

“FULL” VIRAL SUPPRESSION, RESIDUAL VIREMIA AND LOW LEVEL VIREMIA IN HIV-1 ART- TREATED PATIENTS: RISK OF VIROLOGICAL FAILURE AND ASSOCIATION WITH INFLAMMATION MARKERS AND HIV-1 DNA

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Background. The persistence of minimal viremia during antiretroviral treatment could represent a continuous stimulus for the immune system, which underlies to a chronic immune activation and inflammation. In addition the residual viremia could fuel the HIV reservoirs.

Aim. The aim of the study was to clarify the role of RV on virological rebound (VR) and failure (VF), its influence on immune activation status and its relationship with size of the latent reservoir.

Methods. 961 HIV-1 patients from Policlinico Umberto I Hospital were retrospectively examined for 40 months.

HIV-1 RNA was measured by Versant kPCR Molecular System (Siemens Healthcare Diagnostics) [LLOQ=37 copies/mL; qualitative results below the LLOQ are reported as “Target Detected” (TD) or “Target Not Detected” (TND)]. Soluble human CD14 (sCD14), TNF α and IL-6 were measured by ELISA (ENZO Life Sciences). HIV-1 DNA was performed by commercial kit *Generic HIV DNA Cell* (Biocentric, France).

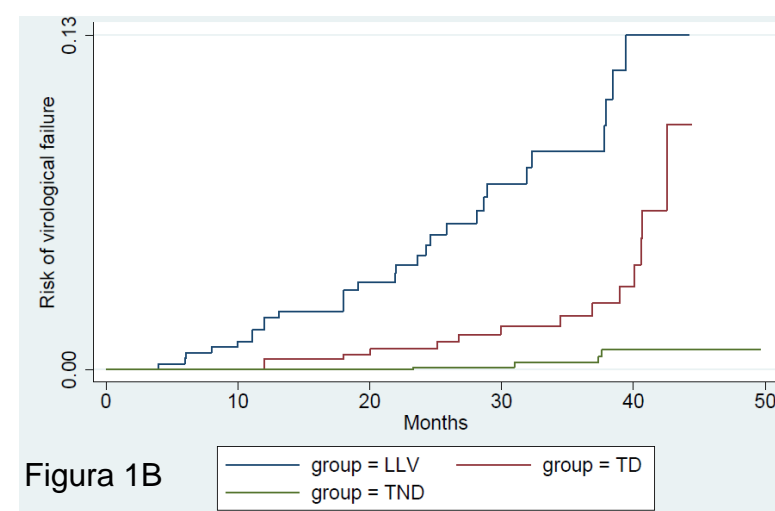
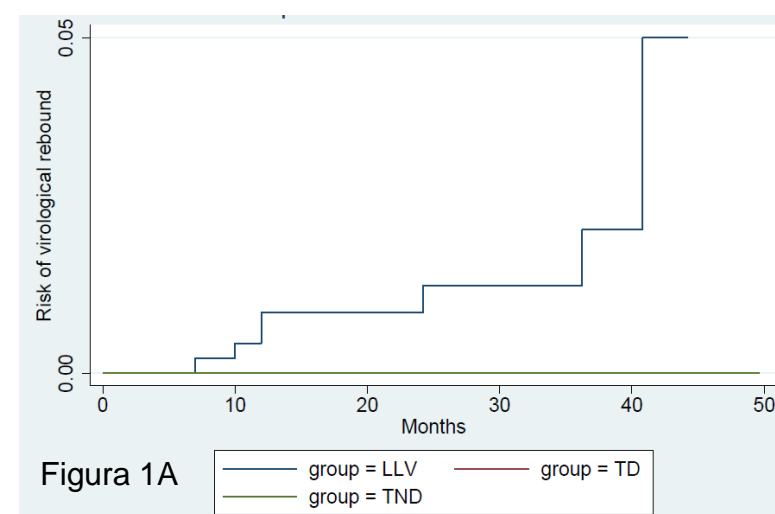
Results. According to plasma HIV-RNA levels, three groups were defined:

full suppression (TND; n=596), residual viremia (TD; n=251), and Low Level Viremia (37-200 copies/ml; n=114).

Virological rebound (VR) was defined as two HIV-1 RNA values >200 copies/mL. Virological failure (VF) was defined as HIV-1 RNA values >400 copies/mL.

Rebound rates were 0.1% for TND 0.1%, for TD, and 6.14% for LLV. After 40 months, the risk of VR were significantly higher in LLV than in TND or TD (p<0.0001) (Figura 1A).

Failure rates were 3.36% for TND 6%, for TD, and 24.6% for LLV. The risk of VF were significantly higher in LLV than in TND or TD (p<0.0001) and higher in TD group than TND (p=0.004) (Figura 1B).



The levels of inflammatory markers were analyzed in 113 patients who had always viremia TND during follow up (group I), 113 patients with residual viremia (RV) during follow up (group II) and 95 patients with at least 2 value of VL> 37 copies/ml (group III). sCD14 levels >10 μ g/ml were detected in 11.7% of group I, 33.3% of group II and 72.3% of group III (I vs II: p<0.0001; I vs III: p<0.0001; II vs III: p=0.001)

In the remaining samples the median (range) values for sCD14 were 7.25 μ g/ml (2.7->10) in group I, 8.8 μ g/ml (3.6->10) in group II and 10 μ g/ml (4->10) in group III (I vs II: p<0.0001; I vs III: p<0.0001; II vs III: p=0.001) (Figura 2). No difference, regarding TNF-alpha and IL-6 levels, was found.

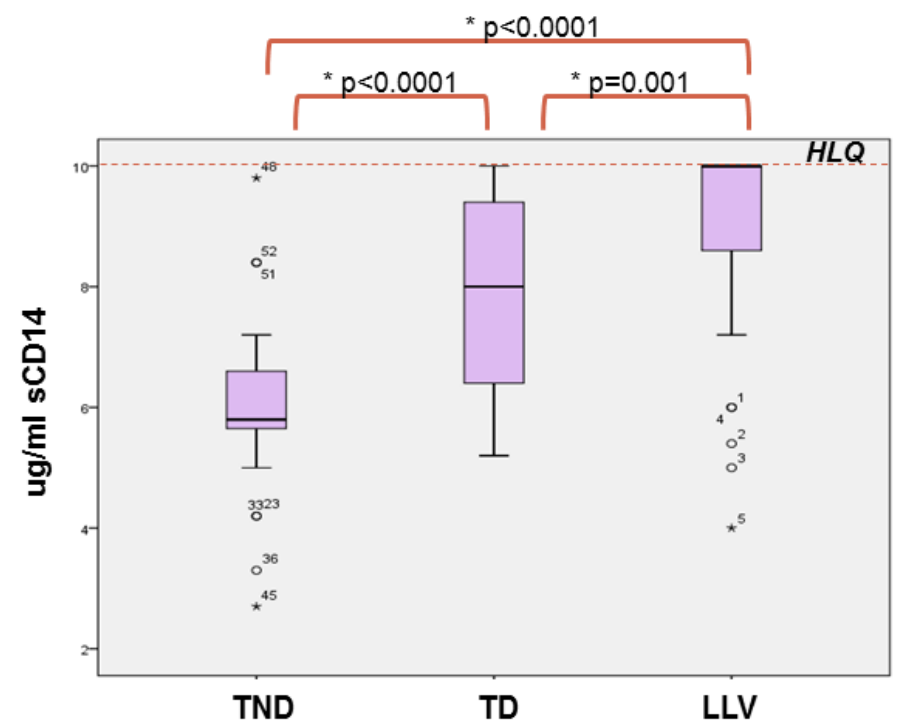


Figura 2

The HIV-1 DNA levels were stratified on the basis of RV. There was a statistically significant difference between individuals with TD versus TND plasma viremia [14,3 (IQR: 12.4-15.9) log₁₀/10⁶ PBMC and 12.23 (IQR: 9.4-14.3) log₁₀/10⁶ PBMC (p=0.001)] and individuals with LLV [15.4 (IQR: 12.3-17.2) log₁₀/10⁶ PBMC (p<0.0001)] (Figura 3).

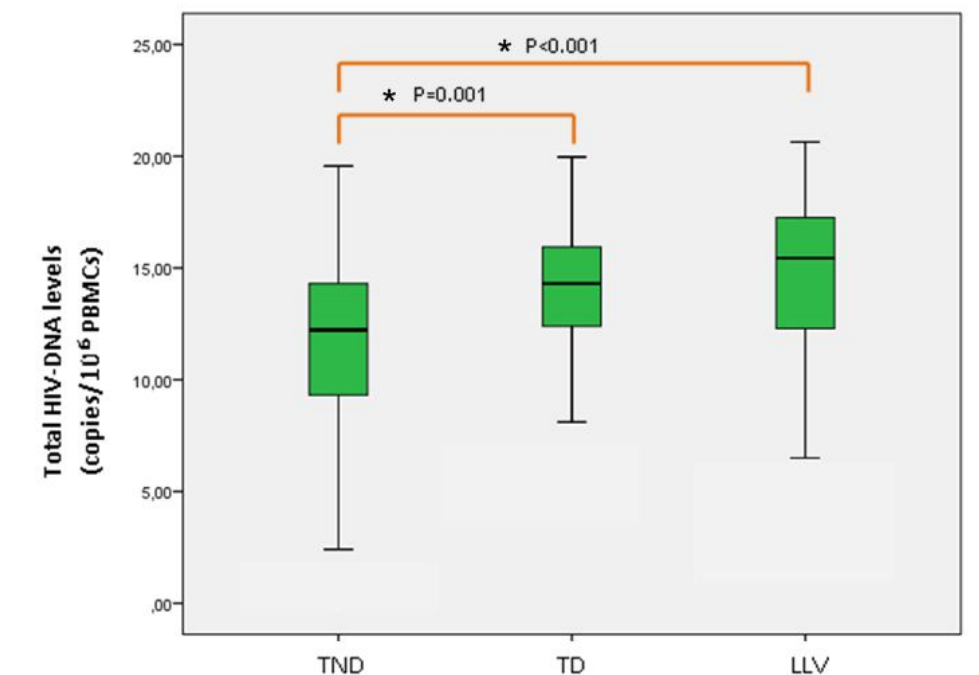


Figura 3

Conclusions. A VL of 37-200 copies/mL was associated with virological rebound; RV and LLV were associated with an increased risk of virological failure. Patients with RV and LLV showed higher levels sCD14 markers than individuals with a persistent TND viremia. In addition, a relationship between RV and HIV-1 DNA was found.

