

**POSTER 54****CHARACTERISATION OF PROTEASE CLEAVAGE SITES IN PROTEASE INHIBITOR-NAÏVE PATIENTS INFECTED WITH HIV-1 SUBTYPE C**

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**Background and Objectives:** HIV-1 subtype C has naturally occurring polymorphisms in protease that are known to cause drug resistance in subtype B. It has been described that mutations in protease are accompanied by compensatory mutations in the protease cleavage sites (CS) in *gag*. As an increasing number of South African patients start their second-line (PI-inclusive) regimen, it is important that analysis be undertaken on subtype C protease sequences, *gag* protease CS and non-CS prior to initiating PI therapy as these mutations may affect drug efficacy.

**Methods:** The *gag* and *pol* genes (incorporating 8 of the CS) were sequenced in 25 HIV subtype C infected PI-naïve patients. These patients had failed their first line therapy (3TC, D4T and NVP or EFV) and were about to switch to second line therapy (AZT, DDI and LPV boosted with RTV). Sequences were aligned using ClustalW and manually edited with the Genetic Data Environment (GDE). Nucleotide and amino acid diversity at the CS was measured using Mega version 4.0.

**Results:** No major PI resistance mutations were seen. Three accessory mutations present were: T74S (8%), L10F (4%) and K20R (4%). 60% of the subtype C PI-naïve viruses exhibited resistance associated mutations at the CS p2/NC (G381S/N), while 4% exhibited the p1p6<sup>gag</sup> mutation L449I. Resistance associated mutations at non-CS were: V390I/A (24%), K436R (20%), H219Q/P (16%), I437V/L (12%), E468G (8%) and P453T (4%). Of the CS analysed, 4 were classified as conserved (variability at <5.0%) [p17/p24, p24/p2, p1/p6<sup>gag</sup>, NC/TFP], 3 as moderately variable [NC/p1, TFP/p6<sup>pol</sup> p6<sup>pol</sup>/PR] (>5.0%<10%), with the most variable being p2p7(25%). When we extended the analyses to 10aa upstream and downstream of the CS, we found an increase in variability in p17/p24, p1/p6<sup>gag</sup> and NC/TFP. Repeat of the PTAP motif in p6<sup>gag</sup> occurred in 44% of the isolates.

**Conclusion:** No major or minor resistance associated mutations were seen in PR. However, many accessory resistance associated mutations were found in *gag*. The effect of the mutations and the PTAP repeats on PI therapy in HIV-1 subtype C infection needs to be further investigated.

**Acknowledgements:**

NRF Grant Holders Scholarship  
HIV Pathogenesis Programme (HPP)