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Does HIV-1 tropism change in patients during virological suppressive therapy?

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Background

Drug toxicities are limiting factors for the lifelong therapy of HIV infection. The CCR5 receptor antagonist maraviroc showed no long-term toxicities so far. Thus switching from a virologically successful but not well tolerated regimen to maraviroc might be an future option. However, testing of viral tropism is mandatory before the use; tests require a plasma viral load >500 c/ml. In the majority of patients (pts) in larger clinical centers, plasma was frozen before starting antiretroviral therapies. These samples would be available to define viral tropism if it can be excluded that viral tropism changes during virological successful therapy.

Methods

Blood samples were obtained at a mean of 7.4 days (0–19) before starting initial ART from seven male pts, with a mean pre-treatment viral load of 36.433 copies/ml (range 1,500–133,500), and a mean CD4 count of 509/µl (356–650). PBMC and plasma were cryopreserved at -80°C. Pts received 3TC, d4T, SQV and NFV in standard dosing for mean of 92 weeks (range 72–180). A predefined STI was performed and samples were collected at a mean of 34 days (28–59) after cessation of ART at a mean viral load of 43,967 c/ml (860–145,000). HIV co-receptor tropism was determined in PBMC and plasma phenotypically using the TrofileTM assay [1]. For comparison a genotypic test was accomplished by amplifying and sequencing the V3 loop of the HIV envelope gene in pre- and post-treatment samples. For sequence analysis and prediction of HIV co-receptor usage the gen2pheno [co-receptor] software was used [2].

Summary of results

In PBMC the genotypic test detected R5 viruses before and after treatment in 7/7 pts with no change of tropism during suppressive therapy. Genotypic results from plasma revealed R5 viruses in 4/4 pre-treatment samples and in all 7/7 post-treatment samples. R5 using viruses were detected in 3/4 pre-treatment samples and 7/7 post-treatment samples by using the standard phenotypic assay. However, in one patient a duotropic D/M population was detected phenotypically in pre-treatment samples with a shift to R5 usage after ART, whereas genotyping failed to detect the duotropic population in this patient.

Conclusion

The genotypic test in PBMC and plasma showed no changes of tropism during virological successful therapy in our patients. No shift from R5 to X4 usage was detected during suppressive therapy by standard phenotype testing which remains the gold standard at the moment. Thus historical samples might be used to screen selected aviremic patients for a switch to maraviroc.

References

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