Online-Only Abstract

The lowest X4 Geno2Pheno false-positive rate is associated with greater CD4 depletion in HIV-1 infected patients

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Abstract

Through this study we evaluated whether the HIV-1 tropism determined by genotypic analysis correlates with HIV-1 markers, such as CD4 cell count and plasma HIV-RNA. The analysis was performed on 1221 HIV-1 B-subtype infected patients with an available V3 sequence (all maraviroc naive). Of them, 532 were antiretroviral therapy (ART) naive and 689 ART experienced. Tropism determination was performed by using the geno2pheno (co-receptor) algorithm set at a false-positive rate (FPR) of 10% and 2%. Potential associations of FPR with CD4 cell count and viraemia were evaluated. Association of V3 mutations with genotypic-determined tropism was also evaluated according to different FPR ranges. About 26% of patients (either ART naive or ART experienced) were infected by X4-tropic viruses (using the classical 10% FPR cut-off). However, a significantly lower proportion of ART-naive patients had FPR ≤ 2% in comparison with ART-experienced patients (4.9% vs. 12.6%, respectively, p <0.001). The risk of advanced HIV-1 infection (with CD4 cell count ≤ 200 cells/mm^3) was significantly greater in X4-infected patients, either ART-naive (OR (95% CI)), 4.2 (1.8–9.2); p 0.0006) or ART-experienced (2.3 (1.4–3.6); p 0.0003), with FPR set at 2% (but not at 10%). This finding was confirmed by multivariable logistic analysis. No relationship was found between viraemia and FPR ≤2%. Some X4-related mutations were significantly associated with FPR ≤2% (ART-naive patients, S11R, Y21V, G24K and G24R, p ≤0.001; ART-experienced patients, Y7K, S11R, H13Y, p ≤0.002). In conclusion, these findings show that within the context of genotypically-assessed CXCR4 tropism, FPR ≤2% defines (far better than 10%-FPR) a viral population associated with low CD4 rank, with potentially greater cytopathic effect, and with more advanced disease.