The evolution of HIV associated lymphoma over three decades

Ramaswami R[1]., Chia G[3]., Dalla Pria A[1]., Pinato DJ[1]., Parker K.[1], Nelson M.[2], and Bower M.[1,3]

Department of Oncology[1] / HIV[2] National Centre for HIV malignancies Chelsea and Westminster Hospital NHS Foundation Trust

Imperial College London, School of Medicine[3]

Introduction

Human Immunodeficiency Virus (HIV) infection increases the risk of cancer and after Kaposi's sarcoma, lymphomas are recognized as the second most common malignancy among people living with HIV (PLWH) from cohorts originating within Europe, Australia and North America.[1]

The emergence of combined antiretroviral therapy (cART) and improvements in the management of opportunistic infections have altered the HIV epidemic over the last 30 years. We aimed to assess changes to the biology and outcomes of HIV-associated lymphomas over this period at the national centre for HIV oncology in the United Kingdom.

Patients and Methods

Clinical characteristics at lymphoma diagnosis have been prospectively collected since 1986, along with details of lymphoma treatment and outcomes. The clinical features and outcomes were compared between 3 decades: pre-cART decade (1986-1995), early cART decade (1996-2005) and late cART decade (2006-2015).

Survival was calculated from lymphoma diagnosis until death (overall survival) or last follow-up. Survival curves were plotted according to the method of Kaplan and Meier.

References

1. Grulich, A.E., van Leeuwen, M. T., Falster, M. O, et al., *Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. .* Lancet, 2007. **370**: p. 59-67.
2. Rubinstein PG, Aboulafia DM, Zloza A., *Malignancies in HIV/AIDS: from epidemiology to therapeutic challenges. .* AIDS, 2014. **28**(4): p. 453-465.
3. Rios A., *HIV-Related Hematological Malignancies: A Concise Review.* Clinical Lymphoma Myeloma and Leukemia, 2014. **14**(Supplement): p. S96-S103.
4. Lim, S.T., et al., *AIDS-related Burkitt's lymphoma versus diffuse large-cell lymphoma in the pre-highly active antiretroviral therapy (HAART) and HAART eras: significant differences in survival with standard chemotherapy.* J Clin Oncol, 2005. **23**(19): p. 4430-8.

Results

	All N=615 (%)	1986-1995 N=158 (%)	1996-2005 N=200 (%)	2006-2015 N=257 (%)	p
Male (%)	547 (89%)	153 (97%)	178 (89%)	216 (84%)	<0.0003
Mean age at HIV (range)	37 (0-73) years	34 (19-58) years	37 (13-73) years	40 (0-71) years	<0.0001
Mean age at lymphoma (range)	42 (19-78) years	38 (22-59) years	42 (21-78) years	45 (19-75) years	<0.0001
Mean duration HIV (range)	61 (0-362) months	46 (0-137) months	64 (0-249) months	68 (0-362) months	0.53
Prior AIDS (%)	196 (32%)	96 (44%)	54 (27%)	46 (18%)	<0.0001
Median CD4 at lymphoma (range)	130 (0-2308) cells/mm^3	36 (0-763) cells/mm^3	132 (0-814) cells/mm^3	221 (2-2308) cells/mm^3	<0.0001
On cART at lymphoma (%)	264 (43%)	0 (0%)	116 (58%)	149 (58%)	<0.0001
On cART with undetectable plasma HIV VL (%)	158/615 (26%)	0	45/116 (38%)	113/149 (76%)	<0.0003
Lymphoma Subtypes					
PCNSL	69 (11%)	39 (25%)	27 (13%)	3 (1%)	
Systemic B cell	426 (69%)	106 (67%)	145 (72%)	175 (68%)	
DLBCL	312 (51%)	99 (63%)	119 (59%)	94 (37%)	
BL	76 (12%)	4 (3%)	20 (10%)	52 (20%)	
PEL	18 (3%)	3 (2%)	2 (1%)	13 (5%)	
Plasmablastic	20 (3%)	0 (0%)	4 (2%)	16 (6%)	
Hodgkins	96 (16%)	7 (4%)	22 (11%)	67 (26%)	
T-cell	18 (3%)	6 (4%)	4 (2%)	8 (3%)	
Low grade	6 (1%)	0 (0%)	2 (1%)	4 (2%)	
Survival					
2 year overall survival -all lymphomas (95%CI)	51.2% (47.2-55.2)	19.7% (13.1-26.3)	48.2% (42.0-54.4)	74.3% (68.7-79.9)	P<0.0001
5 year overall survival -all lymphomas (95%CI)	45.8% (41.6-50.0)	13.2% (7.4-19.0)	44.5% (37.3-51.7)	69.6% (63.4-75.8)	

Table 1 - Total of 615 (547 male) patients diagnosed with HIV associated lymphomas over 30 years between 1986 and 2015.

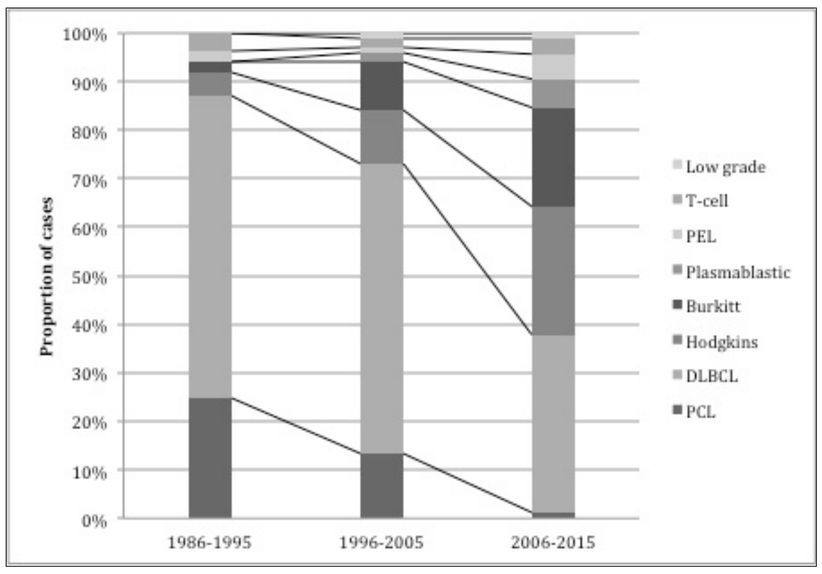

Figure 1: Lymphoma subtypes over three decades, 1986-1995 (pre-cART), 1996-2005 (early cART), 2006-2015 (late cART)

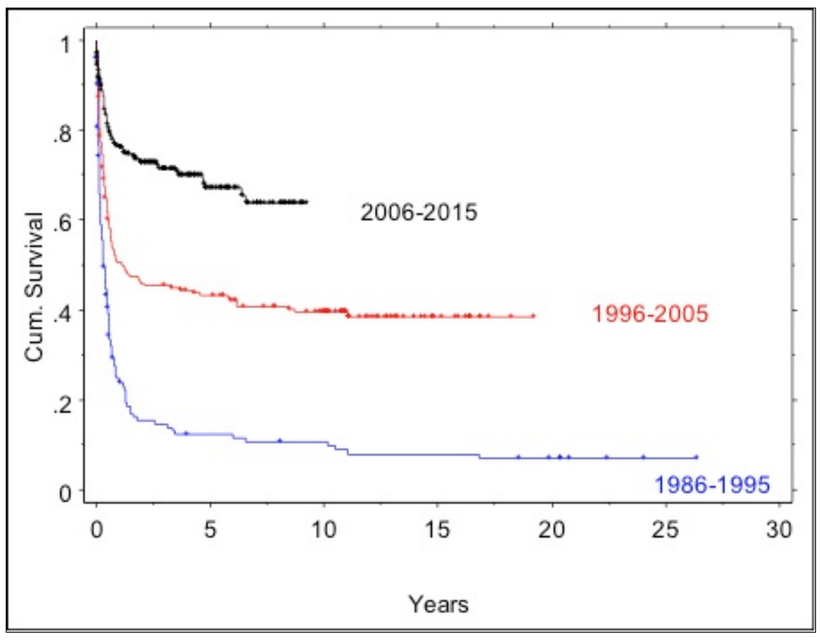

Figure 2: Cumulative survival over three decades among all patients diagnosed with HIV-associated lymphoma.

A total of 615 patients with HIV-associated lymphoma were included in the study: 158 patients in the pre-cART era, 200 patients in the early cART era and 257 patients in the late cART era. In more recent decades patients were older (p<0.0001) and had higher CD4 cell counts (p<0.0001) at lymphoma diagnosis. Over time there has also been a shift in lymphoma histological subtypes, with an increase in lymphoma subtypes associated with moderate immunosuppression. The overall survival for patients with HIV-associated lymphoma has dramatically improved over the 3 decades (p<0.0001).

Conclusion

This study of a single institution prospective cohort of 615 patients over three decades including the pre-cART, early cART and current c-ART eras, demonstrates a change in the baseline characteristics and outcomes of HIV associated lymphoma. The most dramatic evolution has been the rising CD4 cell count at lymphoma diagnosis and the shift towards histological subtypes that are associated with less severe immunosuppression. Within this study, there has been a steady decrease over time in proportion of patients with PCNSL and DLBCL, which are associated with a greater degree of immunosuppression.

The great improvement in overall survival in this study has been well described previously [2, 3, 4] and is attributable to a number of factors including: the use of cART, better focus on opportunistic infection prophylaxis and improved chemotherapy.

Over the last 30 years, the clinical demographic of HIV associated lymphomas has evolved and the outcomes have improved.

SSAT ST STEPHEN'S AIDS TRUST

Chelsea and Westminster Hospital NHS NHS Foundation Trust

Imperial College London