Better Virological Outcomes when Initiating Early ART in the HPTN 071 (PoPART) Trial in South Africa

**BACKGROUND**

- Effective virological suppression (VS) amongst people living with HIV requiring antiretroviral treatment (ART) is essential for both individual benefit and at the population level to reduce HIV transmission.
- There have been concerns about reduced adherence and viral suppression among people living with HIV initiating ART with high pre-ART CD4 counts.
- This study assessed virological outcomes in initiation ART independent of CD4 count in the HPTN 071 (PoPART) trial in South Africa, in which ART initiation irrespective of CD4 count was offered almost three years prior to routine implementation in the country.
- Virological outcomes of people initiating ART were compared in strata of baseline CD4 count.

**METHODS**

- A cohort study including all initiators ART since Jun. 2014 at three primary healthcare facilities was conducted in South Africa, using routinely collected facility-based clinical data.
- These facilities were part of the full intervention arm (PeP) of the HPTN 071 (PoPART) cluster-randomized trial, which offered ART regardless of CD4 count for all adults living with HIV.
- Concomitant antiretroviral therapy was determined by institutional guidelines at the time of ART initiation.
- During the study period, adults attending public clinics were eligible to initiate ART with baseline CD4 count ≥ 500 cells/µL until January 2015 and thereafter with CD4 count ≥ 350 cells/µL.
- Multivariable analyses were used to estimate relative risks of elevated viral load on ART, and Kaplan-Meier analyses and Cox regression were used to analyze time-to-event outcomes.

**RESULTS**

- Among those with baseline CD4 count ≥500 cells/µL, 5% was at risk at one month intervals to 30 months of ART.
- Those with baseline CD4 count <200 cells/µL, 5.3% compared to those with CD4 count 200–499 cells/µL, 5.0%.
- Those with CD4 count >200 cells/µL, had an increased risk of an elevated viral load (25.4%, HR=1.40 (95% CI, 1.33-1.47), P<0.0001), compared to those with baseline CD4 count <200 cells/µL.
- The incidence of VF (two consecutive viral loads >100 copies/ml) was inversely related to baseline CD4 count, declining from 7.0 per 100 person-years for those with baseline CD4 count <200 cells/µL, to 2.0 for those with CD4 count 200–499 cells/µL, to 0.5 for those with CD4 count ≥500 cells/µL (P=0.0002).
- After 24 months, the cumulative probability of VF was 19.6%, 5.3%, and 0.7% in these groups, respectively (Figure 2).
- Multivariable analyses revealed that patients with baseline CD4 count >500 cells/µL, had an independently reduced risk of VF, adjusted hazard ratio (HR)=0.23 (95% CI: 0.05-0.97, P=0.045) (Table 2).

**CONCLUSIONS**

- Despite initial concerns of reduced ART adherence amongst clinically well HIV-positive people initiating ART with high CD4 counts, virological outcomes of participants with CD4 count ≥500 cells/µL, were significantly improved when compared to those with baseline CD4 count <500 cells/µL.
- These findings provide support for and are encouraging in the context of universal ART implementation in Africa.
- Expansion of programs targeting early ART initiation are important to reach the UNAIDS 2nd and 3rd “90” targets of ART coverage and viral suppression.

**Table 1: Proportions with an elevated viral load (> 400 copies/ml) and baseline predictors of an elevated viral load**

<table>
<thead>
<tr>
<th>CD4 Count (cells/µL)</th>
<th>At Baseline</th>
<th>Multivariable analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;200</td>
<td>47/1694 (2.8)</td>
<td>Reference</td>
</tr>
<tr>
<td>200–499</td>
<td>36/1561 (2.3)</td>
<td>2.00 (1.3–3.0)</td>
</tr>
<tr>
<td>≥500</td>
<td>23/1024 (2.2)</td>
<td>0.70–5.71</td>
</tr>
</tbody>
</table>

**Table 2: Predictors of confirmed virological failure after starting antiretroviral treatment**

<table>
<thead>
<tr>
<th>Baseline CD4 Count (cells/µL)</th>
<th>Multivariable analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;200</td>
<td>Reference</td>
</tr>
<tr>
<td>200–499</td>
<td>2.01 (0.82–5.00)</td>
</tr>
<tr>
<td>≥500</td>
<td>0.22 (0.08–0.58)</td>
</tr>
</tbody>
</table>

**Figure 1: Proportion of participants with elevated viral load (>400 copies/ml) according to baseline CD4 count strata and time an antiretroviral treatment.**

**Figure 2: Kaplan-Meier failure estimates of confirmed virological failure (two consecutive viral loads >100 copies/ml) according to baseline CD4 count strata after starting antiretroviral treatment.**

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