Inferior outcome of poor prognostic phenotype non-Hodgkin’s lymphoma treatment among HIV positive patients compared with HIV negative counterparts in the HAART era.

(ASCO abstract June 2007: Othieno-Abinya NA, Abwao HO, Kiarie GW)
- HIV-lymphoma Vs non-HIV lymphoma – 60/1 risk Systemic BL/DLBCL.
- PCNS – DLBCL/BL
- Primary effusion – DLBCL /??? HD.
- From HAART introduction – diminishment of ARL in US/Europe.
- 20 fold drop in PCNSL. *(Kirk et al. Blood 2001)*
  - Controlling HIV critical determinant of ARL.
Clinical Presentation of ARL

Systemic ARLs – Aggressive clinical course

- Extralymphatic
- 20% of ARL – CNS involvement
- EBV in systemic ARL – CNS disease/relapse hence CNS prophylaxis (Cingolani et al. JCO 2000)

- HAART – improvement in prognosis of HIV-DLBCL, but not HIV-BL.
- OS in preHAART HIV-DLBCL – 8.3/12
- OS in HAART-HIV-DLBCL - 43.2/12. This is 6.4 and 5.7 for HIV-BL (Lim ST, et al. J Clin Oncol 2005) - May require more intensive protocols like hyperCVAD.
Factors predicting for negative outcome

- CD4+ CELLS <100
- Age >35 years
- IVD use

(Strauss et al, JCO 1998)

Median Survival Pattern According to:
0-1 of the factors – 46 weeks
2 of the factors – 44 weeks
3 of the factors – 18 weeks
Another study:
- Age > 40 years
- High serum LDH
- CD4+ cells <100
- St III or IV disease
- IVD use
- Impaired performance status

(Gabarre K et al. AM J Med 2001)

High IPI Score – poor outcome in CHOP treated patients.

# Mainly pre-HAART patients included
ARL THERAPY

Half dose m-BACOD – no impact
(Kaplan et al. N Engl J Med 1997)
- Dose attenuated CHOP inferior results (largely abandoned).
- Better efficacy with infusional regimens –
  - EPOCH – 75% durable CR
(Gutierrez et al. J CO 2000)
  - CDE – 58% RR
(Sparano et al. J CO 1996)

CODOX-M/IVAC on HIV-BL or non-HIV-BL –
OTHERS:
R-CHOP/R-CHOE – CR86%; PFS 79%
(Tirelli U et al, Cancer Res 2002)
-Salvage of relapsed or refractory ARL with HDT and AHPC support feasible in HAART era.
Toxicity similar between HIV-DLBCL/BL and nonHIV-DLBCL/BL on HAART/intensive chemotherapy


Drug interactions not a problem between:

- CHOP/Stavudine + lamivudine + indinavir
  - No toxicity
  - Doxorubicin/indinavir pharmacokinetics unperturbed
  - 50% reduction in CTX clearance but no toxicity

Methodology

- We did a retrospective analysis of 75 cases of aggressive and highly aggressive phenotypes of NHL at HURL-ONCO.

- June 1994 to May 2006 (HAART and pre-HAART Era for Kenya)
Methodology cont’d

- Demographic details, DOD, Histology+ IHC, HIV status, CD 4+ cell count, Viral load,
- PS, IPI, Treatment given,
- CR, PR, SD and PD
- Relapse, 2nd line protocol, response to 2nd line, F-up. Analysed using the Fischers exact test and CMH test.
### PATIENT CHARACTERISTICS

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No.</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>43</td>
<td>(57.3%)</td>
</tr>
<tr>
<td>Females</td>
<td>32</td>
<td>(42.7%)</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13-19</td>
<td>4</td>
<td>(5.3%)</td>
</tr>
<tr>
<td>20-29</td>
<td>27</td>
<td>(36%)</td>
</tr>
<tr>
<td>40-59</td>
<td>31</td>
<td>(41.3%)</td>
</tr>
<tr>
<td>60-79</td>
<td>12</td>
<td>(16.0%)</td>
</tr>
</tbody>
</table>
HIV status patients

- Positive 32 (42.7%)
- Negative 32 (42.7%)
- Unknown 11 (14.7%)

According to ethnicity:
- Luo 77% NHL+
- Luhya 44% NHL+
- Others 32% NHL+
### Treatment against HIV status

<table>
<thead>
<tr>
<th>PROTOCOL</th>
<th>CHOP</th>
<th>R-CHOP</th>
<th>MACOP-B</th>
<th>OTHERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>POSITIVE</td>
<td>13 (37%)</td>
<td>6 (54%)</td>
<td>7 (53%)</td>
<td>2 (25%) T=28</td>
</tr>
<tr>
<td>NEGATIVE</td>
<td>17 (49%)</td>
<td>4 (36%)</td>
<td>6 (46%)</td>
<td>4 (50%) T=31</td>
</tr>
<tr>
<td>U.KNOWN</td>
<td>5 (14%)</td>
<td>1 (9.1%)</td>
<td>0</td>
<td>2 (25%) T=8</td>
</tr>
<tr>
<td>HISTOLOGY/STATUS</td>
<td>DLBCL</td>
<td>Transf. Fo</td>
<td>Burkitts L</td>
<td>“Aggressive”</td>
</tr>
<tr>
<td>------------------</td>
<td>---------</td>
<td>------------</td>
<td>------------</td>
<td>--------------</td>
</tr>
<tr>
<td>positive</td>
<td>12 (50%)</td>
<td>2 (28.6%)</td>
<td>2 (67%)</td>
<td>14 (44%)</td>
</tr>
<tr>
<td>negative</td>
<td>7 (29.2%)</td>
<td>4 (57.1%)</td>
<td>1 (33%)</td>
<td>13 (41%)</td>
</tr>
<tr>
<td>Others</td>
<td>5 (20.8%)</td>
<td>1 (14.3%)</td>
<td>0</td>
<td>5 (15%)</td>
</tr>
</tbody>
</table>
Patient Outcome against HIV status \((p<0.0001)\)

<table>
<thead>
<tr>
<th>OUTCOME</th>
<th>CR</th>
<th>PR/SD/PD</th>
<th>DEFAULT</th>
</tr>
</thead>
<tbody>
<tr>
<td>POSITIVE</td>
<td>7 (21%)</td>
<td>5 (36%)</td>
<td>15 (65%)</td>
</tr>
<tr>
<td>NEGATIVE</td>
<td>24 (73%)</td>
<td>5 (36%)</td>
<td>3 (13%)</td>
</tr>
<tr>
<td>U.KNOWN</td>
<td>2 (6%)</td>
<td>4 (28%)</td>
<td>5 (22%)</td>
</tr>
</tbody>
</table>
# IPI Score Against Outcome \((p=0.2192)\)

<table>
<thead>
<tr>
<th>Score Response</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>Unkown</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>2</td>
<td>4</td>
<td>3</td>
<td>14</td>
<td>10</td>
</tr>
<tr>
<td>PR/SD/PD</td>
<td>0</td>
<td>1</td>
<td>11</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>Default</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>14</td>
</tr>
</tbody>
</table>
Patient outcome against CD4⁺

Fischers exact (p=0.1423) CMH p=0.1513

<table>
<thead>
<tr>
<th>CD4⁺/RESPONSE</th>
<th>&lt;50</th>
<th>50-99</th>
<th>100-199</th>
<th>200+</th>
<th>UNKNOWN</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>PR/SD/PD</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>TRD</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 T=2</td>
</tr>
<tr>
<td>UNKNOWN</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>10</td>
</tr>
</tbody>
</table>
## Survival vs Status

**Fischer exact test**

\[ p = 0.0036 \]

\[ (CMH \ p = 0.0060) \]

<table>
<thead>
<tr>
<th>Survival/Status</th>
<th>0-12mth</th>
<th>12-36mths</th>
<th>&gt;36mth</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>15</td>
<td>1</td>
<td>0</td>
<td>16</td>
</tr>
<tr>
<td>Negative</td>
<td>7</td>
<td>5</td>
<td>5</td>
<td>17</td>
</tr>
</tbody>
</table>
Survival differences Between Positive and Negative

- 33 dead after 8/12 median f/up, range 1 – 96,
- Overall median f/up 7.5/12, range 1-136/12, mean 21/12
- HIV Positive
  - Mean f/up - 9/12
  - Median f/up- 5.5/12
- HIV Negative: P=0.0036
  - Mean f/up 17/12
  - Median f/up- 30/12
Summary of Study

- More men, age 20-59yrs PREVALENT, equal HIV +ve and –ve
- Histology: higher aggressive phenotypes in HIV
- Better outcome associated with HIV-ve

* NOTE - CR rates for HIV- cases comparable to best of centres
Summary Continued

- IPI score no significant diff in HIV status
- CD4$^+$ no. sig diff probably due to small no.
- Standard chemotherapy, standard dosing in HIV NHL. Use of supporting factors and HAART.