HIV co-receptor tropism prediction remains stable over time in treatment naive patients

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INTRODUCTION

HIV co-receptor tropism must be established before the initiation of treatment with CCR5 receptor antagonists such as Maraviroc. Tropism largely results from to the hypervariable V3 loop of the gp120 HIV molecule, as this is the specific section that binds the CD4 cells’ co-receptor. Consequently, determining the amino acid sequence of this region can be used to predict co-receptor usage (Beerenwinkel 2003, Jensen 2003, Low 2008), and this forms the basis of genotypic tropism assessment of HIV-1. HIV-1 co-receptor tropism can be grouped as CCR5 (R5), CXCR4 (X4), dual-tropic or dual mixed (D/M, containing both X4 and R5-tropic viruses).

Current UK guidelines suggest genotypic tropism predictions can be considered valid for up to 90% of CCR5 antagonist eligible patients (X4), dual-tropic or dual mixed (D/M, containing both X4 and R5-tropic viruses).

RESULTS

Co-receptor tropism was assessed in 19 ART-naive patients with ongoing viral replication. We retrospectively genotyped samples taken between the baseline, first clinic visit, and final sample before the start of ART, median 53 months (range 33-80 months). Each patient had samples at approximately yearly intervals.

METHODS

We selectively amplified the V3 loop region of the HIV-1 envelope and performed population sequencing of amplicons. Triplicate testing was performed to increase sensitivity of detection of minority X4 variant quasispecies and the Geno2Pheno system used to predict co-receptor tropism. Samples with clonal false positive rates <6% were deemed X4 tropic.

Both clonal and clinical predictions were made. Clonal predictions made upon the genotype V3 sequence alone. Clinical predictions combined the genotypic sequence with clinical data – viral load (VL); Nadir CD4 and Nadir % CD4.

Any samples with false positive rates <6%, in any of the triplicate amplifications, were deemed X4 tropic. This is in line with current clinical practice.

CONCLUSIONS

Co-receptor tropism in treatment naive patients with ongoing viral replication appears to show a high level of stability over time. Including the specific components that determine co-receptor tropism.

100% of CCR5 antagonist eligible patients remained so at 22 months after initial genotyping. Our data suggest that baseline genotypic tropism prediction may be valid for a significant duration in patients delaying the start of anti-retroviral therapy.

This has significant clinical and financial implications, particularly following withdrawal of commercial funding to cover the cost of a tropism test.

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LITERATURE CITED

