Transmitted drug resistance (TDR) in newly diagnosed HIV-1-infected subjects in Estonia in 2013

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Introduction

- Estonian HIV epidemic is typical to Eastern Europe being driven by PWIDs.
- TDR has been 0, 5.5% and 4.5% in 2006, 2008 and 2010, respectively (Figure 1).
- NNRTIs with low resistance barrier, are still first line agents while integrase inhibitors are rarely used.

Objective

To evaluate TDR in newly diagnosed HIV positive subjects in 2013 and find risk groups

Methods

- 325 newly HIV diagnosed subjects between 1st of January 2013 and 31st of December 2013.
- Viral RNA was sequenced in 223 subjects in *pol* region and assembled using Vector NTI software.
- DRMs were determined by Stanford HIV Drug Resistance database (SDRM 2009, CPR v6.0).
- Phylogenetic analysis was conducted using the maximum likelihood method.
- Demographical and clinical data was obtained from Estonian Health Board and E-HIV database.
- LAg-avidity EIA testing was performed to categorize patients to recent (median duration of 130 days) or long term infection.

Abbreviations:
PWID: people who inject drugs
NNRTIs: Non-nucleoside reverse transcriptase inhibitors
E-HIV: Estonian HIV Cohort Study
DRM: HIV-1 drug resistance mutations
IQR: interquartile range
MSM – men having sex with men

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Results

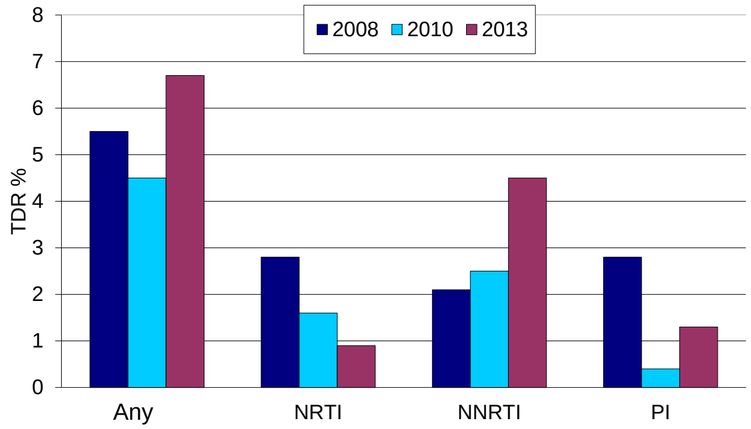

Figure 1.Prevalence of overall TDR and drug class TDR in 2008, 2010 and 2013 in Estonia

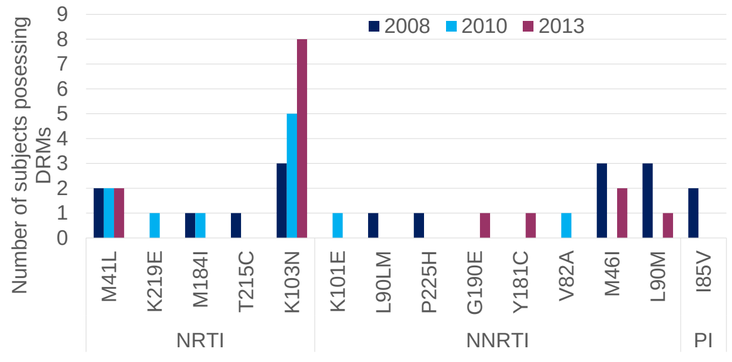

Figure 2.Prevalence of different DRMs in 2008, 2013 and 2013 in Estonia

Table 1. Characteristics of newly HIV-1 diagnosed subjects in 2013.

Number of subjects	325
Males, N (%)	199 (61)
Age in years, median (IQR)	32 (27-35)
Reason for testing, N (%):	
clinical suspicion	88 (27)
screening (pregnancy, blood donors, imprisoned, STD, TB)	65 (20)
known contact with HIV positive person	32 (10)
PWID	20 (6)
unknown	119 (37)
Transmission route, N (%):	
heterosexual	177 (55)
MSM	6 (2)
PWID	70 (22)
other/unknown	72 (22)
CD4+ cell count, median (IQR)	366 (206-540)
HIV viral load in log10, median (IQR)	4.9 (4.2-5.5)

- **15/223 strains (6.7%**; 95% CI 3.9% - 11.0%) **had a DRM** with no dual or triple class resistance observed (Figure 1).
- The prevalence of TDR in recent infections was 3.1% vs 6.8% in long term infections.
- Being imprisoned was associated with higher risk of possessing DRMs, 22.2% of imprisoned subjects vs 5.4% of all other reasons for testing (p=0.023).

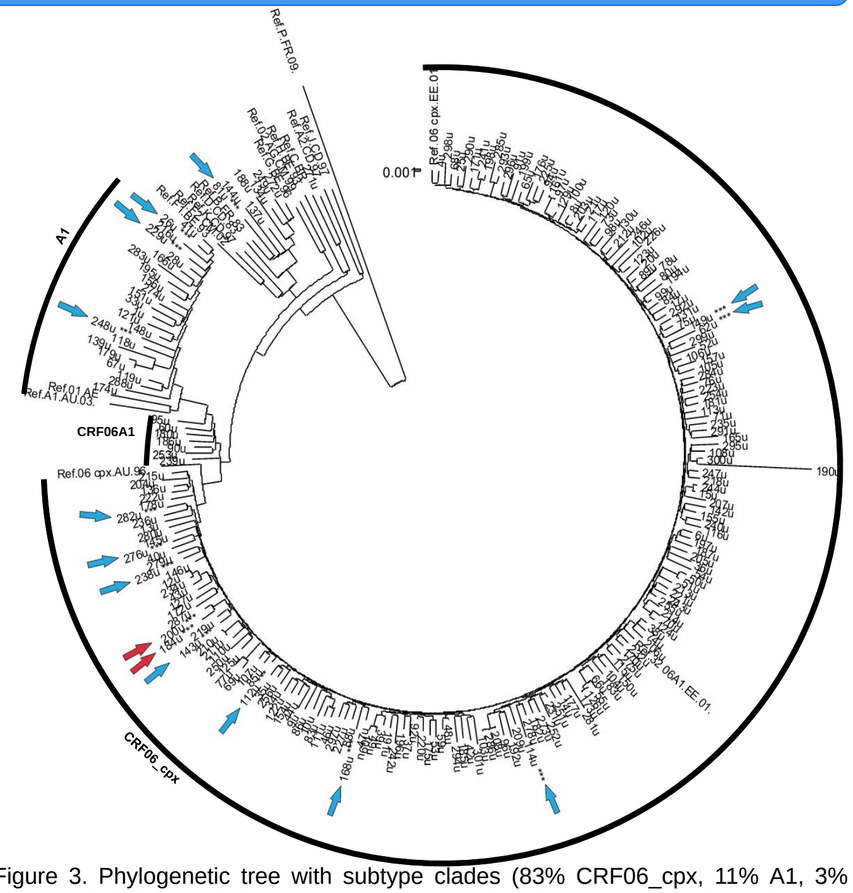

Figure 3. Phylogenetic tree with subtype clades (83% CRF06_cpx, 11% A1, 3% CRF06A1) in black circles, DRMs (blue arrows) and one transmission subcluster (bootstrap=91) with two K103N DRM-possessing viruses (red arrows).

Conclusions

- In Estonia the raising prevalence of TDR of 6.7% with predominance of NNRTI mutation K103N is reflecting wide use of efavirenz.
- There is almost no transmission clusters, but being imprisoned is associated with higher risk of possessing DRMs.
- As TDR has exceeded 5% implementation of resistance testing prior to initiation of antiretroviral treatment is recommended.

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