Temporal trends of transmitted HIV drug resistance following seroconversion

Ashley Olson1, Claudia Kucherer2, Anders Sönnerborg3, Carmen de Mendoza4, Robert Zangerle5, Maria Prins6, John Gill7, Anne-Marie Bakken Kran8, Dimitrios Paraskevis9, Khouloud Porter1 for CASCADE collaboration in EuroCoord

1 Medical Research Council Clinical Trials Unit at University College London, London, UK; 2 Robert Koch Institute, Berlin, Germany; 3 Unit of Infectious Diseases, Department of Medicine Huddinge, Karolinska Institutet, Karolinska University Hospital Huddinge, Stockholm, Sweden; 4 Department of Internal Medicine, Puerta de Hierro Research Institute and University Hospital, Majadahonda, Madrid; 5 Department of Dermatology and Venereology, Innercity Medical University, Austria; 6 Public Health Service of Amsterdam, Cluster of Infectious Diseases, Amsterdam, the Netherlands; 7 University of Calgary, Calgary, Alberta, Canada; 8 Department of Microbiology, Oslo University Hospital, Oslo, Norway; 9 Institute of Clinical Medicine, University of Oslo, Norway; 10 Department of Hygiene, Epidemiology and Medical Statistics, Medical School, University of Athens, Athens, Greece

INTRODUCTION

- Transmitted drug resistance (TDR) may increase with wider use of combination antiretroviral therapy (cART)
- TDR can contribute to cART failure
- In seroprevalent cART naïve individuals, it has been shown that TDR has decreased with calendar time
- It has yet to be established if this decrease can be attributed to lower TDR as the data used are naïve nucleotide samples opposed to nucleotide samples near HIV seroconversion

AIMS

- To analyse the time trends of TDR among individuals with nucleotide sequence data near HIV seroconversion

METHODS

DATA

- CASCADE data on HIV-1 positive individuals with negative and positive HIV test dates ≤ 3 years apart
- Inclusion criteria (4,183 individuals)
- Seroconverted in the cART era (≥ 1996)
- Seroconverted before December 31, 2012
- ≥ 1 cART naïve nucleotide sequence ≤ 1 year of HIV seroconversion

ANALYSIS

- Identify the most common (>10%) TDR mutations by drug class according to the WHO criteria (surveillance drug resistance mutations - SDRMs)
- Virus considered resistant if at least one SDRM mutation was present
- Logistic regression was used to examine the association between TDR and calendar time adjusting for sex, HIV transmission risk group, HIV diagnoses during acute HIV infection (HIV test interval < 30 days or laboratory evidence of acute HIV infection) and age at seroconversion
- We used the Stanford HIV db algorithm to determine susceptibility to cART drugs

RESULTS

Table 1: Baseline characteristics

<table>
<thead>
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<tbody>
<tr>
<td>Age at seroconversion (years)</td>
<td>33 (27, 39)</td>
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<tr>
<td>MSM - N (%)</td>
<td>3341 (80%)</td>
</tr>
<tr>
<td>IDU - N (%)</td>
<td>113 (3%)</td>
</tr>
<tr>
<td>MSM - N (%)</td>
<td>636 (15%)</td>
</tr>
<tr>
<td>Other/Unknown - N (%)</td>
<td>93 (2%)</td>
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</tbody>
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Acute HIV infection - N (%) 1270 (30%)

TDR Mutations - N (%) 457 (11%)

Table 2: Predictors of any TDR

<table>
<thead>
<tr>
<th>Covariate</th>
<th>HR (95% CI)</th>
<th>P- value</th>
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<tbody>
<tr>
<td>Females</td>
<td>1.01 (0.60, 1.71)</td>
<td>0.96</td>
</tr>
<tr>
<td>Risk Group</td>
<td>0.08</td>
<td></td>
</tr>
<tr>
<td>MSM</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>IDU</td>
<td>0.68 (0.35, 1.31)</td>
<td>0.35</td>
</tr>
<tr>
<td>MSW</td>
<td>0.62 (0.42, 1.66)</td>
<td>0.08</td>
</tr>
<tr>
<td>OTH/Unknown</td>
<td>0.82 (0.41, 1.66)</td>
<td>0.26</td>
</tr>
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Age Group (years) 0.86

15-24 1
25-34 1.09 (0.82, 1.47) 0.08
35-44 1.02 (0.74, 1.39) 0.45
45+ 1.11 (0.76, 1.63) 0.26

Seroconversion year 0.92 (0.89, 0.94) < 0.001

Acute Infection 1.18 (0.96, 1.46) 0.12

CONCLUSION

- Transmitted drug resistance has decreased over calendar time which is a realistic estimation of the actual decrease in TDR due to the inclusion nucleotide sequence data close to HIV seroconversion
- Moderate evidence of an association between risk of TDR and diagnoses during acute infection may suggest TDR impacts presentation to care during acute infection (e.g. seroconversion illness) or that we underestimate TDR if not tested immediately following seroconversion.