HIV-1 genetic diversity and naturally occurring polymorphisms in HIV-1 Kenyan isolates Integrase gene: Implications for integrase inhibitors.

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Background: Little is known about the extent and predictors of polymorphisms potentially influencing the susceptibility to HIV integrase inhibitors (INs).

Objectives: To determine the extent of drug resistance mutations in HIV-1 positive antiretroviral naive and those on treatment prior to Intergrase inhibitors intervention.

Methods: HIV-1 positive plasma samples were collected from forty nine (49) subjects: (30) drug naive and (19) treated with ARV, within Nairobi cohort (18 males and 35 females) consenting patients between April and December 2009. The viral RNA from plasma samples were extracted using Qiagen® RNA isolation kit and intergrase (IN) gene was amplified by nested PCR. The amplified products were analysed by gel electrophoresis and visualized under UV light. The successfully amplified products were then labeled with a sequence dye in sequence PCR reaction using the Big Dye® sequence terminator kit (Applied Biosystem®) and the products purified by use of Qiagen purification kit before directly sequenced using an automated ABI 310 sequencer (Applied Biosystem, Foster City CA). In the IN gene (288bp) of the virus was sequenced.

Results: From the partial pol-intergrase sequences the phylogenetic analysis revealed: A1 (38.8%), D (20.4%), A (2%), C (18.4%), AICD (2%), A2D (2%), BG (2%), 02_AG (4%) and URF (6%). The higher levels of unique and circulating recombinant forms detected suggested a possible viral mixing within Nairobi populations. Two (2) % of the study subjects were detected with integrase mutation at position T97A that is associated with reduced susceptibility. This occurred in patients infected with predominant HIV-1 subtype A1. Therefore, drug reduced susceptibility prevalence of 2% prevalence against raltegravir was detected. In addition, 22.4% of the study subjects were found to harbour viral strains with other mutations that are not associated with any intergrase drug resistance. This suggested a possible evolution of the virus due immune and other class of antiretroviral pressure. This study showed that the new class of intergrase inhibitors was eligible to be used in among the rest of cocktail of HAART in treatment of HIV cases.