Immunologic and Virologic Disease Progression and Response to ART Across Geographic Regions: Outcomes from HPTN 052

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Abstract Authors

Outline

• Review HIV disease progression of the HIV infected index participant
  – HIV-1 RNA and CD4 changes over time
  – ART initiation
  – Treatment response

• Explore differences in baseline, behavioral and disease progression characteristics across regions that may explain observed differences in the number of transmissions between participants enrolled at African versus non-African sites
HPTN 052 Study Design

HIV-infected subjects with CD4 350 to 550 cells/mm$^3$
Serodiscordant couples

Randomization

Immediate ART
CD4 350-550
886 index partners

Delayed ART
CD4 <250
877 index partners

184 initiated therapy
HIV-1 RNA and CD4 Over Time (ITT)
21% initiated therapy
   - Mostly (75%) triggered by a decline in CD4 count

Median time to initiation was 3.5 years

Median CD4 at initiation was 225 cells/mm³
   - Q1–Q3: 199 – 247

Time to ART Initiation (Delayed Arm)
## Factors Associated with ART Initiation (Delayed Arm)

<table>
<thead>
<tr>
<th></th>
<th>Univariate</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>p</td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td><strong>Baseline CD4</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>(per 100 cells/mm³)</td>
<td>0.6 (0.5, 0.7)</td>
<td>&lt;.0001</td>
<td>0.6 (0.5, 0.7)</td>
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<tr>
<td><strong>Baseline HIV-1 RNA</strong></td>
<td></td>
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<tr>
<td>(per log₁₀ copies/ml)</td>
<td>1.7 (1.4, 2.1)</td>
<td>&lt;.0001</td>
<td>1.5 (1.2, 1.8)</td>
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<tr>
<td><strong>Index gender</strong></td>
<td></td>
<td></td>
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<tr>
<td>(male vs. female)</td>
<td>1.3 (0.9, 1.8)</td>
<td>0.63</td>
<td>1.2 (0.8, 1.5)</td>
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</table>
# ART Regimens

<table>
<thead>
<tr>
<th>N initiating ART</th>
<th>Immediate Arm</th>
<th>Delayed Arm</th>
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<tbody>
<tr>
<td>N initiating ART</td>
<td>886</td>
<td>184</td>
</tr>
<tr>
<td>(AZT/3TC)/EFV</td>
<td>72%</td>
<td>70%</td>
</tr>
<tr>
<td>(AZT/3TC)/ATV</td>
<td>10%</td>
<td>7%</td>
</tr>
<tr>
<td>(FTC/TDF)/EFV</td>
<td>9%</td>
<td>11%</td>
</tr>
<tr>
<td>(AZT/3TC)/(LPV/RTV)</td>
<td>7%</td>
<td>2%</td>
</tr>
<tr>
<td>Other</td>
<td>2%</td>
<td>10%</td>
</tr>
</tbody>
</table>
CD4 Trends Post ART Initiation

The graph illustrates the CD4 trends post ART initiation, comparing immediate and delayed responses.

- **Immediate**
  - Months 0: 880 CD4 cells/mm³
  - Months 3: 842 CD4 cells/mm³
  - Months 6: 785 CD4 cells/mm³
  - Months 12: 577 CD4 cells/mm³
  - Months 18: 390 CD4 cells/mm³
  - Months 24: 33 CD4 cells/mm³
  - Months 30: 30 CD4 cells/mm³

- **Delayed**
  - Months 0: 183 CD4 cells/mm³
  - Months 3: 149 CD4 cells/mm³
  - Months 6: 96 CD4 cells/mm³
  - Months 12: 55 CD4 cells/mm³
  - Months 18: 33 CD4 cells/mm³

The graph shows a gradual increase in CD4 counts over time, with immediate responders showing a more pronounced increase compared to delayed responders.
## Virologic Failure and Second Line ART

|                                | Immediate Arm | Delayed Arm |
|                                |               |            |
| Enrolled                       | 886           | 877        |
| Initiated primary regimen      | 886           | 184        |
| Experienced virologic failure | 5.1%          | 2.7%       |
| Initiated secondary regimen    | 67%           | 60%        |
Brief Summary So Far

• ART response in the immediate arm was rapid and robust

• In the delayed arm ART was initiated in a minority of participants and was significantly associated with baseline CD4 and viral load

• Virologic failure was uncommon in either arm

• The magnitude of CD4 responses were similar but the absolute CD4 levels achieved were lower in the delayed arm
Regional Analysis

- Regional variance in transmission was apparent
  - 23/28 (82%) linked and 32/39 (82%) unlinked transmissions in sub-Saharan Africa
  - 54% enrollment at African sites

- Differences in baseline HIV RNA and CD4, HIV subtype, adherence and response to ART, sexual behavior on study and/or differential timing of ART initiation in the delayed arm may contribute to these differences
  - Baseline characteristics compared using Wilcoxon rank sum and chi-square tests
  - Time to event outcomes compared using Cox proportional hazards
## Baseline Characteristics by Region

<table>
<thead>
<tr>
<th></th>
<th>Africa (N=954)</th>
<th>Asia/Americas (N=807)</th>
<th>P</th>
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<tbody>
<tr>
<td><strong>Demographic</strong></td>
<td></td>
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<tr>
<td>Female sex</td>
<td>58%</td>
<td>40%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age group</td>
<td></td>
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<tr>
<td>18-25</td>
<td>20%</td>
<td>15%</td>
<td>0.003</td>
</tr>
<tr>
<td>26-40</td>
<td>59%</td>
<td>67%</td>
<td></td>
</tr>
<tr>
<td>&gt;40</td>
<td>21%</td>
<td>19%</td>
<td></td>
</tr>
<tr>
<td><strong>Clinical</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD4 cell count (/mm$^3$)</td>
<td>436 (361, 526)*</td>
<td>448 (370, 518)*</td>
<td>0.95</td>
</tr>
<tr>
<td>HIV-1 RNA (log10 copies/ml)</td>
<td>4.4 (3.8, 4.9)*</td>
<td>4.5 (3.9, 5.0)*</td>
<td>0.006</td>
</tr>
<tr>
<td><strong>Behavioral</strong></td>
<td></td>
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<tr>
<td>Unprotected sex last week</td>
<td>9%</td>
<td>4%</td>
<td>0.0007</td>
</tr>
<tr>
<td>3+ sex acts last week</td>
<td>29%</td>
<td>18%</td>
<td>&lt;0.0001</td>
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*Median (Q1 – Q3)
Time to ART Initiation by Region

HR: 1.4 (1.1, 1.9), P=0.02
Adj.HR: 1.3 (0.9, 1.8), P=0.06
Viral Suppression

- **Immediate arm:** After one year, 90% of total had viral suppression
  - 90% non-Africa
  - 91% Africa

- **Delayed arm:** After one year, 93% of total had viral suppression.
  - 96% from non-Africa region
  - 85% from Africa
## Adherence According to Region

<table>
<thead>
<tr>
<th></th>
<th>Africa</th>
<th>Non-Africa</th>
</tr>
</thead>
<tbody>
<tr>
<td>N on ART</td>
<td>615</td>
<td>533</td>
</tr>
<tr>
<td>N with evaluable adherence</td>
<td>582</td>
<td>517</td>
</tr>
<tr>
<td>Adherence≥75%</td>
<td>95%</td>
<td>96%</td>
</tr>
<tr>
<td>Adherence≥95%</td>
<td>74%</td>
<td>82%</td>
</tr>
<tr>
<td>Mean (SD) adherence (%)</td>
<td>95 (12)</td>
<td>95 (15)</td>
</tr>
<tr>
<td>Median adherence (%)</td>
<td>99</td>
<td>99</td>
</tr>
</tbody>
</table>
Conclusions

• High rates of virologic suppression and CD4 increase for persons on ART (both arms)

• Lower absolute CD4 one year post-ART initiation in subjects with delayed ART (ongoing clinical risk)

• Regional differences seen in baseline characteristics, sexual behavior, and progression to ART initiation (may help explain regional variation in HIV transmission)
Special Thanks

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