Drugs for treatment and prevention, and other novel therapies

PO - (8411) - MOLECULAR CHARACTERIZATION OF GP41 AND GP120 V3 LOOP IN HIV 1C PATIENTS FAILING SALVAGE THERAPY IN BOTSWANA

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Background: Triple class drug resistant HIV-1 infection remains a global challenge in individuals with extensive antiretroviral treatment (ART) experience, in terms of high mortality and probability of onward transmission. New therapeutic options within old drug and new drug classes are therefore essential. We determined if patients failing salvage therapy in Botswana are eligible for Maraviroc(MVC) and Enfuvirtide(T20) viral entry inhibitors based on the coreceptor usage and drug resistant mutations in envelope gp120 and gp41.

Methods: A total of 38 deep salvage patients were included in the analysis. We amplified and sequenced gp41 and V3 regions of HIV-1 envelope. Drug resistance mutations were analyzed according to the IAS-USA 2017 reference mutation lists. Coreceptor usage was determined using PSSM and Geno2Pheno using a false positive rate (FPR) of 10%.

Results: Among 38 participants, 34(89%) were successfully sequenced and amplified gp41 and 26(68%) gp120 V3 loop sequences were obtained. Major T20 mutation G36S was obtained in 1/34 samples (5.8%) within the study population. Polymorphisms I169V(97%), I135L(100%), E151A(70.6%) and N42S(70.6%)were detected in HR1 and HR2 of gp41. CXCR4 coreceptor associated use, mutation L34M in gp41 HR1 was detected in 2 samples (5%). Analysis of coreceptor usage showed (17/26) 65.4% use of CCR5, and a (9/26) 34.6% use of the CXCR4 coreceptor.

Conclusions: A moderately high proportion of treatment experienced (deep salvage) participants had CXCR4 coreceptor using strains. The use of maraviroc in Botswana would require coreceptor tropism testing. Non T20 treatment experience in Botswana reduces the prevalence of the major mutations that confer resistance to the drug. T20 is therefore a potential alternative drug for patients failing salvage therapy in Botswana.