Immune recovery of acute HIV treated patients is characterized by an increase in immune senescence.

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BACKGROUND

Our aim was to characterize the immunophenotypic evolution of T cells during the first year of ART in acute HIV patients focusing on T cell subsets, immune activation, immune-senescence and regulatory T cells.

METHODS

Blood samples were obtained from subjects enrolled in the VIHIA cohort which follows acute HIV patients from 5 different states in Mexico at diagnosis and 2, 6 and 12 months pos-ART.

Flow-cytometry analysis of T-cell-immune-phenotypic characteristics (T cell subsets, immune-activation, immune-senescence, regulatory T cells) was performed.

Wilcoxon matched-pairs signed rank test was used for each value between baseline (Pre-ART) and month 12(Pos-ART).

RESULTS

Table 1. Baseline characteristics	Patients
Fiebig Stage	n (%)
• II	4 (11)
• III	5 (13)
• IV	24 (63)
• V	5 (13)
Age in years (mean; min - max)	32 (21 - 57)
CD4+/CD8+ T cell ratio pre-ART (mean; min – max)	0.4985 (0.096 - 1.26)
CD4+ T cell (mean; min - max)	439 cells/μL (163 – 721)
Viral load (mean; min – max)	1.2 milion copies/mL (23339 – 20000000)

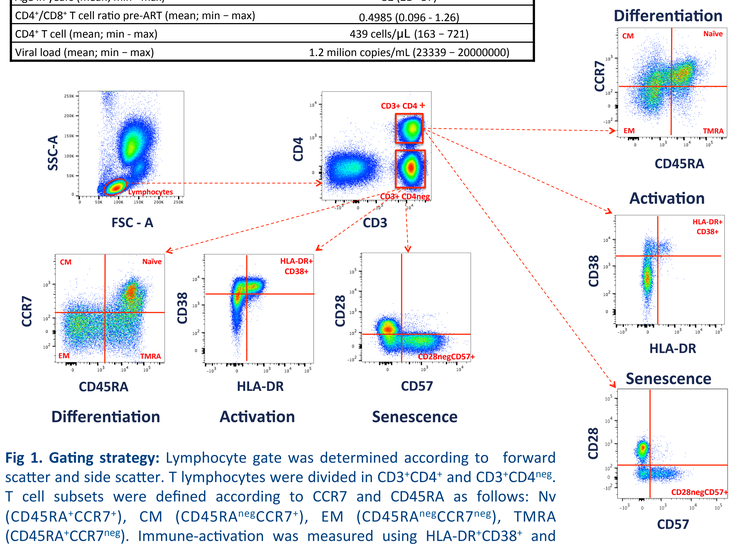

Fig 1. Gating strategy: Lymphocyte gate was determined according to forward scatter and side scatter. T lymphocytes were divided in $CD3^+CD4^+$ and $CD3^+CD4^{neg}$. T cell subsets were defined according to CCR7 and CD45RA as follows: Nv ($CD45RA^+CCR7^+$), CM ($CD45RA^{neg}CCR7^+$), EM ($CD45RA^{neg}CCR7^{neg}$), TMRA ($CD45RA^+CCR7^{neg}$). Immune-activation was measured using $HLA\text{-}DR^+CD38^+$ and immune-senescence was defined as $CD28^{neg}$ $CD57^+$.

$CD4^+$ and $CD4^{neg}$ T Cells Differentiation Dynamics

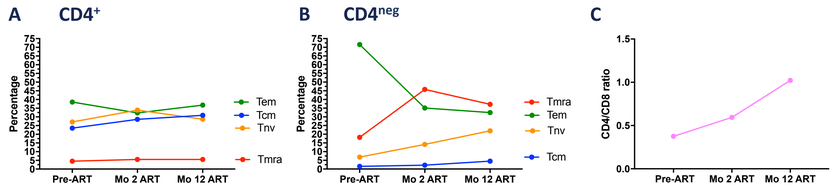

Fig 2. T cell differentiation during 12 months of follow-up. ART: Antiretroviral therapy, Tcm: Central memory T cells, Tnv: Naïve T cells, Tmra: Effector memory RA T cells, Tem: Effector memory T cells. $CD4^+$ T cells **(A)** and $CD4^{neg}$ T cells **(B).** CD4/CD8 ratio during 12 months of follow-up**(C)**.

Regulatory T cells

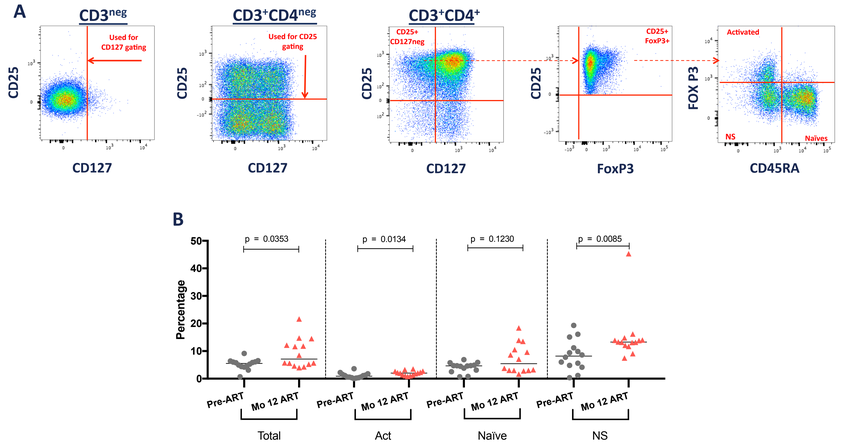

Fig 3. Tregs Analysis: (**A**) Gating strategy for Regulatory T cells. Activated Tregs: $CD4^+CD25^+CD127^{neg}FoxP3^{hi}CD45RA^{neg}$; Naïve Tregs: $CD4^+CD25^+CD127^{-}$ Fox $P3^{low}CD45RA^+$; Non supressors: (NS): $CD4^+CD25^+CD127^{neg}FoxP3^{low}CD45RA^{neg}$. (**B**) Percentage of different Treg subsets pre-ART and at 12 months of follow-up.

$CD4^+$ and $CD4^{neg}$ T Cells Senescence

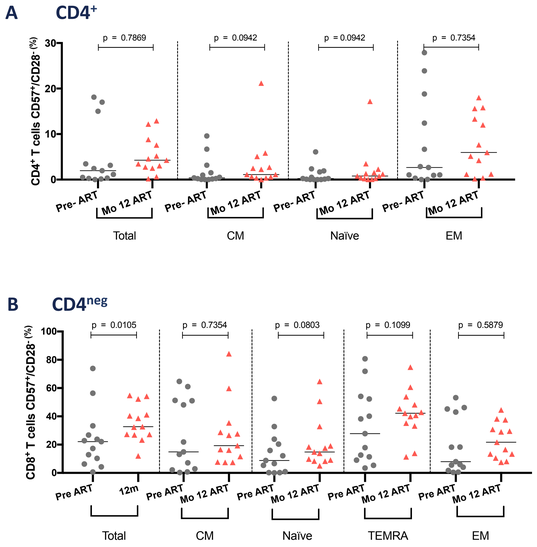

Fig 4. Effects of ART in the percentage of $CD4^+CD28^{neg}CD57^+$ (**A**) and $CD4^{neg}CD28^{neg}CD57^+$ (**B**) T cells. CM: Central memory T cells, Naïve: Naïve T cells, EM: Effector memory T cells, TEMRA: Effector memory RA T cells.

CONCLUSIONS

It has been hypothesized that early ART decreases Tcell immune-senescence, however in our cohort despite treatment during acute HIV infection, we observed that at 1 year follow-up immune-senescence markers increased despite a decrease in immune activation and a recovery of T cell subsets.

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