

Viral and Immune Predictors of HIV Rebound after ART Interruption

SUPPLEMENTAL MATERIALS

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Supplemental Table 1. ART restart criteria

HIV-1 RNA at $\geq 1,000$ copies/mL on two consecutive measurements

A single HIV-1 RNA $\geq 1,000$ copies/mL and an average daily HIV-1 RNA rise of ≥ 0.5 \log_{10} copies/mL based on the most recent two viral load measurements

A single HIV-1 RNA $\geq 10,000$ copies/mL

CD4+ T-cell count < 250 cells/ mm^3 on two consecutive measurements

CD4+ T-cell count $< 50\%$ of the Step 1 entry CD4 count on two consecutive measurements

Clinical progression to CDC Category B or C disease

Diagnosis of Acute Retroviral Syndrome (ARS)

Pregnancy

Re-initiation of ART requested by participant or health care provider

Supplemental Table 2: Demographics for the A5345 study population.

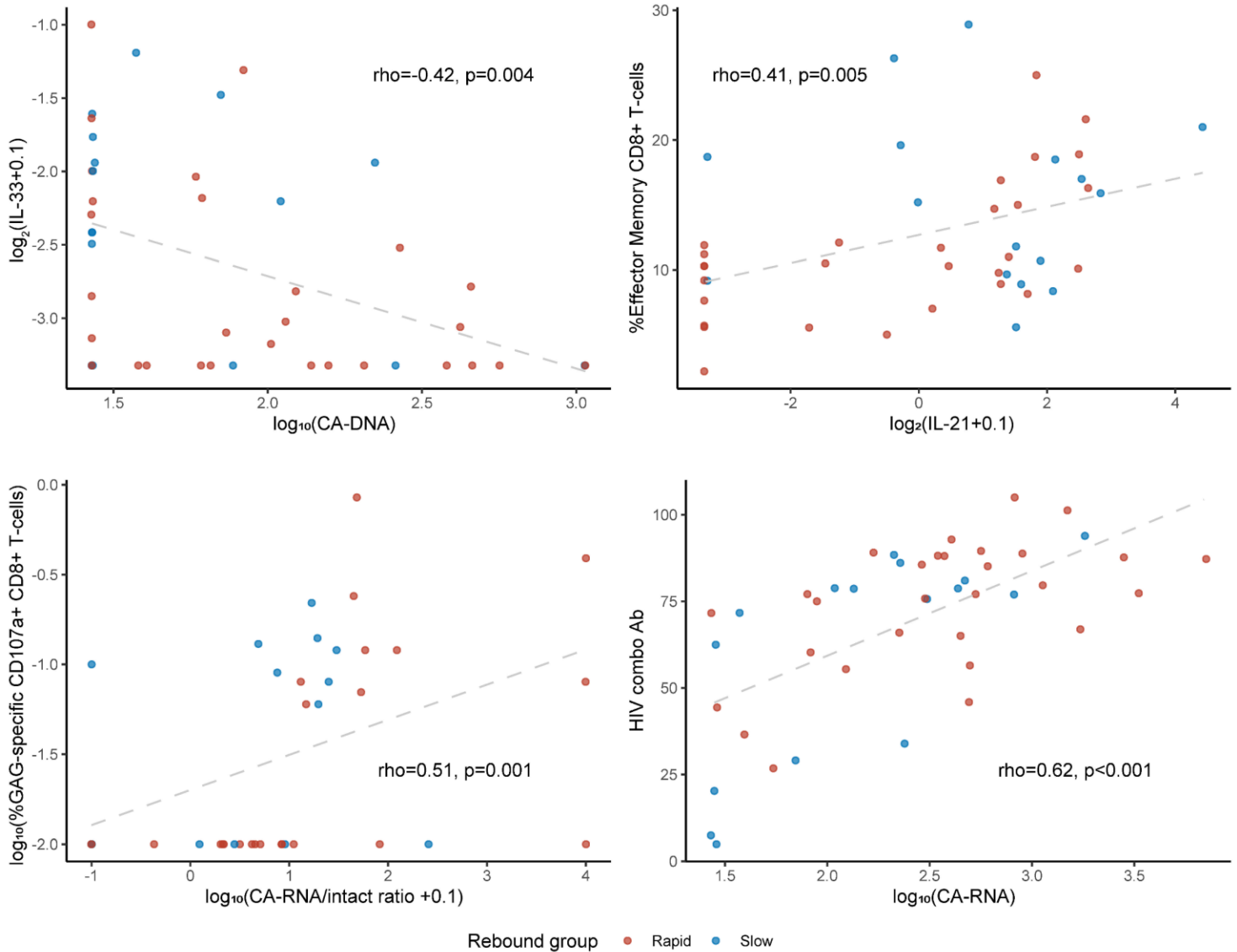
	Chronic-treated (N=33)	Early-treated (N=12)
Age, median (Q1, Q3) years	46 (36, 53)	38 (34, 47)
Sex, % male	88%	100%
Race/ethnicity, %		
White	73%	8%
Black	12%	
Hispanic	12%	33%
Asian		50%
Other	3%	8%
Nadir CD4, cells/mm ³		
<200		
201-500	82%	83%
>500	18%	17%
Pre-ATI CD4, median (Q1, Q3) cells/mm ³	783 (651, 1028)	742 (654, 892)
Pre-ART Viral Load, median (Q1, Q3) log ₁₀ copies/mL	4.5 (4.0, 5.0)	5.7 (4.8, 6.3)
Duration of ART, median (Q1, Q3) years	10.3 (6.1, 15.6)	3.9 (3.1, 4.8)

Supplemental Table 3. Features included in Partial least squares-discriminant analysis (PLS-DA) models.

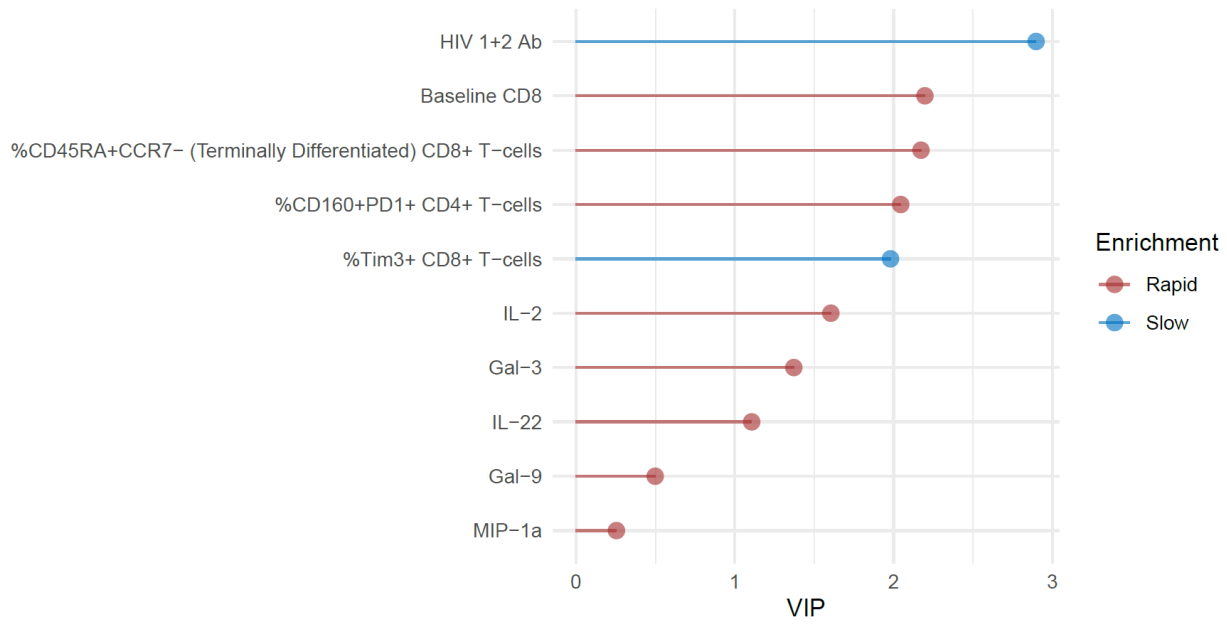
Features	Category	Features	Category
CA-RNA	Viral	HIV 1+2 Ab	Antibody
CA-DNA	Viral	HIV combo Ab	Antibody
SCA	Viral	LAg-Avidity	Antibody
IUPM	Viral	IFN- β	Cytokine/chemokine
CA-RNA/CA-DNA ratio	Viral	IFN- γ	Cytokine/chemokine
Baseline CD4	Cellular	IL-10	Cytokine/chemokine
Baseline CD8	Cellular	IL-13	Cytokine/chemokine
Baseline CD4/CD8 ratio	Cellular	IL-15	Cytokine/chemokine
Nadir CD4 cell count	Cellular	IL-1 β	Cytokine/chemokine
%CD38+HLADR+ CD4+ T-cells	Cellular	IL-21	Cytokine/chemokine
%CD38+HLADR+ CD8+ T-cells	Cellular	IL-33	Cytokine/chemokine
%CD45RA-CCR7+ (Central Memory) CD4+ T-cells	Cellular	IL-6	Cytokine/chemokine
%CD45RA-CCR7+ (Central Memory) CD8+ T-cells	Cellular	TNF- α	Cytokine/chemokine
%CD45RA+CCR7- (Terminally Differentiated) CD4+ T-cells	Cellular	Fractalkine	Cytokine/chemokine
%CD45RA+CCR7- (Terminally Differentiated) CD8+ T-cells	Cellular	IFN- α 2a	Cytokine/chemokine
%CD45RA-CCR7- (Effector Memory) CD4+ T-cells	Cellular	IL-12p70	Cytokine/chemokine
%CD45RA-CCR7- (Effector Memory) CD8+ T-cells	Cellular	IL-2	Cytokine/chemokine
%CD45RA+CCR7+ (Naive) CD4+ T-cells	Cellular	IL-22	Cytokine/chemokine
%CD45RA+CCR7+ (Naive) CD8+ T-cells	Cellular	IL-23	Cytokine/chemokine
%CD73+CD160+ CD4+ T-cells	Cellular	IP-10	Cytokine/chemokine
%CD73+CD160+ CD8+ T-cells	Cellular	MCP-2	Cytokine/chemokine
%CD160+PD1+ CD4+ T-cells	Cellular	MIP-1 α	Cytokine/chemokine
%CD160+PD1+ CD8+ T-cells	Cellular	SDF-1a	Cytokine/chemokine
%CD160+ CD4+ T-cells	Cellular	LBP	Microbial translocation
%CD160+ CD8+ T-cells	Cellular	sCD14	Immune activation/ inflammation
%CD73+ CD4+ T-cells	Cellular	sCD163	Immune activation/ inflammation
%CD73+ CD8+ T-cells	Cellular	b-glucan	Microbial translocation
%LAG3+PD1+ CD4+ T-cells	Cellular	Gal-3	Immunomodulatory lectin
%LAG3+PD1+ CD8+ T-cells	Cellular	Gal-9	Immunomodulatory lectin
%LAG3+ CD4+ T-cells	Cellular	E-selectin	Immunomodulatory lectin
%LAG3+ CD8+ T-cells	Cellular		
%PD1+ CD4+ T-cells	Cellular		
%PD1+ CD8+ T-cells	Cellular		
%TIGIT+ CD4+ T-cells	Cellular		
%TIGIT+ CD8+ T-cells	Cellular		
%Tim3+ CD4+ T-cells	Cellular		
%Tim3+ CD8+ T-cells	Cellular		
%CD8 T-cells expressing CD107a (summing the 3 HIV peptides)	Cellular		
%GAG-specific CD107a+ CD8+ T-cells	Cellular		

Supplemental Table 4: Demographics for the A5345 study population categorized by individuals with rapid (<4 weeks) versus slow (\geq 4 weeks) viral rebound.

	Rapid rebound (N=29)	Slow rebound (N=16)
Age, median (Q1, Q3) years	46 (35, 50)	45 (35, 54)
Sex, % male	90%	94%
Race/ethnicity, %		
White	62%	44%
Black	10%	6%
Hispanic	14%	25%
Asian	7%	25%
Other	7%	0%
Nadir CD4, cells/mm ³		
<200		
201-500	83%	81%
>500	17%	19%
Pre-ATI CD4, median (Q1, Q3) cells/mm ³	783 (651, 1028)	742 (654, 892)
Pre-ART Viral Load, median (Q1, Q3) log ₁₀ copies/mL	4.7 (4.0, 5.2)	4.6 (3.9, 5.8)
Duration of ART, median (Q1, Q3) years	7.1 (4.6, 12.5)	7.7 (3.8, 17.3)
Early-treated, %	21%	38%



Supplemental Figure 1: Examples of significant correlations between HIV reservoir, immune and inflammatory markers. CA-DNA, total cell-associated HIV DNA; CA-RNA, unspliced cell-associated RNA. Red represents participants with HIV rebound <4 weeks and blue represents individuals with slow viral rebound ≥4 weeks.



Supplemental Figure 2: Variable importance in projection (VIP) scores for selected features in the second component of chronically-treated participants.