



Prognostic value of peripheral blood mononuclear cell-associated HIV-1 DNA for virological outcome in asymptomatic HIV-1 chronic infection

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ABSTRACT

Background: Studies in primary HIV-1 infection and advanced HIV-1 disease have demonstrated that HIV-1 DNA associated with peripheral blood mononuclear cells (PBMC HIV-1 DNA) has predictive value for disease progression.

Objectives: To analyse in asymptomatic HIV-1 chronic infection the predictive value of PBMC HIV-1 DNA for virological failure.

Study design: In 115 individuals who had previously participated in study STIR-2102, we retrospectively analysed the PBMC HIV-1 DNA by quantitative real-time PCR. Antiretroviral naïve patients (baseline pre-ART) received 6 weeks of ART prior to randomisation (baseline post-ART). The predictive value of PBMC HIV-1 DNA, HIV-1 RNA in plasma and CD4⁺ T cells, at baselines pre-ART and post-ART, was determined by Kaplan–Meier and Proportional Hazards Regression analyses.

Results: At baseline post-ART, 82% of patients showed suppression of HIV-1 RNA, however they maintained significant amounts of HIV-1 DNA (geometric mean: 690 copies/10⁶ PBMC). Pre-ART and post-ART levels of HIV-1 DNA and pre-ART levels of HIV-1 RNA showed predictive value (Log-Rank test: $p < 0.001$, $p < 0.001$, $p = 0.003$, respectively). In a multivariate model post-ART PBMC HIV-1 DNA was the stronger predictive variable (adjusted HR, 2.51 [95% CI, 1.33–4.73, $p = 0.004$]) independently of HIV-1 RNA (HR 1.74 [95% CI, 1.16–2.61, $p = 0.007$]).

Conclusions: PBMC HIV-1 DNA is an effective prognostic marker for virological outcome in individuals with asymptomatic HIV-1 chronic infection.

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1. Background

Integration of HIV-1 DNA into host cell genomic DNA ensures viral persistence as a latent reservoir despite prolonged antiretroviral therapy (ART).^{1–9} The persistence of HIV-1 DNA in the cellular reservoir is one of the current challenges with regard to the control of the progression of HIV-1 infection.^{10–13}

CD4⁺ T cell counts (CD4) and plasma HIV-1 RNA levels are the surrogate standards for HIV-1 disease progression.^{14–20} However,

cell-associated HIV-1 DNA is a marker associated with the viral reservoir and with the spread of the virus.

Studies in patients with primary HIV-1 infection and with advanced HIV-1 chronic infection, either naïve or experienced for ART, have shown that early levels of HIV-1 DNA in PBMC and in CD4⁺ T cells have predictive value for long-term virologic outcome and for disease progression.^{21–33} However, there is scarce information on the prognostic value of PBMC-associated HIV-1 DNA for predicting the virological outcome of asymptomatic patients with HIV-1 chronic infection who starts ART.

2. Objectives

To evaluate in 115 antiretroviral naïve patients with asymptomatic HIV-1 chronic infection, who had previously participated in STIR-2102 trial,^{34,35} whether or not the levels of PBMC-associated HIV-1 DNA could have prognostic value beyond the current surrogate standards for the long-term virologic outcome.

Abbreviations: ART, antiretroviral therapy; PBMC, peripheral blood mononuclear cells; PCR, polymerase chain reaction; CD4, CD4⁺ T cell counts.

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