



## No Evidence of Primary Resistance to T-20 in Treatment-Naive Patients Infected with Non-B HIV-1 Isolates

F Roman<sup>1</sup>, D Gonzalez<sup>2</sup>, R Boulme<sup>2</sup>, A Fischer<sup>1</sup>, T Baurith<sup>1</sup>, V Arendt<sup>1</sup>, F Schneider<sup>1</sup>, R Hemmer<sup>1</sup> and JC Schmit<sup>1</sup>

1 Retrovirology Laboratory, CRP-Santé, Luxembourg and 2 Advanced Biological Laboratories, Biomedical Information Unit, Luxembourg

**BACKGROUND :** T-20 is a lead compound of a new class of antiretroviral drugs called fusion inhibitors. Resistance-associated mutations to T-20 have been described in vitro: G36S and V38M, and other combinations of the tripeptide motif involving residues 36, 37 and 38 located in the heptad repeat 1 domain of gp41. Other mutations (V38A, Q39H, Q40H and N43D) were identified in HIV-1 isolates from patients participating in T-20 clinical trials. Although primary resistance to T-20 is a rare event in Caucasian patients, little is known on the distribution of these mutations in non-B HIV-1 isolates.

**METHODS :** plasma samples of 45 patients infected with non-B HIV-1 were collected before any antiretroviral treatment. The patients were infected with clade A (N=5), C (N=9), D (N=5), F1 (N=9), G (N=7), H (N=1), CRF01 (N=4), CRF02 (N=2), and complex (cx) recombinant viruses (N=3). After RNA extraction, 550 bp fragments from gp41 were amplified by RT-PCR and sequenced on an automated ABIPrism3100. All sequences were aligned with HXB2 and screened for amino acid changes at positions 36 to 40 and 43.

**RESULTS :** of the 45 patients, none had amino acid substitutions at the T-20 resistance related residues. However, synonymous mutations were detected at codons 36, 39 and 43: 10 of the 45 (22%) isolates exhibited a GGT to GGC substitution at codon 36 (G=4, A=3, C=1, F1=1 and cx=1); 8 of the 9 (89%) F1 isolates had a GGT to GGA change. A CAG to CAA change at codon 39 was detected in the majority of these non-B isolates (N=43). An AAT to AAC mutation at codon 43 was identified in one CRF02 isolate. No silent mutations were identified at codons 37, 38 and 40.

**CONCLUSIONS :** although silent mutations were present, no amino acid substitutions at critical residues for T-20 resistance have been identified in our study. These results suggest that primary resistance to T-20 is rare among patients infected with non-B HIV-1 isolates.

## Abstracts