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Influence of gender in predicting CCR5 coreceptor usage

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Purpose of the study

Factors associated with CCR5 coreceptor usage are not yet extensively evaluated; in some studies high CD4 and low viremia have been considered predictive [1,2]. We evaluated factors predicting the viral tropism in failing patients with long exposure to HIV, screened for Maraviroc Expanded Access Program (A4001050) at San Raffaele Hospital.

Methods

Viral tropism was determined in 98/116 (84%) (Viro-Logic PhenoSense assay). Viral tropism was classified as R5, D/M or X4 for virus that used CCR5 coreceptor, CCR5 and CXCR4 coreceptors or CXCR4 coreceptor, respectively. Variables evaluated for the association with the R5 virus (outcome variable) were: age, gender, CDC stage (C vs. A and B), screening CD4 percentage, CD4+ cells, HIV-1 plasma RNA level, nadir CD4+, risk factor (IVDU vs. other), time since HIV infection. All these characteristics were considered at univariable and multivariable analysis. Logistic regression was applied at multivariable analysis. Data were described as median (Q1–Q3) or frequency (%), as appropriate.

Summary of results

56 (57.1%) patients had R5 virus, 40 (40.1%) had D/M virus, two (4.1%) had X4 virus; only R5 and D/M groups were considered for this analysis; 82 (85.4%) were males, age 45.7 (42.6–50.8) years; 15 (19.5%) were IVDU, HIV exposure 15.8 (12.7–18.7) years, 41 (43%) had a C CDC stage. Screening characteristics were: CD4 240 cells/cmm

(133–364); CD4% 12.7(8.6–19.2); HIV-RNAlog10 copies/mL 4.31(3.82–4.94).

Female were more likely to have D/M virus [10/14 (71%) vs. 30/82 (37%); p = 0.0195]. The D/M group had a significantly lower screening CD4+ cells percentage than R5 group (11.0% (7.3–17.8) vs. 15.3% (9.4–20.6); p = 0.055). No other differences on the screening characteristics were found in relation to coreceptor usage (age: p = 0.296; HIV-1 plasma RNA level: p = 0.855; nadir CD4+: p = 0.070; CD4+: p = 0.079; CDC stage: p = 0.202; risk factor of HIV transmission: p = 0.574, HIV exposure: p = 0.907). Among the screening characteristics up-reported, multivariable analysis showed that females rather than males [OR = 0.124 95% CI: 0.021–0.558; p = 0.011] and patients with CD4% <12.85 (median value) [OR = 0.275 95%CI: 0.077–0.875; p = 0.035] were less likely to harbour R5 virus.

Conclusion

Our study underlines the possibility for gender to influence not only the initial viral set-point as previously shown [3], but also the probability of harbouring R5 viruses.

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