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Long-term early antiretroviral therapy limits the HIV-1 reservoir size as compared to later treatment initiation but not to levels found in long-term non-progressors

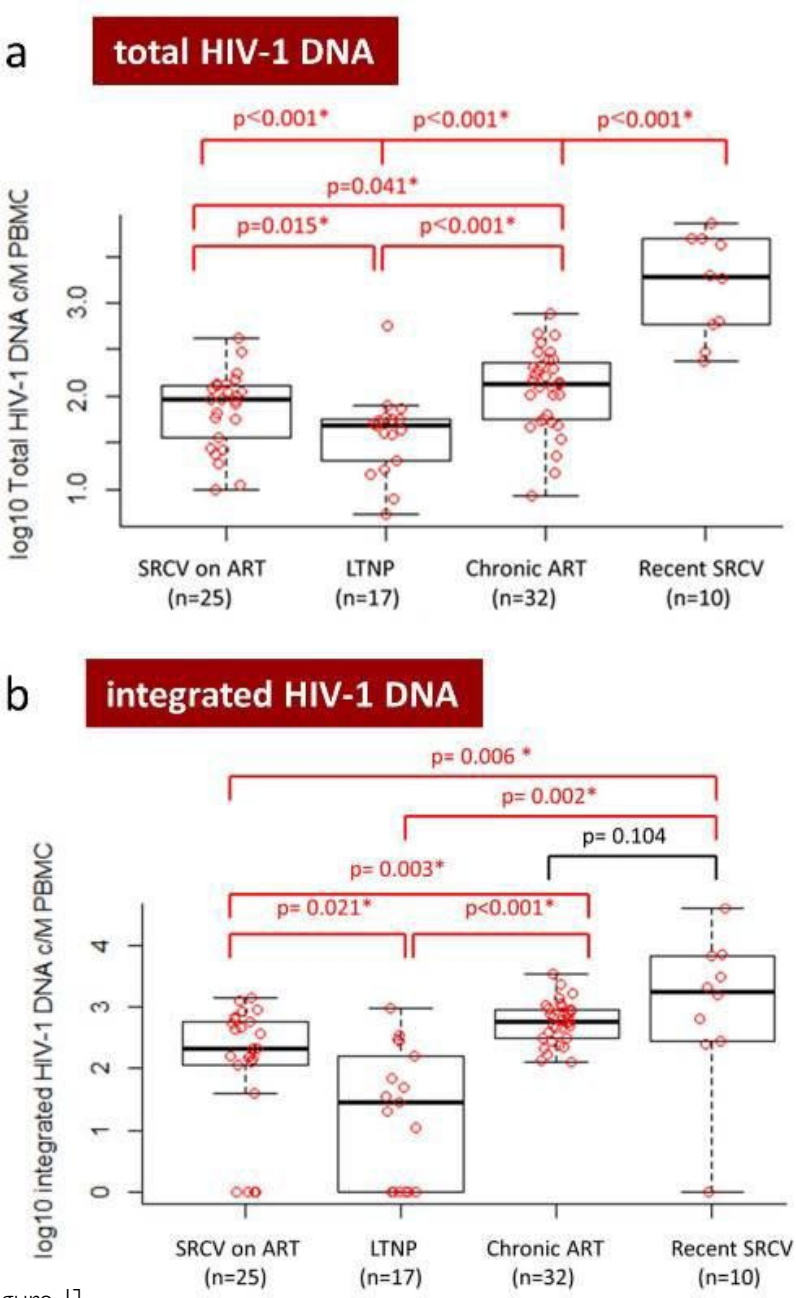
Malatinkova E.[1], De Spiegelaere W.[1], Bonczkowski P.[1], Kiselinova M.[1], Vervisch K.[1], Trypsteen W.[1], Johnson M.[2], de Looze D.[3], Kinloch S.[2], Vandekerckhove L.[1]

[1]Ghent University and University Hospital Ghent, HIV Translational Research Unit, Department of Internal Medicine, Faculty of Medicine and Health Sciences, Ghent, Belgium, [2]University College London, Royal Free Hospital, Division of Infection and Immunity, Royal Free Campus, London, United Kingdom, [3]University Hospital Ghent, Ghent, Belgium

Background: Early initiation of long-term antiretroviral therapy (ART) may lead to viral control after treatment discontinuation. Recent evidence indicates that ART initiated within seroconversion limits the HIV-1 reservoir size. Insight into the reservoir in patients with different timings of ART as well as those who can control HIV-1 without therapy should further inform new treatment strategies.

Methods: A cross-sectional study of HIV-1 reservoir size (total and integrated HIV-1 DNA) and dynamics (2-LTR circles and cell-associated HIV-1 unspliced RNA (usRNA)) was performed in peripheral blood mononuclear cells (PBMCs) in 84 HIV-1 infected patients from 4 cohorts in 2 clinical centers (London, UK and Ghent, BE): long-term treated patients with ART initiated during seroconversion (SRCV on ART; n=25) or chronic infection (Chronic ART; n=32), long-term non-progressors (LTNP; n=17) and ART-naïve recent seroconverters (Recent SRCV; n=10). Total HIV-1 DNA, 2-LTR and usRNA were measured by ddPCR and integrated HIV-1 DNA by Alu-HIV PCR. Clinical parameters including time on ART and aviremia, CD4 count and CD4/CD8 ratio were collected.

Results: Median total HIV-1 DNA copies were: $9^{2,4}8$, 137 and 1901 c/106 PBMCs in SRCV on ART, LTNP, Chronic ART and Recent SRCV, respectively. Significantly lower levels of total (p=0.041) and integrated HIV-1 DNA (p=0.003) were detected in early as compared to chronically treated patients, however these were higher than those found in LTNP (Fig.1a, 1b). Interestingly, similar levels of integrated HIV-1 DNA were found in Recent SRCV compared to the Chronic ART cohort (p=0.104), confirming very fast seeding of the reservoir (Fig 1b). Levels of usRNA were significantly lower in early compared to chronically treated cohort (p=0.007), indicating a lower transcriptional activity in early treated patients and similar to LTNP (p=0.615). Furthermore, early treated patients exhibited a higher CD4/CD8 ratio compared to chronically treated patients (p=0.009), suggesting lower levels of residual immune activation.



[Figure 1]

Conclusions: Our data demonstrate that long-term early treated patients have smaller reservoir size as compared to patients treated during chronic infection, however not reaching levels found in LTNP. Interestingly, the reservoir dynamics in terms of 2-LTR and usRNA as well as the CD4/CD8 ratio in early treated patients are comparable to LTNP.

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