Evaluation of residual HIV-1 replication among individuals receiving different antiretroviral treatment regimens

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Background: Residual HIV-1 replication among individuals under antiretroviral therapy is an obstacle towards reduction of chronic HIV related micro-inflammation.

Objectives: To determine the levels of residual viral replication of HIV-1 in distinct subgroups of patients inferred by quantification of episomal HIV DNA, quantification of total HIV DNA and quantification of HIV-1 specific antibodies.

Methods: 109 patients were divided into 5 groups: first suppressive therapy with efavirenz (26), first suppressive therapy with boosted protease inhibitors (PI) (25), salvage therapy using boosted PI (27), salvage therapy with raltegravir (15) and virological failure (16). Quantification of episomal and total DNA was performed by real-time PCR. Specific antibody quantification was performed using enzyme immunoassay capture.

Results: Episomal DNA amplification was positive in 36 out of 109 patients' samples (33%) and quantification of total DNA was obtained in 94 patients' samples (86.3%). Individuals on salvage therapy using Raltegravir presented lower prevalence and lower quantitation of episomal DNA as compared to other treatment groups ($p=0.03$). There was no differences between groups in quantification of total DNA ($p=0.298$) or antibodies ($p=0.126$). The HIV-1 proviral load was higher among individuals with positive episomal DNA ($p=0.01$). There was a negative correlation between the episomal DNA quantification and *(i)* duration of treatment with undetectable viral load, *(ii)* CD4 counts, and *(iii)* CD8 counts. There was a higher prevalence of episomal DNA and a higher quantification of total DNA in virologic failure group ($p=0.009$ and 0.06 respectively). The antibody quantitation was higher among individuals on initial treatment using efavirenz compared to initial treatment with PIs ($p=0.027$).

Conclusions: Duration of treatment, CD4, CD8 counts, and raltegravir based regimens relate to decreased residual viral replication (episomal DNA). The relationship between episomal DNA and total DNA suggests replenishment of proviral reservoir with potential impact on HIV persistence. Lower antibodies levels among patients with PI based initial treatment may suggest a more effective HIV suppression of these regimens, with higher capacity of decreasing the HIV antigenic component.