HIV Proviral DNA Quantification in a Cohort of Japanese patients on Long-term ART

Kamelia R. Stanoeva1, André König2, Asami Fukuda1, Yoko Kawanami1, Takeo Kuwata1, Yorifumi Satou1 and Shuzo Matsushita1

1Center for AIDS Research, Kumamoto University, Kumamoto, Japan; 2Faculty of Statistics, Technical University Dortmund, Germany

Abstract

• The aim of this study was to measure the levels of total HIV DNA in PBMC and follow up long-term dynamics under ART. As expected higher levels were observed prior to treatment and a decrease was seen during the first regimen. ART achieving viral control with undetectable HIV RNA viral load (VL), however, did not lead to undetectable total HIV DNA levels with the latter most commonly measured in the cluster between 20 and 200 copies/10⁶ PBMC. HIV DNA loads fluctuations were observed without linking to clinical events. Stable total HIV DNA levels were seen with recent PIs and INAs regimens. Our retrospective study shows a glimpse on HIV peripheral reservoir dynamic and suggests better understanding of proviral DNA and influencing factors is needed. Total HIV DNA quantification is relatively easy to perform and could be implemented as clinical monitoring tool.

• Despite successes of ART, the persistence of HIV reservoir and its measurement remain unsolved issues. Understanding the integrated viral DNA [1-3] and the mechanisms of its persistence [4] are important for the future HIV cure.

• Patient populations on ART are growing (7.5 million in 2010 to 17 million in 2015 globally [5]) and accessing how the long-term therapy affects persistence is needed as basis for HIV Cure research.

• Therefore, our aim was to evaluate the total HIV DNA in PBMC and outline the dynamics of part of the peripheral viral reservoir in a cohort of Japanese patient on long-term ART.

Material and methods

Kumamoto University Hospital cohort, Kumamoto, Japan

• PBMC: male, mean age 47 years
• Blood samples collected in the period 2016–2015
• 280 PBMC: DNA samples isolated with QIAamp DNA Blood Kit
• qPCR: quantification of total HIV DNA
• Clinical monitoring and ART regimen data collected and analyzed

Total HIV DNA quantification in PBMC

• Real-time qPCR (on StepOnePlus® Real-Time PCR System)
• modification of a previously described method by Thonk et al. [6]
• qPCR primers: proviral gag Herpesviridae, gag proviral gag Herpesvirus and gag proviral gag Herpesvirus
• Plenty in standards used as standards
• Total HIV DNA calculated in copies/10⁶ PBMC cells

Results

Patient 19: stable ART with HIV RNA VL < detectable (single VL = 8 copies/ml)

Stable total HIV DNA levels under ART achieving viral control

Stable and decreased total HIV DNA levels more frequently associated with switching to newer regimens: PIs and especially INIs.

Conclusions & Discussion

Supports routine clinical monitoring of HIV DNA levels

• Consistent with data that HIV-1 establishes reservoirs in early infection [7]
• Might be partially allowed by detection of uncloned HIV proviral DNA
• Effective antiretroviral therapy (ART) does not necessarily
• Supports routine clinical monitoring of HIV DNA levels

Stable and decreased total HIV DNA levels more frequently associated with switching to newer regimens: PIs and especially INIs.

Acknowledgments:
The Japanese government MEXT programmes provided support to K.R.S. We express our gratitude to the IAS Towards a Cure team for a “2016 Towards an HIV Cure scholarship” awarded to K.R.S as presenting author.

References:
8. 559.97 201.52 201.52 14
9. 2769
10. Kumamoto, Japan
11. 47
12. % male, mean age
13. Mean ages of the 61 selected patients
14. • Clinical monitoring and ART regimen data collected and analyzed
15. • Blood samples collected in the period
16. • Samples available at multiple time points
17. • Proviral DNA calculated in copies/10⁶ PBMC cells.
18. 559.97 201.52 201.52 14
19. 2769