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 JMed 1997)

- Dose attenuated CHOP inferior results

(largely abandoned).

- Better efficacy with infusional regimens –
  - EPOCH – 75% durable CR

(Gutierrez et al. J C O 2000)

  - CDE – 58% RR

(Sparano et al. J C O 1996)

CODOX-M/IVAC on HIV-BL or non-HIV-BL - Better 2-year EFS than less intensive regimens(Wang ES, et al. Cancer 1998)

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.

(Castello RT, et al- Cancer 2004. Re A et al-J Clin Oncol 2003)

Toxicity similar between HIV-DLBCL/BL and nonHIV-DLBCL/BL on HAART/intensive chemotherapy

(Thomas DA, et al. J Clin Oncol 1999)

Drug interactions not a problem between:

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

(AIDS Malignancy Consortium – Ratner et al. J C O 2001)

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

Characteristic	No.	Percentage
Sex		
Males	43	(57.3%)
Females	32	(42.7%)
Age		
13-19	4	(5.3%)
20-29	27	(36%)
40-59	31	(41.3%)
60-79	12	(16.0%)

HIV status patients

- Positive 32 (42.7%)
- Negative 32 (42.7%)
- Unknown 11 (14.7%)
- According to ethinicity:
  - Luo 77% NHL+
  - Luhya 44% NHL +
  - Others 32% NHL+

Treatment against HIV status

PROTOCOL	CHOP	R-CHOP	MACOP-B	OTHERS
POSITIVE	13 (37%)	6 (54%)	7 (53%)	2(25%) T=28
NEGATIVE	17 (49%)	4 (36%)	6 (46%)	4 (50%)T=31
U.KNOWN	5 (14%)	1 (9.1%)	0	2 (25%) T=8

HISTOLOGY AGAINST HIV STATUS

HISTOLOGY/STATUS	DLBCL	Transf.Fo	Burkitts L	“Aggressive”	OTHERS
positive	12 (50%)	2 (28.6%)	2 (67%)	14 (44%)	2 (22%)
negative	7 (29.2%)	4 (57.1%)	1 (33%)	13 (41%)	7 (77.8%)
Others	5 (20.8%)	1 (14.3%)	0	5 (15%)	0

Patient Outcome against HIV status *(p<0.0001)*

OUTCOME	CR	PR/SD/PD	DEFAULT
POSITIVE	7 (21%)	5 (36%)	15 (65%)
NEGATIVE	24(73%)	5(36%)	3 (13%)
U.KNOWN	2 (6%)	4 (28%)	5 (22%)

IPI SCORE AGAINST OUTCOME *(p=0.2192)*

SC0RE / RESP.	0	1	2	3	UNKNOWN
CR	2	4 (6)	3	14 (17)	10
PR/SD/PD	0	1 (1)	11	10 (21)	2
DEFAULT	0	0	0	9	14

Patient outcome against $CD4^+$

fischers exact ***(p=0.1423) CMH p=0.1513***

$CD4^+$ /RESPONSE	<50	50-99	100-199	200+	UKNOWN
CR	1	1	2	1	4
PR/SD/PD	3	2	1	0	0
TRD	1	0	0	0	1 **T=2**
UNKNOWN	1	0	2	2	10

Survival vs Status *fischer exact t=* ***(p=0.0036) (CMH p=0.0060)***

SURVIVAL/STATUS	0-12mth	12-36mths	>36mth	TOTAL
POSTIVE	15	1	0	16
NEGATIVE	7	5	5	17

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.