

**POSTER 59****NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR (NRTI)-ASSOCIATED MUTATIONS IN THE RNASE H REGION IN SOUTH AFRICAN ADULTS AND CHILDREN FAILING HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART)**

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**Background:** The South African national treatment program includes NRTIs in both first and second line regimens. Recently, mutations in the RNase H domain have also been associated with resistance to NRTIs. However, very little data is available for RNase H and HIV-1 subtype C. Therefore, it is important to gather information on the prevalence and impact of RNase H mutations on NRTI resistance in HIV-1 subtype C.

**Methods:** *Pol* and RNase H domain (RT codons 439 to 560) sequences of 58 NRTI treated viral isolates and 10 ART-naïve viral isolates from South African HIV positive adults (51) and children (7) were generated and analyzed. In addition, sequences from 48 subtype C drug-naïve isolates were downloaded from the Stanford HIV Drug Resistance Database to give a total of 58 sequences from ART-naïve individuals for the analysis. Spearman rank correlation (nonparametric correlation) was used to explore relationships between mutations occurring in the RNase H domain and NRTI mutations.

**Results:** 56/58 samples were determined as subtype C, with one subtype A and one subtype B. All sequences from ART-naïve patients were classified as subtype C. Analysis of the residues at the primer grip motif and catalytic site of RNase H showed high levels of conservation. Frequency of L469I/F {22% (13/58 isolates)} was significantly higher in treated isolates when compared to subtype C naïves 5.2% (3/58 isolates) ( $p=0.007$ ). Similarly, T470P/A/D/S was found in 36.8% of treatment-experienced isolates, while seen in 13.8% of subtype C naïves ( $p=0.005$ ) and K530R/G was also found in 82.8% of treated when compared to 56% of subtype C naïves ( $p=0.001$ ). Significant correlations between RNase H and NRTI mutations were noted: L469I with T215IY ( $p=0.05$ ) and positive correlations for several mutations were also noted. A negative correlation was seen for K530R with V118IV, L74LV and E44EK. Interestingly, six treatment experienced samples had mutations in the RNase H domain but did not have any of the classical NRTI mutations (RT domain).

**Conclusion:** These preliminary findings suggest that drug resistance can be caused by mutation in the RNase H domain either alone or in combination with mutations in the *pol* region. Mutations in the RNase H domain should be taken into consideration when assessing resistance to NRTIs.