Characterization of HIV-1 Drug Resistance mutations from plasma and peripheral blood mononuclear cells in patients failing antiretroviral treatment in Bela- Bela, South Africa

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Submitted By

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Abstract

BACKGROUND: The current expansion of antiretroviral treatment (ART) in developing countries, such as South Africa, which lacks routine virological monitoring raises concerns on the outcome of the strategy in terms of virological success and the drug resistant burden. With an estimated 3.7% of the patients failing first-line treatment after 2 years and 17.9% after 4 years on treatment, there is qualified need for practical and routine drug resistance testing to provide data to clinicians in order to improve the lives of these patients. Thus, this study was conducted to characterize and compare HIV-1 drug resistance mutations in peripheral blood mononuclear cells (PBMCs) and in the plasma of patients whose therapeutic regimen is failing.

METHOD: The study was nested within the Bela-Bela Wellness clinic, Limpopo Province South Africa. Approval for the study was obtained from the Health, Safety and Research Ethics Committee of the University of Venda. Blood specimens were collected from 23 HIV-infected drug experienced, individuals between July 2013 and October 2014 who met the following criteria: (1) two consecutive viral loads on treatment greater than 1000 copies/ml after previous suppression; (2) one viral load greater than 1000 copies/ml after previous suppression followed by a change in treatment; and (3) one viral load greater than 1000 copies/ml after 180 days on ART without suppression. The protease (PR) and reverse transcriptase (RT) genes of the 23 treatment exposed HIV infected patients failing therapy were PCR amplified, sequenced, subtyped and analysed for the presence of drug resistance mutations.

RESULTS: Twenty one (91%), out of 23 specimens were successfully amplified. Comparison of the amino acid sequence of the PR and RT genes in the cell-associated variants of HIV-1 with that of plasma revealed that 17(81%), out of the 21 specimens tested, exhibited major drug resistance both in PBMCs and plasma. However, the greatest number of mutations were found

in plasma (D67N, K103N, V106M, Y181C and M184V) occurred most frequently. On the other hand, V106M, K103N and M184V were observed most often in PBMCs. The prevalence of predicted resistance mutations in our study corresponding to respective ART usage were thus: NRTI, (n=11), NNRTI, (n=13) and PI, (n=4). The most common mutations for RT were M184V>K103N>V106M>D67N. It is noteworthy that M230I an NNRTI was found in PBMCs only. Major mutations for PR were M46I> D30N>V82A. Seventeen of the 21 viruses (81%) were HIV-1 subtype C in the polymerase gene; one virus was subtype B (4.8%) and one was a C/B recombinant (4.8%). One virus (4.8%) could not be conclusively typed.

In conclusion, this study firstly, confirmed previous findings that the cellular compartment of blood may contain an archive of drug resistant variants making an interesting compartment for analysing the evolution of drug resistance in a given patient. Secondly, the prevalence of drug resistance mutations observed in Bela-Bela drug experienced individuals is very fairly high; and finally, there appears to be a continual presence of recombinant viruses circulating in the study region.

Key words: Virologic failure; Highly active antiretroviral therapy; Drug resistance; Peripheral blood mononuclear cell; Plasma; Bela-Bela; South Africa.