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Persistence of anal squamous intraepithelial lesions and anal HPV infection in HIV-infected patients despite immune restoration under cART

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Background
A high prevalence of anal squamous intraepithelial lesions (ASIL) and HPV infection have been observed in HIV-infected MSM in the pre-cART era. To date, the impact of cART on the natural history of HPV infection and ASIL is poorly documented.

Methods
94 HIV-infected MSM naïve of cART were enrolled in a longitudinal study before starting a first-line regimen of cART. Each patient provided anal samples for cytology, histology, and HPV DNA testing at baseline, month 12, and month 24 of cART. HPV DNA was detected by real-time PCR and Roche Linear Array assay. Anal cytologic was processed by the Thin Prep™ method (Hologic). CD4+ and CD8+ T cell responses to HPV-16 E6 and E7 proteins were measured in a subgroup of individuals exhibiting HPV-16 anal infection at inclusion.

Results
Prevalence of low-grade SIL, high-grade SIL, and HPV infection was similar at M12 compared to baseline. Among patients with normal cytology and/or histology at baseline, 44% progressed to SIL at M12 whereas 31% of patients with ASIL at baseline exhibited a regression at M12. Specific anti-HPV CD4 T cell responses were mostly undetectable both at baseline and M12. (Table 1 and 2)

At month 12, prevalence of anal HPV DNA detection was similar than at baseline. High-risk HPV was detected at month 12 in 92% of the patients with high-risk HPV infection at baseline. Low-risk HPV was detected at month 12 in 91% of the patients with low-risk HPV infection at baseline. HPV-16 and HPV-18 were detected at month 12 in 13% and 3.7% of patients with no HPV-16 and HPV 18 infection at baseline, respectively. HPV-16 was detected in 100% and 70% of high-grade SIL at baseline and month 12, respectively.

Table 1 The median age of the patients was 39.7 years (33.2-43.5). Baseline and month 12 cytologic and/or histologic results

<table>
<thead>
<tr>
<th></th>
<th>CD4/mm³ median (Q1-Q3)</th>
<th>Plasma HIV RNA log10 copies/mL</th>
<th>VL &lt;50</th>
<th>Prior AIDS event</th>
<th>Visible lesion</th>
<th>Presence of condyloma</th>
<th>Anal SIL</th>
<th>Low-grade SIL; High-grade SIL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>299 (242 – 342)</td>
<td>4.8 (4.17 – 5.26)</td>
<td>1%</td>
<td>4 (4%)</td>
<td>40/94 (43%)</td>
<td>23/94 (25%)</td>
<td>51 (54%)</td>
<td>30 (32%); 8 (9%)</td>
</tr>
<tr>
<td>M12</td>
<td>500 (411 – 575)</td>
<td>1.6 (1.6 – 1.6)</td>
<td>93%</td>
<td></td>
<td>25/71 (35%)</td>
<td>5/71 (7%)</td>
<td>41 (59%)</td>
<td>24 (34%); 10 (14%)</td>
</tr>
</tbody>
</table>

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Conclusion
Our results demonstrate a high prevalence and incidence of ASIL and anal HPV infection in HIV-infected MSM despite CD4 reconstitution under cART. These data suggest that all HIV-positive MSM, even under antiretroviral therapy, remain at risk of anal SIL.

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Table 2 Baseline and month 12 virological results

<table>
<thead>
<tr>
<th></th>
<th>Number of HPV</th>
<th>Number of high-risk and low-risk type</th>
<th>High risk HPV</th>
<th>HPV-16</th>
<th>HPV-18</th>
<th>HPV-16 DNA log_{10} copies/10^6 cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>5 (2 – 7)</td>
<td>3 (2 – 5); 2 (1 – 4)</td>
<td>83 (90%)</td>
<td>49 (53%)</td>
<td>28 (30%)</td>
<td>6.1 (5.3 – 7.1)</td>
</tr>
<tr>
<td>M12</td>
<td>5 (2 – 6)</td>
<td>3 (1 – 4); 2 (1 – 4)</td>
<td>59 (87%)</td>
<td>28 (41%)</td>
<td>15 (22%)</td>
<td>6.1 (2.0 – 7.2)</td>
</tr>
</tbody>
</table>

http://www.infectagentscancer.com/content/5/S1/A59