HSCT in Burkitt Lymphoma

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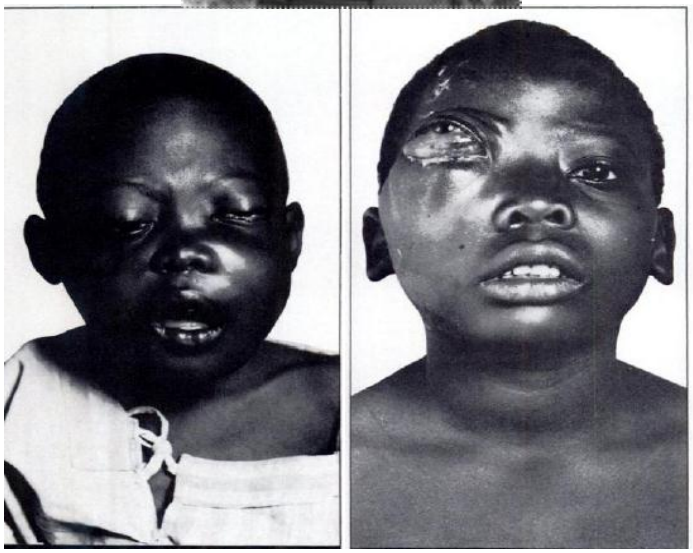
KFSHRC, Riyadh Saudi Arabia

3rd WBMT Scientific Symposium
Cape Town
16 Nov 2014

Burkitt Lymphoma: A story of many stories

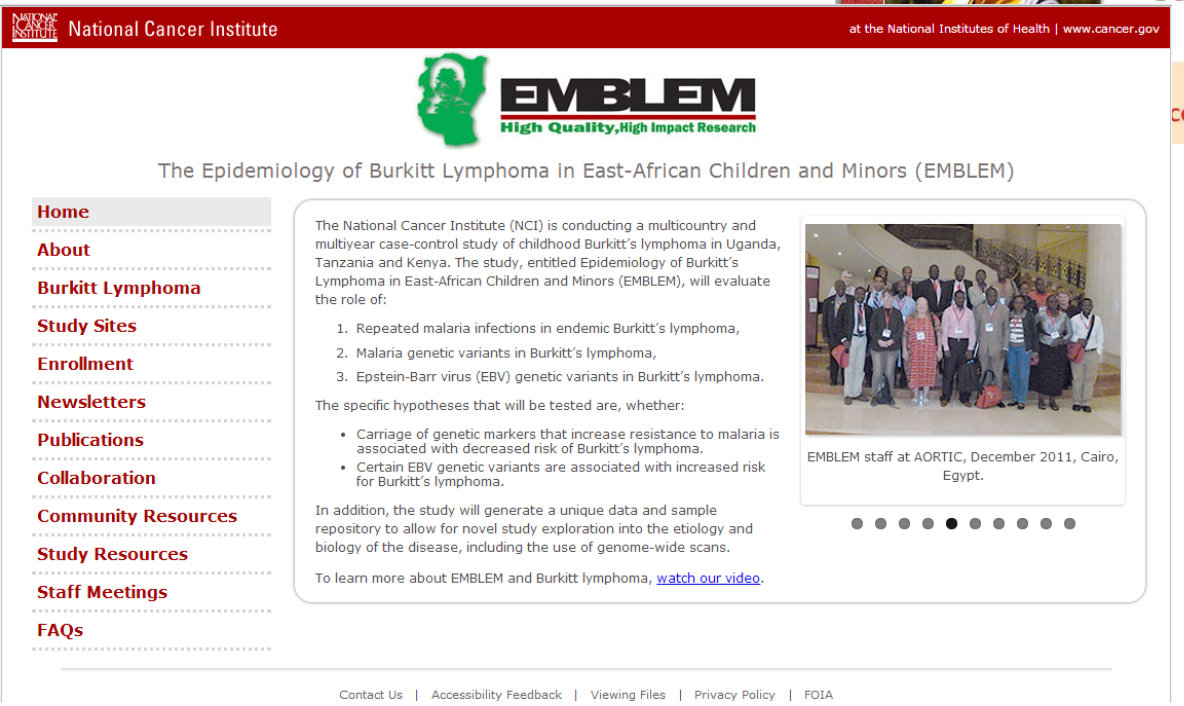
- Denis Burkitt 1958
- Infection and Cancer
  - Epstein-Barr virus
  - Malaria
  - HIV
- Genetics of cancer
  - Discovery of t(8;14) in BL cells
    - (Zech 1976)



Burkitt Lymphoma: A story of many stories

- Collaboration
  - NCI and Uganda Cancer Institute
    - COM
  - INCTR
  - EMBLEM
  - AORTIC
  - BIG CAT
- ?WBMT

Collaboration



http://emblem.cancer.gov/

Progress and setbacks..

- Progress
  - Remissions with cyclophosphamide
  - Newer agents
    - Intensive chemotherapy
    - Rituximab
- And setbacks
  - HIV + associated lymphomas
  - Social /political

BURKITT'S LYMPHOMA (BL)

- High grade NHL
  - Sporadic form 1-2% of NHL in N.america and W.Europe
  - Endemic form : Africa , Papua New Guinea
  - Immunodeficiency associated

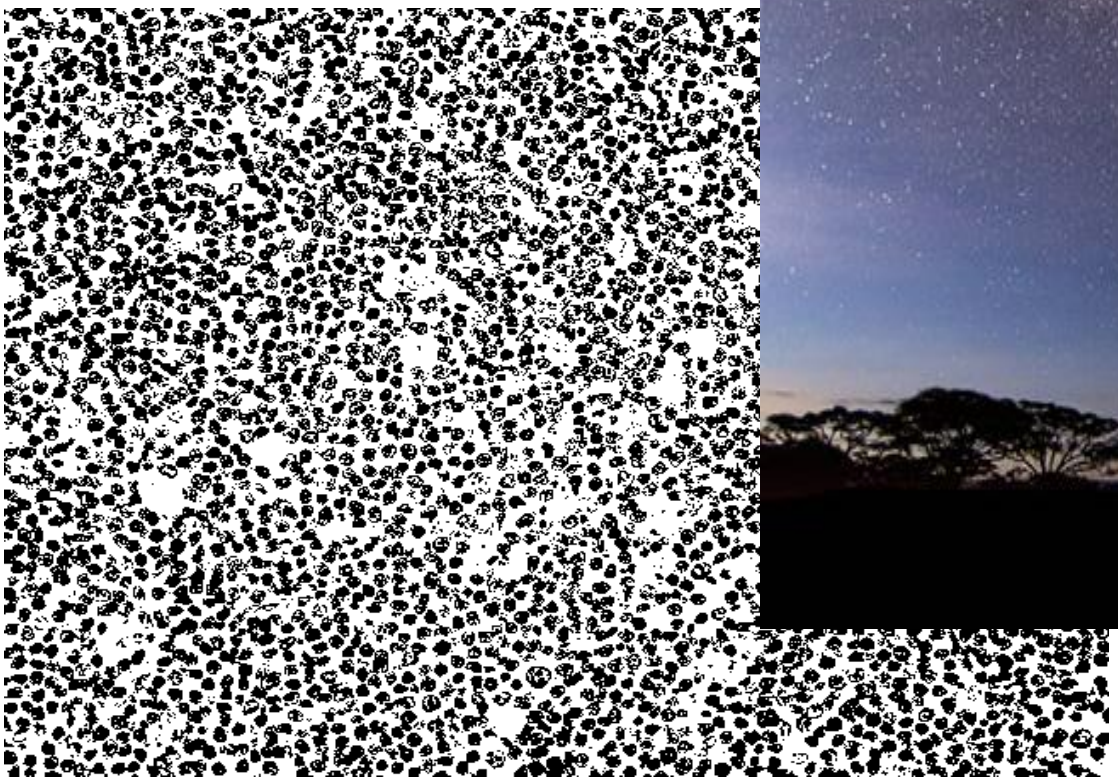
- Characteristic Morphology
  - Medium sized, clumped chromatin,
  - Diffuse monotonous pattern
  - High proliferative index – Ki-67 >95-100%

- Immunophenotype:
  - IgM+ (vs ALL), Bcl-6+, CD19+, CD20+, CD22+, CD10+, CD79a+
  - CD5-, CD23-, Bcl2-, TdT- (vs ALL)

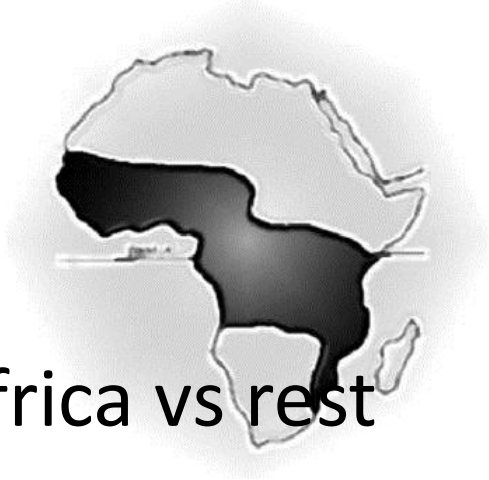
- Cytogenetic evidence of c-myc rearrangement

- Burkitt-like lymphoma (BLL)
  - WHO 2008:
  - B cell lymphoma unclassifiable with features intermediate between diffuce large b-cell lymphoma and burkitt's lymphoma
    - ?(BCLUFI-DLBCL/BL)

Starry sky ....



Why HSCT in BL



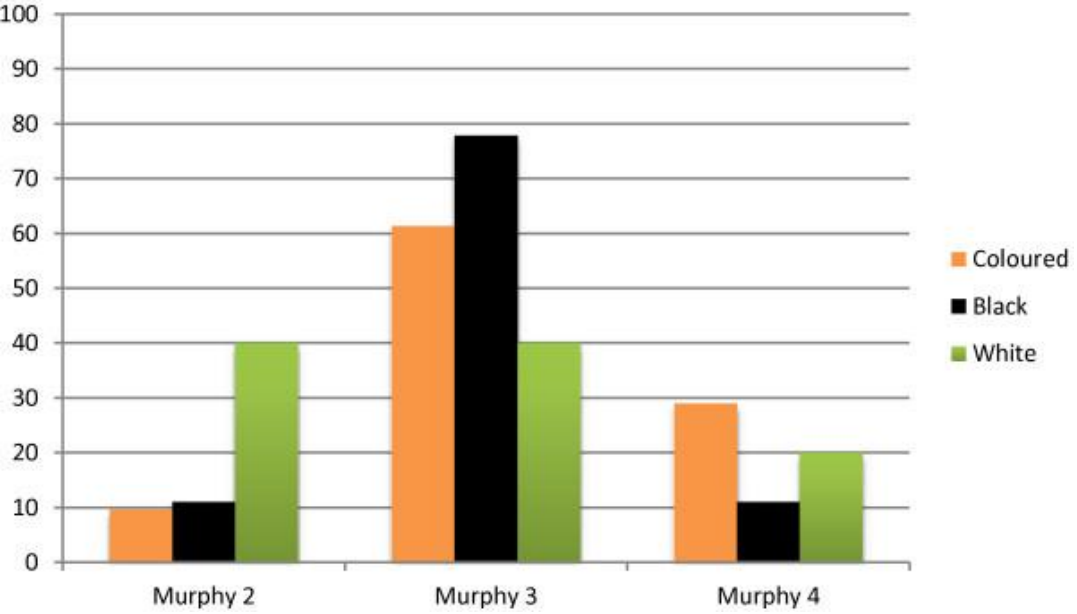
- Higher incidence in Sub-Saharan Africa vs rest of the world
  - Endemic
    - Tanzania 50-70% of all childhood cancers
    - Overall crude BL incidence was 4.2 per 100,000 M>F,
  - HIV
- Chemotherapy outcomes still inferior to outcomes in west

Aka et al , Ped Blood and Ca, 2012

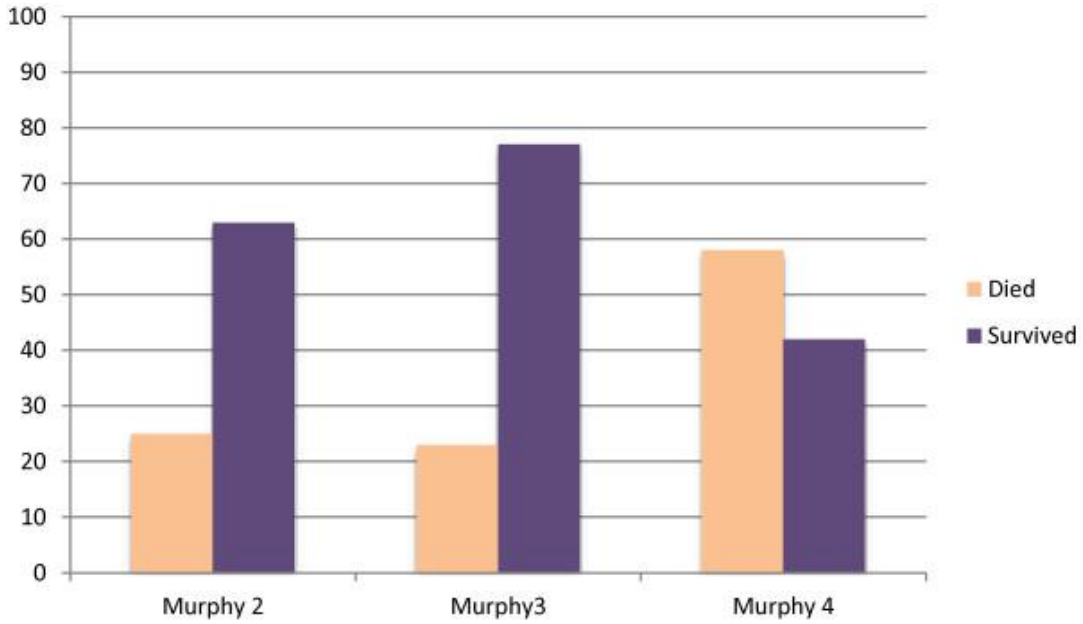
S.Africa –Centre experience

- NHL 120 cases /year
  - 70% HIV +ve
  - DLBCL 40%
  - BL 25%
  - BL-like 15%

Patel, personal communication
McGrath et al, Ecancermedicalscience. 2009; 3: 159.



Median age: 6y
OS = 64%



Stefan et al

Chemotherapy in BL

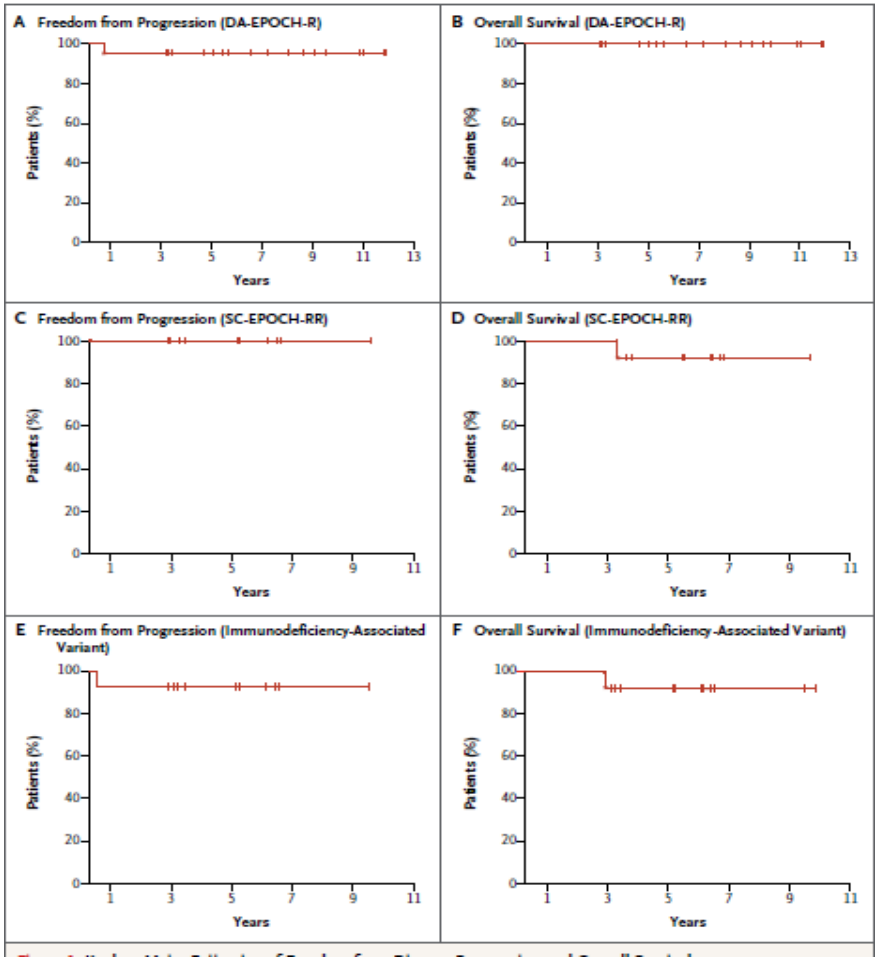
- Standard of Care
  - Hyper-CVAD
  - CODOX-M /IVAC
  - DA-EPOCH
  - LMB / FAB

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

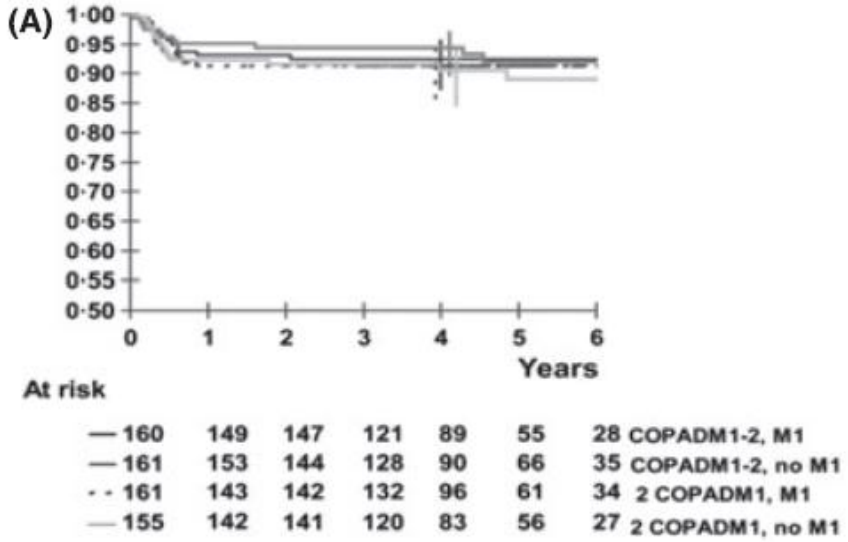
Low-Intensity Therapy in Adults with Burkitt's Lymphoma

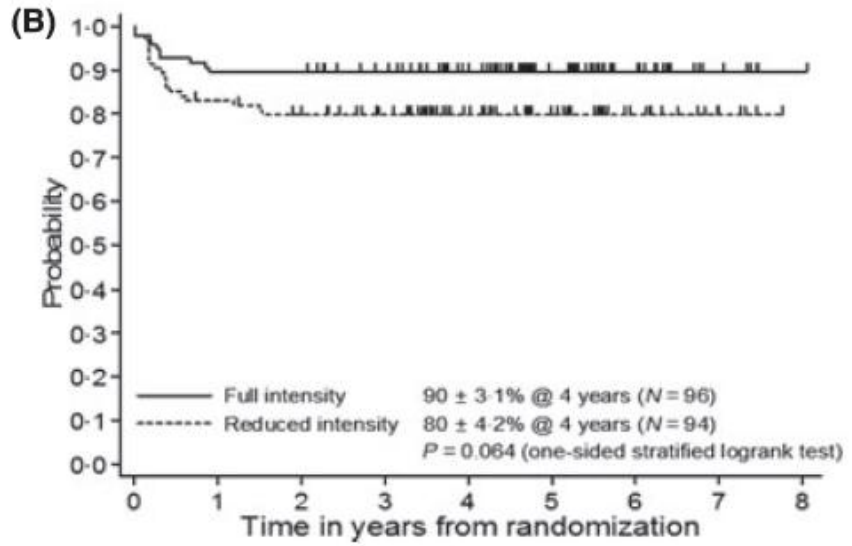
Kieron Dunleavy, M.D., Stefania Pittaluga, M.D., Ph.D., Margaret Shovlin, R.N., Seth M. Steinberg, Ph.D., Diane Cole, M.S., Cliona Grant, M.D., Brigitte Widemann, M.D., Louis M. Staudt, M.D., Ph.D., Elaine S. Jaffe, M.D., Richard F. Little, M.D., and Wyndham H. Wilson, M.D., Ph.D.



- N=30
- HIV+ =11
- SC-EPOCH-RR
  - HIV+

Pediatric FAB-LMB96 protocols





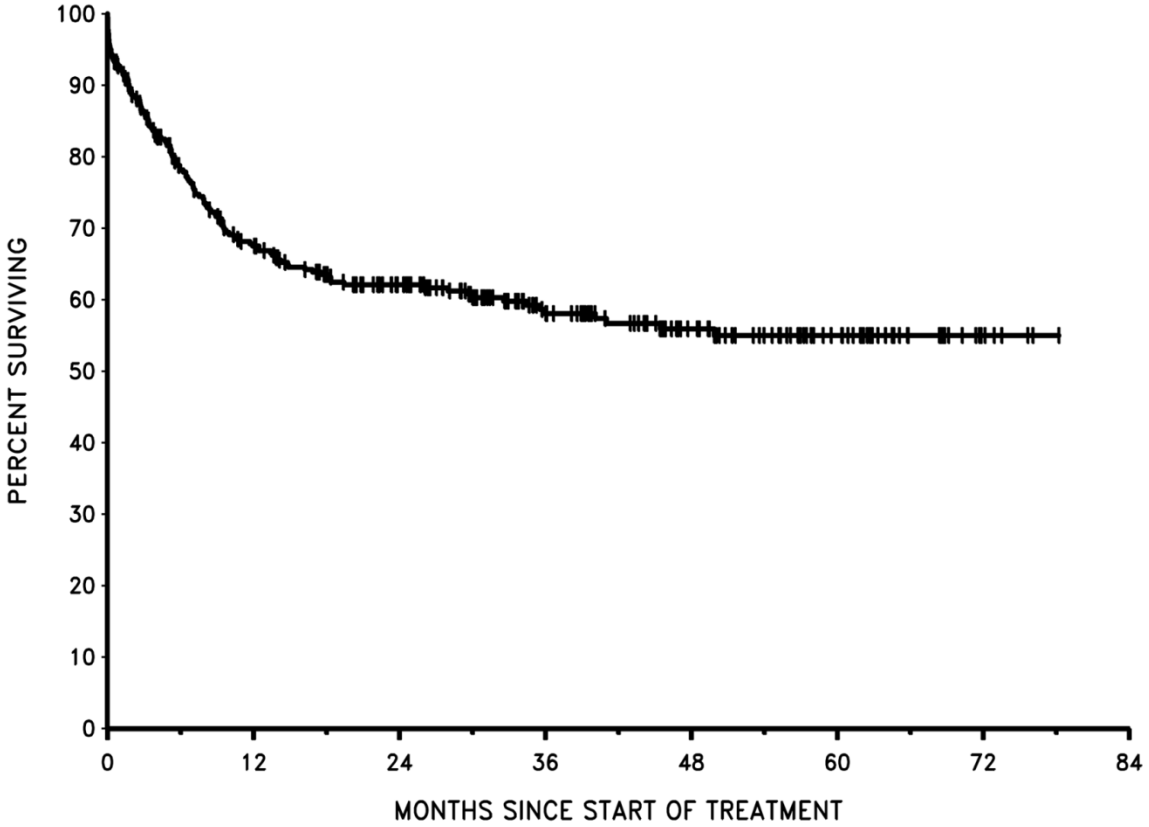
INCTR Protocol

Regimen Chemotherapy Dose and schedule
First Line (FL)1
Cyclophosphamide 1200 mg/m2 i.v., day 1
Vincristine 1.4 mg/m2, i.v., day 1
Methotrexate 75 mg/m2, i.v., day 1
Methotrexate 12 mg, IT days 1 and 83
Cytarabine 50 mg, IT, day 44

Second Line (SL)5 Etoposide 60 mg/m2, i.v., days 1–3
Ifosfamide 1500 mg/m2, i.v., days 1–3
Mesna 300 mg/m2, i.v. with Ifosfamide, then × 3 doses every 3 hours post Ifosfamide, days 1–3
Cytarabine 100 mg/m2, i.v., days 1–3
Cytarabine 50 mg. IT, day 44
Methorexate 12 mg, IT days 1 and 83
Repeat First Line (RFL) Same as FL Same as FL

Ngoma et al .Br J Haematol. 2012

INCTR protocol
Tanzania, Kenya, Nigeria



N=356
Median age: 7 (2-59)
HIV + = 4.6%

Ngoma et al .Br J Haematol. 2012

EMBLEM reports

- OS at Tygeberg 2y OS =47%
  - 96% HIV+, 82% LMB
  - 22% infectious deths
  - 22% disease progression
  - Non-compliance 40%
- Cote D'Ivoire
  - Children
  - CR 35%, PR 65% ; 24% relapse
- Nigeria
  - COM / COMP
  - 2y OS 57% ; EFS 53%

Role of SCT in BL

- Not well defined
- Limitations of available evidence:
  - Most studies from transplants ‘pre-rituximab’
  - Patients with BL analysed with patients with Burkitt’s like (BLL) +/- lymphoblastic lymphoma
  - Paediatric cases included
  - Small numbers of BL patients in prospective studies that have investigated role of SCT in aggressive lymphomas

Limitations to transplantation

- Alternatives
  - Second line salvage therapy
- Toxicity
  - > chemotherapy
- HIV
- Cost

Autologous SCT in BL

Autologous SCT

- Who may benefit

- Is there a role for ASCT upfront in BL?

Autologous SCT

- Who may benefit
- Is there a role for ASCT upfront in BL?
  - Generally – NO
- What is the role in resource poor setting

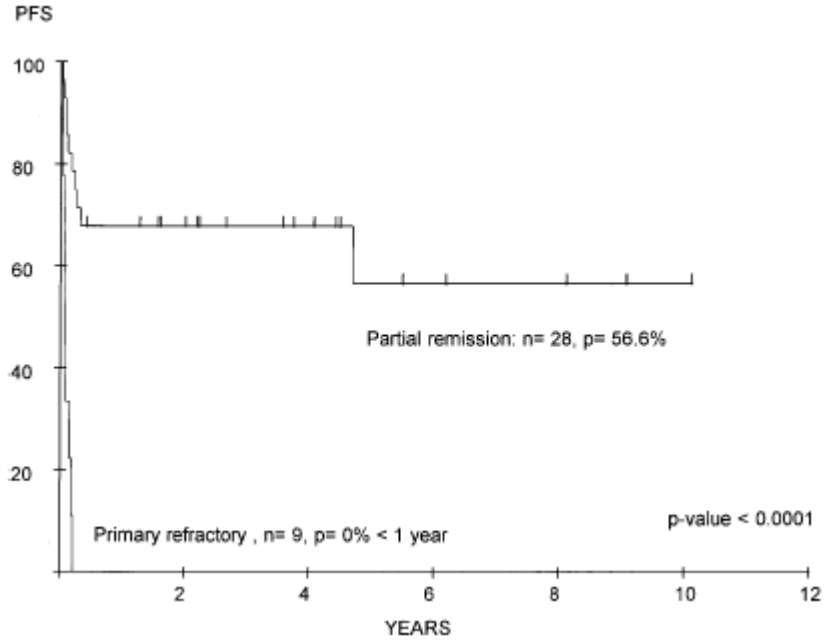
Studies of ASCT including BL : Adult

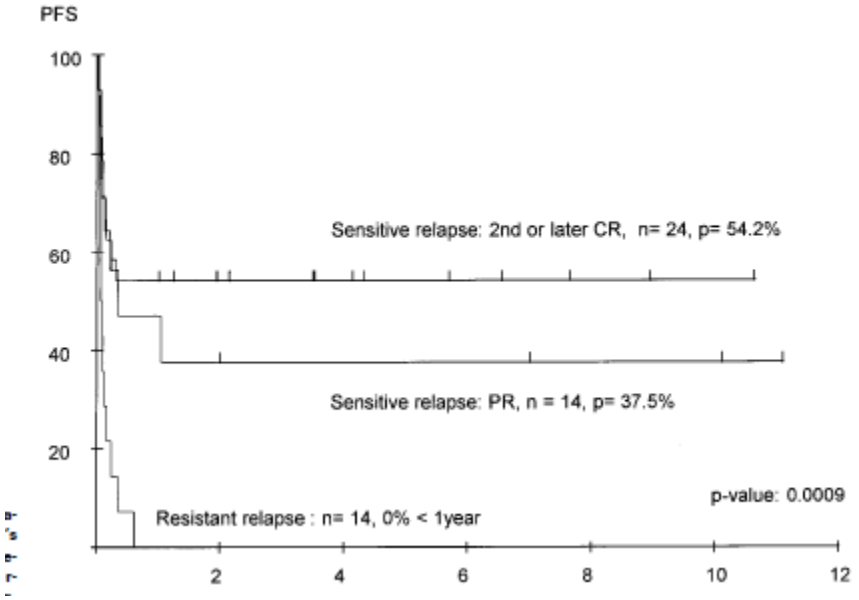
Ref and year	N=	No BL/BLL (%) in study	Median Age, Y	Conditioning	Risk group / features, %	Median follow-up	Disease status, %	Survival	EFS / PFS	NRM
Sweetenham *et al.* (1996)[33]	117	117 (100%)	31 (16-57)	BEAM 21% Cy/TBI 33% Other TBI based 13%	St III-IV : 63% >1Ocm mass:49% BM+:13% CNS+:13%	26 (1-126)	CR1 : 60% CR2: 10% PR : 9% RRel / PRD: 12%	53% @3y CR1 pts : 72% ChemoS rel: 37% ChemoR : 7%	54%	8.5%
Majhail *et al.* (2009)[41]	1367	70 (5.1%)** NHL:960 (70%)	31 (7-77)*	TBI in 44% **	St III-IV : 68%‡	104(25-203)	CR1: 51%; Rel1: 13%	87% @ 5y**	77%**	8% 5y**
Nademanee *et al.* (2000)[39*]	264	28 (11%)	44 (5-69)	TBI/Cy/VP16 BCNU/VP16/Cy	St III-IV:74%; 63% Extranodal:63 %; BM+ : 19%	53 (12-154)	CR1/PR1: 36%; IF: 15%; Rel: 49%	55% @ 5y	47% overall CR/PR :73%; Rel :34%; IF: 30%	10%
Van Imhoff *et al.* (2005)[31]	42	27 (64%)	36 (15-64)	BEAM	UKLG HR:89% aaIPI 2-3:37% >10cm mass:44% Raised LDH: 67%	61	Newly diagnosed/ upfront	81% @ 5y	73%	0%
Nademanee *et al.* (1997)[24]	52	10 (18%)	38 (22-56)	TBI/Cy/VP16 TBI BCNU/VP16	aaIPI high 90% aaIPI high-int 10%	44	CR1 : 70% PR1 : 30%	60% @3Y	60% 3y	10% for SNCL (2% overall)
Jost *et al.* (1995)[29]	26	9 (34%)	25 (16-59)	Cy/TBI Cy/BCNU/VP16	Elevated LDH:71% >St III-IV : 88%	45	Upfront	48%*	EFS 44% @ 3y *	0%*

AutoSCT in Burkitt: Disease status

High-Dose Chemotherapy With Autologous Bone Marrow Rescue in Children With Poor-Risk Burkitt's Lymphoma: A Report From the European Lymphoma Bone Marrow Transplantation Registry

By Ruth Ladenstein, Rachel Pearce, Olivier Hartmann, Catherine Patte, Tony Goldstone, and Thierry Philip





Ladenstein et al 97

Challenges in patient selection

- Histology:
  - Burkitt, or
  - B cell lymphoma unclassifiable with features intermediate between diffuce large b-cell lymphoma and burkitt's lymphoma
    - ?(BCLUFI-DLBCL/BL)

Differentiating BL from 'BCLu'

bjh research paper

Diagnosis of Burkitt lymphoma using an algorithmic approach – applicable in both resource-poor and resource-rich countries

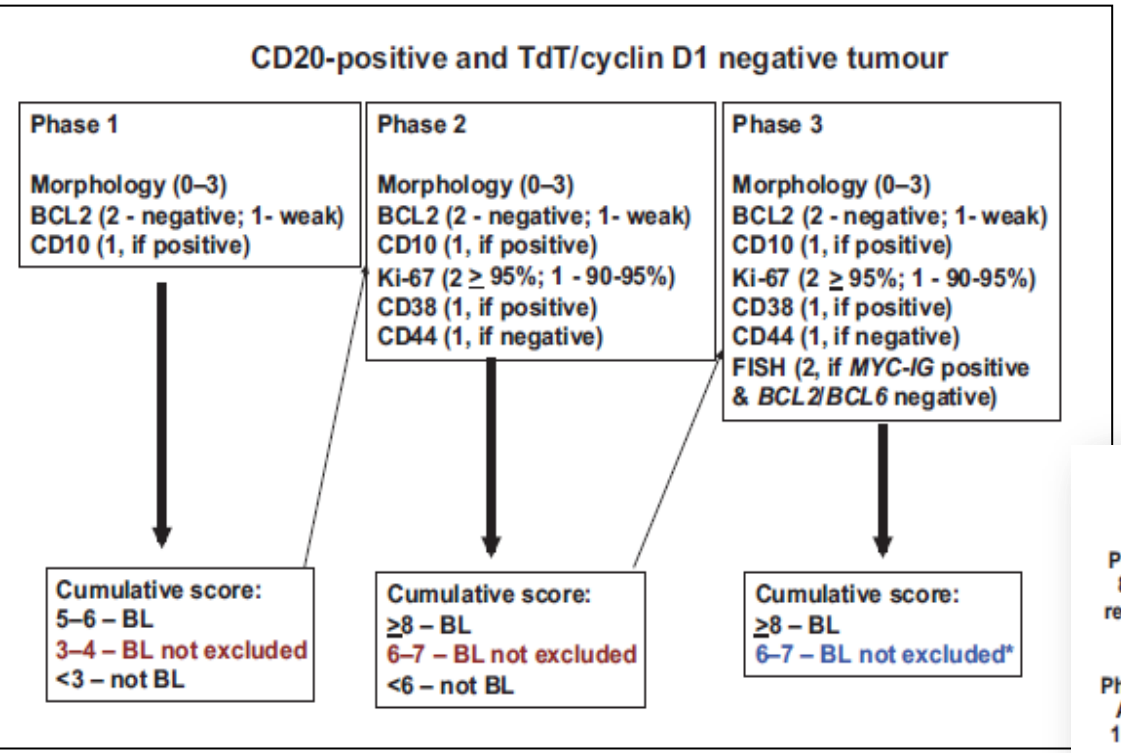
Kikkeri N. Naresh,[1] Hazem A. H. Ibrahim,[1,12] Stefano Lazzi,[2] Patricia Rince,[3] Monica Onorati,[2] Maria R. Ambrosio,[2] Chrystèle Bilhou-Nabera,[3] Furrat Amen,[1] Alistair Reid,[4] Michael Mawanda,[5] Valeria Calbi,[5] Martin Ogwang,[5] Emily Rogena,[6] Bessie Byakika,[7] Shahin Sayed,[8] Emma Moshi,[9] Amos Mwakigonja,[9,10] Martine Raphael,[3] Ian Magrath[11] and Lorenzo Leoncini[2]

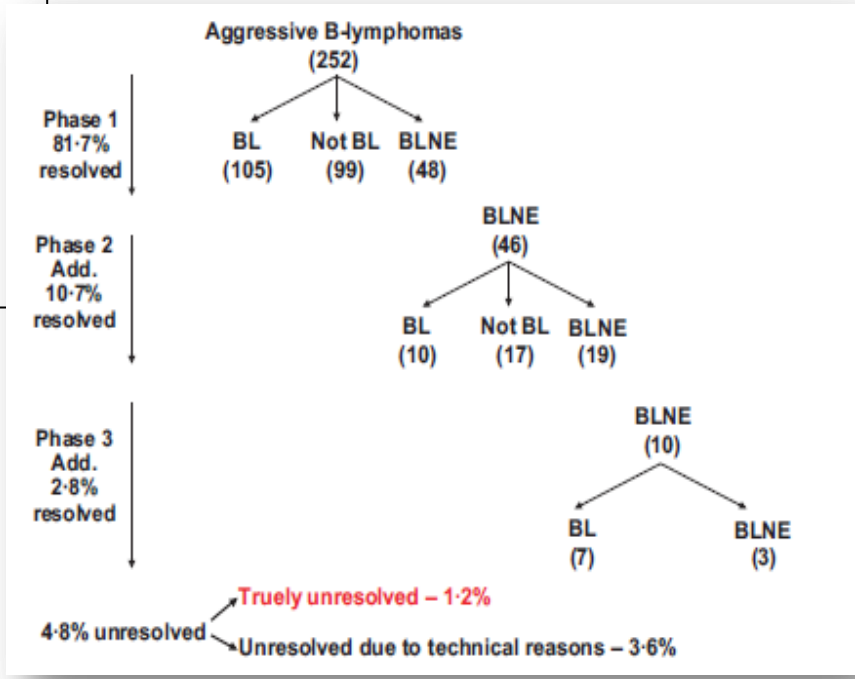
bjh review

Lymphomas in sub-Saharan Africa – what can we learn and how can we help in improving diagnosis, managing patients and fostering translational research?

Kikkeri N. Naresh,[1] Martine Raphael,[2] Leona Ayers,[3] Nina Hurwitz,[4] Valeria Calbi,[5] Emily Rogena,[6] Shahin Sayed,[7] Omar Sherman,[7] Hazem A.H. Ibrahim,[1,8] Stefano Lazzi,[9] Vasileios Mourmouras,[9] Patricia Rince,[2] Jessie Githanga,[6] Bessie Byakika,[10] Emma Moshi,[11] Muheez Durosinmi,[12] Babatunde J. Olasode,[12] Olayiwola A. Oluwasola,[13] Effiong E. Akang,[13] Yetunde Akenòva,[13] Melissa Adde,[14] Ian Magrath[14] and Lorenzo Leoncini[9]

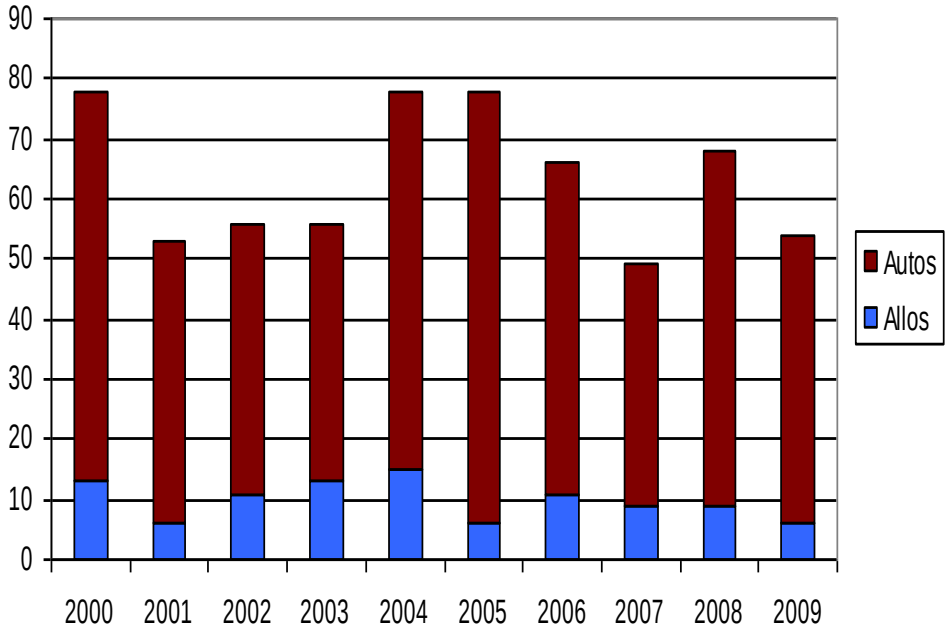
[1]Hammersmith Hospital & Imperial College, London, UK, [2]Univ Paris-Sud, Paris, France, [3]The Ohio State University, Columbus, Ohio, USA, [4]University of Basel, Basel, Switzerland, [5]Saint Mary Hospital, Lacor, Gulu, Uganda, [6]University of Nairobi, [7]Aga Khan University Hospital, Nairobi, Kenya, [8]Mansoura University, Mansoura, Egypt, [9]University of Siena, Siena, Italy, [10]Nairobi Hospital, Nairobi, Kenya; Nairobi, Kenya, [11]Muhimbili National Hospital, Dares salaam, Tanzania, [12]Obafemi Awolowo University, Ile Ife, Nigeria, [13]U.C.H, Ibadan, Nigeria, and [14]INCTR, Brussels, Belgium


CD20-positive and TdT/cyclin D1 negative tumour
Phase 1
Morphology (0–3)
BCL2 (2 - negative; 1- weak)
CD10 (1, if positive)
Phase 2
Morphology (0–3)
BCL2 (2 - negative; 1- weak)
CD10 (1, if positive)
Ki-67 (2 ≥ 95%; 1 - 90-95%)
CD38 (1, if positive)
CD44 (1, if negative)
Phase 3
Morphology (0–3)
BCL2 (2 - negative; 1- weak)
CD10 (1, if positive)
Ki-67 (2 ≥ 95%; 1 - 90-95%)
CD38 (1, if positive)
CD44 (1, if negative)
FISH (2, if MYC-IG positive & BCL2/BCL6 negative)
Cumulative score:
5–6 – BL
3–4 – BL not excluded
<3 – not BL
Cumulative score:
≥8 – BL
6–7 – BL not excluded
<6 – not BL
Cumulative score:
≥8 – BL
6–7 – BL not excluded*


Aggressive B-lymphomas
(252)
Phase 1
81·7%
resolved
BL
(105)
Not BL
(99)
BLNE
(48)
BLNE
(46)
Phase 2
Add.
10·7%
resolved
BL
(10)
Not BL
(17)
BLNE
(19)
BLNE
(10)
Phase 3
Add.
2·8%
resolved
BL
(7)
BLNE
(3)
4·8% unresolved
Truely unresolved – 1·2%
Unresolved due to technical reasons – 3·6%

Adult Allo & Auto Cohorts 2000-2009 in BL ('Rituximab-era')

	Allo	Auto	Total
2000	13	65	78
2001	6	47	53
2002	11	45	56
2003	13	43	56
2004	15	63	78
2005	6	72	78
2006	11	55	66
2007	9	40	49
2008	9	59	68
2009	6	48	54
TOTAL	99	537	636



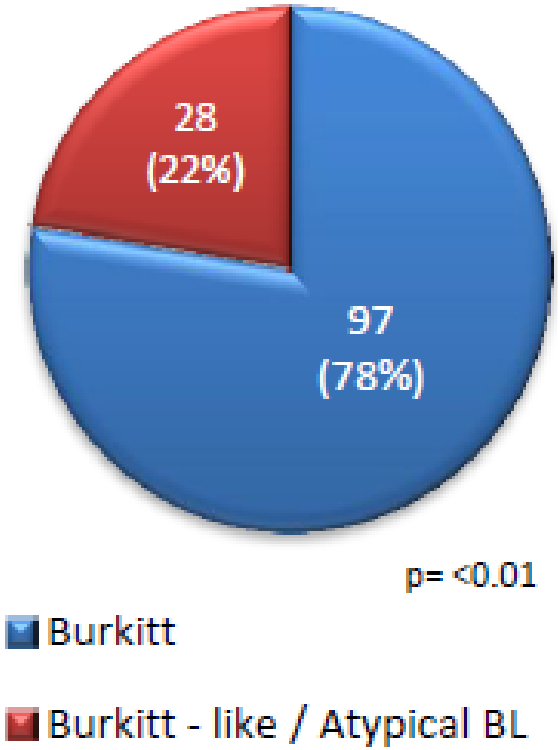
- Burkitt's Lymphoma (PROMISE code=50)
- First transplants
- Age 18-65
- Includes HIV+

Autologous Stem Cell Transplantation For Adult Burkitt Lymphoma In The Rituximab Era: A Retrospective Study Of The Lymphoma Working Party (LWP) Of The European Group For Blood and Marrow Transplantation (EBMT)

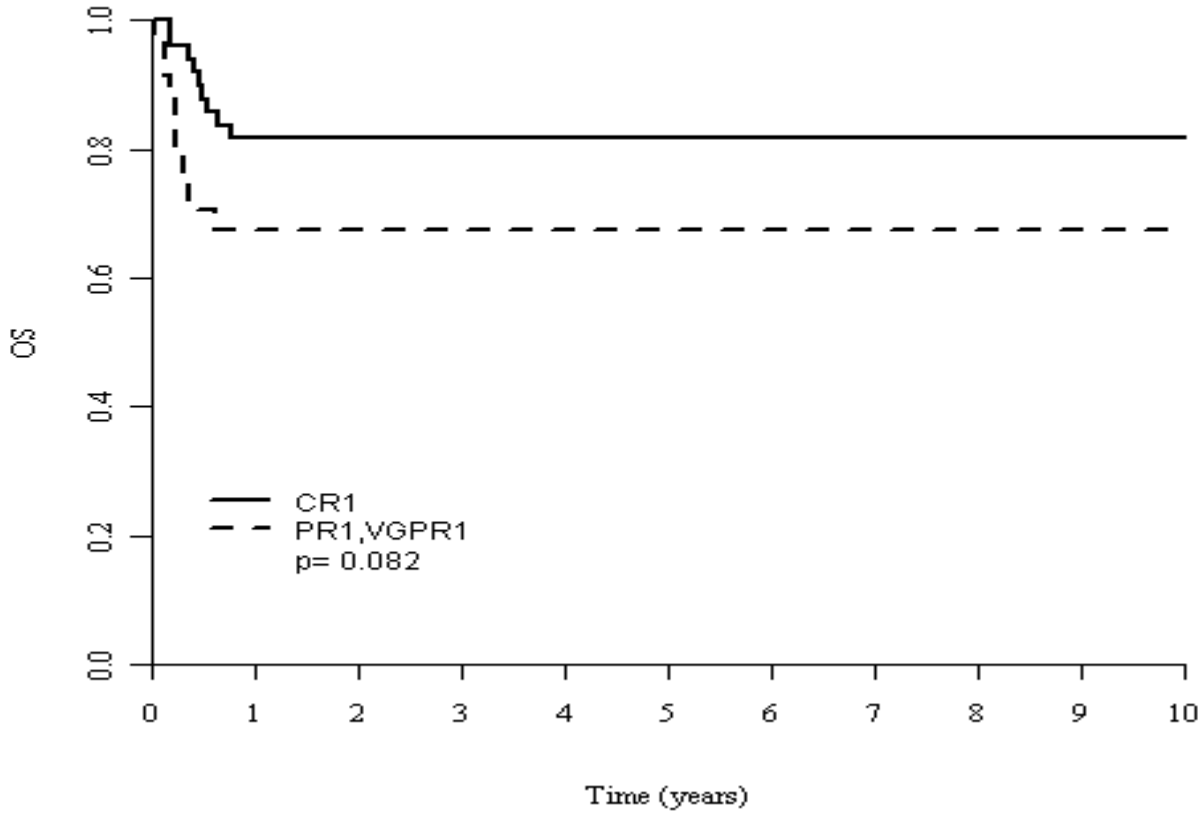
Table 1. Patient and Disease Characteristics (N=125)

Characteristics at diagnosis	N (%)
Median Age, y	36 (16-64)
Stage III/IV	20 (16%) / 79 (64%)
Elevated LDH	60 (70%)
Bulky Mass >10 cm	27 (23%)
Disease Status at ASCT	**N (%)**
• CR1/ VGPR1/PR1	90 (72%)
• CR>1 / AD	31 (25%)

Fig. 1. Histological subtype



Outcomes in CR1 vs VGPR/PR1



AutoSCT can successfully salvage patients who fail to achieve remission after initial chemotherapy

HCT in HIV+ BL

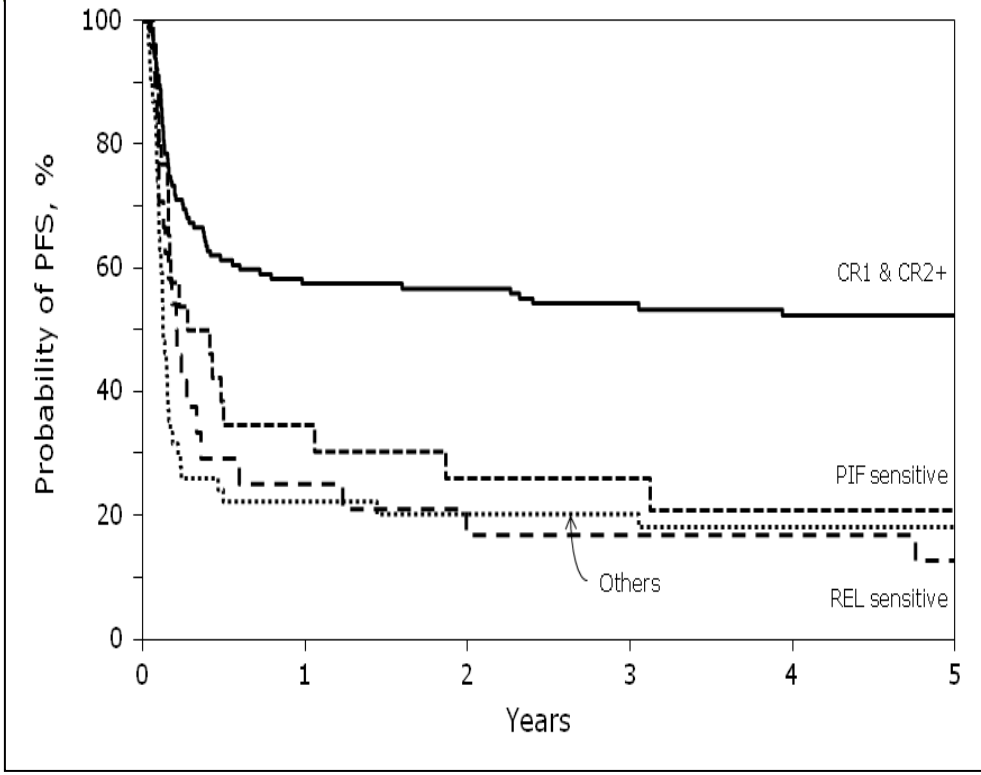
Ref and year	N=	BL/BLL	Age	Disease status	Conditioning	NRM	Survival	PFS
Balsalobre *et al.* (2009)[71]	68	8 (12%)	41 (29-62)	CR 51%, PR/ChemoS rel. 37%; IF/ChemoR rel. 12%	BEAM (95.5%); TBI (4.5%)	7.5%	61% @ 3yrs	56%
Diez-Martin *et al.* (2009)[72]	53	3(6%)	40.7 (29-62)	CR 47%; PR/ChemoS relapse 43.5%	TBI ; BEAM ; other	8%	58.5% @ 2.5yrs *	57.5%
Krishnan *et al.* (2005)[73]	20	6 (30%)	44 (11-68)	CR 30%; Refractory/Relapse 70%;	BCNU/VP16/Cy or TBI/VP16/Cy	5%	70% @ 2.6 yrs	85%

Blood (ASH Annual Meeting Abstracts) 2010; **116**(21)**:** 2390-.

CIBMTR Analysis of 241 Transplants for BL, 1985-2007 - *Gajewski et al 2010*

Variable	AUTO	SIB	UNR/MM
N	**113**	**80**	**48**
Median age	31 (5-76)	24 (3-55)	22 (2-54)
Bone marrow involvement @ diagnosis	22%	21%	27%
CR1 status prior to HCT	42%	34%	6%
Chemosensitive prior to HCT	86%	77%	71%
TRM @ 1 yr (95% CI)	5 (2-10)	26 (17-37)	28 (16-41)
PFS @ 5 yr (95% CI)	48 (39-58)	30 (20-41)	22 (12-35)
OS @ 5 yr (95%CI)	**54 (44-63)**	**32 (22-43)**	**23 (12-36)**

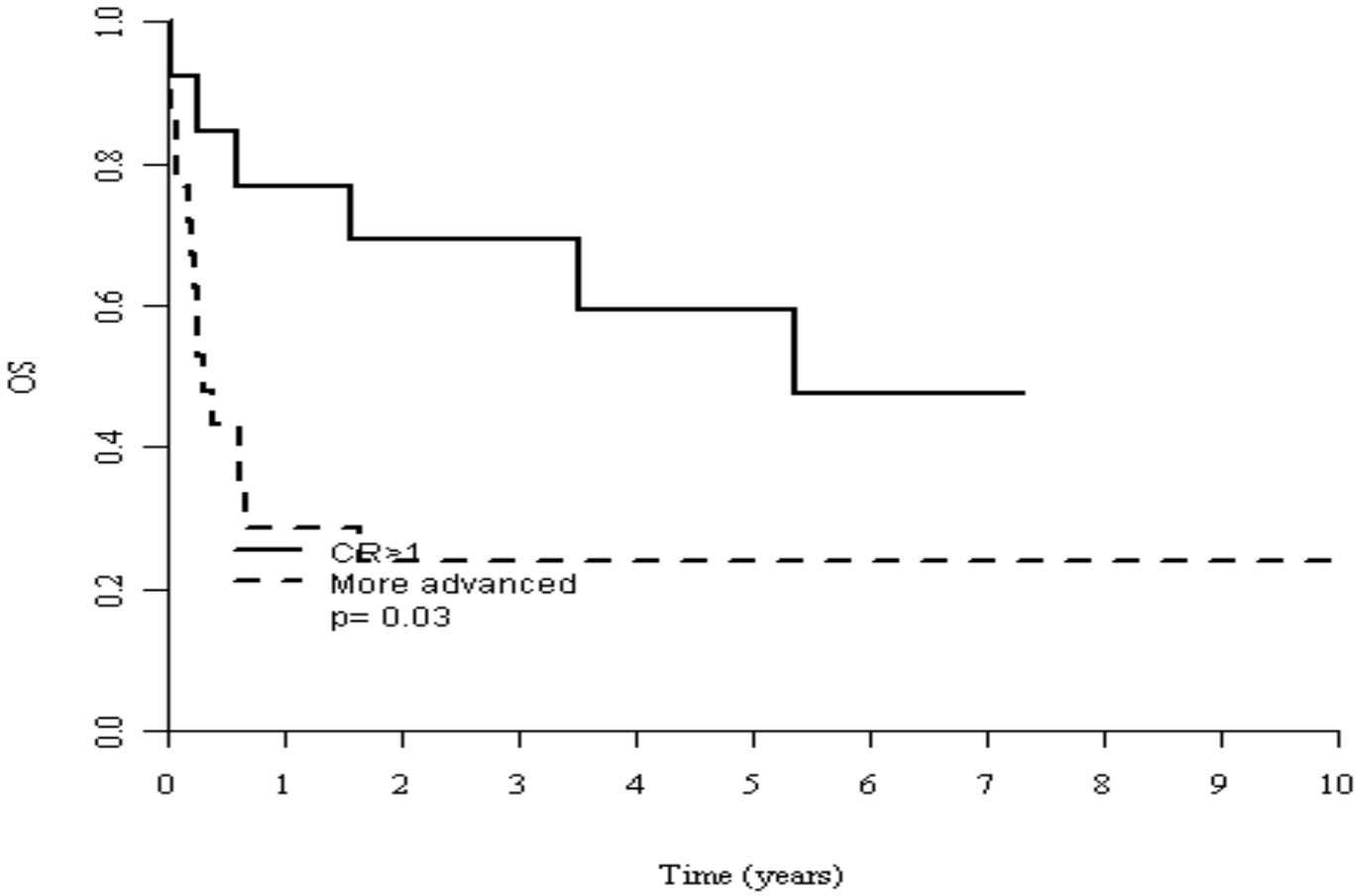
- Adult + paediatric
- Worse outcome in relapse, PIF
- Survival in AUTO superior to ALLO



Blood 2010; **116**(21)**:** 2390a

Autologous Stem Cell Transplantation For Adult Burkitt Lymphoma In The Rituximab Era: A Retrospective Study Of The Lymphoma Working Party (LWP) Of The European Group For Blood and Marrow Transplantation (EBMT)

ASCT after Relapse
EBMT Study:
N=35



Autologous Stem Cell Transplantation For Adult Burkitt Lymphoma In The Rituximab Era: A Retrospective Study Of The Lymphoma Working Party (LWP) Of The European Group For Blood and Marrow Transplantation (EBMT)

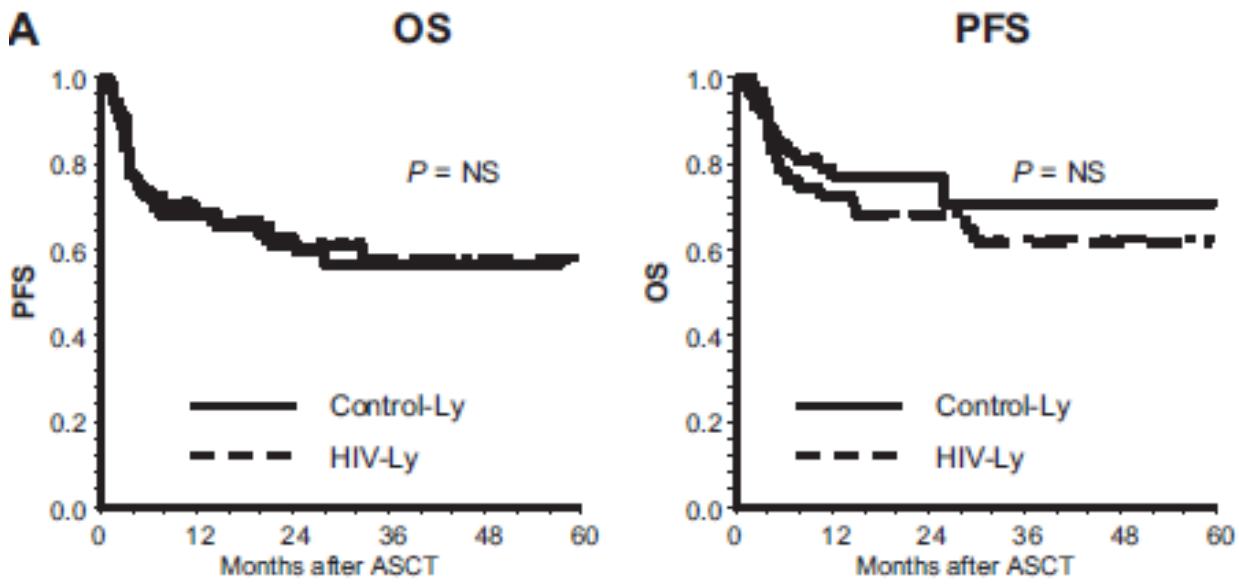
- Patients treated after 2000
- Histology report review
- HIV not excluded

AutoSCT in HIV+ BL

blood

2009 113: 6011-6014
Prepublished online March 23, 2009;
doi:10.1182/blood-2008-12-195388

Comparable survival between HIV^{+} and HIV^{-} non-Hodgkin and Hodgkin lymphoma patients undergoing autologous peripheral blood stem cell transplantation



Mobilization in HIV+ patients

Stem cell mobilization in HIV seropositive patients with lymphoma

Alessandro Re,[1] Chiara Cattaneo,[1] Cristina Skert,[2] Pascual Balsalobre,[3] Mariagrazia Michieli,[4] Mark Bower,[5] Andrés J. M. Ferreri,[6] Marcus Hentrich,[7] José M. Ribera,[8] Bernardino Allione,[9] Philipp Schommers,[10] Silvia Montoto,[11] Camillo Almici,[12] Pierino Ferremi,[12] Mario Mazzucato,[13] Salvatore Gattillo,[14] Salvatore Casari,[15] Michele Spina,[16] José L. Diez-Martin,[3] Umberto Tirelli,[16] and Giuseppe Rossi[1] on the behalf of GECAT (Cooperative European Group on AIDS and Tumors)

- 155 mobilizations
  - 127 NHL, 35 HL
  - 23 BL
- Mobilisation failure:
  - Low CD4 count
  - Refractory disease
- Optimal mobilization:
  - Cyclophosphamide >3g/m2

Table 3. Univariate and multivariate statistical analysis of factors influencing optimal mobilization ($CD34^+$ >$5x10^6$/kg) in 155 first mobilization attempts.

Prognostic factor*	Optimal mobilization Univariate P OR (95% CI)	Multivariate P OR (95% CI)
Lymphoma refractory	0.04 0.34 (0.11-0.98)	NS
Platelet < 160 x 10^9/L	0.001 0.37 (0.2-0.7)	0.004 0.33 (0.1-0.7)
$CD4^+$ count < 237/mcL	0.08 0.55 (0.30-1.05)	0.001 0.52 (0.26-0.8)
Mobilizing strategy (G-CSF *vs.* G-CSF + CT)	0.02 0.31 (0.12-0.80)	0.008 0.21 (0.07-0.7)
CTX > 3 g/m² as mobilizing tx	0.01 2.1 (1.20-3.80)	0.006 3.1 (1.4-6.8)
CTX 1.5 g/m² as mobilizing tx	0.03 0.20 (0.05-0.90)	NS

*Only those parameters that achieved statistical significance ($P<0.05$) are listed.

Re et al, 2014

Allogeneic SCT in Burkitt

Allogeneic SCT in BL

Reference	No. HCT	N: BL (%)	Median Age, years (Range)	Auto-HCT vs allo-HCT	NRM / TRM	OS	DFS/PFS
Gajewski *et al.* (2010)[32]	241	241 (100)	31 (5-76)	113 Auto-HCT	5%	54% @ 5y	48% @ 5y
			24 (3-55)	80 Sib allo-HCT	26%	32% @5y	30% @ 5y
			22 (2-54)	48 MUD/MMRD	28%	23% @5y	22% @ 5y
Peniket *et al.* (2003)[48]	15872	71 (6)	22.6 (4.8-48)	1185 allo -HCT(BL:71)	30.9% @ 4y	37% @ 4y; Median OS 4.7 months post allo-HCT	PFS: 34.9% @ 4y
				14687 auto-HCT			
Van Biesen *et al.* (2009)[50]	283	68 (24)**	37 (2-65)	Allo only	44%* @1y RR 1.97 (vs FL)	24% 5y OS* (HA-NHL RR :2.25 **)	PFS: 22% 5y * (HA-NHL RR:1.92**)
Gada *et al.* (2005)[63]	38	38(100)	16 (4-65)	25 Auto	8% 1 yr	23% @ 10y	21% @10y
			13 (4-62)	13 Allo	15% 1 yr	31% @ 10y	31% @ 10y
Song *et al.* (2006)[30]	27	27 (100)	36 (16-32)	21 auto 6 allo	NA	52% 0S for all pts	3y EFS 51%
Soussain *et al.* (1995)[13]	18	18 (100)	29(17-42)	11 Auto	9%	45%	NA
			29 (21-33)	7 allo	29%	43%	
Schimmer *et al.* (2000)[82]	429	21(5)	46(16-73)	15 Auto	6%*	62% 3y	52%
				3 Allo	23%*	72% (NS vs auto)	71%
Kwon *et al.* (2010)[83]	13	13 (100)	41 (24-67)	11 auto 2 allo	23%	75% 2yr OS	NA
Divine *et al.* (2005)[14]	9	9 (100)	33 (18-76)	8 Auto 2 Allo	NA	12% 0%	NA
Troussard *et al.* (1990)[46]	9	9 (100)	27(15-36)	Allo	22%	77% @43m	NA
Hamadani *et al.* (2009)[47]	46	3 (6.5%)	47 (22-59)*	Allo	0%	OS: 33% 5y OS	PFS: 33% 5y
Kusumi *et al.* (2005)[84]	112	2 (2%) (HA- NHL:9)	50(22-72)[§]	RIC allo	33.3%[§]	0% 3yr OS[§]	NA

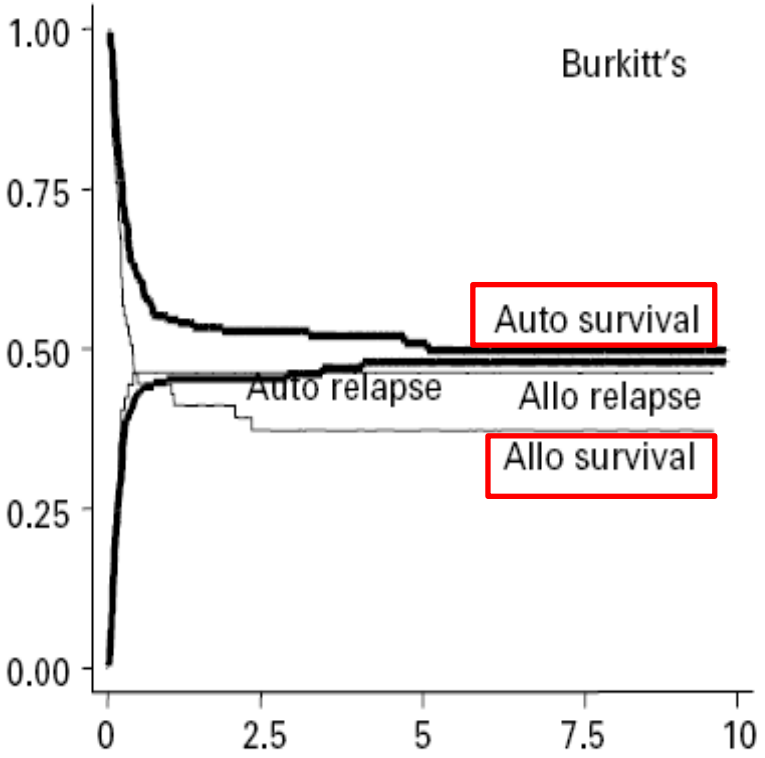
EBMT data: Comparison of Auto vs Allo in all patients having a first SCT for BL, 2000-2009 (N=636)

	6m	6m	1y	1y	2y	2y	3y	3y
	AUTO	**ALLO**	**AUTO**	**ALLO**	**AUTO**	**ALLO**	**AUTO**	**ALLO**
NRM	6%	26%	**7%**	**29%**	8%	29%	9%	29%
RR	22%	41%	28%	42%	31%	42%	31%	44%
OS	77%	38%	**71%**	**30%**	65%	30%	65%	29%
PFS	71%	33%	64%	29%	61%	29%	60%	27%

- Autogous patients, N=537
- Allogeneic transplants, N=99
- Age 18-65
- Exclusion of " Burkitt-like" as registered on PROMISE
- Better overall survival for Auto group

Allo vs Autologous SCT in BL/BLL

- EBMT study Peniket et al.
  - All lymphomas
  - 71 BL allo
  - Retrospective comparison with ASCT cohort
  - OS better for autologous vs allogeneic in all lymphomas
  - Relapse rate in BL
    - allo = ASCT
- Transplants carried out between 1982-1998



Peniket et al (2003) BMT 31:667-678

Allogeneic SCT in Burkitt

- Possible option in the presence of sibling donor:
  - Relapse post auto
  - BM+ / unable to mobilise cells

- Disease status

RIC transplants

- Lower efficacy in highly aggressive lymphoma
  - RIC alografts in aggressive/ resistant NHL:
    - 12.9 % PFS at 2 yrs

MUD

CIBMTR analysis including 68 (24%) lymphoblastic lymphoma/BL/BLL.

- Heterogeneous group
- Increased relative risk of treatment-related mortality (TRM)
  - (relative risk (RR) of 1.97) and
  - disease progression/relapse (RR 3.53) compared with those with follicular lymphoma;
  - Relapse accounted for 39% of deaths in the former group.

- Volunteer unrelated donor transplants had an inferior outcome to sibling transplants (PFS 22 vs 30%)

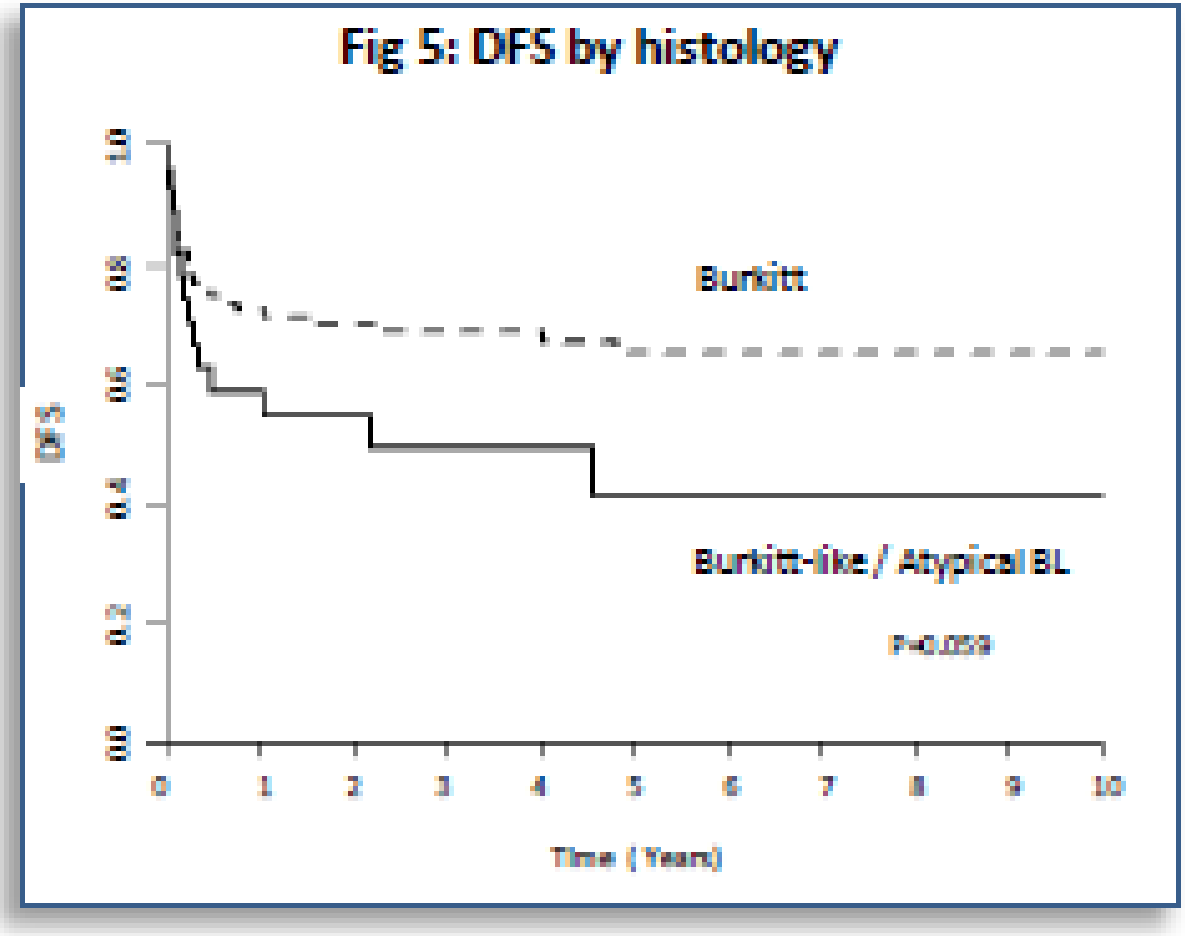
SCT in BCLu / Burkitt- Like

Ref and year	N=	BLL/BCLU	Age	No. SCT	Procedure	Survival	PFS
Johnson *et al.*(2009)[65]	54	DHL (100%)	NA	4 (7%)	3 Auto 1 Allo	Median OS 3m*	PFS reported as similar to OS
Le Gouill *et al.*(2007)[58]	16	DHL (100%)	60(36-73)	5 (31%)	3 ASCT 2 alloSCT	OS 5 months	PFS: Median 4 months
Tholouli *et al.*(2009)[74]	13	Complex CGN (100%), including DHL (30%)	42 (19-69)	4 (31%)	1 ASCT 3 allo	OS 5 months **	PFS: Median 3 months **
Snuderl *et al.*(2010)[83]	20	DHL (100%)		2 (10%)	2 ASCT	OS 4.5 months**	NA
Macpherson *et al.*(1999) [4]	39	c-myc (28%), DHL (33%),other CGN (39%)	53 (16-93)	8 (20%)	4 auto-SCT 4 allo-SCT	Median OS 2.5 months for DHL patients; OS: DHL 0%; c-myc 32% @ 2y; other CGN 25% @ 2y	NA
Dann *et al.* (1997)[66]	27	HL (22%), BLL (15%), Other NHL (63%)	36 (18-60)	4 (19%)	Allo	Median OS 2.7 months**; OS 25% for BLL pts	DFS: 22%**

*Including 2 patients who received ALL like treatment

*For all patients

Burkitt vs BCLu

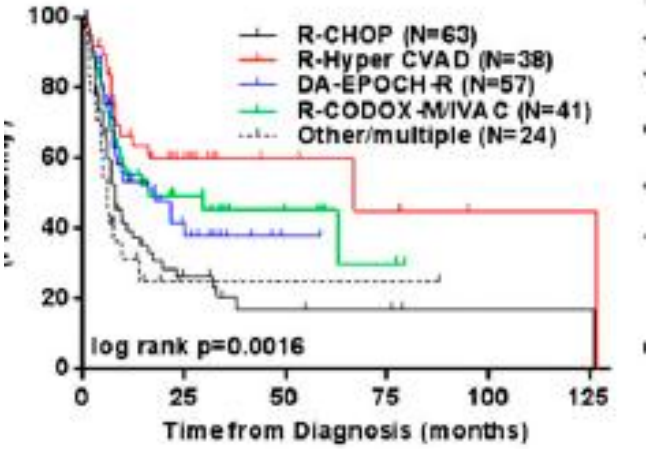


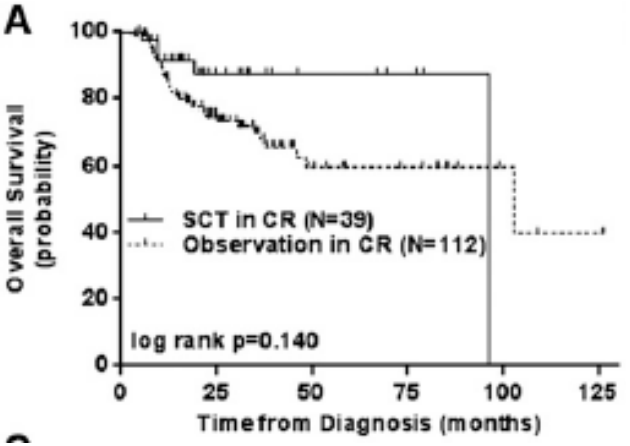
Regular Article

CLINICAL TRIALS AND OBSERVATIONS

Impact of induction regimen and stem cell transplantation on outcomes in double-hit lymphoma: a multicenter retrospective analysis

Adam M. Petrich,[1] Mitul Gandhi,[1] Borko Jovanovic,[1] Jorge J. Castillo,[2] Saurabh Rajguru,[3] David T. Yang,[4] Khushboo A. Shah,[5] Jeremy D. Whyman,[5] Frederick Lansigan,[5] Francisco J. Hernandez-Ilizaliturri,[6] Lisa X. Lee,[7] Stefan K. Barta,[7] Shruthi Melinamani,[8] Reem Karmali,[8] Camille Adeimy,[9] Scott Smith,[9] Neil Dalal,[10] Chadi Nabhan,[11] David Peace,[12] Julie Vose,[13] Andrew M. Evens,[14] Namrata Shah,[15] Timothy S. Fenske,[15] Andrew D. Zelenetz,[16] Daniel J. Landsburg,[17] Christina Howlett,[18,19] Anthony Mato,[17,18] Michael Jaglal,[20] Julio C. Chavez,[20] Judy P. Tsai,[21] Nishitha Reddy,[21] Shaoying Li,[22] Caitlin Handler,[23] Christopher R. Flowers,[23] Jonathon B. Cohen,[23,24] Kristie A. Blum,[24] Kevin Song,[25] Haowei (Linda) Sun,[25] Oliver Press,[26] Ryan Cassaday,[26] Jesse Jaso,[27] L. Jeffrey Medeiros,[27] Aliyah R. Sohani,[28] and Jeremy S. Abramson[29]





Conclusions-I

- Upfront auto-SCT has been reported to be feasible in patients who have high-risk features at presentation, and in whom it is a clinical option.

- In patients with relapsed disease, auto-SCT can result in a PFS of 30–40%.

- Allo-SCT is an option in relapsing patients with a sibling or matched related donor who may not be eligible for, or may have previously received, an auto-SCT; Role of RIC and T-cell depletion is not well defined.
- Disease status at transplant is the most significant predictor of outcome in patients undergoing SCT.

HSCT in BL in Africa

- Indication for ASCT
  - PR1 (vs salvage chemo?)
  - In CR2
- Allo
  - Limited use

- One size doesn't fit all
- Development of African registries
  - Regional answers
    - Endemic BL and SCT (cf NCI chemotherapeutic regimes)
- Collaboration with WBMT
  - Regional transplant centres

Thank You

Thank You

Prostate	7069	13·8	4975	24·5	2908	5·8	4778	40·5	9947	19·3	29 663	16·0
Oesophagus												
Males	11 174	19·1	369	1·5	1140	2·1	2804	19·7	802	1·3	16 289	7·8
Females	5411	8·0	62	0·2	875	1·4	1301	7·0	410	0·6	8058	3·4
Non-Hodgkin lymphoma												
Males	7264	7·1	1525	4·5	3124	4·4	846	4·8	4868	5·7	17 626	5·6
Females	4741	4·4	2249	6·9	1830	2·4	614	3·0	2995	3·5	12 428	3·9
Stomach												
Males	4687	7·4	3283	13·4	2550	4·4	1183	8·2	2131	3·4	13 836	6·2
Females	3883	5·5	3780	12·6	1671	2·5	686	3·7	2331	3·6	12 350	4·9
Colon/rectum												
Males	4019	6·1	627	2·3	3150	5·1	1553	11·3	3430	5·1	12 778	5·4
Females	2997	4·1	951	3·3	2707	4·0	1644	8·9	2655	3·5	10 903	4·2
Bladder												
Males	2787	2·1	440	0·9	11 863	13·0	1348	5·4	2458	2·1	18 893	4·5
Females	2575	1·9	157	0·3	2356	2·6	630	2·5	980	0·8	6700	1·6
Cervix uteri	33 903	42·7	8201	28	8175	12·1	7698	38·2	20 919	29·3	78 897	29·3
Breast (females)	15 564	19·5	5173	16·5	16 588	23·2	6474	33·4	21 397	27·8	65 197	23·4
Ovary	4706	5·8	1182	3·3	1892	2·6	1003	5·2	3601	4·6	12 384	4·3
All sites (except skin)												
Males	118 903	158·7	39 212	141·9	60 011	99	31 626	213·7	61 610	90	311 363	126
Females	129 029	156·7	38 857	121·5	59 603	85·2	32 170	163·2	78 740	104·4	338 397	121

BURKITT'S LYMPHOMA (BL)

- High grade NHL
  - Sporadic form 1-2% of NHL in N.america and W.Europe
- Characteristic Morphology
  - Medium sized, clumped chromatin,
  - Diffuse monotonous pattern
  - High proliferative index – Ki-67 >95-100%
- Immunophenotype:
  - IgM+ (vs ALL), Bcl-6+, CD19+, CD20+, CD22+, CD10+, CD79a+
  - CD5-, CD23-, Bcl2-, TdT- (vs ALL)
- Cytogenetic evidence of c-myc rearrangement
- Burkitt-like lymphoma (BLL) / DLBCL (unclassified) to be excluded in study

- Burkitt's lymphoma is a rare yet very aggressive high grade lymphoma .
- There are three clinical variants.
  - The endemic form –
    - equatorial Africa in areas of high malaria prevalence
    - most common childhoods malignancy – jaw tumours that often presents with extranodal – especially abdominal – disease and leukemia2, 3. There is a correlation with endemic malaria.
  - Sporadic BL occurs in the rest of the world, where the incidence is 1-2% of all lymphomas and is again a disease of the young. There is a male preponderance in both the sporadic and endemic forms.
  - Immunodeficiency associated BL is associated with HIV infection.

- Burkitt’s variant
- Burkitt-like lymphoma (BLL)
  - Now called :
  - B cell lymphoma unclassifiable with features intermediate between diffuce large b-cell lymphoma and burkitt’s lymphoma
    - ?(BCLUFI-DLBCL/BL)

Pathology

- High proliferation index and rapid doubling time
- Monotonous pattern, small noncleaved cells
- ‘Starry sky’