

**POSTER 52****PRE-EXISTING LOW-LEVELS OF THE K103N HIV-1 RT MUTATION IS A RISK FACTOR FOR TREATMENT-NAÏVE PATIENTS FAILING A 3TC+ZDV+EFV REGIMEN**

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**Background:** Study GS-01-934 was a randomized phase III study comparing FTC+TDF+EFV to 3TC+ZDV+EFV in treatment-naïve HIV-1 infected patients. Patients with detectable NNRTI-resistance at baseline by standard population sequencing were excluded from the primary analysis. Following 144 weeks of therapy, virological failure (VF) was observed in 50/487 patients (FTC+TDF+EFV, n=19; 3TC+ZDV+EFV, n=31). The most common mutations developing were K103N (FTC+TDF+EFV, 8/19; 3TC+ZDV+EFV, 17/29) followed by M184V/I (FTC+TDF+EFV, 2/19; 3TC+ZDV+EFV, 10/29). In this study, a correlation between pre-existing low-levels of the K103N and M184V/I RT mutations at baseline and VF was investigated.

**Methods:** A MultiCode-RTx real-time PCR platform (EraGen Biosciences, Madison, WI) that utilizes allele-specific PCR primers for K103N (AAC and AAT codons) and M184V/I detection was developed with cut-offs of mutant detection of 0.5%. Baseline plasma samples from patients with VF (n=48) were tested for low-level K103N and M184V/I starting from RT-PCR products. In addition, a subset of non-VF subjects (n=66) with similar distributions of age, CD4 counts, and viral load as the VF patients was selected and samples from these subjects were also tested for low-level K103N at baseline.

**Results:** Among treatment-naïve patients who failed therapy by week 144 (n=48), no M184V/I mutations were detected at baseline whereas low-level K103N was detected in a total of seven patients (3TC+ZDV+EFV, 6/29; FTC+TDF+EFV, 1/19). The level of K103N ranged from 0.8% to 19.3% in these samples and was not detected by standard population sequencing. To establish a correlation between the pre-existing low-levels of K103N and VF, we also assessed the prevalence of K103N among a subset of patients who did not fail therapy by week 144. In this subset of patients, only two patients had detectable K103N (3TC+ZDV+EFV, 0/38; FTC+TDF+EFV, 2/28). Statistical analysis showed a strong correlation between the pre-existing low-levels of K103N and VF in the 3TC+ZDV+EFV treated group (p=0.005, Fisher's Exact test), but not in the FTC+TDF+EFV treated group (p=1.00).

**Conclusions:** The results of this study suggest that pre-existing low-levels of the K103N HIV-1 RT mutation correlated with treatment-naïve patients failing a 3TC+ZDV+EFV combination regimen. In this preliminary analysis, no such correlation was observed for FTC+TDF+EFV combination therapy.