Long-term ART Reduces HIV-1 Reservoir Functionality and Chronic Inflammation in PWH

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BACKGROUND

- Although antiretroviral treatment (ART) successfully blocks HIV-1 replication and restores CD4+ T cells in people with HIV (PWH), its long-term effects on the viral reservoir and chronic inflammation remain unclear.
- **Objective**: To assess the impact of time on ART on the viral reservoir, immune exhaustion and senescence, and plasma cytokine levels.

METHODS

Cross-sectional study with PWH (n= 80) who were on ART for different durations:

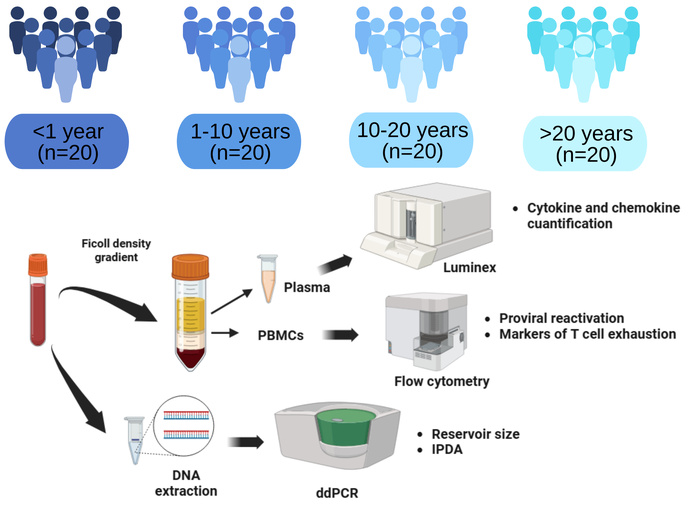


Table 1. Clinical and sociodemographic characteristics of the participants.

	<1y	1-10y	10-20y	>20y	p-value
	n= 20	n= 20	n= 20	n= 20	
Demographic characteristics					
Age (years): median (IQR)	24 (26.0-31.0)	37.5 (2808-43.0)	48.5 (43.5-52.5)	55.5 (53.8-60.3)	**<0.0001**
Gender (male): n (%)	17 (85)	16 (80.0)	16 (80.0)	15 (75.0)	0.4039
Clinical chacteristcics of HIV-1 infection					
Time since HIV infection (years): median (IQR)	<1	7.0 (4.0-9.0)	15.0 (13.8-19.0)	28.5 (24.8-31.5)	**<0.0001**
Time on ART (years): median (IQR)	<1	6.5 (4.0-8.0)	14.5 (12.0-17)	25.0 (23.0-31.0)	**<0.0001**
Nadir CD4 (cells/mm3): median (IQR)	248 (206.0-521.0)	301.0 (135.8 -418.5)	345.0 (195.3-462.5)	257.5 (176.3-449.3)	0.8737
CD4 count (cells/mm3): median (IQR)	570.0 (398.0-862.0)	787.0 (513.0-998.0)	966.5 (602.3-1133.5)	894.5 (709.5-991.0)	0.0819
CD8 count (cells/mm3): median (IQR)	1183.0 (805.5-1327.0)	673.0 (607.0-920.5)	761.5 (598.5-902.5)	862.0 (610.8-1366.3)	0.1374
CD4/CD8 ratio (cells/mm3): median (IQR)	0.53 (0.34-0.81)	0.80 (0.56-1.37)	1.16 (0.92-1.48)	0.91 (0.69-1.23)	**0.0038**
Viral load (undetectable): n (%)	16 (80.0)	19 (95.0)	18 (90.0)	20 (100)	0.1975

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Sustained ART is associated with CD4 recovery, reduced immune exhaustion and inflammatory cytokines, and a decline in intact proviruses, supporting improved immune control and a lower reservoir reactivation potential

RESULTS

Figure 1. Pro-inflammatory and anti-inflammatory/regulatory cytokines decreased in >20y. Bar charts (right or top) show the percentage of participants with detectable (positive) or undetectable (negative) cytokines in plasma. Dot plots (left or bottom) show individual patient data.

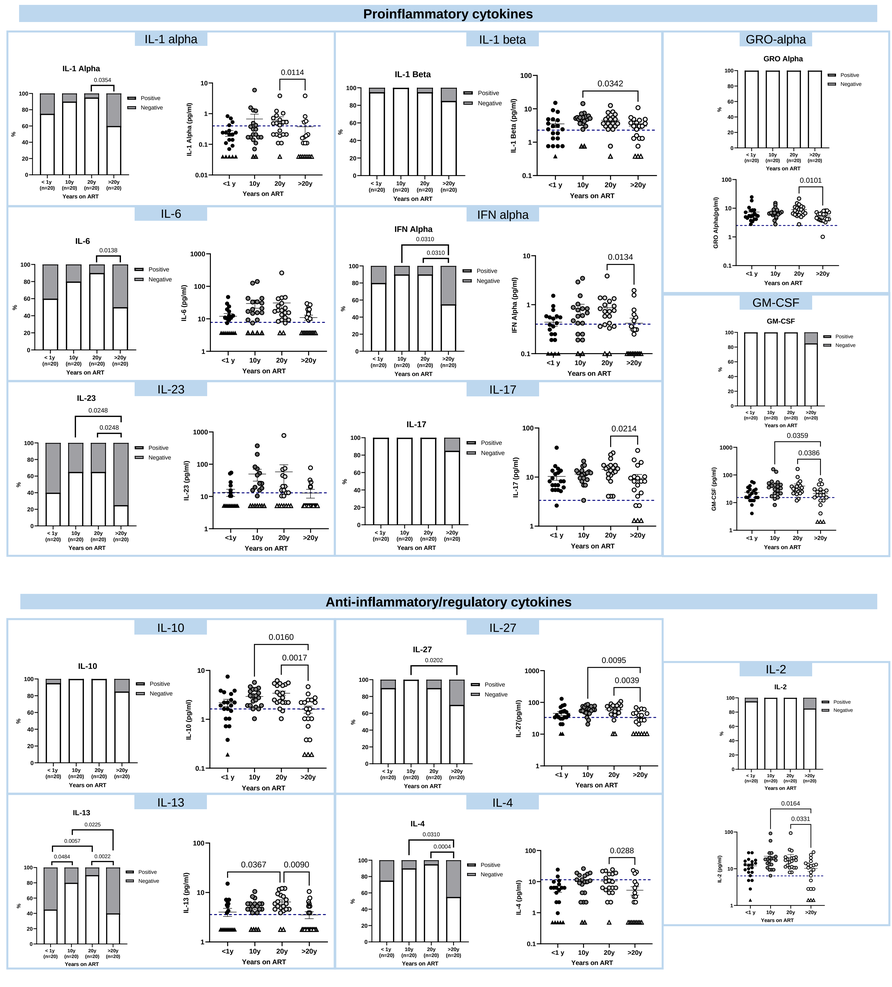


Figure 2. No changes in chemokines or growth factors across cohorts. Representative markers are shown, additional markers showed similar results (data not shown).

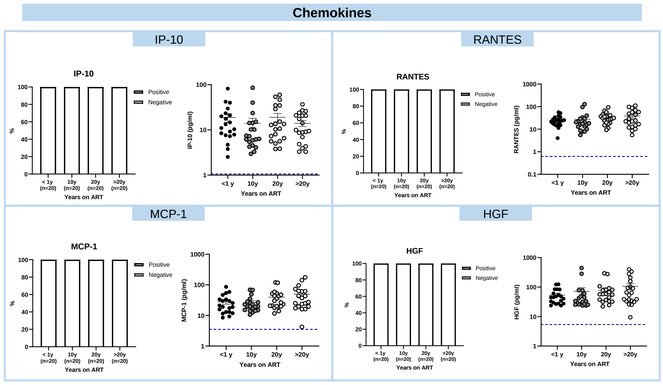


Figure 3. Total CD4+ counters increased with longer ART, but exhaustion markers LAG-3 and PD-1 decreased with ART duration.

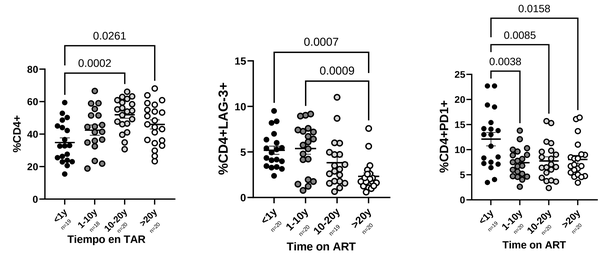
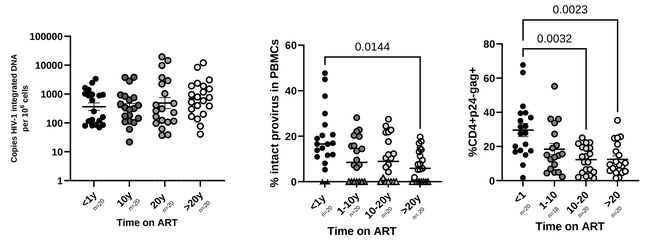


Figure 4. Total reservoir size remained stable, but the proportion of intact proviruses declined, as did reactivation capacity



CONCLUSIONS

- PWH on long-term ART showed sustained CD4 recovery, reduced immune exhaustion, and a significant decrease in intact proviruses, indicating a direct impact on the viral reservoir and its reactivation capacity.
- The reduction in both pro- and anti-inflammatory cytokines, along with stable growth factors and chemokines, suggests a less activated but functionally preserved immune system.