Mortality and Causes of Death Among HIV/HCV Co-Infected Persons in the Eastern European Country of Georgia

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## Background: HIV and HCV in Georgia

### HIV
- Estimated prevalence: 0.4%
- Estimated number: 10 500
- Progress towards 90-90-90:
  - 48% diagnosed
  - 81% of diagnosed on ART
  - 89% virally suppressed

### HCV
- HCV in general population:
  - Anti-HCV+: 7.7% (208 000 persons)
  - HCV RNA+: 5.4% (150 000 persons)
- HCV in PLHIV
  - Anti-HCV+: 40% (4 200 persons)
  - HCV RNA+: 34% (3 500 persons)

In April 2015, in partnership with US CDC and Gilead Sciences, Georgia launched the world’s first National Hepatitis C Elimination Program.
Standard of Care in Georgia

• Universal access to ART since 2004; ART regardless of CD4 cell count for HIV/HCV since 2013 and for all since 2015

• anti-HCV screening at the entry into HIV care

• HCV RNA testing for anti-HCV+

• HCV genotyping and liver fibrosis assessment for HCV RNA+

• HCV Treatment
  – 12.2011-05.2015: PEG/RBV
  – 06.2015-03.2016: SOF/PEG/RBV; SOF/RBV weeks
  – Since 03.2016: SOF/LDV ± RBV for 12 or 24 wks
  – Since 11.2018: SOF/VEL ± RBV
Objective

• Evaluate impact of universal availability of HCV treatment on mortality and causes of death among people living with HIV in Georgia
Methods

• **Population:**
  – Adult (age ≥18 years) HIV-infected individuals diagnosed from 2004 through 2016 followed until December 31, 2017

• **Data source:**
  – National AIDS Health Information System (AIDS HIS)

• **HIV/HCV co-infection**
  – HIV positive persons with anti-HCV+

• **Statistical analysis:**
  – Mortality rates per 100 person-years of follow-up were calculated
  – Predictors of mortality were assessed in Cox proportional hazards regression model
  – Causes of death were classified according to Coding of Death in HIV (CoDe) protocol
# Study Population

<table>
<thead>
<tr>
<th></th>
<th>All (n=4560)</th>
<th>anti-HCV+ (n=2058)</th>
<th>anti-HCV- (n=2502)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, median years (IQR)</strong></td>
<td>36.6 (30.0-43.8)</td>
<td>39.0 (33.7-44.7)</td>
<td>33.9 (27.1-42.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Sex, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Men</td>
<td>3343 (73.3)</td>
<td>1823 (88.6)</td>
<td>1520 (60.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Women</td>
<td>1217 (26.7)</td>
<td>235 (11.4)</td>
<td>982 (39.2)</td>
<td></td>
</tr>
<tr>
<td><strong>Mode of HIV transmission, n (%)</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Injection drug use</td>
<td>1864 (40.9)</td>
<td>1575 (76.5)</td>
<td>289 (11.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Heterosexual contact</td>
<td>2150 (47.2)</td>
<td>420 (20.4)</td>
<td>1730 (69.1)</td>
<td></td>
</tr>
<tr>
<td>Sex between men</td>
<td>485 (10.6)</td>
<td>48 (2.3)</td>
<td>437 (17.5)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>61 (1.3)</td>
<td>15 (0.7)</td>
<td>46 (1.8)</td>
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</tr>
<tr>
<td><strong>HBV infection, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBsAg+</td>
<td>247 (5.4)</td>
<td>116 (5.6)</td>
<td>131 (5.2)</td>
<td>0.55</td>
</tr>
<tr>
<td>HBsAg-</td>
<td>4323 (94.6)</td>
<td>1942 (94.4)</td>
<td>2371 (94.8)</td>
<td></td>
</tr>
<tr>
<td><strong>Baseline CD4 cell count, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;350</td>
<td>2481 (54.4)</td>
<td>1261 (61.3)</td>
<td>1220 (48.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>≥350</td>
<td>2079 (45.6)</td>
<td>797 (38.7)</td>
<td>1282 (51.2)</td>
<td></td>
</tr>
<tr>
<td><strong>History of ART, n (%)</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Never started ART</td>
<td>630 (13.8)</td>
<td>285 (13.8)</td>
<td>345 (13.8)</td>
<td>0.95</td>
</tr>
<tr>
<td>Ever started ART</td>
<td>3930 (86.2)</td>
<td>1773 (86.2)</td>
<td>2157 (86.2)</td>
<td></td>
</tr>
</tbody>
</table>
Mortality

- After the median 4.1 years of follow-up 20.9% (954/4560) persons died, including:
  - 29.9% (615/2058) among HIV/HCV co-infected persons and 13.5% (339/2502) among HIV mono-infected persons (p<0.0001)

<table>
<thead>
<tr>
<th></th>
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<th>Anti-HCV+</th>
<th>Anti-HCV-</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality per 100 PY</td>
<td>4.27</td>
<td>5.76</td>
<td>2.91</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Annual Mortality Rates by HCV Status

- **anti-HCV+**
- **anti-HCV-**

Mortality rate per 100 PY

- 2008: p=0.02
- 2009: p=0.02
- 2010: p=0.03
- 2011: p=0.005
- 2012: p=0.002
- 2013: p=0.05
- 2014: p=0.04
- 2015: p=0.002
- 2016: p=0.05
- 2017: p=0.06
# Factors Associated with Mortality

<table>
<thead>
<tr>
<th>Factor</th>
<th>HR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>anti-HCV+</td>
<td>1.33 (1.13-1.57)</td>
<td>0.0006</td>
</tr>
<tr>
<td>Age per year increase</td>
<td>1.03 (1.02-1.04)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Men</td>
<td>1.33 (1.07-1.66)</td>
<td>0.01</td>
</tr>
<tr>
<td>Injection drug use vs. MSM</td>
<td>3.77 (2.40-5.93)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Heterosexual contact vs. MSM</td>
<td>2.55 (1.61-4.03)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HBsAg+</td>
<td>0.74 (0.53-1.04)</td>
<td>0.08</td>
</tr>
<tr>
<td>Baseline CD4 cell count &lt;350</td>
<td>1.89 (1.64-2.17)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Never started ART</td>
<td>5.55 (4.82-6.40)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Top 5 Causes of Death

**anti-HCV+**
- AIDS; 43.1%
- ESLD; 20.8%
- Drug abuse; 3.4%
- Cancer; 5.5%
- Ishemic heart dis; 4.7%

**anti-HCV-**
- AIDS; 45.7%
- Stroke; 3.8%
- Cancer; 7.1%
- Ishemic heart dis; 4.4%
- Non-AIDS infection; 2.9%

AIDS remained leading cause of death before and after availability of HCV treatment.
Conclusions

• Wide availability of ART and anti-HCV therapy translated into significant decline in mortality including due to liver related causes

• HIV/HCV co-infected persons continue to have higher mortality

• AIDS is the leading cause of death because of high rates of late diagnosis

• Improving earlier diagnosis will decrease excess AIDS-related mortality among HIV/HCV co-infected persons.
Acknowledgement

All Care Provider Centers