Intact HIV Remains Similar in Early and Late-Treated Patients with Comparable Immunological Status

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BACKGROUND

The HIV reservoir stablished in the early stages of the acute HIV infection (AHI) and at the time of antiretroviral therapy (ART) initiation is a major barrier to curing HIV. Our objective was to assess the longitudinal impact of initiating ART during early HIV infection on the composition of the viral reservoir, in comparison to a cohort of individuals with similar immunological status treated during the chronic phase of the infection.

METHODS

-The VHAHI cohort is an ongoing ambispective cohort (n=147) including patients with confirmed AHI in Barcelona, Spain (Suanzes et al, IJID, 2023).

-We included 41 participants: 25 individuals from the VHAHI cohort that started ART within 180 days (early treated: ET), and 16 individuals with similar immunological status that started ART during the chronic phase of HIV infection (late treated: LT).

-We performed a longitudinal analysis after 0, 6, 12 and 36 months of ART in 13 ET and 7 LT participants. A cross-sectional analysis using samples from 23 ET and 14 LT participants who had been on ART a median of 68 months (IQR: 45-101) was performed.

-PBMCs were isolated by Ficoll-Plaque density gradient centrifugation and cryopreserved in liquid nitrogen. We measured total HIV DNA (qPCR) and frequencies of intact and defective proviruses (IPDA), in CD4+ T-cells (Bruner et al, Nature, 2019).

-Statistical analysis were performed using IBM SPSS (Version 21) and GraphPad Prism (version 8.3).

	Total (n=41)	Early treated (n=25)	Late treated (n=16)	p-value
Age, years, median (IQR)	30 (27-40)	30 (25-39)	38 (28-41)	0.307
Sex, female, n (%)	38 (92.7)	24 (96)	14 (87.5)	0.550
Pre-ART HIV VL, copies/mL, median (IQR)	302,000 (85,950-1,561,603)	629,000 (123,500-6,380,000)	228,000 (85,925-323,750)	0.035
Pre-ART CD4+ T-cells, cells/mm3, median (IQR)	470 (353-570)	480 (345-585)	455 (351-530)	0.467
Pre-ART 48 CD8+ T-cells, cells/mm3, median (IQR)	931 (658-1,301)	925 (590-1,268)	931 (774-1,433)	0.672
Pre-ART CD4+/CD8+ ratio, median (IQR)	0.51 (0.30-0.68)	0.51 (0.30-0.71)	0.49 (0.30-0.61)	0.521

Table 1. Demographic and immunovirological characteristics.

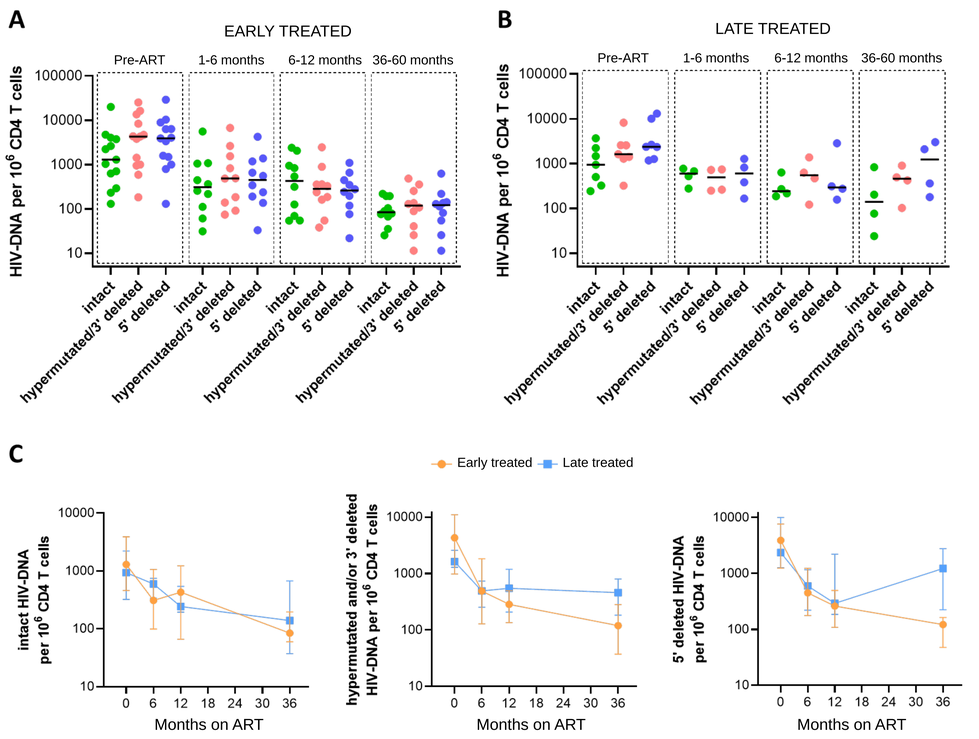


Figure 1. Changes in the composition of the HIV reservoir overtime. Intact and defective proviruses were measured by IPDA.

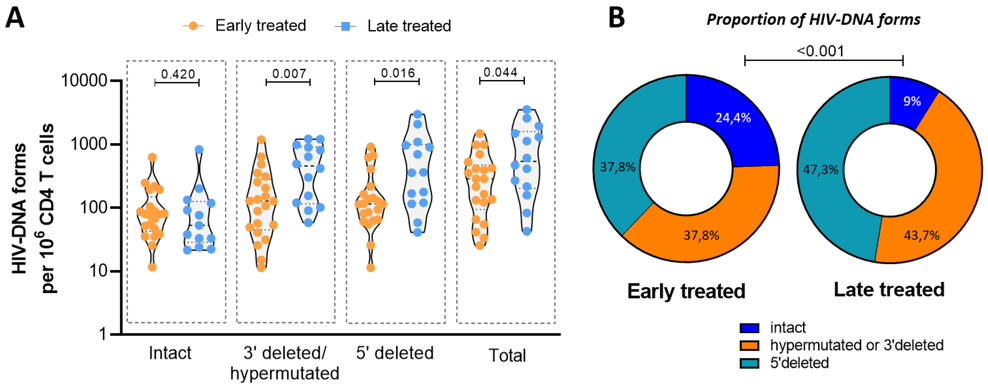


Figure 2. Composition of the HIV reservoir. A) Total, intact and defective proviruses were measured by qPCR or IPDA in early and late treated individuals after ≥36 months of ART. B) Proportions of proviral forms are shown.

RESULTS

-The median time from the estimated date of infection to ART initiation was 75 days (IQR: 42-128) in the ET group and >180 days in the LT group.

-In the longitudinal analysis (Fig.1), all viral forms, including intact DNA, declined over time in both cohorts. However, defective proviruses plateaued after 6-12 months of ART in LT participants, while continuous decay was observed in the ET group (p=0.01).

-Participants in the cross-sectional analysis maintained virological suppression for a median of 63 months (IQR: 39-95) without significant differences between ET and LT (p>0.05). Total HIV DNA and defective proviral DNA levels were significantly higher in LT participants (Fig.2A). Although we did not observe differences in intact proviral DNA between groups (Fig.2A), the contribution of the intact form to the total pool of HIV-DNA was significantly higher in ET participants (Fig.2B).

CONCLUSIONS

The HIV intact reservoir declines over time both in early and late treated people with HIV. However, while the decay of defective proviruses continues in early treated individuals, it plateaus after 6-12 months of ART in late treated participants (Fig.1). After a median of 63 months of ART, both total and defective proviral DNA levels were higher in the late treated group, but the intact reservoir remained similar between early and late treated individuals (Fig.2).

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ADDITIONAL KEY INFORMATION

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