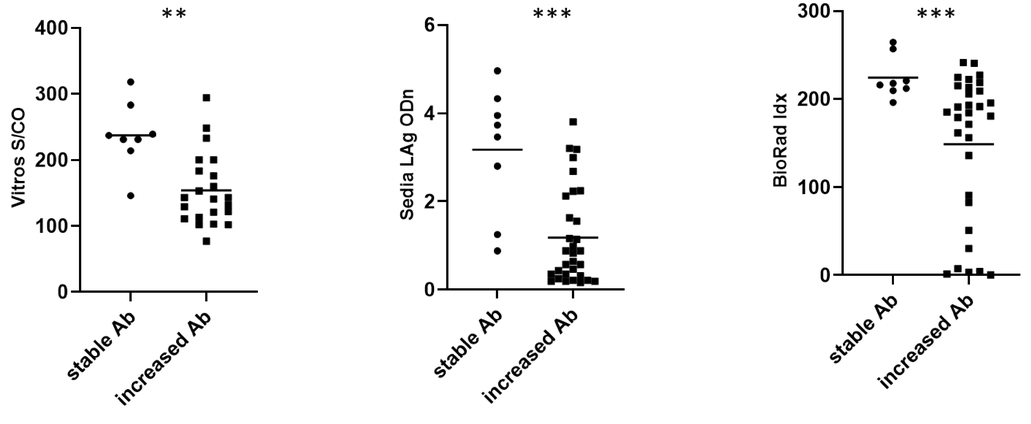
Fig.1 Longitudinal Ab levels in 41 participants during ATI, day 0 is ATI start, green dot is ATI end.

During ATI, HIV antibodies levels increase following VL rebound. Antigens remain undetectable until VL reached 10^4 RNA copies/mL.

Ab levels at ATI initiation in participants who started ART during acute or chronic infection



Ab levels at ATI initiation in participants whose Ab level increased >10% or not during ATI



RESULTS

- Neither Ab nor Ag levels increased before VL rebound. Among 41 participants, 31 (76%) showed increased antibody serological reactivity—two timepoints above 10% from baseline—after RNA rebound, which decreased after restarting ART. The 8 participants without increased seroreactivity had higher antibody levels at the start of ATI (mean Ortho Combo S/CO 237 vs. 154, p<0.001). Early-treated participants had lower antibody levels at ATI initiation (S/CO 80 vs. 173, p=0.0004).

- Two participants with post-treatment control showed a progressive increase in seroreactivity that mirrored slow or intermittent VL increases. While p24 antigen was undetectable without denaturation, samples with VL >10^4 RNA copies/mL tested positive for p24 Ag after immune-complex dissociation, showing a strong correlation with VL levels (Spearman r=0.89)

CONCLUSIONS

Commercial HIV serological assays detected an anamnestic Ab induction following VL rebound after ATI in 76% of cases. p24 Ag was detectable at rebound VL>10^4 RNA copies/mL only following IC dissociation. Longitudinal p24 Ag/Ab quantitation provides insights into post-rebound viral replication and impact of ART reinitiation and could be useful for monitoring of ATIs.

ADDITIONAL KEY INFORMATION

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