The prognosis of HIV-1 infection with transmitted drug resistance in Denmark 2001-2008

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Objective

• Estimate the prevalence of transmitted drug resistance in Denmark
  – How does transmitted drug resistance affects the prognosis of an HIV-1 infection
  • Longitudinal follow-up
Materials

- Two nationwide population-based cohort studies:
  - SERO-project
  - Danish HIV Cohort
Materials

• SERO-project
  – National surveillance of resistance among newly diagnosed treatment naïve individuals
  – Genotypic resistance test
  – Standardised questionnaires (Epidemiological-data, VL and CD4 etc.)
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• SERO-project
  – National surveillance of resistance among newly diagnosed treatment naïve individuals
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• Danish HIV Cohort
  – National surveillance of all HIV-1 infected patients treated in Danish HIV clinics since January 1998.
Method

• **Transmitted resistance**
  – Population based sequencing
    ViroSeq™ HIV-1 genotyping System v. 2 (Abbot Diagnostics).

  – Transmitted resistance
    > 1 resistance mutation, primary PI and/or RTI

Results
Total number of patients: 1197
Total transmitted drug resistance: 70
Prevalence: 5.8%
Results - gender

No resistance
- Male: 76%
- Female: 24%

Transmitted resistance
- Male: 76%
- Female: 24%
Results – country of origin

No resistance

Transmitted resistance

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Results - Subtype

No resistance

- B: 32%
- non-B: 68%

Transmitted resistance

- B: 27%
- non-B: 73%

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Results – route of transmission

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Prevalence of transmitted drug resistance

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Phylogenetics
Transmission of resistance described by phylogenetics

• Material
  – Danish HIV sequence database
    • Sequences from HIV-1 patients with treatment failure
  – Phylogenetic documented transmitted resistance
    • NJ, with F84 distance estimate
    • Bootstrap > 90 %
    • Intra-cluster avs. Branch length < 0.03 nt substitutions

• Phylogenetic trees (2001-2009)
  – 85 TDR patients >< 85 TDR patients
  – 85 TDR patients >< patients failing treatment
Phylogenetic results

• 45% (n=40) of TDR could be linked phylogenetically to either Danish treatment failing sequence or another TDR sequence
  – 12 clusters in subtype B
  – 1 clusters in subtype D
  – 1 clusters in subtype G
• MSM
• PI mutation 85V
• diagnosed in the last half of the study period (2005-2009)
• 5 sero converters
The consequence of TDR
70 TDR patients

10 No HAART

21 Sub-optimal HAART

39 HAART Acc. Res.

1 months – 4 years

5 Follow-up resistance tests

7 % of TDR patients have therapeutic virologic failure
Follow-up

Viral Load after start of HAART

Median CD4 after start of HAART

TDR in Danish HIV-1 patients has no impact on response to HAART regarding:

- VL
- CD4
- Time to development of AIDS/death (relative risk = 0.59 [95%CI 0.33-1.26])

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Conclusion

- The prevalence of transmitted drug resistance is low in Denmark

- Transmitted drug resistant virus carried resistance towards 1-2 drug-groups
  - No multiple-drug-class resistance

- Half of TDR sequences could be linked to Danish origin phylogenetically

- TDR has no impact on response to HAART
  (VL-suppression, increase in CD4 count or time to AIDS/death)
  - Success of the surveillance program?
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