Outcome of TB in HIV Infected Patients in Eastern Europe

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Disclosure

- I do not have any conflicts of interests
WHO definition of TB treatment outcome

- Treatment success
  - Cure
  - Treatment completed

- Unfavorable
  - Death
  - Failure
  - Lost to follow up
WHO definition of TB treatment outcome

- Treatment success
  - Cure
  - Treatment completed
- Unfavourable
  - Death
  - Failure
  - Lost to follow up
WHO TB report 2014

- TB treatment success 2012: African region 81% vs. European region 75%
- Treatment outcomes for patients treated on second-line regimens: 50% or less in most regions
TB/HIV EPIDEMIC IN EASTERN EUROPE
TB/HIV Epidemic in Eastern Europe
Example of Belarus

A. Skrahina. Personal communication
MDR-TB Epidemic - Example of Belarus

A. Skrahina. Personal communication
Primary MDR-TB in TB/HIV patients in St. Petersburg, Russia

A Panteleev. Personal communication
MDR-TB and HIV co-infection
A study from Belarus

A Skrahina et al., Bull World Health Organ 2013;91:36–45
Who are TB/HIV patients in Eastern Europe?  
The TB:HIV Study

<table>
<thead>
<tr>
<th></th>
<th>Eastern Europe N = 844</th>
<th>Western Europe N = 152</th>
<th>Southern Europe N = 164</th>
<th>Latin America N = 253</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (median, IQR)</td>
<td>35 (31 - 40)</td>
<td>37 (32 - 48)</td>
<td>42 (33 - 48)</td>
<td>38 (30 - 45)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Gender (female, %)</td>
<td>24.9</td>
<td>44.1</td>
<td>27.4</td>
<td>26.5</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Ethnicity (white, %)</td>
<td>95.2</td>
<td>26.2</td>
<td>72.3</td>
<td>19.0</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>CD4 count (median, IQR)</td>
<td>107 (35 - 254)</td>
<td>149 (35 - 360)</td>
<td>129 (38 - 315)</td>
<td>96 (35 - 289)</td>
<td>0.12</td>
</tr>
<tr>
<td>HIV+ more than 3 months before TB diagnosis</td>
<td>75.2</td>
<td>54.0</td>
<td>60.4</td>
<td>62.1</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>HIV treatment, cART (%)</td>
<td>16.6</td>
<td>39.5</td>
<td>43.9</td>
<td>35.2</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>TB Risk Group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- IDU (%)</td>
<td>61.1</td>
<td>9.2</td>
<td>29.3</td>
<td>15.0</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>- In prison last 2 years (%)</td>
<td>18.6</td>
<td>2.6</td>
<td>4.9</td>
<td>6.7</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>TB in the past, yes (%)</td>
<td>13.4</td>
<td>10.1</td>
<td>14.5</td>
<td>16.5</td>
<td>0.36</td>
</tr>
<tr>
<td>Current OST, yes¹ (%)</td>
<td>3.7</td>
<td>66.7</td>
<td>48.8</td>
<td>0</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

AMW Efsen, HIV Drug Therapy, Glasgow 2014
MDR-TB prevalence among those tested for MDR. The TB:HIV Study

- **576** had baseline DST performed
  - **495** (86%) had data on both R and H resistance

A Schultze et al., IAS 2015, Vancouver, Canada
HIV and TB epidemics in Eastern Europe

- TB
- MDR-TB
- HIV
- HCV
MANAGEMENT OF TB AND HIV IN EASTERN EUROPE
Organisational set-up of TB services - results from a survey

All, p<0.001; OST: opiate substitution therapy

M Mansfeld et al, HIV Med 2015
Availability of anti-TB drugs
Reported ‘unlimited access’ to 2\textsuperscript{nd} and 3\textsuperscript{rd} line anti-TB drugs

\[ P<0.001 \]

M Mansfeld et al, HIV Med 2015
Number of active drugs in the initial regimen. The TB:HIV Study

- 576 (41%) had baseline DST performed

<table>
<thead>
<tr>
<th></th>
<th>EE</th>
<th>WSE</th>
<th>LA</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 or more N(%)</td>
<td>201 (69)</td>
<td>197 (98)</td>
<td>90 (75)</td>
</tr>
<tr>
<td>2 or fewer N(%)</td>
<td>90 (31)</td>
<td>5 (2)</td>
<td>8 (10)</td>
</tr>
</tbody>
</table>

p < 0.0001

A Schultze et al, IAS 2015
Number of active drugs in the initial regimen TB/HIV cohort from St. Petersburg, 2013

N=81

<table>
<thead>
<tr>
<th>Mortality, %</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>57.1</td>
<td>39.1</td>
<td>33.3</td>
<td>23.8</td>
</tr>
</tbody>
</table>

A. Panteleev. Personal communication
Management of TB/HIV patient in Western Europe

ID department

TB treatment + cART

Discharged

Outpatient follow-up cART + TB treatment

+ social support

OST

Methadone
cART
TB treatment
Management of TB/HIV patient in Eastern Europe

ID Hospital → MTB+ → TB Hospital → Discharged

Consultation of HIV specialist

TB outpatient unit

AIDS Centre

cART

TB treatment

OST???

Social support???
TB OUTCOMES IN TB AND TB/HIV PATIENTS IN EASTERN EUROPE
Probability of TB death, according to geographical region. The TB:HIV Study
Overall Mortality and Causes of Death
The TB:HIV Study

- 265 individuals (19%) died within 12 months
  - 188 (71%) of these deaths could be classified as TB-related

<table>
<thead>
<tr>
<th></th>
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<th>WSE</th>
<th>LA</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB N(%)</td>
<td>175 (79)</td>
<td>3 (23)</td>
<td>10 (36)</td>
</tr>
<tr>
<td>Other N(%)</td>
<td>34 (15)</td>
<td>9 (69)</td>
<td>12 (43)</td>
</tr>
<tr>
<td>Unknown N(%)</td>
<td>14 (6)</td>
<td>1 (8)</td>
<td>6 (21)</td>
</tr>
</tbody>
</table>

A Schultze et al, IAS 2015
Probability of TB death, according to number of active drugs in the initial regimen. The TB:HIV Study

A Schultze et al, IAS 2015
Treatment outcomes for MDR-TB patients without and with HIV. A study from Belarus

A Skrahina. Personal communication
Mortality of TB/HIV patients depending on CD4 cell count
A study from St. Petersburg

A Panteleev. Personal communication
Mortality of TB/HIV patients after cART initiation
A study from St. Petersburg

<table>
<thead>
<tr>
<th>Months after cART initiation</th>
<th>MDR-TB</th>
<th>Disseminated TB</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>23.3%</td>
<td>82.1%</td>
</tr>
<tr>
<td>2</td>
<td>21.7%</td>
<td>84.3%</td>
</tr>
<tr>
<td>3</td>
<td>15%</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>6.7%</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>5%</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>7.0%</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>6.7%</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>3.3%</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>3.3%</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>3.3%</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>1.7%</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>1.7%</td>
<td></td>
</tr>
</tbody>
</table>

A Panteleev. Personal communication

p<0.05
57.5%
51.5%
Final treatment outcomes for patients with multidrug-resistant tuberculosis (MDR TB), Georgia, March 2009–October 2012

141 pulmonary MDR TB patients

1 patient on treatment and excluded

140 evaluated for treatment outcomes

Acquired drug resistance n = 19

2 (11%) favorable
1 (5.2%) Cured
1 (5.2%) Completed

17 (89%) poor
6 (32%) Death
5 (26%) Failure
6 (32%) LFU*

No acquired drug resistance n = 121

77 (64%) favorable
37 (31%) Cured
40 (33%) Completed

44 (36%) poor
5 (4%) Death
1 (1%) Failure
38 (31%) LFU*
### Treatment outcomes among drug-susceptible tuberculosis patients in Latvia, 2006–2010

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cured</td>
<td>79.9</td>
</tr>
<tr>
<td>Treatment completed</td>
<td>7.6</td>
</tr>
<tr>
<td>Died</td>
<td>6.4</td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>5.4</td>
</tr>
<tr>
<td>Failure</td>
<td>0.4</td>
</tr>
<tr>
<td>Other</td>
<td>0.2</td>
</tr>
</tbody>
</table>

### Factors, significantly associated with unsuccessful treatment

<table>
<thead>
<tr>
<th>Factor</th>
<th>Adjusted RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV+</td>
<td>2.0 (1.4–2.8)</td>
</tr>
<tr>
<td>Unemployment</td>
<td>3.4 (2.3–5.0)</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>1.5 (1.2–1.9)</td>
</tr>
</tbody>
</table>

*Public Health Action. 2014 Oct 21;4(Suppl 2)*
WHAT CAN BE DONE TO IMPROVE TB OUTCOMES IN EASTERN EUROPE
Effect of cART duration on TB incidence

Girardi, CID 2005
Timing of ART Initiation in patients initiating TB treatment

• SAPiT study: higher incidence of death in patients deferring ART therapy to end of TB treatment (sequential) vs initiation during TB therapy (integrated)[1]

• CAMELIA study: significant reduction in mortality with ART initiation at Wk 2 vs Wk 8 of TB therapy in pts with CD4+ counts ≤ 200 cells/mm3 [2]

• SAPiT and ACTG5221 studies: suggest all pts with CD4+ counts < 50 cells/mm3 should begin ART within 2-4 wks of TB therapy initiation[3,4]

Cohort of 614 MDR-TB patients in Tomsk, Russia

Aggressive MDR-TB regimen:
- Intensive phase: $\geq 5$ likely effective drugs
- Cont. phase: $\geq 4$ likely effective drugs

Adjusted hazard ratio 0.52 [95% CI 0.29–0.94]
Integrated health care works  
A study from Ukraine

Quality Healthcare Indicators (QHI) based on service delivery setting: HIV-Related Quality Healthcare Indicators

296 HIV+ IDUs
- Integrated co-located care
  - On site care for HIV, TB, OST
- Non-co-located care
  - OST only
- Harm reduction and outreach
  - but no OST

*C Bachireddy et al., Drug Alcohol Depend. 2014*
Opiate substitution therapy works
A study from Ukraine


Observational study of 110 TB patients (68% HIV+)
MMT (methadone maintenance): N=57 / non-MMT N = 53

Time to discontinuation of TB treatment over 90-day observation period

90-day retention on tuberculosis treatment was significantly associated with MMT:
• adjusted OR (95% CI) 3.05 (1.08–8.66)
Summary:
Actions to improve TB outcomes in HIV+ people in Eastern Europe

- Integration of health care systems (HIV/TB/OST)
- Strong infection control to stop spread of TB/MDR-TB and HIV infections
  - Early case detection
- Adequate treatment of TB based on the results of the Drug Susceptibility Testing
  - Rapid DST
- Adequate treatment of HIV infection
  - Early initiation of ART
- Treatment of concomitant conditions (IDU/HCV)
- Political will and commitment
Acknowledgement

- CHIP, Copenhagen
  - Jens D. Lundgren
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- Royal Free Hospital, London
  - Amanda Mocroft
  - Anna Schultze
- Colleagues from Eastern Europe
  - Alena Skrahina
  - Aza Rakhmanova
  - Alexander Panteleev
Thank you very much for your attention!

CAN YOU IMAGINE A WORLD WITHOUT TB?
WE CAN.