Decreasing Prevalence of Transmitted Drug Resistance among ART-naïve, HIV-1-infected Patients in Iceland, 1996-2012

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❖ Introduction

- HIV-1 treatment and prevention largely depend on antiretroviral treatment (ART).
- Resistance to ART can complicate the management of HIV-1 infection and impair control of its spread.
- The aim of the current study was to investigate the prevalence and patterns of HIV-1 drug resistance among ART-naïve patients in Iceland.

❖ Methods

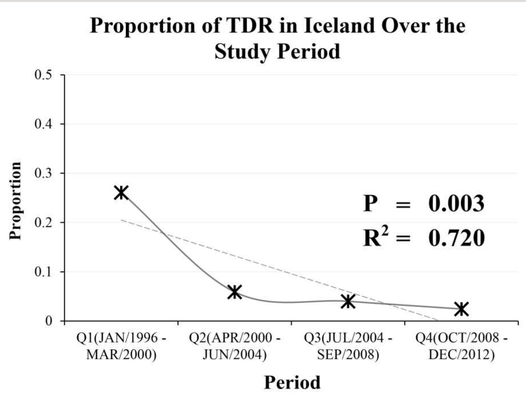
- Partial HIV-1 *pol* sequences (1020 bases) from 106 ART-naïve patients diagnosed in Iceland between 1996 and 2012 were subjected to drug resistance analysis using the Calibrated Population Resistance (CPR) tool based on the Stanford Surveillance Drug Resistance Mutation list (SDRM).
- To assess epidemiologic linkages, the Icelandic sequences were analysed phylogenetically before and after removal of drug resistance mutation codon sites.

❖ Prevalence and patterns of TDR

- Among ART-naïve patients, the overall prevalence of TDR was 8.5% (95% CI: 4.5%-15.4%). Of these, 6.6% to NRTIs, 0.9% to NNRTIs, and 1.9% to PIs.
- The major NRTI mutations detected were T215C/D (n=7, 5.7%) and M41L (n=1, 0.9%). The only major NNRTI mutation detected was K103N (n=1, 0.9%). The major PI mutations detected were M46I (n=1, 0.9%) and L90M (n=1, 0.9%). One patient had resistance mutations to both NRTI and PI.

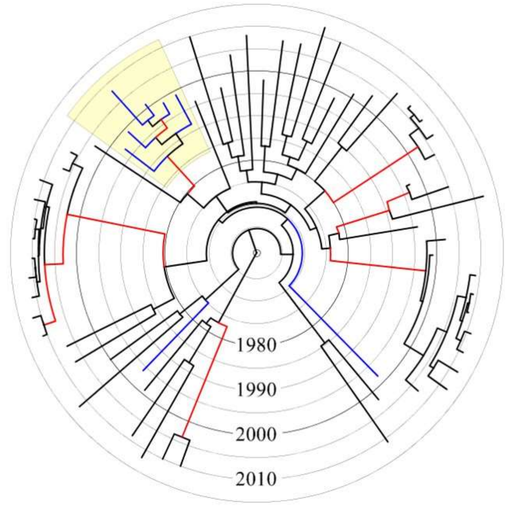
❖ Temporal trend of TDR

- Drug resistance mutations were more likely to be found among patients diagnosed before mid-2004 compared to patients diagnosed after mid-2004 (p=0.025; Fisher exact test).
- Trend analysis showed a significant decrease in the prevalence of TDR over the study period (p=0.003; Linear-by-linear test for association).



❖ Domestic spread of TDR

- Six patients with T215C/D mutation were found to be epidemiologically linked in a phylogenetic cluster with high statistical support (posterior probability=1.0).
- An identical cluster was found after removal of resistance mutation codons from the sequence alignment. This excludes the possibility of incorrect clustering due to convergent evolution.



Maximum clade credibility tree of the clade B Icelandic sequences. Branches with posterior probability value of 1.0 are shown in red. Terminal branches highlighted in blue represent sequences harbouring at least one TDR mutation. The yellow highlighted area represents the monophyletic cluster with T215C/D mutation.

❖ Conclusions

- The prevalence of TDR in Iceland was found to be at a moderate level and has decreased during 2000s.
- The most common TDR mutation observed in Iceland was thymidine analogue 215 revertant mutant, with an evidence of domestic spread, similar to findings in UK and Spain. This finding might be explained by the weak effect of this mutation on the replicative fitness of the virus.
- Screening ART-naïve patients for TDR should continue in order to optimize treatment of HIV-1-infected patients and also to prevent further HIV-1 spread.

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