

Baseline drug-resistant HIV-1 in adults initiating first-line HAART at an urban private clinic in South Africa

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Background: Widespread dissemination of drug-resistant HIV-1 (HIVDR), either acquired during previous use of antiretroviral (ARV) drugs or through drug-resistant infection, has the serious potential to compromise the response to antiretroviral therapy (HAART). Data in the context of the rapid treatment scale-up in resource-limited countries is limited. The aim of this analysis was to assess baseline HIVDR among adults initiating first-line HAART at an urban private clinic in Pretoria, South Africa.

Materials & Methods: A cross-sectional analysis within the PASER Monitoring Cohort. Study participants were HIV-1 infected adults who were eligible to initiate first-line HAART; they were either "ARV-naive" or "ARV-experienced", defined as a history of any ARV use (for prophylaxis and/or treatment) more than 1 month prior to HAART initiation. Population-based nucleotide sequence analysis of the HIV-1 *pol* gene was performed on plasma (in-house assay). Sequences were analyzed through Stanford hivdb website, using the International AIDS Society (IAS)–USA 2007 major mutation list. HIV-1 subtypes were assessed using the REGA HIV-1 subtyping tool (v2.0).

Results: Between May 2007 through July 2008, 207 participants were enrolled, of whom 114 (55%) were females. Mean age was 38.0 (SD±8.7) years. 121 (60%) of participants had WHO clinical stage III/IV disease. A total of 182 (88%) participants were ARV-naive. Of the 25 (12%) ARV-experienced participants 22 (88%) were females; their ARV history included HAART (n=9), combination therapy for prevention of mother-to-child transmission of HIV-1 (pMTCT) (n=13), but no single-dose NVP for pMTCT. Median CD4 cell count was 142 cells/mm³ (interquartile range (IQR), 51-233) and 209 cells/mm³ (IQR, 134-284) in ARV-naive and ARV-experienced participants, respectively (p=0.2418). Mean HIV-1 load (±SD) was 5.0 (0.9) and 4.6 (0.8) log₁₀ copies/ml in ARV-naive and ARV-experienced participants, respectively (p=0.1875). HIV-1 sequence results were available for n=126. All participants but 1 (subtype A1) had HIV-1 subtype C. Overall, the frequency of any major HIVDR mutations was 5/126=4.0% (95% confidence interval (CI), 1.3-9.0), and 0.8% (0.02-4.3) for NRTI, 3.2% (0.9-7.9) for NNRTI, and 0% (0.0-2.9) for PI. In ARV-naive participants HIVDR frequency was 1/110=0.9% (CI, 0.02-4.9), and in ARV-experienced 4/16=25% (CI, 7.3-52.4) (p<0.0001). Observed mutations were: A62V (1), K65R (1), D67N (1), K70R (1), V75I (1), M184V (1), K219E (1), K103N (4), V106M (1). No multiclass resistance was observed. Of the 5 participants with ≥1 major HIVDR mutation, 4 had previously used ARVs. Of note, 1 participant harbored A62V, K65R, D67N, K70R, V75I, M184V and K219E, following exposure to ZDV and 3TC for pMTCT in 2006, and 1 ARV-naive participant harbored K103N, either due to HIVDR transmission or undisclosed previous ARV use.

Conclusions: Baseline HIVDR in an urban private clinic in South Africa was low (0.9%), indicating that for ARV-naive patients the standard NNRTI-based first-line drug regimen seems to be effective. By contrast, considerable HIVDR (25%) was observed in persons who were previously exposed to HAART or pMTCT, suggesting that HIVDR surveillance is particularly important in this patient group. Coordinated surveillance studies are warranted to confirm these preliminary findings and to better guide selection of optimal regimens in resource-limited settings.