Journal of the International AIDS Society

Poster presentation

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Patterns of drug resistance mutations after failure of first-line NNRTI-based antiretroviral therapy in Western India

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from Ninth International Congress on Drug Therapy in HIV Infection
Glasgow, UK. 9–13 November 2008

Published: 10 November 2008

Journal of the International AIDS Society 2008, **11**(Suppl 1):P193 doi:10.1186/1758-2652-11-S1-P193

This abstract is available from: http://www.jiasociety.org/content/11/S1/P193

Background

There is limited information on the pattern of drug resistance mutations (DRMs) after failure of NNRTI-based first-line ART in India (subtype C viruses). We assessed the prevalence of DRMs after first-line failure and explored risk factors associated with development of thymidine analog mutations (TAMs).

Methods

Patients with confirmed first-line therapy failure (d4T or ZDV/3TC/NVP or EFV) as defined virologic (VF), immunologic (IF) and clinical (CF) (according to WHO ARV scale-up guidelines), were eligible. Genotypic drug resistance testing (GRT) was done by viral RNA extraction, RT-PCR and in-house sequencing and interpretation done according to the Stanford database. The frequency of DRMs (NNRTI mutations-K103N, V106M, Y181C, G190A and others, 3TC-M184V/I and TAMs: 41, 210, 215 or 67, 70, 219 or no specific pathway) were determined. Univariate analysis were used to determine the risk of development of >3 TAMs according to age, gender, type of failure, duration on regimen, duration of HIV infection, exposure to suboptimal regimens, CD4 counts and PVL at time of GRT.

Summary of results

Data from 89 patients (80.6% male) with median age 38 years were available. Median duration on ART at the time of GRT was 43.5 (IQR 23–67) months, and the median PVL and CD4 count were 4.5 log copies/ml (IQR 4.1–5.3) and 168/mm3(IQR 67–289), respectively. 83% patients had PVL>4 logs. Amongst patients with failure, 42% were VF, 39.7% IF and 18.3% CF. All patients were infected with subtype c virus. 92%, 66.6% and 31.1% patients had NNRTI mutations (K103N:44.4%, Y181C:32.1%), M184V and both, respectively. At least one TAM was documented in 71.9% patients, 38.2% had >3 TAMs, with 38.2% and 35.5% following the 67/70/219 and 41/210/215 pathway. 4.4% had K65R. A last CD4 count<200/mm3 and PVL >4 log copies/ml were associated with a trend towards harbouring >3 TAMs, though they failed to achieve statistical significance.

Conclusion

Patterns of resistance mutations after failure of NNRTI-based first-line regimens amongst subtype C viruses is similar to that documented in other subtypes in literature. After failure of first-line therapy most patients have NNRTI and/or 3TC resistance. The frequency of TAMs is high and is associated with high viral loads and low CD4 counts at the time of GRT.