



## New Mutations at Residue Positions Critical for T-20 Resistance in T-20 Naïve Patients Infected with Clade B HIV-1 Isolates

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**BACKGROUND:** T-20 is a lead compound of the new class of antiretroviral drugs called fusion inhibitors. Resistance-associated mutations to T-20 located in the heptad repeat 1 (HR-1) domain of gp41 have been described in vitro or in clinical trials: G36S, V38M, V38A, Q39H, Q40H, N43D and other combinations of the tripeptide motif involving residues 36, 37 and 38. We determined the prevalence of these mutations in B and non-B HIV-1 viruses of T-20 naïve individuals at the beginning of their follow-up in the Luxembourg HIV cohort. For B isolates, we also studied the polymorphism of the HR-1 domain in the course of HIV-1 infection.

**METHODS:** plasma samples of patients infected with B (N=48) and non-B (N=48) isolates were collected at the beginning of their follow-up in the cohort. After RNA extraction, 550 bp fragments from gp41 were amplified by RT-PCR and directly sequenced on an automated ABIPrism 3100. Available sequences were aligned with HXB2 and screened for amino acid changes at positions 36 to 40 and 43. A similar analysis was performed for all B isolates, after an average duration of infection of 5.8 years (range, 3-8.9 years).

**RESULTS :** sequences were obtained for 43 non-B isolates and 42 B isolates at the beginning of the follow-up, and for 42 B isolates at the time of the second analysis. None of the non-B sequences had amino acid substitutions at the T-20 resistance-related residues. In contrast, 3 B isolates (6.2%) exhibited substitutions at residues 37 or 39. A Q39R mutation was present in 2 isolates before initiation of antiretroviral treatment and at the time of the second analysis. An I37V mutation appeared in another isolate after 4.8 years of HIV-1 infection and 3.6 years of antiretroviral treatment.

**CONCLUSIONS :** no classical resistance-associated mutations to T-20 were identified in B or non-B isolates in our study. However, we identified 2 new mutations in B isolates in a region critical for T-20 activity: I37V and Q39R. The impact of these mutations on T-20 sensitivity has not been determined in vitro. These findings emphasize the need to develop phenotypic resistance testing for fusion inhibitors.

## Abstracts