

POSTER 70

INTEGRASE GENOTYPIC DIVERSITY IN HIV-1 INFECTED PATIENTS NAÏVE TO INTEGRASE INHIBITOR THERAPY

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Objective: Antiretroviral therapies (ART) that target HIV-1 reverse transcriptase (RT) may potentially select mutations in the integrase gene (IN) due to functional interactions between the two viral enzymes.

Methods: Genotypic and statistical analyses (Fisher's Exact test) were performed on HIV-1 RT sequences from 200 antiretroviral treatment-naïve and 248 NRTI and/or NNRTI treatment-experienced patients with a majority of subtype B HIV-1. The analysis focused on amino acids (AA) 1-240 of RT and the entire IN gene (AA 1-288). Statistical significance was determined as a p-value ≤ 0.010 with $\geq 95\%$ conservation in the treatment-naïve group or 100% conservation in the treatment-experienced group.

Results: As expected, the RT domain had statistically significant differences between the groups at 36 AA positions, including many that are known resistance sites. Within IN, D25, K156 and A205 had statistically significant changes between the groups (p-values = 0.009, 0.002 and 0.007 respectively); none are associated with resistance to existing INIs. Only one AA substitution was observed at IN residue D25; D25E occurred in 3.5% of treatment-naïve patients and 10.1% of treatment-experienced. Similarly, for IN residue K156, only one AA substitution was observed; K156N occurred in 5% of treatment-naïve patients and 13.7% of treatment-experienced. For IN residue A205, multiple AA substitutions were observed in 5% of treatment-naïve patients and 0.8% of treatment-experienced patients. Of the treatment-naïve patients with a substitution at residue A205 (n=10), 5 had A205S, 4 had A205P, and 1 had A205T, while the treatment-experienced showed one each of A205S and A205P. In the 25 treatment-naïve patients with IN substitutions, 2 (8%) had both K156N and A205A/P, while in the 55 treatment-experienced patients with IN substitutions, 6 (11%) patients had both D25E and K156N.

Conclusions: Currently available ART that targets RT of HIV-1 was found to be associated with enrichment of mutations in IN at positions D25 of the N-terminal zinc finger domain and K156 and A205 of the central catalytic core domain. However, none of these three AA residues correlate with sites of known primary or secondary INI resistance. Future studies are needed to determine if these mutations affect IN function or influence susceptibility to current INIs.