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Drug Resistance Mutations in Treatment-Naïve HIV-Infected Patients 2000-2013

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Introduction

- Cases of transmission of HIV-1 containing drug resistance-associated mutations (RAMs) in protease (PR) and reverse transcriptase (RT) have been documented, with up to 9% of antiretroviral (ARV) treatment-naïve HIV-1 infected individuals harboring HIV-1 containing PR/RT RAMs[1]
- The presence of such pre-existing PR/RT RAMs in ARV treatment-naïve individuals can impact the effectiveness of ARV therapy
- PR/RT drug resistance testing prior to ARV treatment initiation is now included in the standard of care for HIV-1 treatment
- Data on transmitted drug resistance (TDR) for integrase (IN) strand transfer inhibitors (INSTIs) such as raltegravir (RAL), elvitegravir (EVG), and dolutegravir (DTG) are limited
- Results of a retrospective genotypic analysis (IN, PR, and RT) of ARV treatment-naïve subjects in phase 3 clinical studies over a 13-year period are reported here

Methodology

- Plasma samples from 4 Phase 3 studies (GS-99-903 (903), GS-01-934 (934), GS-US-292-0104 (104), and GS-US-292-0111 (111)) in ARV treatment-naïve HIV-1 infected patients were collected at screening before any drug treatment
- HIV-1 extracted from plasma was sequenced at the IN, RT and PR segments of HIV-1 *pol* by population sequencing and compared to the HIV-1 reference sequence NL4-3 (Monogram Biosciences; Gilead Sciences)
- Characteristics such as presence of RAMs, HIV-1 subtype, and enrollment year were analyzed
- The number of amino acid changes from reference was also tabulated and compared across the studies, and statistical analyses were performed (Fisher's exact test, Chi-square test, Mann-Whitney test)
- Mixtures of mutant/wild-type amino acids were treated as a full mutations unless otherwise noted

Results

Figure 1. Resistance-Associated Mutations by Drug Class

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