Kaposi Sarcoma Risk in Children on Antiretroviral Therapy from Africa, Europe and Asia
Eliane Rohner1 and Julia Bohlhus1 on behalf of the International Epidemiologic Databases to Evaluate AIDS Southern Africa, the Collaboration of Observational HIV Epidemiological Research in Europe in EuroCoord, and the TREAT Asia Pediatric HIV Observational Database

Background
Epidemic Kaposi sarcoma (KS) is caused by human herpesvirus 8 (HHV-8) infection and HIV-induced immunosuppression. HHV-8 prevalence varies between geographical regions: HHV-8 prevalence is higher in Eastern Africa than Southern Africa, and lower in Europe and Asia.

Methods (1)
Databases
We analyzed data from the International Epidemiologic Databases to Evaluate AIDS Southern Africa; the TREAT Asia Pediatric HIV Observational Database; and the Collaboration of Observational HIV Epidemiological Research in Europe in EuroCoord.

Methods (2)
Inclusion criteria and definitions
We included HIV-infected children aged <16 years at ART initiation after 1995. Geographic regions were defined according to the United Nations classification.

Statistical methods
Time at risk was measured from ART initiation to KS diagnosis, last follow-up visit, death, or database closure.

Results (1)
Study population
We included data on 25,033 children from 16 countries in Eastern Africa (Zimbabwe, Zambia); Southern Africa (South Africa); Europe (Denmark, France, Germany, Ireland, Netherlands, Spain, and the UK); and Asia (Cambodia, India, Indonesia, Malaysia, Thailand, Vietnam).

Median age at ART start was 5.0 years (interquartile range 1.8-9.1) and varied across regions (Table). Overall, 10% (n=2,429) of children and adolescents initiated ART in CDC stage C.

Table: Characteristics of included children at ART start

<table>
<thead>
<tr>
<th>Region</th>
<th>Children (N)</th>
<th>Boys (%)</th>
<th>Median age (years)</th>
<th>Median CD4 cell</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eastern Africa</td>
<td>11,197</td>
<td>50%</td>
<td>6.1 (2.3-10.3)</td>
<td>241</td>
</tr>
<tr>
<td>Southern Africa</td>
<td>9,182</td>
<td>50%</td>
<td>3.4 (1.0-7.3)</td>
<td>256</td>
</tr>
<tr>
<td>Europe</td>
<td>658</td>
<td>51%</td>
<td>3.7 (5.0-12.1)</td>
<td>259</td>
</tr>
<tr>
<td>Non-SSA region</td>
<td>934</td>
<td>49%</td>
<td>8.7 (6.0-8.8)</td>
<td>190</td>
</tr>
<tr>
<td>Asia</td>
<td>3,062</td>
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ART: combination antiretroviral therapy; KS: Kaposi sarcoma; SSA: sub-Saharan African. Medians are presented with interquartile ranges.

Results (2)
KS incidence rates and risk factors
- During 74,617 person-years (py) of follow-up time, 26 children developed KS after ART initiation. Incidence rates per 100,000 yrs were 85 in Eastern Africa (95% CI 55-132), 11 in Southern Africa (95% CI 4-35), and 81 (95% CI 26-251) in children of sub-Saharan African (SSA) origin in Europe; no incident KS cases were observed in children of non-SSA origin in Europe and in Asia.
- The overall KS incidence rate was highest in the first three months on ART (206 per 100,000 yrs, 95% CI 117-363), and declined steeply thereafter (Figure).
- KS risk was lower in girls than boys (adjusted hazard ratio [aHR] 0.3, 95% CI 0.1-0.9), and increased with age (10-15 versus 0-4 years: aHR 3.4; 95% CI 1.2-10.1) and advanced HIV/AIDS stage (CDC stage C versus A/B; aHR 2.4; 95% CI 0.8-7.3) at ART initiation.

Conclusions
HIV-infected children from sub-Saharan Africa, but not those from other regions, have a high risk of developing KS after ART initiation. In these children early ART initiation might reduce KS risk.

Contact: Eliane Rohner; MD, Institute of Social and Preventive Medicine, University of Bern, Switzerland; E-mail: eliane.rohner@ispm.unibe.ch

Funding: Supported by the National Institute Of Allergy and Infectious Diseases (NIAID); National Institute of Child Health and Human Development (NICHD); the National Cancer Institute (NCI); the U.S. National Institutes of Health (NIH) under Award Numbers Southern Africa: U10MD020394, Asia Pacific: U10MD020397, and the AIDES Network Coordinating Center of ViHIVdd (U10MD020398). The COHERE study group has received unrestricted funding from Agence Nationale de Recherche sur le Sida et les Maladies V%C3%A9rales (ANRS); France; HIV Monitoring Foundation, the Netherlands; and the Augustinus Foundation, Denmark. The research leading to these results has received funding from the European Union Seventh Framework Programme (FP7-HEALTH-2010-109618) under EuroCoord grant agreement # 200944. A list of publications by models of KS incidence among children included in COHERE can be found on the Regional Coordinating Centre website at http://www.cohere.ch/CoHERE/Stat/2004_Default.asp and http://www.sida-et-maladies-virales.fr/cohere. The full acknowledgement section for COHERE in EuroCoord is shown next to the poster.

Abstract #619

Background
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Methods (2)
Inclusion criteria and definitions
We included HIV-infected children aged <16 years at ART initiation after 1995. Geographic regions were defined according to the United Nations classification.

Statistical methods
Time at risk was measured from ART initiation to KS diagnosis, last follow-up visit, death, or database closure. We calculated KS incidence rates for the overall observation period, and by time periods after ART initiation. We ignored ART interruptions or treatment changes. We used Cox models to calculate hazard ratios (HR), adjusted for region and origin, sex, age at ART initiation, CDC stage at ART initiation and ART start year.

Limitations
- Only children on ART included
- KS ascertainment (mainly clinical versus histological confirmation) varies between regions

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Study population
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