SUPPLEMENTARY APPENDIX

Incidence and risk factors for relapses in HIV-associated non-Hodgkin lymphoma as observed in the German HIV-related lymphoma cohort study

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 doi:10.3324/haematol.2017.180893

Received: September 17, 2017.

Accepted: February 2, 2018.

Pre-published: February 8, 2018.

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Cycle day(s)	Drug	Dose	Route
Pre-phase			
1–5	Cyclophosphamide	200 mg/m^2	iv over 1 h
1–5	Prednisone	60 mg/ m^2	iv bolus
Cycle A			
7	Rituximab	375 mg/ m^2	iv progressive infusion (4 h)
8	Vincristine	2 mg (absolute)	iv bolus day 1
8	Methotrexate	1500 mg/ m^2	iv over 24 h†‡
8–12	Ifosfamide	800 mg/ m^2	iv over 1 h
8–12	Dexamethasone	10 mg/ m^2	iv bolus
11–12	Teniposide (VM26)	100 mg/ m^2	iv over 1 h
11–12	Cytarabine	150 mg/ m^2	iv over 1 h every 12 h
Cycle B			
28	Rituximab	375 mg/ m^2	iv progressive infusion (4 h)
29	Vincristine	2 mg (absolute)	iv bolus day 1
29	Methotrexate	1500 mg/ m^2	iv over 24 h
29–33	Cyclophosphamide	200 mg/ m^2	iv over 1 h
29–33	Dexamethasone	10 mg/ m^2	iv bolus
32–33	Doxorubicin	25 mg/ m^2	iv over 15 min
Cycle C			
49	Rituximab	375 mg/ m^2	iv progressive infusion (4 h)
50	Vindesine	3 mg/m2 (max. 5 mg)	iv bolus
50	Methotrexate	1500 mg/ m^2	iv over 24 h†
50–54	Dexamethasone	10 mg/ m^2	iv bolus
53–54	Etoposide (VP16)	250 mg/ m^2	iv over 1 h
54	Cytarabine	2000 mg/ m^2	iv over 3 h every 12 h
Central nervous system prophylaxis			
1–8–12–29–33	Methotrexate	15 mg	Intrathecal
	Cytarabine	40 mg	
	Dexametasone	20 mg	

iv, intravenous; G-CSF, granulocyte-colony stimulating factor.
†Folinic acid rescue from 12 h after the end of infusion.
‡Half to one-third in patients over 55 years.

Supplementary Table 1

B-ALL (GMALL) Protocol Treatment (adapted from B-ALL/NHL2002, ClinicalTrials.gov identifiers NCT00199082 and NCT00388193)

Cycles A–C were repeated from days 77 to 124 for a total of six treatment cycles after the pre-phase. Patients received eight intrathecal doses as a central nervous system prophylaxis. Two additional doses of rituximab were given at the end of the regular treatment cycles (weeks 21 and 24 at standard dose) making a total of eight doses of rituximab for the complete treatment. Growth factors (G-CSF) were allowed for use from neutrophils < 0.5 × 109/L until recovery for each cycle.

Cycle day(s)	Drug	Dose	Route
1	Rituximab	375 mg/ m^2	Iv over 2 hours
2	Cyclophosphamide	750 mg/m^2	iv over 1 h
2	Doxorubicin	50 mg/m^2	iv over 1 h
2	Vincristine	1,4 mg/ m^2	iv bolus
2-6	Prednisone	100 mg (absolute)	taken orally

Supplementary Table 2
R-CHOP Protocol Treatment
Cycles are repeated at day 22 (R-CHOP 21).

	Treat-ment delay (*N*=85)	No Treat-ment delay (*N*=134)	*P*-value	Reduced Therapy Intensity (*N*=37)	Regular Therapy Intensity (*N*=197)	*P*-value	Reduced # of Cycles (*N*=42)	Regular # of Cycles (*N*=204)	*P*-value	No Full Therapy (≥1 criteria applies, *N*=118)	Full Therapy (in all 3 criteria, *N*=96)	*P*-value
Male	78 (94%)	115 (88%)	0.162[c]	20 (94%)	175 (90%)	0.542[c]	36 (86%)	183 (92%)	0.235[c]	106 (91%)	83 (88%)	0.495[c]
Median Age (years)	44	44	0.568[b]	48	43	**<0.001**[b]	40	44	0.549[b]	45	42	**0.042**[b]
Prior AIDS-defining illness	22 (27%)	25 (19%)	0.236[c]	11 (31%)	39 (20%)	0.181[c]	13 (33%)	40 (20%)	0.099[c]	30 (26%)	15 (16%)	0.092[c]
HIV-RNA below limit of detection	20 (26%)	44 (34%)	0.385[c]	11(31%)	57 (30%)	0.946[c]	11 (28%)	59 (30%)	0.902[c]	34 (30%)	30 (33%)	0.743[c]
Median CD4+ T cells (x10^9/L)	268	238	0.470b	273	248	0.819b	288	245	0.419[b]	265	242	0.660[b]
CD20+ lymphoma	74 (93%)	109 (89%)	0.623[c]	26 (84%)	173 (92%)	0.189[c]	41 (98%)	165 (89%)	0.088[c]	100 (91%)	81 (90%)	1.000[c]
BM Involvement	24 (31%)	18 (14%)	**0.004**[c]	6 (19%)	36 (19%)	1.000[c]	11 (28%)	35 (19%)	0.190[c]	26 (24%)	15 (16%)	0.220[c]
CNS Involvement	8 (11%)	6 (6%)	0.260[c]	1 (3%)	13 (8%)	0.699[c]	3 (8%)	12 (7%)	0.733[c]	8 (8%)	6 (8%)	1000[c]
IPI score												
Low	25 (30%)	61 (49%)		8 (24%)	83 (44%)		19 (46%)	75 (41%)		41 (37%)	44 (49%)	
Intermediate	42 (51%)	47 (38%)		16 (49%)	80 (43%)		14 (34%)	86 (46%)		50 (44%)	50 (44%)	
High	16 (19%)	16 (13%)	**0.023**[a]	9 (27%)	24 (13%)	**0.032**[a]	8 (20%)	25 (14%)	0.339[a]	23 (20%)	9 (10%)	0.066[a]
Chemotherapy												
CHOP	36 (43%)	102 (79%)		25 (74%)	123 (63%)		17 (42%)	140 (71%)		59 (51%)	76 (82%)	
GMALL	47 (57%)	28 (22%)	**<0.001**[c]	9 (27%)	71 (37%)	0.253[c]	24 (59%)	58 (29%)	**0.001**[c]	57 (49%)	17 (18%)	**<0.001**[c]

[a] Pearson's χ^2, two-sided.
[b] Kruskal-Wallis test.
[c] Fisher's exact test

Supplementary Table 3

Dose intensity of first line chemotherapy in patients with CR.
IPI, International Prognostic Index; VL bd, viral load below limit of detection; BM, bone marrow; CNS, central nervous system

	R-CHOP-treated DLBCL (*N*=121)				GMALL-treated BL (*N*=76)			
		5-year Relapse-free Survival (5yRFS)	*P*-value (uni-variate)	*P*-value (multi-variate)		5-year Relapse-free Survival (5yRFS)	*P*-value (uni-variate)	*P*-value (multi-variate)
Sex	Male (*N*=106)	87%			Male (*N*=74)	94%		
	Female (*N*=15)	93%	0.523		Female (*N*=2)	100%	0.726	
Age	>60Y (*N*=15)	85%			>60Y (*N*=5)	95%		
	<60Y (*N*=106)	88%	0.803		<60y (*N*=71)	80%	0.121	
CNS involvement	Yes (*N*=3)	100%			Yes (*N*=7)	71%		
	No (*N*=89)	91%	0.587		No (*N*=67)	97%	**0.005**	0.895
BM involvement	Yes (*N*=16)	74%			Yes (*N*=22)	90%		
	No (*N*=96)	91%	**0.049**	0.870	No (*N*=51)	96%	0.377	
Bulky Disease	Yes (*N*=21)	85%			Yes (*N*=13)	90%		
	No (*N*=52)	89%	0.564		No (*N*=34)	96%	0.365	
CD4+ T cells <50x10^9/l	Yes (*N*=16)	88%			Yes (*N*=6)	83%		
	No (*N*=97)	87%	0.938		No (*N*=67)	95%	0.155	
Prior AIDS-defining illness	Yes (*N*=28)	89%			Yes (*N*=14)	85%		
	No (*N*=90)	87%	0.813		No (*N*=60)	98%	**0.033**	0.934
IPI score	Low (*N*=49)	100%		Indicator	Low (*N*=30)	96%		
	Intermediate (*N*=53)	80%		0.937	Intermediate (*N*=28)	96%		
	High (*N*=9)	78%	**0.005**	0.937	High (*N*=13)	91%	0.803	
Ann Arbor stage	I/II (*N*=47)	100%			I/II (*N*=26)	96%		
	III/IV (*N*=71)	79%	**0.002**	0.936	III/IV (*N*=49)	93%	0.698	
Extranodal involvement	Yes (*N*=28)	93%			Yes (*N*=26)	98%		
	No (*N*=92)	86%	0.422		No (*N*=48)	8%	0.062	0.924
ECOG score	0-1 (*N*=83)	90%			0-1 (*N*=46)	98%		
	2-5 (*N*=28)	81%	0.226		2-5 (*N*=26)	92%	0.293	
Elevated LDH	Yes (*N*=47)	82%			Yes (*N*=26)	92%		
	No (*N*=65)	98%	**0.015**	0.333	No (*N*=48)	97%	0.276	
Antiretroviral Treatment	Viral load b.d. (*N*=32)	87%			Viral load b.d. (*N*=25)	96%		Indicator
	Naive (*N*=61)	85%			Naive (*N*=42)	97%		0.909
	Therapy failure (*N*=24)	95%	0.375		Therapy failure (*N*=8)	75%	**0.041**	0.942
cART during Chemotherapy	Yes (*N*=106)	86%			Yes (*N*=72)	97%		
	No (*N*=6)	100%	0.358		No (*N*=1)	0%	**<0.001**	0.915
CD20 positive lymphoma	Positive(*N*=108)	88%			Positive (*N*=76)	94%		
	Negative (n=2)	100%	0.564		Negative (*N*=0)	-	-	
Chemotherapy reduced doses	Yes (*N*=16)	87%			Yes (*N*=8)	100%		
	No (*N*=94)	88%	0.969		No (*N*=62)	95%	0.572	
Chemotherapy treatment delay	Yes (*N*=27)	88%			Yes (*N*=41)	95%		
	No (*N*=77)	88%	0.848		No (*N*=25)	96%	0.855	
Chemotherapy reduced # of cycles	Yes (*N*=15)	87%			Yes (*N*=21)	84%		
	No (*N*=102)	88%	0.934		No (*N*=51)	98%	**0.046**	0.934
Full Therapy	Full Chemotherapy (*N*=59)	85%			Full Chemotherapy (*N*=15)	100%		
	≥ 1 Reduction (*N*=43)	91%	0.412		≥ 1 Reduction (*N*=50)	93%	0.330	

Supplementary Table 4

Evaluation of risk factors for five-year relapse-free survival (5yRFS) in R-CHOP-treated DLBCL GMALL-treated BL.

Includes all DLBCL and BL with a R-CHOPs- and GMALL-treatment, respectively that reached a CR with their first-line chemotherapy (n=121 and n=76, respectively). Univariate statistics: Log rank test Multivariate statistics: Cox regression. Viral load b.d., Viral load below limit of detection; cART, combination antiretroviral therapy; BL,

Burkitt lymphoma; DLBCL, diffuse large B-cell lymphoma; IPI, International Prognostic Index; BM, bone marrow; CNS, central nervous system