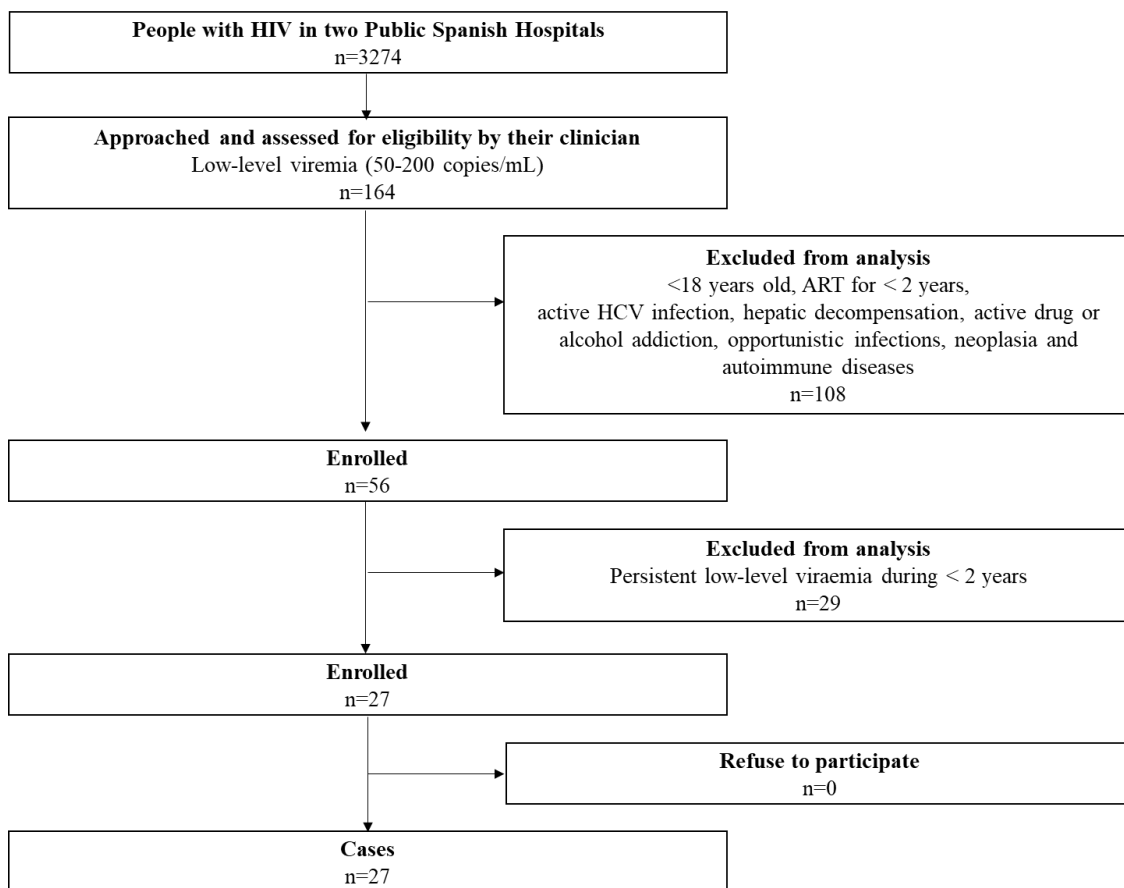


## APPENDIX

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## Supplementary Material 1. Flow-chart of participant's selection.



**Notes:** Cases were defined as people with HIV with low-level viremia described as at least two consecutive viral loads between 50-200 copies/mL for the last two years before sample collection (LLV group). For each case, an HIV control with suppressed viremia (<50 copies/mL) during the last two years (SV group) and a non-HIV control (PCR negative, HIV antibodies negative) (NHC group) were selected. Exclusion criteria were pregnancy, individuals below 18 years old, active HCV infection, lack of optimized treatment based on resistance studies, lack of good adherence, clinical evidence of hepatic decompensation, active drug or alcohol addiction, opportunistic infections, and other concomitant diseases such as autoimmune disease, and neoplasia.

## Supplementary Material 2. Protocol of 14-color flow cytometry

To characterize CD4<sup>+</sup> and CD8<sup>+</sup> T-cells subpopulations, the expression of surface markers was evaluated in  $1.5 \times 10^6$  cryopreserved PBMCs stained with Fixable Viability Dye eFluor 455UV (ThermoFisher) 30 min at 4°C. After washing with PBS+2%FBS, non-specific antibody binding was blocked using the Human TruStain FcX (BioLegend) for 10 min at room temperature. After surface staining for 30 min at 4°C and washing, cells were finally fixed with 2% PFA for analysis on an Aurora Spectral flow cytometer with five lasers (Cytek Biosciences). Data were analysed with FlowJo™ v10 software (Tree Star, Ashland).

### Supplementary Material 3. Fluorescently conjugated antibody panel

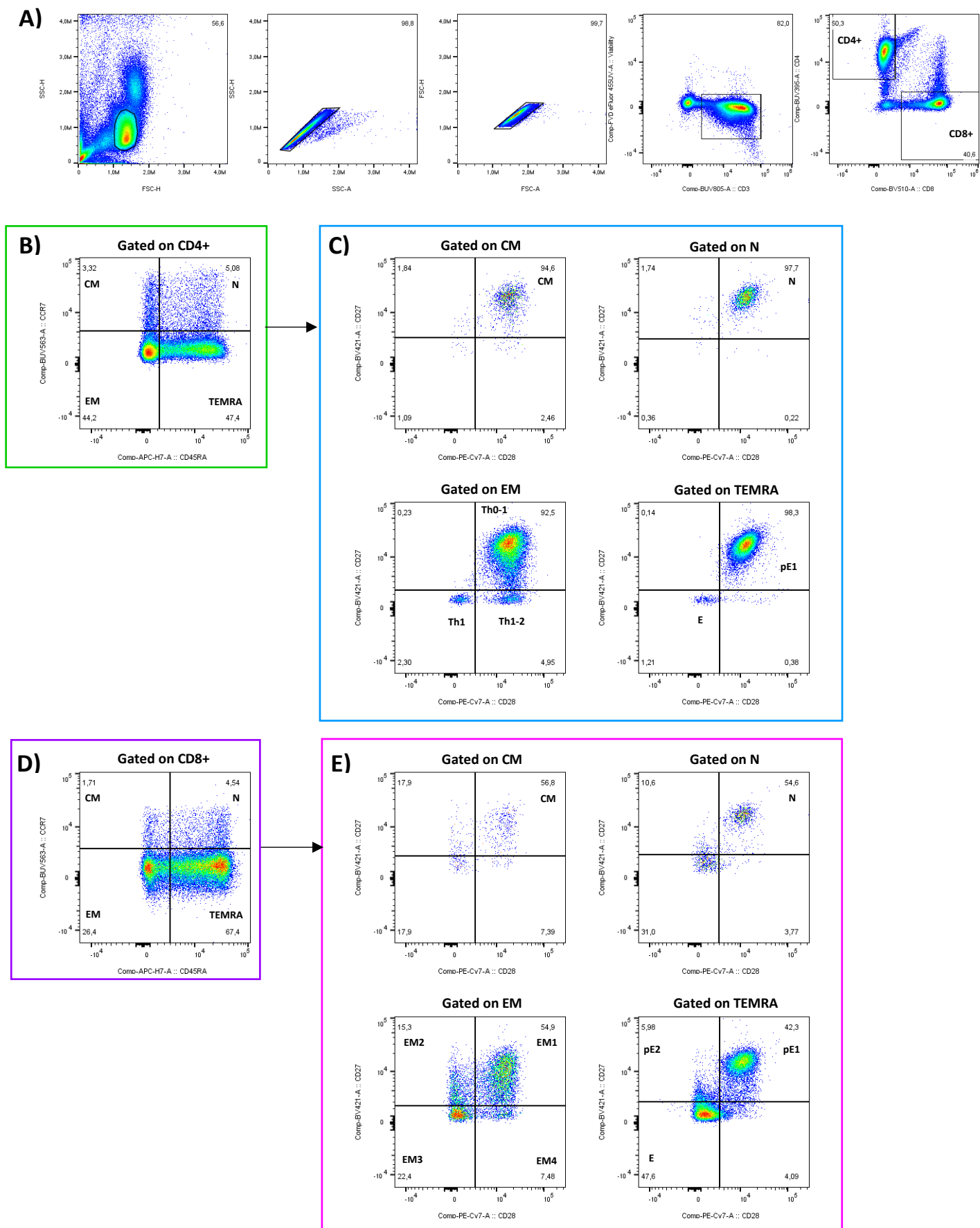
Markers	Antibodies	Reference
<i>Viability</i>	Fixable Viability Dye eFluor 455UV	ThermoFisher
<i>T-cell development</i>	CD3-BUV805	Beckton-Dickinson
	CD4-BUV395	Beckton-Dickinson
	CD8-BV510	Beckton-Dickinson
	CCR7-BUV563	Beckton-Dickinson
	CD45RA-APC/H7	Beckton-Dickinson
	CD27-BD421	Beckton-Dickinson
	CD28-PE/Cy7	Beckton-Dickinson
<i>Activation</i>	CD25-BV711	BioLegend
	HLA-DR-AF647	BioLegend
	CD38-cFluor R720	BioLegend
<i>Senescence</i>	CD57-PE/Dazzle 594	BioLegend
	PD1-BB700	Beckton-Dickinson
	TIM-3-BV785	BioLegend

### Supplementary Material 4. Immunophenotypic characterization of subpopulation CD4+ and CD8+ T cells.

Population	Phenotypic	Ref
<b>CD4+</b>		
Naïve (N)	CD3+, CD4+, CD45RA+, CCR7+, CD27+, CD28+	1,2,3,4
Central memory (CM)	CD3+, CD4+, CD45RA-, CCR7+, CD27+, CD28+	1,2,3,4
Effector memory (EM)	CD3+, CD4+, CD45RA-, CCR7-	1,2,3,4
Effector memory 0 and 1 (EM Th0-1)	CD3+, CD4+, CD45RA-, CCR7-, CD28+, CD27+	4
Effector memory 1 (EM Th1)	CD3+, CD4+, CD45RA-, CCR7-, CD28-, CD27-	4
Effector memory 1 and 2 (EM Th1-2)	CD3+, CD4+, CD45RA-, CCR7-, CD28+, CD27-	4
Terminally differentiated effector memory RA+ (TEMRA)	CD3+, CD4+, CD45RA+, CCR7-	1,5
Pre-terminally differentiated effector memory RA+ 1 (pE1)	CD3+, CD4+, CD45RA+, CCR7-, CD28+, CD27+	1,5
Terminally differentiated effector memory RA+ effector (E)	CD3+, CD4+, CD45RA+, CCR7-, CD28-, CD27-	1,5
<b>CD8+</b>		
Naïve (N)	CD3+, CD8+, CD45RA+, CCR7+, CD27+, CD28+	1,2,3,4,5
Central memory (CM)	CD3+, CD8+, CD45RA-, CCR7+, CD27+, CD28+	1,2,3,4,5
Effector memory (EM)	CD3+, CD8+, CD45RA-, CCR7-	1,2,3,4,5
Effector memory type 1 (EM1)	CD3+, CD8+, CD45RA-, CCR7-, CD27+, CD28+	1,5,6
Effector memory type 2 (EM2)	CD3+, CD8+, CD45RA-, CCR7-, CD27+, CD28-	1,5,6
Effector memory type 3 (EM3)	CD3+, CD8+, CD45RA-, CCR7-, CD27-, CD28-	1,5,6
Effector memory type 4 (EM4)	CD3+, CD8+, CD45RA-, CCR7-, CD27-, CD28+	1,5,6
Terminally differentiated effector memory RA+ (TEMRA)	CD3+, CD8+, CD45RA+, CCR7-	1,5,6
Pre-terminally differentiated effector memory RA+ 1 (pE1)	CD3+, CD8+, CD45RA+, CCR7-, CD27+, CD28+	1,5,6
Pre-terminally differentiated effector memory RA+ 2 (pE2)	CD3+, CD8+, CD45RA+, CCR7-, CD27+, CD28-	1,5,6
Terminally differentiated effector memory RA+ effector (E)	CD3+, CD8+, CD45RA+, CCR7-, CD27-, CD28-	1,5,6

**References:** [1] Koch, S.; Larbi, A.; Derhovanessian, E.; Ozelik, D.; Naumova, E.; Pawelec, G. Multiparameter Flow Cytometric Analysis of CD4 and CD8 T Cell Subsets in Young and Old People. *Immunity Ageing* 2008, 5, 6. <https://doi.org/10.1186/1742-4933-5-6>; [2] Larbi, A.; Fulop, T. From “Truly Naïve” to “Exhausted Senescent” T Cells: When Markers Predict Functionality. *Cytometry Part A* 2014, 85 (1), 25–35. <https://doi.org/10.1002/cyto.a.22351>; [3] Mahnke, Y. D.; Brodie, T. M.; Sallusto, F.; Roederer, M.; Lugli, E. The Who’s Who of T-Cell Differentiation: Human Memory T-Cell Subsets. *Eur J Immunol* 2013, 43 (11), 2797–2809. <https://doi.org/10.1002/eji.201343751>; [4] Okada, R.; Kondo, T.; Matsuki, F.; Takata, H.; Takiguchi, M. Phenotypic Classification of Human CD4+ T Cell Subsets and Their Differentiation. *Int Immunol* 2008, 20 (9), 1189–1199. <https://doi.org/10.1093/intimm/dxn075>; [5] Romero, P., Zippelius, A., Kurth, I., Pittet, M. J., Touvrey, C., Iancu, E. M., Corthesy, P., Devevre, E., Speiser, D. E., & Rufer, N. (2007). Four functionally distinct populations of human effector-memory CD8+ T lymphocytes. *Journal of immunology* (Baltimore, Md.: 1950), 178(7), 4112–4119. <https://doi.org/10.4049/jimmunol.178.7.4112>; [6] Tilburgs, T.; Schonkeren, D.; Eikmans, M.; Nagtzaam, N. M.; Datema, G.; Swings, G. M.; Prins, F.; van Lith, J. M.; van der Mast, B. J.; Roelen, D. L.; Scherjon, S. A.; Claas, F. H. Human Decidual Tissue Contains Differentiated CD8+ Effector-Memory T Cells with Unique Properties. *The Journal of Immunology* 2010, 185 (7), 4470–4477. <https://doi.org/10.4049/jimmunol.0903597>

## Supplementary Material 5. Gating strategy



**Notes:** Differential expression of CD45RA, CCR7, CD27 and CD28 cell surface molecules on total CD4+ and CD8+ T cells from participants acquired on a Spectral Flow Cytometry Instrument (Cytek Biosciences). **A**, the FSC-Height (H) vs. Side scatter (SSC)-H is used to gate lymphocytes population. The FSC-H vs. FSC-A and SSC-H vs. SSC-A and are to gate on single cells and to exclude doublets. Next, the eFluor 455 UV-negative and the CD3-positive was used to gated live CD3+ lymphocytes and excluded dead or damage cells. **B**, CD4+ gated cells were separated into four subsets N (CCR7+CD45RA+), CM

(CCR7+CD45RA-), EM (CCR7-CD45RA-), and TEMRA (CCR7-CD45RA+) based on CD45RA and CCR7 labeling. **C**, Each of these subsets was analyzed for CD27 and CD28 coexpression and seven subpopulations of CD4+ T cells could be distinguished: N (CD27+CD28+), CM (CD27+CD28+), EM Th0 and Th1 (CD27+CD28+), EM Th1 (CD27-CD28-) and EM Th1 and Th2 (CD27-CD28+), TEMRA pE1 (CD27+CD28+) and TEMRA E (CD27-CD28-). **D**, CD8+ gated cells were divided into four subsets N (CCR7+CD45RA+), CM (CCR7+CD45RA-), EM (CCR7-CD45RA-), and TEMRA (CCR7-CD45RA+) based on CD45RA and CCR7 labeling. **E**, Each of these subsets was analyzed for CD27 and CD28 coexpression and nine subpopulations of CD8+ T cells could be distinguished: N (CD27+CD28+), CM (CD27+CD28+), EM1 (CD27+CD28+), EM2 (CD27-CD28+), EM3 (CD27-CD28-), EM4 (CD27+CD28-), TEMRA pE1 (CD27+CD28+), TEMRA pE2 (CD27+CD28-) and TEMRA E (CD27-CD28-). On all these CD4+ T and CD8+ T subpopulations, the profile of intermediate activation (CD25 and HLADR), advanced activation (HLADR and CD38), intermediate senescence (CD57 and PD1) and advanced senescence (PD1 and TIM3) were analyzed. Abbreviations: N, naïve; CM, central memory; EM, effector memory; Th, T helper, TEMRA pE1, pre-terminally differentiated effector memory RA+ type 1; TEMRA pE2, pre-terminally differentiated effector memory RA+ type 2; TEMRA E, terminally differentiated effector memory RA+.

### Supplementary Material 6. Markers of systemic inflammation evaluated in plasma of participants.

Marker name	Official Protein Symbol	Official Gene Symbol	Official Full Name
<b><i>Th1/Th2</i></b>			
GM-CSF	GM-CSF	CSF2	Granulocyte-macrophage colony-stimulating factor
IFN- $\gamma$	IFN- $\gamma$	IFNG	Interferon gamma
IL-1 $\beta$	IL-1 $\beta$	IL1B	Interleukin 1 beta
IL-2	IL-2	IL2	Interleukin 2
IL-4	IL-4	IL4	Interleukin 4
IL-5	IL-5	IL5	Interleukin 5
IL-6	IL-6	IL6	Interleukin 6
IL-8	IL-8	CXCL8	C-X-C motif chemokine ligand 8
IL-12p70	IL-12p70	IL12B	Interleukin 12
IL-13	IL-13	IL13	Interleukin 13
IL-18	IL-18	IL18	Interleukin 18
TNF- $\alpha$	TNF- $\alpha$	TNF	Tumor necrosis factor alpha
<b><i>Th9/Th17/Th22/Treg</i></b>			
IL-9	IL-9	IL9	Interleukin 9
IL-10	IL-10	IL10	Interleukin 10
IL-17A (CTLA-8)	IL-17A	IL-17A	Interleukin 17A
IL-21	IL-21	IL21	Interleukin 21
IL-22	IL-22	IL22	Interleukin 22
IL-23	IL-23	IL23A	Interleukin 23
IL-27	IL-27	IL27	Interleukin 27
<b><i>Inflammatory cytokines</i></b>			
IFN- $\alpha$	IFN- $\alpha$	IFNA1	Interferon alpha 1
IL-1 $\alpha$	IL-1 $\alpha$	IL1A	Interleukin 1 alpha
IL-1RA	IL-1RA	IL1RN	Interleukin-1 receptor antagonist
IL-7	IL-7	IL7	Interleukin 7
IL-15	IL-15	IL15	Interleukin 15
IL-31	IL-31	IL31	Interleukin 31
TNF beta	LT $\alpha$	LTA	Lymphotoxin alpha
<b><i>Chemokines</i></b>			
Eotaxin	Eotaxin	CCL11	C-C motif chemokine ligand 11
GRO- $\alpha$	GRO- $\alpha$	CXCL1	C-X-C motif chemokine ligand 1
IP-10	CXCL10	CXCL10	C-X-C motif chemokine ligand 10
MCP-1	CCL2	CCL2	C-C motif chemokine ligand 2
MIP-1 $\alpha$	CCL3	CCL3	C-C motif chemokine ligand 3
MIP-1 $\beta$	CCL4	CCL4	C-C motif chemokine ligand 4
RANTES	CCL5	CCL5	C-C motif chemokine ligand 5
SDF-1 $\alpha$	CXCL12	CXCL12	C-X-C motif chemokine ligand 12
<b><i>Growth factors</i></b>			
BDNF	BDNF	BDNF	Brain derived neurotrophic factor
EGF	EGF	EGF	Epidermal growth factor
FGF-2	FGF-2	FGF-2	Fibroblast growth factor 2
HGF	HGF	HGF	Hepatocyte growth factor
NGF- $\beta$	$\beta$ -NGF	NGF	Nerve growth factor
LIF	LIF	LIF	Leukemia inhibitory factor
PDGF-BB	PDGF-BB	PDGFB	Platelet derived growth factor subunit B
PIGF-1	PIGF-1	PGF	Placental growth factor
SCF	KITLG	KITLG	KIT ligand
VEGF-A	VEGF-A	VEGFA	Vascular endothelial growth factor A
VEGF-D	VEGF-D	VEGFD	Vascular endothelial growth factor D

**Supplementary Material 7. Epidemiological characteristics of all group of patients enrolled in this study.**

	<b>Total</b>	<b>LLV</b>	<b>SV</b>	<b>NHC</b>	<b>p<sup>a</sup></b>	<b>p<sup>b</sup></b>	<b>p<sup>c</sup></b>	<b>p<sup>d</sup></b>
<b>No.</b>	81	27	27	27	--	--	--	--
<b>Sex at birth [n (%)]</b>								
Male	63 (77.80%)	21 (77.80%)	21 (77.80%)	21 [77.80%]	1.000	1.000	1.000	1.000
<b>Ethnicity [n (%)]</b>								
Caucasian	76 (95.00%)	25 (92.60%)	25 (92.60%)	27 (100.00%)	1.000	1.000	1.000	1.000
<b>Age (years)</b>	53.00 [48.00-58.00]	53.00 [47.50-58.00]	54.00 [49.00-59.00]	52.00 [49.00-55.00]	0.502	0.775	0.376	0.275
<b>Height (cm)</b>	173.0 [166.0-178.0]	170.0 [165.5-179.0]	174.0 [165.8-178.0]	173.0 [169.5-176.9]	0.936	0.789	0.727	0.884
<b>Weight (kg)</b>	76.20 [69.43-89.72]	76.00 [69.74-89.83]	76.65 [68.29-89.86]	76.20 [72.00-87.35]	0.970	0.993	0.818	0.841
<b>BMI (kg/m<sup>2</sup>)</b>	25.86 [23.82-28.70]	26.90 [24.65-28.70]	24.90 [23.00-28.10]	25.99 [24.00-29.00]	0.373	0.228	0.713	0.237

**Statistics:** values are expressed as the absolute numbers (%) and median [interquartile range]. *P-values* were estimated by Kruskal-Wallis and Mann-Whitney U test for continuous variables and chi-squared or Fisher's exact test for categorical variables. Statistically significant values are highlighted in bold. **a:** comparison between all the three groups enrolled in this study; **b:** comparison between LLV and SV; **c:** comparison between LLV and NHC; **d:** comparison between SV and NHC. **Abbreviations:** LLV, PWH with persistent low-level viremia (50-200 copies/mL); SV, PWH with suppressed viremia (<50 copies/mL); NHC, non-infected HIV controls; BMI, body mass index.

**Supplementary Material 8. Biochemical and metabolic characteristics of all group of patients enrolled in this study.**

No.	Total 81	LLV 27	SV 27	NHC 27	p <sup>a</sup> --	p <sup>b</sup> --	p <sup>c</sup> --	p <sup>d</sup> --
Platelets (cell/ $\mu$ L)	229.00 [193.00- 278.750]	250.00 [196.00-282.50]	218.00 [203.50-298.00]	228.00 [189.25-258.75]	0.547	0.986	0.274	0.417
<b>Lipid profile</b>								
Glucose (mg/dL)	93.50 [87.75- 101.25]	94.00 [88.75- 116.00]	97.50 [93.25- 102.00]	88.50 [84.75- 92.00]	<b>&lt;0.001</b>	0.898	<b>0.002</b>	<b>&lt;0.001</b>
Glucose $\geq$ 110 (%)	12 (15.80%)	8 (30.80%)	4 (15.40%)	-	<b>0.009</b>	0.324	<b>0.004</b>	0.111
Creatinine (mg/dL)	1.00 [0.88- 1.02]	0.95 [0.90- 1.00]	1.00 [0.90- 1.10]	0.90 [0.70- 1.00]	0.189	0.484	0.288	0.066
TC (mg/dL)	199.50 [168.25- 219.00]	200.50 [165.00- 227.75]	187.50 [157.25- 209.00]	205.50 [182.75- 220.00]	0.115	0.151	0.771	<b>0.037</b>
TC $\geq$ 200 (%)	38 (50.00%)	13 (50.00%)	10 (38.50%)	15 (62.50%)	0.243	0.577	0.407	0.156
LDL (mg/dL)	117.80 [94.10- 136.45]	115.00 [94.00- 147.00]	114.00 [89.00- 131.00]	118.50 [101.00- 136.75]	0.719	0.547	0.904	0.435
LDL $\geq$ 130 (%)	28 (37.80%)	10 (40.00%)	9 (36.00%)	9 (37.50%)	1.000	1.000	1.000	1.000
HDL (mg/dL)	49.00 [41.00- 60.00]	47.00 [41.00- 57.00]	43.00 [35.50- 50.25]	60.00 [49.75- 71.50]	<b>&lt;0.001</b>	0.122	<b>0.006</b>	<b>&lt;0.001</b>
HDL $>$ 40 (%)	16 (21.30%)	5 (20.00%)	10 (38.5%)	1 (4.2%)	<b>0.009</b>	0.220	0.189	<b>0.005</b>
TG (mg/dL)	121.00 [87.50- 159.75]	128.00 [95.75- 178.00]	127.00 [100.25- 167.50]	97.00 [71.50- 138.75]	<b>0.020</b>	0.861	<b>0.016</b>	<b>0.016</b>
TG $\geq$ 200 (%)	11 (14.90%)	5 (20.80%)	6 (23.10%)	-	<b>0.029</b>	1.000	0.050	<b>0.023</b>
LDL/HDL (mg/dL)	2.38 [1.87- 2.73]	2.39 [1.85- 2.73]	2.44 [2.00- 3.14]	2.19 [1.45- 2.59]	0.113	0.547	0.174	<b>0.038</b>
AI (%)	3.90 [3.32- 4.45]	4.00 [3.57- 4.56]	3.97 [3.66- 4.83]	3.64 [2.72- 4.11]	<b>0.022</b>	0.692	0.050	<b>0.006</b>
AIP (%)	0.43 [0.28- 0.59]	0.48 [0.22- 0.64]	0.48 [0.37- 0.64]	0.31 [0.22- 0.45]	0.124	0.560	0.169	<b>0.039</b>
<b>Biochemical parameters of liver function</b>								
AST (mg/dL)	20.00 [17.00- 26.00]	23.50 [19.00- 29.00]	21.00 [16.50- 26.00]	19.00 [15.75- 20.25]	<b>0.025</b>	0.199	<b>0.005</b>	0.179
AST $\geq$ 40 (%)	3 (3.90%)	3 (11.50%)	--	-	0.063	0.111	0.236	--
ALT (mg/dL)	24.00 [18.00- 34.00]	32.00 [22.75- 45.75]	30.00 [20.00- 41.00]	17.00 [13.75- 21.00]	<b>&lt;0.001</b>	0.373	<b>&lt;0.001</b>	<b>&lt;0.001</b>
ALT $\geq$ 40 (%)	14 (18.40%)	8 (30.8%)	6 (23.1%)	-	<b>0.008</b>	0.755	<b>0.004</b>	<b>0.023</b>
GGT (mg/dL)	25.00 [19.75- 34.50]	25.50 [22.25- 39.50]	25.50 [22.00- 35.50]	21.50 [16.00- 28.50]	0.124	0.564	0.058	0.122
GGT $\geq$ 50 (%)	7 (9.20%)	6 (23.10%)	1 (3.80%)	-	<b>0.014</b>	0.099	<b>0.023</b>	1.000
TB (mg/dL)	0.60 [0.40- 0.80]	0.60 [0.50- 0.80]	0.60 [0.43- 1.00]	0.54 [0.37- 0.70]	0.235	0.512	0.188	0.134
Hemoglobin (g/dL)	150.35 [140.83-160.10]	150.30 [140.45-160.00]	150.60 [150.10-160.40]	150.10 [140.45-160.02]	0.147	0.113	0.727	0.080

**Statistics:** values are expressed as the absolute numbers (%) and median [interquartile range]. *P-values* were estimated by Kruskal-Wallis and Mann-Whitney U test for continuous variables and chi-squared or Fisher's exact test for categorical variables. Statistically significant values are highlighted in bold. **a:** comparison between all the three groups enrolled in this study; **b:** comparison between LLV and SV; **c:** comparison between LLV and NHC; **d:** comparison between SV and NHC. **Abbreviations:** LLV, PWH with persistent low-level viremia (50-200 copies/mL); SV: PWH with virologic suppression; NHC, non-infected HIV controls; TC, total cholesterol; LDL, low-density lipoprotein; HDL, high-density lipoprotein; TG, triglycerides; AI, Atherogenic index (low risk <5% for men and <40.5% for women, moderate risk 5-9 men and 40.5-7 women); AIP, Atherogenic index for plasma (high risk AIP>0.21); AST, Aspartato aminotransferasa; ALT, Alanina aminotransferase; GGT, Gamma glutamil transferasa; TB, total bilirubin.

**Supplementary Material 9. Comparison of T-cell development, activation, and senescence levels of CD4+ T-cells between all groups of study.**

CD4+ subpopulations	LLV	SV	NHC	aAMR <sup>a</sup> [IC95%]	p <sup>a</sup>	q <sup>a</sup>	aAMR <sup>b</sup> [IC95%]	p <sup>b</sup>	q <sup>b</sup>	aAMR <sup>c</sup> [IC95%]	p <sup>c</sup>	q <sup>c</sup>
<b>Development</b>												
CD4+	47.70 [41.05-55.55]	53.75 [44.55-59.70]	60.10 [53.50-65.50]	0.67 [0.51-0.87]	<b>0.005</b>	<b>0.051</b>	0.71 [0.55-0.91]	<b>0.010</b>	<b>0.092</b>	0.79 [0.59-1.06]	0.118	0.915
TEMRA	36.10 [22.20-44.75]	33.30 [29.27-45.45]	42.00 [26.95-49.65]	0.76 [0.56-1.04]	0.092	0.385	0.65 [0.46-0.90]	<b>0.013</b>	<b>0.094</b>	1.17 [0.82-1.66]	0.391	0.808
<b>Activation (HLADR+)</b>												
N	9.39 [5.70-19.85]	8.84 [7.08-12.27]	4.05 [2.97-8.97]	1.78 [1.14-2.78]	<b>0.014</b>	<b>0.113</b>	1.60 [1.07-2.41]	<b>0.029</b>	0.297	1.16 [0.78-1.71]	0.463	0.956
EM Th1	45.30 [31.50-75.45]	44.15 [24.25-51.00]	26.55 [14.90-41.25]	2.54 [1.47-4.39]	<b>0.002</b>	<b>0.028</b>	1.62 [1.03-2.55]	<b>0.044</b>	0.317	1.75 [1.05-2.93]	<b>0.037</b>	0.590
TEMRA E	62.50 [30.40-74.30]	36.60 [27.90-56.05]	21.20 [8.40-32.00]	3.30 [1.89-5.78]	<b>&lt;0.001</b>	<b>0.005</b>	2.29 [1.41-3.74]	<b>0.002</b>	0.157	1.65 [0.97-2.80]	0.072	0.651
<b>Activation (CD38+)</b>												
CD4+	25.40 [19.70-29.60]	16.20 [11.73-24.90]	12.40 [7.69-23.85]	1.68 [1.20-2.35]	<b>0.004</b>	<b>0.055</b>	1.11 [0.81-1.53]	0.524	0.727	1.54 [1.17-2.03]	<b>0.004</b>	<b>0.100</b>
N	48.90 [38.65-59.85]	18.05 [14.10-26.15]	18.20 [11.50-31.10]	2.77 [1.90-4.90]	<b>&lt;0.001</b>	<b>&lt;0.001</b>	0.81 [0.54-1.21]	0.299	0.570	3.75 [2.83-4.98]	<b>&lt;0.001</b>	<b>&lt;0.001</b>
CM	18.70 [12.40-21.45]	13.40 [10.90-18.82]	8.62 [7.36-16.25]	1.69 [1.26-2.27]	<b>0.001</b>	<b>0.024</b>	1.39 [1.04-1.87]	<b>0.034</b>	0.297	1.22 [0.98-1.53]	0.085	0.651
EM Th0-1	11.70 [8.30-14.25]	10.45 [7.33-13.62]	6.96 [5.34-9.23]	1.47 [1.10-1.95]	<b>0.012</b>	<b>0.113</b>	1.32 [1.03-1.70]	<b>0.035</b>	0.297	1.07 [0.81-1.40]	0.646	0.956
TEMRA pE1	46.70 [40.20-57.30]	12.05 [7.59-18.20]	12.55 [9.72-25.15]	3.55 [2.35-5.38]	<b>&lt;0.001</b>	<b>&lt;0.001</b>	0.66 [0.43-1.01]	0.066	0.344	6.16 [4.43-8.57]	<b>&lt;0.001</b>	<b>&lt;0.001</b>
<b>Late activation (HLADR+CD8+)</b>												
N	3.45 [2.05-5.07]	3.27 [2.18-5.94]	1.54 [0.71-6.03]	1.61 [1.14-2.28]	<b>0.010</b>	<b>0.110</b>	1.41 [1.00-2.01]	0.059	0.335	1.17 [0.87-1.59]	0.307	0.956
EM Th1	4.60 [2.74-9.48]	3.97 [2.17-6.10]	2.07 [0.74-3.35]	1.75 [1.08-2.83]	<b>0.027</b>	0.192	1.65 [1.18-2.31]	<b>0.006</b>	0.225	1.21 [0.79-1.86]	0.391	0.956
<b>Senescence (PD1+)</b>												
CD4+	15.40 [10.75-20.10]	10.02 [7.94-13.65]	9.45 [7.06-11.05]	1.61 [1.24-2.08]	<b>0.001</b>	<b>0.002</b>	1.14 [0.92-1.43]	0.241	0.344	1.35 [1.05-1.73]	<b>0.025</b>	<b>0.144</b>
N	74.90 [68.55-82.70]	78.55 [72.10-85.08]	39.60 [19.60-61.70]	2.71 [1.69-4.32]	<b>&lt;0.001</b>	<b>0.001</b>	3.49 [2.23-5.46]	<b>&lt;0.001</b>	<b>&lt;0.001</b>	0.78 [0.56-1.09]	0.158	0.382
CM	59.50 [50.35-69.45]	55.15 [41.52-63.25]	67.60 [40.30-77.30]	1.88 [1.24-2.85]	<b>0.005</b>	<b>0.011</b>	2.57 [1.73-3.83]	<b>&lt;0.001</b>	<b>&lt;0.001</b>	0.72 [0.53-0.97]	<b>0.036</b>	0.159
EM Th0-1	11.00 [6.96-16.45]	15.15 [10.88-21.27]	7.18 [5.87-10.73]	1.18 [0.78-1.77]	0.440	0.512	1.75 [1.20-2.56]	<b>0.006</b>	<b>0.017</b>	0.57 [0.42-0.76]	<b>&lt;0.001</b>	<b>0.011</b>
TEMRA pE1	1.01 [0.42-1.60]	1.93 [1.08-3.84]	0.56 [0.32-1.26]	1.26 [0.81-1.96]	0.321	<b>0.410</b>	2.61 [1.67-4.07]	<b>&lt;0.001</b>	<b>0.001</b>	0.47 [0.31-0.72]	<b>0.001</b>	<b>0.019</b>
<b>Senescence (HAVCR2+)</b>												
CD4+	3.93 [2.82-5.88]	3.26 [2.19-4.65]	2.54 [1.77-3.74]	1.52 [1.19-1.93]	<b>0.001</b>	<b>0.004</b>	1.18 [0.94-1.48]	0.168	0.270	1.29 [1.05-1.58]	<b>0.019</b>	<b>0.125</b>
N	36.70 [27.10-43.55]	30.25 [21.98-37.60]	21.40 [13.20-29.40]	1.73 [1.15-2.61]	<b>0.012</b>	<b>0.025</b>	1.29 [0.81-2.03]	0.288	0.397	1.40 [0.95-2.06]	0.093	0.125
EM Th0-1	0.91 [0.66-1.71]	0.55 [0.38-0.91]	0.38 [0.27-0.72]	1.97 [1.41-2.77]	<b>&lt;0.001</b>	<b>0.001</b>	1.23 [0.84-1.80]	0.304	0.404	1.24 [0.75-1.50]	0.051	0.159
EM Th1	2.30 [1.50-3.51]	2.77 [1.60-5.59]	0.61 [0.27-1.26]	2.53 [1.63-3.93]	<b>&lt;0.001</b>	<b>0.001</b>	2.59 [1.56-4.29]	<b>0.001</b>	<b>0.003</b>	0.80 [0.53-1.22]	0.303	0.597
EM Th1-2	1.56 [1.17-2.62]	0.86 [0.55-1.44]	0.71 [0.30-1.07]	1.76 [1.27-2.46]	<b>0.002</b>	<b>0.004</b>	1.25 [0.82-1.90]	0.297	0.403	1.37 [0.95-1.98]	0.097	0.278
TEMRA pE1	1.20 [0.72-1.84]	0.70 [0.35-1.18]	0.38 [0.26-0.54]	2.53 [1.69-3.78]	<b>&lt;0.001</b>	<b>&lt;0.001</b>	1.62 [1.16-2.27]	<b>0.007</b>	<b>0.020</b>	1.73 [1.21-2.49]	<b>0.005</b>	<b>0.043</b>
TEMRA E	3.57 [2.64-10.80]	1.78 [1.33-9.70]	0.63 [0.00-1.34]	2.56 [1.35-4.88]	<b>0.007</b>	<b>0.015</b>	1.78 [0.92-3.43]	0.095	0.178	1.27 [0.72-2.25]	0.419	0.657
<b>Intermediate senescence (PD1+CD57+)</b>												
N	3.19 [1.50-8.82]	3.59 [1.98-5.87]	2.39 [0.89-4.06]	1.50 [0.96-2.32]	0.080	0.132	1.54 [1.07-2.21]	<b>0.026</b>	<b>0.063</b>	1.03 [0.69-1.55]	0.886	0.998
CM	18.50 [10.66-27.55]	16.40 [9.37-26.60]	13.50 [7.56-25.80]	1.52 [1.07-2.16]	<b>0.023</b>	<b>0.046</b>	1.39 [1.04-1.85]	<b>0.029</b>	<b>0.069</b>	1.13 [0.83-1.53]	0.446	0.674
EM Th1-2	3.51 [1.44-6.15]	3.23 [2.38-4.28]	1.60 [0.91-2.99]	1.23 [0.82-1.83]	0.322	0.410	1.50 [1.02-2.20]	<b>0.044</b>	<b>0.102</b>	0.85 [0.60-1.21]	0.376	0.639
<b>Advanced senescence (PD1+HAVCR2+)</b>												
CD4+	4.81 [3.41-6.42]	3.22 [2.23-4.94]	2.73 [1.77-3.98]	1.52 [1.18-1.97]	<b>0.002</b>	<b>0.006</b>	1.12 [0.86-1.46]	0.398	0.489	1.41 [1.12-1.76]	<b>0.005</b>	<b>0.043</b>
N	67.10 [45.55-80.65]	62.60 [48.25-74.00]	28.85 [9.18-48.75]	4.08 [2.48-6.70]	<b>&lt;0.001</b>	<b>&lt;0.001</b>	3.55 [2.25-5.60]	<b>&lt;0.001</b>	<b>&lt;0.001</b>	1.23 [0.87-1.73]	0.253	0.533
CM	79.80 [71.50-84.55]	72.55 [69.75-79.28]	37.70 [27.10-50.00]	4.15 [2.67-6.47]	<b>&lt;0.001</b>	<b>&lt;0.001</b>	3.24 [2.19-4.80]	<b>&lt;0.001</b>	<b>&lt;0.001</b>	1.39 [1.00-1.92]	0.053	0.184
EM Th0-1	1.10 [0.60-2.18]	0.44 [0.25-0.86]	0.06 [0.02-0.13]	4.04 [2.46-6.64]	<b>&lt;0.001</b>	<b>&lt;0.001</b>	2.38 [1.44-3.93]	<b>0.001</b>	<b>0.004</b>	1.77 [1.24-2.08]	<b>0.007</b>	<b>0.054</b>
TEMRA E	0.92 [0.00-2.30]	0.52 [0.00-1.33]	0.00 [0.00-0.00]	0.98 [0.44-2.15]	0.954	0.954	0.53 [0.25-1.13]	0.111	0.189	1.78 [1.11-2.83]	<b>0.021</b>	<b>0.129</b>

**Note:** Values are expressed as median of cell frequency [interquartile range]. **Statistics:** The AMR values [interquartile range] were obtained using a GALMSS with zero-one inflated beta distribution and multivariate analysis was performed with age, sex, and antiretroviral therapy. **a:** comparison between LLV and NHC groups; **b:** comparison between SV and NHC groups; **c:** comparison between LLV and SV groups. **Abbreviations:** LLV, PWH with persistent low-level viremia (50-200 copies/mL); SV: PWH with virologic suppression (<50 copies/mL); NHC; non-infected HIV controls; aAMR, adjusted Arithmetic Median Ratio; q, corrected level of significance by false discovery rate; N, naïve T-cells; CM, central memory T cells; EM, memory effector T-cells, TEMRA pE1, pre-terminally differentiated effector memory RA+ 1 T cells; TEMRA pE2, intermediate differentiated effector memory RA+ 2 T cells; TEMRA E, terminally differentiated effector memory RA+ T cells; HAVCR2 also known as TIM3.

**Supplementary Material 10. Comparison of T-cell development, activation, and senescence levels of CD8+ T-cells between all groups of study.**

CD8+ subpopulations	LLV	SV	NHC	aAMR <sup>a</sup> [IC95%]	p <sup>a</sup>	q <sup>a</sup>	aAMR <sup>b</sup> [IC95%]	p <sup>b</sup>	q <sup>b</sup>	aAMR <sup>c</sup> [IC95%]	p <sup>c</sup>	q <sup>c</sup>
<b>Development</b>												
CD8+	45.60 [37.40-53.45]	38.35 [35.27-48.73]	31.60 [26.40-35.20]	1.60 [1.21-2.12]	<b>0.002</b>	<b>0.013</b>	1.49 [1.14-1.94]	<b>0.005</b>	<b>0.079</b>	1.25 [0.95-1.66]	0.120	0.374
N	1.67 [1.15-2.76]	2.54 [1.64-4.03]	2.89 [1.67-3.67]	0.67 [0.48-0.92]	<b>0.019</b>	<b>0.077</b>	0.96 [0.71-1.28]	0.761	0.888	0.67 [0.50-0.89]	<b>0.034</b>	0.285
EM	55.00 [40.75-69.30]	48.65 [44.10-54.35]	39.30 [32.85-45.90]	1.84 [1.33-2.53]	<b>0.001</b>	<b>0.008</b>	1.41 [1.09-1.82]	<b>0.011</b>	<b>0.079</b>	1.32 [1.00-1.74]	0.054	0.285
EM1	45.60 [37.25-56.05]	55.80 [39.17-59.98]	45.60 [32.80-67.65]	1.06 [0.68-1.67]	0.789	0.830	1.31 [0.85-2.03]	0.226	0.475	0.66 [0.46-0.96]	<b>0.034</b>	0.285
TEMRA	35.60 [26.10-51.90]	46.15 [38.98-50.00]	55.00 [46.25-59.55]	0.57 [0.42-0.77]	<b>0.001</b>	<b>0.008</b>	0.72 [0.57-0.91]	<b>0.010</b>	<b>0.079</b>	0.78 [0.59-1.02]	0.075	0.313
CD4/CD8 ratio	1.04 [0.77-1.49]	1.43 [0.92-1.69]	1.91 [1.59-2.44]	0.64 [0.47-0.87]	<b>0.007</b>	<b>0.051</b>	0.68 [0.51-0.91]	<b>0.013</b>	<b>0.092</b>	0.79 [0.59-1.05]	0.113	0.915
<b>Activation (HLADR+)</b>												
CD8+	45.90 [32.20-61.00]	42.75 [37.70-50.05]	22.00 [14.55-32.15]	2.22 [1.42-3.49]	<b>0.001</b>	<b>0.015</b>	2.06 [1.45-2.94]	<b>&lt;0.001</b>	<b>0.005</b>	1.40 [0.91-2.15]	0.131	0.923
CM	40.60 [27.15-57.75]	32.25 [21.88-40.27]	21.00 [8.82-32.60]	2.10 [1.34-3.29]	<b>0.002</b>	<b>0.028</b>	1.54 [1.01-2.32]	<b>0.049</b>	0.181	1.47 [1.01-2.13]	<b>0.048</b>	0.993
EM2	65.00 [45.90-77.75]	52.10 [44.92-61.00]	25.00 [13.70-48.50]	2.94 [1.70-5.06]	<b>&lt;0.001</b>	<b>0.015</b>	2.18 [1.37-3.46]	<b>0.002</b>	<b>0.020</b>	1.50 [0.99-2.29]	0.064	0.923
EM3	59.60 [30.75-74.55]	47.90 [30.40-56.68]	31.20 [6.87-51.80]	2.35 [1.28-4.33]	<b>0.009</b>	<b>0.084</b>	1.68 [0.98-2.89]	0.066	0.202	1.59 [0.99-2.54]	0.061	0.923
EM4	42.30 [32.65-64.95]	49.40 [38.12-55.30]	25.10 [12.82-38.35]	1.86 [1.10-3.15]	<b>0.025</b>	<b>0.120</b>	1.68 [1.06-2.67]	<b>0.034</b>	0.163	1.17 [0.78-1.75]	0.450	0.980
TEMRA pE2	40.50 [21.55-62.05]	37.10 [20.25-45.82]	22.00 [10.40-39.50]	1.83 [1.05-3.19]	<b>0.039</b>	<b>0.143</b>	1.32 [0.80-2.20]	0.284	0.474	1.48 [0.93-2.35]	0.107	0.923
TEMRA E	60.90 [38.60-77.40]	45.40 [29.23-55.85]	36.70 [22.90-55.55]	1.99 [1.19-3.34]	<b>0.012</b>	<b>0.089</b>	1.12 [0.73-1.71]	0.616	0.800	1.85 [1.15-2.97]	<b>0.015</b>	0.736
<b>Activation (CD38+)</b>												
N	14.00 [11.45-24.20]	14.00 [8.93-23.62]	11.65 [4.63-17.52]	1.72 [1.12-2.63]	<b>0.017</b>	<b>0.098</b>	1.67 [1.07-2.61]	<b>0.030</b>	0.163	1.01 [0.71-1.44]	0.965	0.993
EM2	5.31 [2.63-7.18]	5.70 [3.43-8.97]	0.50 [0.08-2.27]	2.65 [1.54-4.56]	<b>0.001</b>	<b>0.015</b>	3.39 [2.04-5.63]	<b>&lt;0.001</b>	<b>0.002</b>	0.95 [0.61-1.49]	0.823	0.980
EM3	4.26 [2.02-9.01]	5.58 [2.36-8.80]	1.61 [0.17-5.33]	2.11 [1.23-3.59]	<b>0.009</b>	<b>0.084</b>	2.99 [1.85-4.84]	<b>&lt;0.001</b>	<b>0.002</b>	0.65 [0.40-1.05]	0.083	0.993
EM4	2.13 [1.62-3.08]	2.43 [1.52-4.20]	0.72 [0.39-2.79]	1.63 [1.06-2.52]	<b>0.032</b>	<b>0.136</b>	1.59 [1.06-2.39]	<b>0.029</b>	0.163	1.06 [0.73-1.53]	0.760	0.980
TEMRA pE2	6.15 [4.18-10.16]	5.57 [3.04-11.77]	1.65 [0.58-3.59]	2.51 [1.55-4.05]	<b>0.001</b>	<b>0.015</b>	2.36 [1.51-3.70]	<b>&lt;0.001</b>	<b>0.006</b>	1.16 [0.77-1.73]	0.482	0.980
<b>Late activation (HLADR+CD38+)</b>												
EM1	3.09 [2.14-5.15]	3.23 [1.95-5.37]	1.79 [1.09-3.08]	1.55 [1.01-2.39]	0.052	0.165	1.59 [1.06-2.39]	<b>0.031</b>	<b>0.129</b>	0.99 [0.69-1.42]	0.957	0.994
EM2	6.01 [2.84-8.53]	6.80 [3.64-9.67]	2.94 [1.19-4.53]	1.69 [1.02-2.81]	0.050	0.165	2.02 [1.30-3.13]	<b>0.003</b>	<b>0.028</b>	0.96 [0.61-1.51]	0.856	0.980
EM3	6.95 [2.72-13.75]	6.96 [3.38-10.75]	4.77 [1.21-6.90]	1.39 [0.84-2.32]	0.212	0.388	1.61 [1.06-2.45]	<b>0.032</b>	<b>0.129</b>	0.97 [0.62-1.49]	0.874	0.993
<b>Senescence (PD1+)</b>												
CD8+	12.90 [9.57-17.60]	14.35 [10.28-17.33]	5.35 [3.70-7.88]	1.96 [1.27-3.04]	<b>0.004</b>	<b>0.016</b>	1.77 [1.16-2.70]	<b>0.011</b>	<b>0.044</b>	1.13 [0.88-1.45]	0.346	0.617
N	61.10 [37.50-69.20]	50.40 [39.03-62.38]	35.75 [13.30-55.35]	1.97 [1.21-3.19]	<b>0.009</b>	<b>0.029</b>	1.62 [1.02-2.55]	<b>0.045</b>	<b>0.136</b>	1.26 [0.91-1.73]	0.165	0.434
EM1	8.78 [6.29-16.85]	12.25 [7.70-19.62]	8.99 [5.65-13.70]	0.99 [0.71-1.39]	0.965	0.975	1.34 [0.95-1.88]	0.098	0.251	0.64 [0.45-0.91]	<b>0.017</b>	<b>0.088</b>
EM2	11.10 [6.24-17.75]	21.30 [10.97-25.90]	8.81 [4.91-20.90]	0.85 [0.50-1.45]	0.555	0.712	1.19 [0.72-1.95]	0.503	0.671	0.59 [0.39-0.87]	<b>0.012</b>	<b>0.069</b>
EM4	3.66 [1.52-6.97]	10.80 [6.80-15.63]	5.96 [3.09-10.68]	0.59 [0.36-0.95]	<b>0.037</b>	<b>0.082</b>	1.28 [0.83-1.97]	0.280	0.444	0.41 [0.28-0.62]	<b>&lt;0.001</b>	<b>0.002</b>
TEMRA pE1	1.13 [0.55-2.04]	2.25 [1.33-4.00]	1.60 [0.84-3.00]	0.61 [0.40-0.92]	<b>0.019</b>	<b>0.055</b>	1.04 [0.70-1.55]	0.858	0.943	0.43 [0.29-0.64]	<b>&lt;0.001</b>	<b>0.002</b>
TEMRA pE2	3.04 [1.36-6.16]	2.88 [1.47-5.44]	4.06 [2.50-6.40]	0.63 [0.42-0.95]	<b>0.032</b>	<b>0.074</b>	0.60 [0.42-0.87]	<b>0.011</b>	<b>0.044</b>	1.00 [0.65-1.55]	0.999	0.999
<b>Senescence (HAVCR2+)</b>												
CD8+	3.07 [2.40-4.42]	2.24 [1.41-2.81]	1.77 [1.15-2.34]	1.71 [1.31-2.22]	<b>&lt;0.001</b>	<b>0.002</b>	1.17 [0.87-1.58]	0.301	0.457	1.46 [1.14-1.85]	<b>0.004</b>	<b>0.027</b>
N	27.40 [17.60-40.75]	25.55 [15.48-36.25]	6.96 [3.28-12.53]	3.82 [2.59-5.63]	<b>&lt;0.001</b>	<b>&lt;0.001</b>	3.22 [2.11-4.92]	<b>&lt;0.001</b>	<b>&lt;0.001</b>	1.15 [0.83-1.59]	0.418	0.663
CM	25.10 [13.15-30.95]	27.30 [14.80-38.27]	15.50 [9.41-24.90]	1.53 [1.07-2.20]	<b>0.026</b>	<b>0.064</b>	1.93 [1.15-3.25]	<b>0.017</b>	<b>0.059</b>	0.60 [0.36-0.99]	0.054	0.226
EM1	2.92 [1.53-4.09]	1.00 [0.80-1.66]	0.82 [0.48-1.24]	2.73 [1.85-4.04]	<b>&lt;0.001</b>	<b>&lt;0.001</b>	1.28 [0.93-1.75]	0.134	0.285	2.34 [1.66-3.31]	<b>&lt;0.001</b>	<b>&lt;0.001</b>
EM2	3.26 [2.29-4.30]	1.77 [1.43-2.76]	1.35 [0.63-3.04]	1.62 [1.16-2.26]	<b>0.008</b>	<b>0.025</b>	0.95 [0.67-1.35]	0.784	0.900	1.74 [1.29-2.36]	<b>0.001</b>	<b>0.008</b>
EM3	0.92 [0.70-1.54]	0.92 [0.68-1.35]	0.63 [0.28-0.86]	1.56 [1.08-2.24]	<b>0.022</b>	<b>0.058</b>	1.46 [0.96-2.22]	0.082	0.222	1.05 [0.74-1.50]	0.785	0.855
EM4	2.63 [2.10-3.50]	1.27 [0.70-1.98]	0.60 [0.20-1.33]	3.17 [2.11-4.76]	<b>&lt;0.001</b>	<b>&lt;0.001</b>	1.48 [0.93-2.36]	0.106	0.264	1.99 [1.38-2.87]	<b>0.001</b>	<b>0.007</b>
TEMRA pE1	2.07 [1.50-3.65]	1.30 [1.04-1.95]	0.63 [0.38-1.23]	2.16 [1.46-3.19]	<b>&lt;0.001</b>	<b>0.002</b>	1.47 [0.87-2.47]	0.155	0.308	1.16 [0.72-1.86]	0.556	0.742
TEMRA pE2	3.99 [2.58-4.67]	1.62 [1.22-2.49]	1.45 [0.69-2.09]	2.28 [1.59-3.26]	<b>&lt;0.001</b>	<b>0.001</b>	1.10 [0.77-1.57]	0.614	0.758	2.22 [1.64-3.00]	<b>&lt;0.001</b>	<b>&lt;0.001</b>
<b>Intermediate senescence (PD1+CD57+)</b>												
EM1	6.58 [3.99-12.45]	7.31 [4.32-10.35]	4.44 [2.88-6.25]	1.64 [1.12-2.40]	<b>0.015</b>	<b>0.044</b>	1.43 [1.02-2.00]	<b>0.046</b>	<b>0.136</b>	1.17 [0.84-1.64]	0.361	0.617
EM3	5.19 [4.13-10.46]	4.46 [3.40-7.45]	10.50 [5.42-20.00]	0.80 [0.50-1.30]	0.373	0.532	0.54 [0.34-0.85]	<b>0.011</b>	<b>0.044</b>	1.35 [0.84-2.16]	0.221	0.513
TEMRA E	7.23 [2.32-22.50]	4.69 [2.44-11.80]	11.38 [5.00-19.50]	0.79 [0.54-1.15]	0.222	0.358	0.61 [0.41-0.90]	<b>0.016</b>	<b>0.057</b>	1.36 [1.01-1.85]	0.052	0.226
<b>Advance senescence (PD1+HAVCR2+)</b>												
CD8+	3.45 [2.29-4.42]	3.66 [2.28-4.48]	1.18 [0.43-2.23]	1.85 [1.23-2.80]	<b>0.005</b>	<b>0.020</b>	1.81 [1.20-2.72]	<b>0.007</b>	<b>0.030</b>	0.91 [0.73-1.15]	0.443	0.682
N	67.10 [45.55-80.65]	62.60 [48.25-74.00]	28.85 [9.18-48.75]	3.20 [1.82-5.61]	<b>&lt;0.001</b>	<b>0.002</b>	2.69 [1.58-4.59]	<b>0.001</b>	<b>0.006</b>	1.27 [0.87-1.85]	0.220	0.513
CM	79.80 [71.50-84.55]	72.55 [69.75-79.28]	37.70 [27.10-50.00]	2.33 [1.38-3.94]	<b>0.003</b>	<b>0.012</b>	1.93 [1.17-3.18]	<b>0.013</b>	<b>0.050</b>	1.26 [0.84-1.88]	0.264	0.550
EM3	0.55 [0.37-1.31]	0.26 [0.11-0.59]	0.00 [0.00-0.04]	3.25 [1.72-6.16]	<b>0.001</b>	<b>0.004</b>	1.69 [0.89-3.21]	0.118	0.270	1.99 [1.33-2.99]	<b>0.002</b>	<b>0.014</b>
TEMRA pE1	0.81 [0.46-1.43]	0.69 [0.37-1.05]	0.07 [0.01-0.17]	2.75 [2.41-6.05]	<b>&lt;0.001</b>	<b>0.001</b>	2.22 [1.34-3.67]	<b>0.003</b>	<b>0.016</b>	1.22 [0.83-1.81]	0.318	0.589
TEMRA E	0.45 [0.28-0.92]	0.09 [0.02-0.18]	0.00 [0.00-0.01]	4.12 [2.02-8.42]	<b>&lt;0.001</b>	<b>0.002</b>	1.70 [0.88-3.32]	0.124	0.276	2.61 [1.67-4.07]	<b>&lt;0.001</b>	<b>0.002</b>

**Note:** Values are expressed as median of cell frequency [interquartile range]. **Statistics:** The AMR values [interquartile range] were obtained using a GALMSS with zero-one inflated beta distribution and multivariate analysis was performed with age, sex, and antiretroviral therapy by stepwise. **a:** comparison between LLV and NHC groups; **b:** comparison between SV and NHC groups; **c:** comparison between LLV and SV groups. **Abbreviations:** LLV, PWH with persistent low-level viremia (50-200 copies/mL); SV, PWH with suppressed viremia (<50 copies/mL); NHC, non-HIV

controls; aAMR, adjusted Arithmetic Median Ratio; q, corrected level of significance by false discovery rate; N, naïve T-cells; CM, central memory T cells; EM, memory effector T-cells, TEMRA pE1, pre-terminally differentiated effector memory RA+ 1 T cells; TEMRA pE2, intermediate differentiated effector memory RA+ 2 T cells; TEMRA E, terminally differentiated effector memory RA+ T cells; HAVCR2 also known as TIM3.

**Supplementary Material 11. Comparison of systemic inflammation between all groups of study.**

	LLV	SV	NHC	aAMR <sup>a</sup> [IC95%]	p <sup>a</sup>	q <sup>a</sup>	aAMR <sup>b</sup> [IC95%]	p <sup>b</sup>	q <sup>b</sup>	aAMR <sup>c</sup> [IC95%]	p <sup>c</sup>	q <sup>c</sup>
<b>Th1/Th2</b>												
GM-CSF	18.50 [14.75-21.50]	17.00 [13.00-20.75]	15.25 [11.00-20.75]	1.29 [0.91-1.81]	0.153	0.376	1.14 [0.86-1.52]	0.358	0.597	1.12 [0.83-1.51]	0.467	0.948
IFN-γ	160.50 [124.75-194.00]	124.00 [97.25-175.50]	23.00 [19.25-30.00]	5.43 [4.01-7.36]	<0.001	<0.001	4.96 [3.57-6.89]	<0.001	<0.001	1.11 [0.89-1.39]	0.368	0.948
IL1-β	23.00 [18.50-26.00]	23.00 [19.00-31.50]	18.00 [11.75-21.50]	1.02 [0.73-1.44]	0.901	0.943	1.15 [0.84-1.57]	0.401	0.607	0.91 [0.78-1.07]	0.250	0.948
IL-2	18.00 [15.25-21.00]	16.00 [14.00-21.50]	16.00 [13.25-21.00]	1.00 [0.58-1.72]	0.988	0.998	0.90 [0.59-1.39]	0.644	0.874	1.06 [0.74-1.50]	0.767	0.948
IL-4	27.00 [23.50-31.00]	28.00 [23.50-31.00]	17.50 [13.00-23.75]	1.46 [1.12-1.89]	<b>0.007</b>	<b>0.026</b>	1.47 [1.15-1.88]	<b>0.003</b>	<b>0.014</b>	0.98 [0.79-1.20]	0.819	0.948
IL-5	22.00 [20.25-27.00]	20.00 [18.00-24.50]	19.00 [13.00-26.25]	1.07 [0.82-1.38]	0.630	0.777	1.02 [0.79-1.32]	0.872	0.957	1.05 [0.88-1.26]	0.578	0.948
IL-6	16.50 [15.50-21.50]	18.00 [13.75-24.25]	16.50 [12.00-23.00]	1.10 [0.75-1.61]	0.640	0.777	1.17 [0.83-1.64]	0.373	0.600	0.95 [0.63-1.43]	0.806	0.948
IL-8	92.00 [82.12-158.25]	102.00 [76.00-126.00]	62.50 [51.75-75.50]	1.68 [1.30-2.18]	<0.001	<b>0.002</b>	1.82 [1.30-2.55]	<b>0.001</b>	<b>0.005</b>	0.93 [0.66-1.30]	0.658	0.948
IL-12	23.00 [19.00-25.50]	21.25 [17.12-29.38]	19.00 [15.25-22.75]	1.06 [0.84-1.33]	0.652	0.777	1.03 [0.82-1.30]	0.774	0.942	1.01 [0.86-1.19]	0.885	0.948
IL-13	24.50 [16.75-28.75]	21.25 [17.00-24.75]	14.50 [10.75-16.50]	1.49 [1.10-2.03]	<b>0.014</b>	<b>0.045</b>	1.28 [0.98-1.66]	0.076	0.222	1.18 [0.93-1.49]	0.187	0.948
IL-18	745.00 [599.50-1039.75]	652.00 [421.50-836.25]	67.00 [48.00-92.50]	10.72 [8.45-13.60]	<0.001	<0.001	10.20 [7.47-13.92]	<0.001	<0.001	0.91 [0.66-1.25]	0.567	0.948
TNF-α	30.50 [25.75-34.00]	29.00 [25.00-33.25]	15.00 [12.50-20.50]	1.64 [1.24-2.15]	<b>0.001</b>	<b>0.005</b>	1.77 [1.37-2.30]	<0.001	<0.001	0.99 [0.82-1.21]	0.939	0.961
<b>Th9/Th17/Th22/Treg</b>												
IL-9	28.50 [24.25-34.00]	26.50 [21.75-31.50]	27.00 [22.50-38.75]	0.96 [0.67-1.36]	0.804	0.905	0.85 [0.66-1.09]	0.204	0.417	1.18 [0.87-1.62]	0.297	0.948
IL-10	22.00 [17.00-25.50]	18.50 [13.25-26.50]	17.50 [16.00-22.25]	1.13 [0.90-1.43]	0.296	0.506	1.02 [0.77-1.36]	0.880	0.957	1.10 [0.86-1.41]	0.449	0.948
IL-17A	21.00 [17.00-26.00]	16.00 [13.75-26.00]	18.50 [13.75-23.50]	1.17 [0.73-1.86]	0.514	0.747	0.99 [0.69-1.42]	0.959	0.981	1.11 [0.74-1.66]	0.607	0.948
IL-21	30.00 [24.25-72.50]	30.00 [20.50-36.00]	31.50 [22.00-57.50]	1.70 [0.78-3.69]	0.188	0.404	2.01 [0.83-4.90]	0.129	0.324	0.86 [0.34-2.13]	0.738	0.948
IL-22	49.00 [33.00-123.75]	35.50 [29.50-60.00]	65.00 [35.50-82.00]	1.33 [0.59-3.04]	0.495	0.742	1.78 [0.70-4.51]	0.230	0.443	0.75 [0.27-2.05]	0.579	0.948
IL-23	22.25 [18.25-28.00]	20.00 [16.50-26.00]	17.50 [14.00-26.25]	1.22 [0.57-2.60]	0.611	0.777	1.35 [0.83-2.22]	0.236	0.443	1.23 [0.69-2.20]	0.479	0.948
IL-27	20.00 [14.50-24.75]	17.00 [11.50-21.50]	15.00 [12.75-23.75]	1.36 [0.87-2.13]	0.189	0.404	0.99 [0.69-1.41]	0.938	0.981	1.38 [0.88-2.15]	0.163	0.948
<b>Inflammatory cytokines</b>												
INF-α	32.00 [24.50-35.25]	30.00 [23.75-36.50]	29.50 [24.25-51.00]	1.10 [0.71-1.72]	0.665	0.777	1.04 [0.67-1.61]	0.864	0.957	1.06 [0.62-1.83]	0.830	0.948
IL-1α	42.00 [36.75-75.75]	42.00 [34.50-60.75]	40.00 [34.75-62.50]	1.48 [0.76-2.88]	0.249	0.487	1.25 [0.74-2.09]	0.405	0.607	1.10 [0.58-2.09]	0.767	0.948
IL-1RA	254.50 [183.75-449.25]	217.00 [143.50-386.25]	31.50 [20.00-35.00]	10.70 [7.31-15.65]	<0.001	<0.001	9.67 [6.41-14.57]	<0.001	<0.001	1.08 [0.76-1.55]	0.665	0.948
IL-7	21.25 [17.12-25.00]	22.00 [18.75-25.50]	17.50 [15.00-26.25]	0.99 [0.77-1.28]	0.966	0.988	1.02 [0.80-1.30]	0.893	0.957	0.98 [0.85-1.14]	0.825	0.948
IL-15	24.00 [19.50-30.50]	24.00 [19.00-30.50]	22.00 [19.00-31.00]	1.09 [0.75-1.59]	0.643	0.777	0.95 [0.73-1.23]	0.680	0.874	1.12 [0.84-1.49]	0.445	0.948
IL-31	29.50 [26.12-33.75]	28.00 [24.75-32.25]	27.00 [23.50-32.25]	1.13 [0.90-1.43]	0.304	0.506	1.04 [0.88-1.21]	0.673	0.874	1.12 [0.92-1.36]	0.276	0.948
LTα	52.00 [45.00-58.75]	50.00 [43.00-60.00]	50.00 [41.50-56.25]	1.10 [0.80-1.52]	0.563	0.777	0.93 [0.72-1.21]	0.606	0.852	1.18 [0.90-1.55]	0.243	0.948
<b>Chemokines</b>												
Eotaxin	253.00 [137.25-391.00]	296.50 [160.00-423.50]	98.00 [78.00-158.00]	2.77 [1.91-4.02]	<0.001	<0.001	3.12 [2.03-4.79]	<0.001	<0.001	0.90 [0.57-1.43]	0.655	0.948
Gro-α	48.50 [38.50-63.88]	48.00 [38.00-58.00]	38.00 [34.25-52.25]	1.25 [0.98-1.58]	0.075	0.226	1.22 [0.91-1.64]	0.180	0.385	0.90 [0.69-1.16]	0.411	0.948
CXCL10	177.00 [126.50-221.25]	129.00 [106.75-252.75]	109.00 [87.25-154.00]	1.51 [1.15-1.98]	<b>0.005</b>	<b>0.020</b>	1.55 [1.08-2.22]	<b>0.021</b>	<b>0.074</b>	0.97 [0.69-1.38]	0.881	0.948
CCL2	233.00 [190.75-294.25]	163.50 [102.75-467.25]	161.00 [107.00-267.75]	1.22 [0.85-1.77]	0.287	0.506	1.24 [0.83-1.87]	0.300	0.520	0.75 [0.46-1.21]	0.245	0.948
CCL3	50.25 [35.12-74.75]	47.00 [34.75-75.00]	38.50 [30.00-67.50]	1.10 [0.71-1.72]	0.674	0.777	1.04 [0.66-1.63]	0.866	0.957	1.06 [0.68-1.64]	0.799	0.948
CCL4	175.00 [111.50-307.75]	181.50 [134.25-332.50]	137.50 [99.50-190.50]	1.42 [0.88-2.30]	0.155	0.376	1.50 [0.93-2.43]	0.106	0.280	0.83 [0.50-1.37]	0.460	0.948
CCL5	6663.50 [5530.38-7681.00]	6589.00 [5266.75-7019.00]	5365.00 [4275.00-6217.00]	1.23 [1.07-1.41]	<b>0.005</b>	<b>0.021</b>	1.19 [1.04-1.37]	<b>0.015</b>	<b>0.054</b>	1.03 [0.92-1.15]	0.636	0.948
CXCL12	258.00 [164.75-376.75]	226.00 [183.50-275.50]	199.50 [154.00-317.00]	1.16 [0.79-1.71]	0.460	0.735	1.19 [0.78-1.81]	0.426	0.619	0.98 [0.63-1.52]	0.922	0.961
<b>Growth factors</b>												
BDNF	1986.00 [1126.00-3194.50]	2050.50 [1211.75-3187.75]	557.00 [410.00-994.50]	3.12 [2.19-4.44]	<0.001	<0.001	3.35 [2.36-4.77]	<0.001	<0.001	0.93 [0.65-1.32]	0.690	0.948
EGF	47.00 [36.50-96.50]	50.50 [33.50-88.00]	26.00 [22.00-49.00]	1.74 [1.21-2.50]	<b>0.005</b>	<b>0.020</b>	1.67 [1.17-2.37]	<b>0.007</b>	<b>0.027</b>	1.03 [0.73-1.44]	0.879	0.948
FGF-2	42.00 [34.50-65.00]	40.00 [34.50-57.75]	35.50 [29.00-46.50]	0.97 [0.67-1.41]	0.883	0.943	0.94 [0.65-1.36]	0.755	0.942	1.03 [0.82-1.30]	0.794	0.948
HGF	29.00 [22.25-31.25]	27.00 [24.75-33.25]	20.00 [16.50-26.50]	1.19 [0.94-1.52]	0.159	0.376	1.27 [0.98-1.65]	0.079	0.222	0.95 [0.81-1.11]	0.499	0.948
LIF	23.00 [17.25-25.00]	18.00 [15.75-21.25]	17.00 [13.50-23.00]	1.25 [0.84-1.84]	0.272	0.506	1.00 [0.76-1.32]	0.990	0.990	1.20 [0.89-1.62]	0.232	0.948
NGF-β	27.50 [24.25-34.00]	26.50 [24.25-29.50]	28.00 [22.25-31.75]	1.09 [0.86-1.38]	0.474	0.735	1.28 [0.91-1.79]	0.160	0.370	0.90 [0.61-1.33]	0.599	0.948
PDGF-BB	274.00 [104.00-446.00]	352.50 [212.50-419.00]	119.00 [93.50-231.25]	2.44 [1.35-4.43]	<b>0.005</b>	<b>0.020</b>	2.29 [1.54-3.39]	<0.001	<b>0.001</b>	1.00 [0.57-1.78]	0.987	0.948
PIGF-1	240.00 [161.75-329.25]	234.00 [193.50-310.00]	196.00 [162.00-246.00]	1.21 [0.90-1.63]	0.206	0.421	1.25 [1.00-1.55]	0.057	0.183	1.03 [0.79-1.35]	0.813	0.948
KITLG	66.00 [54.75-94.50]	69.00 [57.00-101.00]	70.00 [49.00-97.00]	1.02 [0.80-1.30]	0.871	0.943	1.16 [0.88-1.52]	0.300	0.520	0.88 [0.67-1.15]	0.339	0.948
VEGF-A	100.00 [67.00-197.00]	116.00 [83.75-157.25]	44.00 [33.50-70.00]	2.70 [1.72-4.24]	<0.001	<b>0.001</b>	2.43 [1.49-3.94]	<b>0.001</b>	<b>0.004</b>	0.95 [0.54-1.67]	0.855	0.948
VEGF-D	43.00 [36.50-65.00]	51.00 [35.75-56.50]	39.00 [32.25-50.00]	1.19 [0.97-1.47]	0.106	0.297	1.17 [0.94-1.46]	0.164	0.370	0.93 [0.74-1.18]	0.567	0.948

**Note.** Values are expressed as median of fluorescence [interquartile range]. **Statistics:** The AMR values [interquartile range] were obtained using generalized linear model with a gamma distribution and multivariate analysis was performed with age, sex, and antiretroviral therapy by stepwise. **a:** comparison between LLV and NHC groups; **b:** comparison between SV and NHC groups; **c:** comparison between LLV and SV groups. **Abbreviations:** LLV, PWH with persistent low-level viremia (50-200 copies/mL); SV: PWH with suppressed viremia (<50 copies/mL); NHC; non-HIV controls; aAMR, adjusted Arithmetic Median Ratio; q, corrected level of significance by false discovery rate, LTα, also known as TNF-β.

