Clinical and virologic outcomes of six first-line regimens in a large ART program in Nigeria


1Northwestern University PEPFAR / APIN Program since mid-2005.
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ABSTRACT

Background: Over 35,000 volunteers have received antiretroviral therapy (ART) through the Northwestern University PEPFAR / APIN Program providing access to ART in 95% of all CD4+ cell counts. This study documents the clinical outcomes of patients on the first-line regimens as part of their ongoing treatment in the Northwestern University PEPFAR / APIN Program.

Methods: We conducted a retrospective cohort study to evaluate the virologic and clinical outcomes in a large ART program in Nigeria. Estimating the proportion of patients who switch ART and the rates of virologic failure were conducted by using Pearson’s chi-square and Student’s t-test as appropriate.

Results: Overall, the study population was 61.9% female and had an age median of 35.4 years (standard deviation, SD), 9.0. Of all patients reinitiating ART, 36.4% of patients had a CD4 count ≤ 100 cells/mm3 (95%, 0-12mo). The proportion of patients with average adherence < 95% during the study period varied by regimen. The highest rates of virologic failure were observed among patients starting with the efavirenz (EFV) regimen, with a VF rate of 16.1% compared to azidovudine (AZT)/3TC/NVP (9.5%, p < 0.001).

Conclusion: The data from the Northwestern University PEPFAR / APIN Program provide an important opportunity to understand the clinical and virologic outcomes of ART regimens in a large ART program in Nigeria. The results suggest that, while the usage of EFV is common, the high rates of virologic failure observed among patients starting with the EFV regimen may be due to lack of adherence or treatment failure. Further studies are needed to determine the factors contributing to the high rates of virologic failure among patients starting with EFV.

METHODS (Continued)

• Exclusion criteria for VF analysis were:
  - Do not switch to a PI-based regimen due to VF.
  - Misreporting of VL result (≤ 2x results after baseline).
  - Missing baseline CD4 or VL.

• Secondary endpoints include: change in CD4 cell count between baseline and 12 months, and adherence to ART over 12 months.

• Univariate analysis of associations across the six first-line regimens or between NNRTI-based regimens (defined as NVP or EFV with any NRTI or NNRTI-containing regimens (defined as AZT/3TC, TDF/3TC, or d4T/3TC with any NRTI) was conducted using Pearson’s chi-square or Student’s t-test as appropriate.

RESULTS

• During the study period, 12,200 ART-naïve patients from four sites initiated ART with AZT/3TC or TDF/3TC or d4T/3TC plus NVP or EFV or EFV.

Table 1: Comparison of discontinue and ARV switch rates across all first-line ART groups (n = 12,200)

<table>
<thead>
<tr>
<th>ART Regimen</th>
<th>N (n=12,200)</th>
<th>Discontinue (n=524)</th>
<th>Discontinue rate (95% CI)</th>
<th>ARV switch (n=1607)</th>
<th>ARV switch rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZT/3TC</td>
<td>1744</td>
<td>18</td>
<td>1.0% (0.8-1.2)</td>
<td>115</td>
<td>6.6% (5.7-7.5)</td>
</tr>
<tr>
<td>TDF/3TC</td>
<td>2287</td>
<td>26</td>
<td>1.1% (0.9-1.3)</td>
<td>126</td>
<td>5.5% (4.7-6.3)</td>
</tr>
<tr>
<td>d4T/3TC</td>
<td>194</td>
<td>1</td>
<td>0.5% (0.3-0.7)</td>
<td>31</td>
<td>16.1% (14.2-18.0)</td>
</tr>
<tr>
<td>AZT/3TC/EFV</td>
<td>184</td>
<td>4</td>
<td>2.2% (1.5-2.9)</td>
<td>33</td>
<td>18.0% (15.3-20.7)</td>
</tr>
<tr>
<td>TDF/3TC/EFV</td>
<td>729</td>
<td>14</td>
<td>1.9% (1.5-2.3)</td>
<td>69</td>
<td>9.5% (7.7-11.3)</td>
</tr>
<tr>
<td>d4T/3TC/EFV</td>
<td>414</td>
<td>21</td>
<td>5.1% (4.0-6.2)</td>
<td>102</td>
<td>24.9% (21.8-28.0)</td>
</tr>
</tbody>
</table>

• The identified difference in VF rates between TDF/3TC/NVP and AZT/3TC/NVP groups was statistically significant (16.1% versus 9.5%, p < 0.001).

• Though notably in the switch analysis, rates of VF switch were higher in patients on EFV versus NVP-based ART (16.1% versus 11.1%, respectively, p < 0.001).

• Previous clinical trials have documented the superiority of TDF/3TC/NVP over EFV/3TC/NVP in our purely virologic-based endpoint (which excludes discontinues, switches, and missing data).

• Rates of VF were similar between these two groups (p = 1.0).

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• Rates of VF switch were higher among patients initiating AZT/3TC containing ART. Though this high rate of switches can be explained by programmatic changes in preferred NNRTI backbone during the study period, interestingly rates of VF were also highest among patients receiving d4T/3TC (16.9% with either NVP or EFV).

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CONCLUSION

• Now that access to various ARV agents is more widespread, it is important to better understand how different ARV regimens impact rates of LTFU, switch, and virologic failure.

• The identified difference in VF rates between TDF/3TC/NVP and AZT/3TC/NVP groups was further evaluated in our cohort, see Abstract: THPE-0117, AIDS 2010.

REFERENCES

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