Risk of Kaposi Sarcoma in HIV-Positive Adults on ART: a Global Analysis

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Background
Kaposi sarcoma (KS) is one of the most common tumors in HIV-positive persons. Epidemic KS is caused by human herpesvirus 8 (HHV-8) infection and HIV-related immunosuppression. The prevalence of HIV and HHV-8 varies between different geographic regions. HHV-8 prevalence in the general population is much higher in sub-Saharan Africa than in Europe and North America, for example.

Objectives
• To compare KS incidence rates in HIV-positive adults on combination antiretroviral therapy (ART) globally
• To examine risk factors for developing KS in HIV-positive adults on ART

Methods
• We analyzed data from the International Epidemiologic Databases to Evaluate AIDS (IeDEA) and the Collaboration of Observational HIV Epidemiological Research in Europe (COHERE) in EuroCoord.
• We included HIV-positive adults (≥16 years) who initiated ART after enrollment into cohort from 1996 onwards.
• We compared the risk of incident KS after starting ART between regions using flexible parametric survival models with region-specific baseline hazards, adjusted for age, sex and its interaction with region, time-updated CD4 cell counts and years of ART started.
• We excluded the Asia-Pacific and Australia from multivariate analyses due to the small sample size.
• We present hazard ratios (HR) and 95% confidence intervals (CI) by time since ART start and at 2 years after start.

Table: Characteristics of included adults at ART initiation.

<table>
<thead>
<tr>
<th>Region</th>
<th>Asia-Pacific</th>
<th>Australia</th>
<th>Southern Africa</th>
<th>Latin America</th>
<th>North America</th>
<th>Europe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults (N)</td>
<td>2,649</td>
<td>344</td>
<td>172,863</td>
<td>8,599</td>
<td>16,756</td>
<td>160,178</td>
</tr>
<tr>
<td>Median age [years]</td>
<td>36</td>
<td>32</td>
<td>35</td>
<td>36</td>
<td>40</td>
<td>37</td>
</tr>
<tr>
<td>MSM</td>
<td>23%</td>
<td>67%</td>
<td>NR</td>
<td>42%</td>
<td>50%</td>
<td>59%</td>
</tr>
<tr>
<td>Median CD4 cell count [cells/μl]</td>
<td>137</td>
<td>283</td>
<td>(210-398)</td>
<td>(72-210)</td>
<td>(61-273)</td>
<td>(93-378)</td>
</tr>
</tbody>
</table>

Results
• We included 361,389 HIV-positive adults from the Asia-Pacific, Australia, Southern Africa, Latin America, North America, and Europe (Table).
• Over 1.4 million person-years (py) 2,725 adults developed KS for an overall incidence rate of 196/100,000 pyrs (95% CI 188-203).
• After 2 years on ART KS incidence was higher in women from Southern Africa than in European women (adjusted HR 2.2, 95% CI 1.8-2.8) and similar to European women in women from Latin and North America.
• In men crude KS risk after 2 years on ART was higher in North America compared to Europe (HR 1.5, 95% CI 1.2-1.9), in multivariable analyses this risk declined to HR 1.1 (95% CI 0.9-1.4). The change was mainly explained by adjusting for time-updated CD4 cell counts. KS risk was similar in men from other regions (Figure).

Limitations
• Migration data were not available for all regions and hence not considered in the analyses
• No data on HHV-8 status of included adults available
• KS diagnoses not in all regions histologically confirmed

Conclusions
Women in Southern Africa had a higher KS risk than women in Europe which was not explained by HIV-related risk factors. In men KS risk was similar across regions after adjusting for HIV-related risk factors. This pattern likely reflects different HHV-8 risk profiles: while men were at high risk of HHV-8 infection in most MSM (most risk in HHV-8 endemic regions) the main risk factor for HHV-8 infection in women was residence in HHV-8 endemic regions.

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Figure: Adjusted HR and 95% CI for the risk of developing KS in different regions.

ART, combination antiretroviral therapy; CI, confidence interval; HR, hazard ratio; KS, Kaposi sarcoma.