Risk of non-AIDS-defining events amongst HIV-infected patients not yet on antiretroviral therapy

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Background

• Certain non-AIDS-defining illnesses in HIV-infected patients on combination antiretroviral therapy (cART) have been associated with low CD4 cell counts and high HIV RNA levels.
• We aimed to further investigate these associations in patients not yet on cART when potential antiretroviral drug-related toxicities are absent and there is more variation in RNA levels.

Methods

Patient population

• 13,077 patients from the ATHENA national observational HIV cohort who were
  - diagnosed with HIV-1 ≥1998.
  - not yet treated with cART.

Analysis

• Poisson regression model for the association between time-updated CD4 counts and HIV RNA and a composite non-AIDS endpoint.
• Composite endpoint included:
  - major cardiovascular disease: myocardial infarction, stroke, invasive coronary procedures.
  - liver fibrosis/cirrhosis.
  - non-AIDS malignancies.
• Non-AIDS events were considered from the time of the first CD4 count onwards.
• Patients were followed until start of treatment or last follow-up visit.

Results

• 18,641 person-years of follow-up.
• 208 (1.6%) patients with one or more non-AIDS events; 5 patients had ≥2 events:
  - 53 cardiovascular disease.
  - 79 liver fibrosis/cirrhosis.
  - 82 non-AIDS malignancies.

Table 1: Association between latest CD4 count and HIV RNA and the composite non-AIDS endpoint. Multivariate analyses were adjusted for demography, history of smoking, alcohol use, CDC stage, hepatitis B and C co-infection, diabetes, and hypertension. RR: relative risk; CI: confidence interval; ref: reference.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 [cells/mm³]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;200</td>
<td>8.96</td>
<td>4.36</td>
</tr>
<tr>
<td>200-349</td>
<td>2.51</td>
<td>2.13</td>
</tr>
<tr>
<td>350-499</td>
<td>1.35</td>
<td>1.23</td>
</tr>
<tr>
<td>≥500</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>HIV RNA [copies/ml]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20,000</td>
<td>0.48</td>
<td>0.77-1.66</td>
</tr>
<tr>
<td>20,000-99,999</td>
<td>0.75</td>
<td>0.93-1.93</td>
</tr>
<tr>
<td>≥100,000</td>
<td>ref</td>
<td>ref</td>
</tr>
</tbody>
</table>

Conclusions

• In persons not yet receiving cART, a more severe degree of immunodeficiency rather than HIV RNA appears to be associated with an overall risk of our composite non-AIDS event endpoint.
• Larger studies will be needed to address these associations for each individual non-AIDS disease event.