Stable transmission rate of resistant HIV in Germany despite the introduction of new drugs in combination antiretroviral therapy

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Background

HIV primary resistance in drug-naïve newly infected patients is due to transmission of drug resistant HIV (TDR) from patients failing combination antiretroviral treatment (cART) and also to onward transmission of resistant HIV from patients in the early viremic phase of infection. During recent years, new drug classes were introduced in cART regimens improving sustained treatment success.

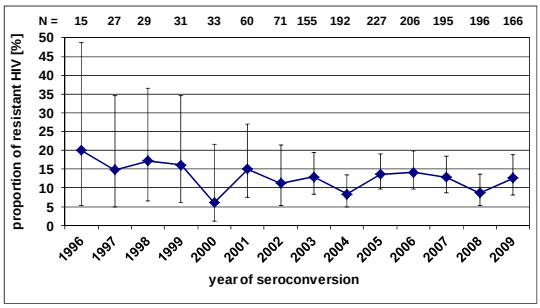
Aims

The prevalence of TDR and patterns of the viral resistance profiles over time with respect to drug classes and resistance mutations were analysed in patients with a known date of infection in the German HIV-1 Seroconverter Cohort.

Materials & Methods

Between 1996 and 2009 (year of infection) from 1639/1858 patients with a known date of HIV-infection a blood sample was obtained prior to treatment initiation. Genotypic resistance was determined from 1603 samples using the ViroSeq® HIV Genotyping System or an inhouse *pol*-RT-PCR. Mutations were identified according to the surveillance drug mutation list (Bennett *et al.* 2009). The χ2 test or the Fisher exact test was used, as appropriate, to compare categorical variables. Logistic regression was used to calculate time trends.

Results



Study population
94.7% of study patients were male and 57.7% were living in Berlin. Route of transmission distributed as follows: 87.2% MSM, 8.4% HET, 0.8% HPL, 1.3% IVD and 2.1% unknown.

Fig. 1: Trend of TDR from 1996 to 2009
The overall prevalence of TDR was 12.2% (195/1603), [CI95% 10.8-13.7], p_{trend}=0.37.

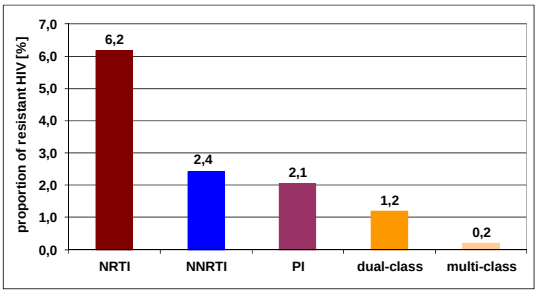


Fig. 2: Prevalence of TDR by resistance class
NRTI resistance predominated with 6.2% (99/1603) [CI95% 5.07-7.50], followed by 2.4% (39/1603) [CI95% 1.76-3.34] NNRTI resistance and 2.1% (33/1603) [CI95% 1.44-2.91] PI resistance. Dual-class resistance was observed in 1.2% (20/1603) [CI95% 0.78-1.96] and multi-class resistance in 0.2% (4/1603) [CI95% 0.79-6.56].

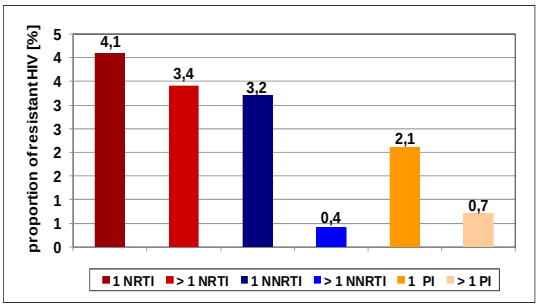


Fig. 3: Prevalence of singleton mutations
NRTI resistance was mainly caused by TAMs (86.5%) and 67.3% of TAMs were T215 revertants. Resistance to NNRTI und PI was predominantly caused by singleton mutations (89.5% and 73.0%, respectively).

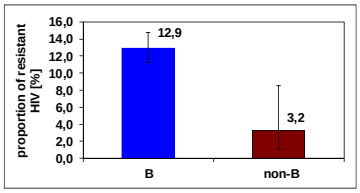


Fig. 5: Correlation of TDR and subtype B
12.9% (191/1480) of infections with subtype B were resistant [CI95% 11.3-14.8], whereas only 3.2% (4/123) of infections with non-B subtypes were resistant [CI95% 1.1-8.6], p=0.002.

Fig. 4: Trends of drug classes from 1996 to 2009
Resistances of each drug class were cumulated from mono-, dual- and multiresistant viruses.
Prevalence of NRTI resistance decreased over time (4a), whereas NNRTI and PI resistance remained stable (4b, 4c).

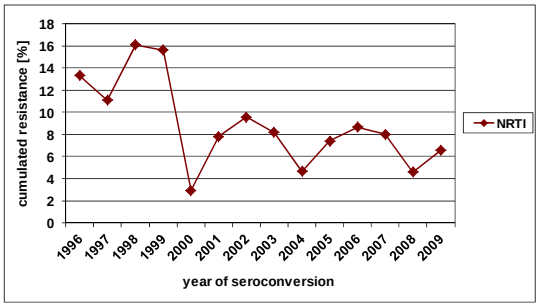


Fig. 4a: Trend of NRTI resistance , p_{trend}=0.04

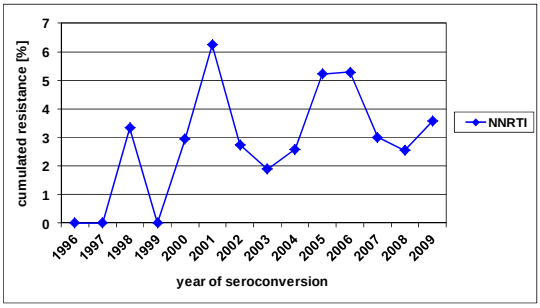


Fig. 4b: Trend of NNRTI resistance, p_{trend}=0.39

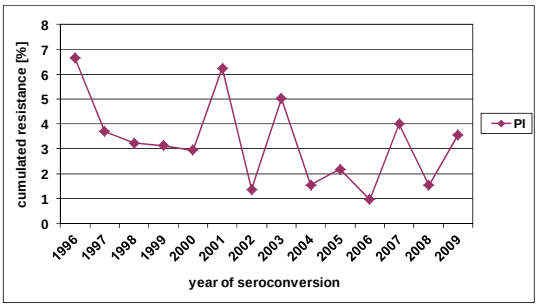


Fig. 4c: Trend of PI resistance, p_{trend}=0.29

Conclusion

Overall prevalence of TDR remained stable during the period of observation. The increase of transmitted NNRTI resistance reported in earlier years of the epidemic (1996-2007) did not continue. Resistance development is declining in treated patients since improved regimens have been introduced. Decrease of treatment failure seems to be reflected by the decrease of transmitted NRTI resistance. However, the stable rate of TDR over time implicates that onward transmission of resistant HIV between drug-naïve newly infected patients contributes to an important extent to the persistence of HIV resistance in the infected population.

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