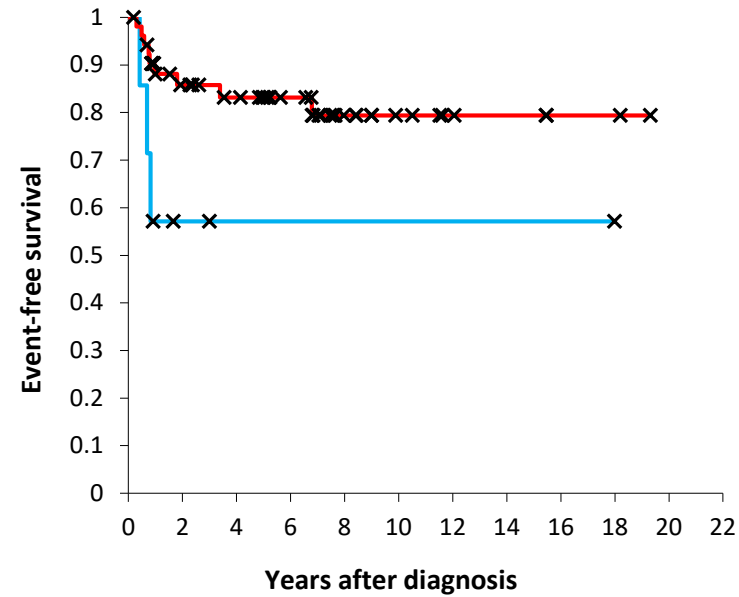


Supplemental Figure 1: 60* PCNSL patients without a pre-existing disorder



— Pediatric NHL-type therapy (n=53): 5-year EFS: 83%±5%
— Miscellaneous therapy (n=7): 5-year EFS: 57%±19%
p=0.044

*one pt. was excluded as therapy was not started for 3 months due to logistic reasons.

Supplemental Table 1: Initial characteristics of the 75 PCNSL study patients

Pt. No.	Age (y)	Lansky	Gender	pre-existing disorder	Time to diagnosis	B-Symptoms	Cranial nerve palsies	Histology	LDH level	Intracranial mass(es)	Intraspinal mass(es)	CSF only	Number of lesions
1	3.59	≥80%	male	/	11 weeks	no	no	DLBCL	≥500 U/l	yes	no	no	1 lesion
2	4.32	≥80%	male	/	2 weeks	no	yes	ALCL	≥500 U/l	yes	no	no	1 lesion
3	18.87	not applicable	male	/	8 weeks	no	no	DLBCL	<500 U/l	yes	no	no	1 lesion
4	7.41	<20%	male	HIV infection	3 weeks	no	unknown	DLBCL	≥500 U/l	yes	no	no	≥2 lesions
5	9.20	60-79%	male	/	12 weeks	no	no	DLBCL	<500 U/l	yes	no	no	1 lesion
6	12.53	60-79%	female	/	40 weeks	yes	yes	DLBCL	<500 U/l	yes	no	no	≥2 lesions
7	4.19	40-59%	male	/	1 week	no	yes	Burkitt lymphoma	<500 U/l	yes	no	no	≥2 lesions
8	12.12	≥80%	male	/	2 weeks	no	yes	Burkitt lymphoma	<500 U/l	yes	no	no	1 lesion
9	17.00	≥80%	male	/	4 weeks	no	no	DLBCL	≥500 U/l	yes	no	no	≥2 lesions
10	13.26	20-39%	female	/	4 weeks	no	yes	DLBCL	<500 U/l	yes	no	no	1 lesion
11	13.51	20-39%	female	/	6 weeks	no	no	ALCL	<500 U/l	yes	no	no	1 lesion
12	15.27	60-79%	female	/	2 weeks	no	no	DLBCL	<500 U/l	yes	no	no	1 lesion
13	8.90	≥80%	male	/	1 day	no	no	ALCL	unknown	yes	no	no	1 lesion
14	17.33	≥80%	female	/	28 weeks	no	no	ALCL	≥500 U/l	yes	no	no	1 lesion
15	3.15	unknown	female	BCP-LBL	unknown	unknown	unknown	DLBCL	unknown	yes	no	unknown	≥2 lesions
16	12.55	≥80%	female	/	2 weeks	yes	yes	ALCL	<500 U/l	yes	yes	unknown	≥2 lesions
17	14.05	≥80%	male	/	10 weeks	no	no	DLBCL	<500 U/l	yes	yes	no	≥2 lesions
18	13.99	≥80%	female	/	4 weeks	no	yes	DLBCL	<500 U/l	yes	no	no	1 lesion
19	14.22	60-79%	male	/	2 months	no	no	DLBCL	unknown	yes	no	no	unknown
20	7.21	≥80%	female	/	1 day	unknown	yes	DLBCL	unknown	yes	no	no	1 lesion
21	12.79	unknown	female	/	unknown	no	no	ALCL	<500 U/l	yes	unknown	no	unknown
22	12.50	≥80%	male	/	1,4 weeks	no	no	DLBCL	<500 U/l	yes	no	no	1 lesion
23	14.79	unknown	female	SLE	8 weeks	no	no	DLBCL	unknown	yes	no	no	1 lesion
24	9.04	unknown	male	/	12 weeks	no	no	DLBCL	unknown	yes	no	no	1 lesion
25	7.85	20-39%	female	HIV infection	12 weeks	no	yes	Burkitt lymphoma	≥500 U/l	yes	no	no	≥2 lesions
26	16.50	unknown	male	/	6,4 weeks	no	yes	Burkitt lymphoma	<500 U/l	yes	no	no	1 lesion
27	16.82	≥80%	male	/	12,9 weeks	no	yes	DLBCL	<500 U/l	yes	no	no	1 lesion
28	8.76	unknown	female	/	unknown	unknown	no	mature B-NHL NOS	<500 U/l	yes	no	no	1 lesion
29	16.07	unknown	male	/	unknown	unknown	no	Burkitt lymphoma	<500 U/l	yes	no	no	≥2 lesions
30	12.76	40-59%	female	/	unknown	no	yes	ALCL	<500 U/l	yes	no	no	unknown
31	10.26	unknown	female	kidney transplantation	3 weeks	no	no	DLBCL	unknown	yes	no	no	1 lesion
32	17.30	40-59%	male	JMML and allo-SCT	4 weeks	no	yes	DLBCL	<500 U/l	yes	no	no	≥2 lesions
33	1.56	60-79%	female	PID n. f. sp.	2 weeks	unknown	yes	DLBCL	<500 U/l	yes	no	no	≥2 lesions
34	7.60	20-39%	male	/	10 weeks	unknown	yes	ALCL	<500 U/l	no	no	yes	/
35	6.92	60-79%	male	/	2 weeks	no	yes	PTCL	unknown	yes	no	no	1 lesion
36	15.19	20-39%	female	/	15 weeks	no	yes	mature B-NHL NOS	<500 U/l	yes	no	no	≥2 lesions
37	15.30	40-59%	male	/	8 weeks	no	yes	Burkitt lymphoma	<500 U/l	yes	no	no	≥2 lesions

38	7.78	<20%	male	/	20 weeks	no	no	ALCL	<500 U/l	yes	no	no	≥2 lesions
39	12.58	60-79%	female	/	4 weeks	no	no	ALCL	<500 U/l	yes	no	no	1 lesion
40	17.86	40-59%	male	/	12 weeks	no	yes	ALCL	<500 U/l	yes	no	no	≥2 lesions
41	13.96	≥80%	male	/	2 weeks	no	no	mature B-NHL NOS	<500 U/l	yes	no	no	1 lesion
42	14.16	20-39%	male	/	12 weeks	no	yes	DLBCL	<500 U/l	yes	no	no	≥2 lesions
43	9.57	40-59%	male	heart transplantation	3 weeks	no	no	DLBCL	<500 U/l	yes	no	no	1 lesion
44	1.25	40-59%	female	CVID	7 weeks	no	yes	ALCL	<500 U/l	yes	no	no	≥2 lesions
45	14.25	40-59%	male	/	12 weeks	no	no	DLBCL	<500 U/l	no	yes	no	1 lesion
46	10.78	40-59%	male	/	6 weeks	yes	no	DLBCL	<500 U/l	yes	no	no	≥2 lesions
47	17.80	20-39%	female	colitis ulcerosa	2 weeks	no	no	DLBCL	<500 U/l	yes	no	no	≥2 lesions
48	15.26	<20%	male	/	20 weeks	yes	yes	DLBCL	<500 U/l	yes	no	no	≥2 lesions
49	10.13	40-59%	female	/	3 weeks	yes	yes	mature B-NHL NOS	<500 U/l	yes	no	no	1 lesion
50	11.50	60-79%	female	/	2 weeks	no	yes	DLBCL	<500 U/l	yes	no	no	1 lesion
51	11.07	unknown	male	/	3 weeks	no	no	DLBCL	<500 U/l	yes	no	no	≥2 lesions
52	11.41	unknown	female	/	unknown	yes	no	BCP-LBL	<500 U/l	yes	no	no	1 lesion
53	8.11	40-59%	male	/	36 weeks	no	yes	BCP-LBL	<500 U/l	no	no	yes	/
54	9.63	≥80%	male	/	3 weeks	no	no	ALCL	unknown	yes	no	no	unknown
55	17.32	20-39%	male	/	68 weeks	yes	yes	ALCL	<500 U/l	yes	yes	no	≥2 lesions
56	9.69	20-39%	female	/	24 weeks	yes	yes	Burkitt lymphoma	<500 U/l	no	yes	no	≥2 lesions
57	14.50	40-59%	male	/	16 weeks	no	no	DLBCL	<500 U/l	yes	no	no	1 lesion
58	11.33	≥80%	male	/	2,7 weeks	no	no	DLBCL	<500 U/l	yes	no	no	1 lesion
59	4.63	60-79%	male	/	12 weeks	no	no	Burkitt lymphoma	<500 U/l	yes	no	no	1 lesion
60	4.25	40-59%	male	/	2,9 weeks	no	no	Burkitt lymphoma	<500 U/l	yes	yes	no	≥2 lesions
61	12.55	≥80%	female	/	40 weeks	no	no	DLBCL	<500 U/l	yes	no	no	1 lesion
62	16.66	40-59%	male	/	16 weeks	no	yes	DLBCL	<500 U/l	yes	no	no	1 lesion
63	14.38	unknown	female	/	16 weeks	no	yes	EN MZL	<500 U/l	yes	no	no	≥2 lesions
64	13.06	≥80%	male	/	44 weeks	no	no	ALCL	≥500 U/l	yes	no	no	1 lesion
65	17.07	40-59%	male	/	8 weeks	yes	yes	DLBCL	≥500 U/l	yes	no	no	1 lesion
66	9.14	20-39%	male	/	2 weeks	no	yes	ALCL	≥500 U/l	yes	no	no	≥2 lesions
67	11.07	≥80%	male	/	1 week	no	yes	DLBCL	<500 U/l	yes	no	no	1 lesion
68	9.75	unknown	male	/	5 weeks	no	yes	BCP-LBL	unknown	yes	no	no	1 lesion
69	15.79	20-39%	male	CLIPPERS	11 weeks	no	no	DLBCL	<500 U/l	yes	no	no	≥2 lesions
70	5.50	40-59%	male	liver transplantation	16 weeks	no	no	DLBCL	<500 U/l	yes	no	no	≥2 lesions
71	4.01	unknown	female	PID n. f. sp.	0,6 weeks	no	no	DLBCL	≥500 U/l	yes	no	no	≥2 lesions
72	11.48	40-59%	male	/	2 weeks	unknown	unknown	mature B-NHL NOS	unknown	yes	no	no	≥2 lesions
73	14.00	60-79%	female	Factor VIII deficiency	8 weeks	no	no	ALCL	unknown	yes	no	no	≥2 lesions
74	12.00	≥80%	male	/	8 weeks	no	no	PTCL	<500 U/l	yes	no	no	≥2 lesions
75	18.00	not applicable	female	/	0,4 weeks	no	no	BCP-LBL	<500 U/l	no	no	yes	/

Abbreviations: No., number; y, years; BCP-LBL, B-cell precursor lymphoblastic lymphoma; SLE, systemic lupus erythematosus; HIV, human immunodeficiency virus; JMML, juvenile myelomonocytic leukemia; allo-SCT, allogeneic stem cell transplantation; PID n. f. sp., primary immunodeficiency not further specified; CVID, common variable immunodeficiency; CLIPPERS, chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids; DLBCL, diffuse large B-cell lymphoma; ALCL, anaplastic large cell lymphoma; B-NHL NOS, B-cell non-Hodgkin's lymphoma not otherwise specified; PTCL, peripheral T-cell lymphoma; EN MZL, extra-nodal marginal zone lymphoma; LDH, lactate dehydrogenase; CSF, cerebrospinal fluid.

Supplemental Table 2: Therapy details of the 75 PCNSL study patients

Pt. No.	Therapy components	Type of therapy	MTX in mg/m2/cycle	ARA-C in mg/m2/cycle	Anthracyclines and cumulative dose in mg/m2	Alkylating agents and cumulative dose in mg/m2/cycle	ith. therapies	RT
1	Chemo + RT	miscellaneous therapy	5000	no ARA-C	no anthracyclines	cyclophosphamide, 400	yes	yes
2	Chemo only	miscellaneous therapy	3500	8000	no anthracyclines	no alkylating agents	yes	no
3	Chemo + RT	miscellaneous therapy	8000	no ARA-C	no anthracyclines	no alkylating agents	yes	yes
4	Chemo + Rituximab	miscellaneous therapy	no MTX	no ARA-C	doxorubicin, 50	cyclophosphamide, 400 - 1000	yes	no
5	Chemo + RT	miscellaneous therapy	1000	no ARA-C	doxorubicin, 100	cyclophosphamide, 1000	yes	yes
6	Chemo only	pediatric NHL therapy	8000	12000	doxorubicin, 180	cyclophosphamide, 300 - 1000 - 1500 - 3000	yes	no
7	Chemo only	pediatric NHL therapy	5000 + 8000	no ARA-C	daunorubicin, 120 + doxorubicin, 120	cyclophosphamide, 1000 - 1500 - 3000	yes	no
8	Chemo only	pediatric NHL therapy	8000	12000	doxorubicin, 180	cyclophosphamide, 300 - 1000 - 1500 - 3000	yes	no
9	Chemo only	miscellaneous therapy	8000	3000	unknown	no alkylating agents	yes	no
10	Chemo + Rituximab	pediatric NHL therapy	5000	12000	doxorubicin, 100	cyclophosphamide, 400 - 1000 + ifosphamide, 4000	yes	no
11	no therapy due to logistic reasons	/	no MTX	no ARA-C	no anthracyclines	no alkylating agents	no	no
12	Chemo only	pediatric NHL therapy	8000	12000	doxorubicin, 240	cyclophosphamide, 300 - 1000 - 1500 - 3000	yes	no
13	Chemo + RT	pediatric NHL therapy	8000	12000	doxorubicin, 240	cyclophosphamide, 300 - 1000 - 1500 - 3000	yes	yes
14	Chemo + RT	pediatric NHL therapy	8000	12000	doxorubicin, 240	cyclophosphamide, 300 - 1000 - 1500 - 3000	yes	yes
15	Chemo + RT	pediatric NHL therapy	8000	12000	doxorubicin, 60	yes, but drug and dose not reported	yes	yes
16	Chemo + RT	pediatric NHL therapy	8000	12000	doxorubicin, 240	cyclophosphamide, 300 - 1000 - 1500 - 3000	yes	yes
17	Chemo + Rituximab	pediatric NHL therapy	8000	12000	doxorubicin, 240	cyclophosphamide, 300 - 1000 - 1500 - 3000	yes	no
18	Chemo only	pediatric NHL therapy	8000	12000	doxorubicin, 240	cyclophosphamide, 300 - 1000 - 1500 - 3000	yes	no
19	Chemo only	pediatric NHL therapy	8000	12000	doxorubicin, 240	cyclophosphamide, 300 - 1000 - 1500 - 3000	yes	no
20	Chemo + RT	pediatric NHL therapy	8000	12000	doxorubicin, 240	cyclophosphamide, 300 - 1000 - 1500 - 3000	yes	yes
21	Chemo + RT	pediatric NHL therapy	5000	12000	doxorubicin, 100	cyclophosphamide, 400 - 1000 + ifosphamide, 4000	yes	yes
22	Chemo only	pediatric NHL therapy	8000	12000	doxorubicin, 180	cyclophosphamide, 300 - 1000 - 1500 - 3000	yes	no
23	Chemo + RT	miscellaneous therapy	no MTX	no ARA-C	no anthracyclines	no alkylating agents	no	yes
24	Chemo only	pediatric NHL therapy	8000	12000	doxorubicin, 240	cyclophosphamide, 300 - 1000 - 1500 - 3000	yes	no
25	Chemo + Rituximab	miscellaneous therapy	5000 + 6000 + 8000	no ARA-C	no anthracyclines	no alkylating agents	yes	no
26	Chemo only	pediatric NHL therapy	5000	12000	daunorubicin, 100	cyclophosphamide, 400 - 1000 + ifosphamide, 8000	yes	no
27	Chemo only	pediatric NHL therapy	5000	12000	daunorubicin, 100	cyclophosphamide, 400 - 1000 + ifosphamide, 8000	yes	no
28	Chemo only	pediatric NHL therapy	5000	6000	doxorubicin, 240	cyclophosphamide, 450 - 1500 -2000	yes	no
29	Chemo only	pediatric NHL therapy	5000	6000	doxorubicin, 240	cyclophosphamide, 450 - 1500 -2000	yes	no
30	Chemo only	pediatric NHL therapy	5000	no ARA-C	doxorubicin, 100	cyclophosphamide, 400 - 1000; ifosphamide, 4000	yes	no
31	Chemo + Rituximab	miscellaneous therapy	8000	no ARA-C	no anthracyclines	cyclophosphamide, 2400	yes	no
32	Chemo + Rituximab	pediatric NHL therapy	8000	12000	doxorubicin, 180	cyclophosphamide, 300 - 1000 - 1500 - 3000	yes	no
33	no therapy - palliation	miscellaneous therapy	no MTX	no ARA-C	no anthracyclines	no alkylating agents	unknown	no
34	Chemo + RT	pediatric NHL therapy	5000	12000	doxorubicin, 100	cyclophosphamide, 400 - 1000 + ifosphamide, 4000	yes	yes
35	no chemo - wait-and-see	pediatric NHL therapy	no MTX	no ARA-C	no anthracyclines	no alkylating agents	no	no
36	Chemo only	pediatric NHL therapy	5000	12000	doxorubicin, 100	cyclophosphamide, 400 - 1000 + ifosphamide, 4000	yes	no
37	Chemo only	pediatric NHL therapy	5000	12000	doxorubicin, 100	cyclophosphamide, 400 - 1000 + ifosphamide, 4000	yes	no

38	Chemo + RT	pediatric NHL therapy	5000	12000	doxorubicin, 100	cyclophosphamide, 400 - 1000 + ifosphamide, 4000	yes	yes
39	Chemo + RT	pediatric NHL therapy	5000	12000	doxorubicin, 100	cyclophosphamide, 400 - 1000 + ifosphamide, 4000	yes	yes
40	Chemo + RT	pediatric NHL therapy	5000	12000	doxorubicin, 100	cyclophosphamide, 400 - 1000 + Ifosphamide, 4000	yes	yes
41	Chemo only	pediatric NHL therapy	5000	12000	doxorubicin, 100	cyclophosphamide, 400 - 1000 + ifosphamide, 4000	yes	no
42	Chemo only	pediatric NHL therapy	5000	12000	doxorubicin, 100	cyclophosphamide, 400 - 1000 + ifosphamide, 4000	yes	no
43	Chemo only	pediatric NHL therapy	2500	6000	doxorubicin, 50	cyclophosphamide, 400 - 1000 + ifosphamide, 4000	yes	no
44	Chemo + RT	pediatric NHL therapy	5000	12000	doxorubicin, 100	cyclophosphamide, 400 - 1000 + ifosphamide, 4000	yes	yes
45	Chemo only	pediatric NHL therapy	5000	12000	doxorubicin, 100	cyclophosphamide, 400 - 1000 + ifosphamide, 4000	yes	no
46	Chemo only	pediatric NHL therapy	5000	12000	doxorubicin, 100	cyclophosphamide, 400 - 1000 + ifosphamide, 4000	yes	no
47	Chemo only	pediatric NHL therapy	5000	12000	doxorubicin, 100	cyclophosphamide, 400 - 1000 + ifosphamide, 4000	yes	no
48	Chemo + Rituximab	pediatric NHL therapy	5000	12000	doxorubicin, 100	cyclophosphamide, 400 - 1000 + ifosphamide, 4000	yes	no
49	Chemo only	pediatric NHL therapy	5000	12000	doxorubicin, 100	cyclophosphamide, 400 - 1000 + ifosphamide, 4000	yes	no
50	Chemo only	pediatric NHL therapy	5000	12000	doxorubicin, 100	cyclophosphamide, 400 - 1000 + ifosphamide, 4000	yes	no
51	Chemo only	pediatric NHL therapy	5000	12000	doxorubicin, 100	cyclophosphamide, 400 - 1000 + ifosphamide, 4000	yes	no
52	Chemo + RT	pediatric NHL therapy	5000	no ARA-C	daunorubicin, 120 + doxorubicin, 120	cyclophosphamide, 1000 - 1000 - 1000	yes	yes
53	Chemo only	pediatric NHL therapy	5000	4000	daunorubicin, 150 + doxorubicin, 120	cyclophosphamide, 1000 - 1000 - 1000 - 1000	yes	no
54	Chemo + RT	pediatric NHL therapy	8000	12000	doxorubicin, 180	cyclophosphamide, 300 - 1000 - 1500 - 3000	yes	yes
55	Chemo + RT	pediatric NHL therapy	5000	6000	doxorubicin, 100	cyclophosphamide, 400 - 1000 + ifosphamide, 4000	yes	yes
56	Chemo + Rituximab	pediatric NHL therapy	5000	6000	doxorubicin, 100	cyclophosphamide, 400 - 1000 + ifosphamide, 4000	yes	no
57	Chemo + Rituximab	pediatric NHL therapy	5000	6000	doxorubicin, 100	cyclophosphamide, 1000 + ifosphamide, 4000 + ifosphamide, 9000	yes	no
58	Chemo + Rituximab	pediatric NHL therapy	unknown	unknown	unknown	unknown	yes	no
59	Chemo + Rituximab	pediatric NHL therapy	5000	6000	doxorubicin, 100	cyclophosphamide, 400 - 1000 + ifosphamide, 4000	yes	no
60	Chemo + Rituximab	pediatric NHL therapy	5000	6000	doxorubicin, 100	cyclophosphamide, 1000 + ifosphamide, 4000 + ifosphamide, 9000	yes	no
61	Chemo + Rituximab	pediatric NHL therapy	5000	6000	doxorubicin, 100	cyclophosphamide, 400 - 1000 + ifosphamide, 4000	yes	no
62	Chemo + RT + Rituximab	miscellaneous therapy	5000	12000	doxorubicin, 100	cyclophosphamide, 400 - 1000 + ifosphamide, 4000	yes	yes
63	Chemo + RT	miscellaneous therapy	no MTX	no ARA-C	no anthracyclines	no alkylating agents	yes	yes
64	Chemo only	pediatric NHL therapy	8000	12500	doxorubicin, 240	cyclophosphamide, 300 - 1500 - 3000 - 1000 - 1000	yes	no
65	Chemo + Rituximab	pediatric NHL therapy	8000	12000	doxorubicin, 180	cyclophosphamide, 300 - 1000 - 1500 - 3000	yes	no
66	Chemo + RT	pediatric NHL therapy	5000	12000	doxorubicin, 100	cyclophosphamide, 400 - 1000 + ifosphamide, 4000	yes	yes
67	Chemo + Rituximab	pediatric NHL therapy	8000	12000	doxorubicin, 180	cyclophosphamide, 300 - 1000 - 1500 - 3000	yes	no
68	Chemo + RT	pediatric NHL therapy	5000	no ARA-C	daunorubicin, 120 + doxorubicin, 120	cyclophosphamide, 1000	yes	yes
69	Chemo + RT + Rituximab	miscellaneous therapy	3500	no ARA-C	no anthracyclines	cyclophosphamide, 300	yes	yes
70	Chemo only	miscellaneous therapy	1000 + 5000	no ARA-C	no anthracyclines	no alkylating agents	yes	no
71	Chemo + RT	miscellaneous therapy	1000	no ARA-C	doxorubicin, 25	cyclophosphamide, 1000	yes	yes
72	Chemo only	pediatric NHL therapy	8000	12000	doxorubicin, 180	cyclophosphamide, 300 - 1000 - 1500 - 3000	unknown	no
73	Chemo + RT	miscellaneous therapy	5000	6000	no anthracyclines	procarbazine	yes	yes
74	Chemo only	adult NHL therapy	8000	1600	no anthracyclines	temozolomide	no	no
75	Chemo + RT	pediatric NHL therapy	5000	no ARA-C	daunorubicin, 100 + doxorubicin, 100	cyclophosphamide, 1000 - 1000 - 1000	yes	yes

Abbreviations: No., number; Chemo, chemotherapy; RT, radiotherapy; NHL, non-Hodgkin's lymphoma; MTX, methotrexate; ARA-C, cytarabine; ith., intrathecal; RT, radiotherapy.

Supplemental Table 3: Disease outcome, long-term side effects and follow-up of the 75 PCNSL study patients

Pt. No.	Relapse/progression	Death	Cause of Death	Neurological long-term toxicity	Cardiac long-term toxicity	Endocrine long-term toxicity	Other late effects	Follow-up (y)
1	no	no	/	no	no	no	no	1.65
2	no	no	/	no	no	no	no	2.99
3	yes	no	/	no	no	no	osteonecrosis	15.03
4	no	yes	TRM (septicemia)	no	no	no	no	/
5	no	no	/	no	no	no	no	17.98
6	no	no	/	no	no	partial hypopituitarism	no	8.98
7	yes	yes	relapse	no	no	no	no	/
8	no	no	/	no	no	no	no	2.36
9	no	no	/	no	no	no	osteonecrosis	0.90
10	no	no	/	no	no	no	no	0.92
11	yes	no	/	no	no	no	no	0.96
12	no	no	/	no	unknown	no	no	5.14
13	no	no	/	no	unknown	no	no	6.56
14	no	no	/	cognitive impairment	unknown	unknown	unknown	19.31
15	no	no	/	unknown	unknown	unknown	unknown	25.59
16	yes	yes	relapse	unknown	unknown	unknown	unknown	/
17	no	no	/	no	unknown	no	no	8.42
18	no	no	/	no	no	no	no	11.61
19	yes	yes	relapse	no	unknown	no	no	/
20	no	no	/	unknown	unknown	unknown	unknown	15.44
21	no	no	/	unknown	no	no	no	7.58
22	no	no	/	speech and movement difficulties	no	no	no	0.93
23	no	yes	unknown	transverse myelitis causing paraplegia and neurogenic bladder (SLE or PCNSL?)	unknown	no	no	/
24	no	no	/	right hemiplegia, epilepsy	no	no	no	18.19
25	no	no	/	no	no	no	no	0.49
26	no	no	/	no	no	no	no	6.75
27	no	no	/	left hand tremor	no	no	no	5.22
28	no	no	/	unknown	unknown	unknown	unknown	7.04
29	no	no	/	unknown	unknown	unknown	unknown	7.11
30	yes	no	/	unknown	no	unknown	unknown	4.58
31	no	no	/	epilepsy	no	no	no	12.70
32	yes	no	/	left arm paresis, club foot and epilepsy	no	no	no	3.21
33	no	yes	PCNSL without any therapy	no	no	no	no	/
34	yes	yes	relapse	optic nerve atrophy on both sides	no	no	no	/
35	no	no	/	no	no	no	no	11.52
36	no	no	/	balance and sensory disturbances, facial nerve paresis, bladder/bowel evacuation disorder	no	no	no	7.45
37	no	no	/	diplopia	no	panhypopituitarism	osteonecrosis	8.40
38	no	no	/	complete amaurosis of the left eye, epilepsy	no	no	no	15.45

39	no	no	/	no	no	no	6.79	
40	no	no	/	no	no	no	7.65	
41	no	no	/	no	no	no	12.05	
42	no	no	/	hearing loss, optic nerve atrophy on the right side	no	no	9.88	
43	no	yes	TRM (heart graft failure)	no	no	no	/	
44	no	yes	TRM (pneumonia)	left hemiparesis	no	no	/	
45	no	no	/	N. peroneus palsy	no	no	10.49	
46	no	no	/	no	no	psychosocial problems	4.83	
47	no	yes	TRM (not specified)	no	no	no	/	
48	yes	yes	relapse	no	no	no	/	
49	no	no	/	vincristine neuropathy	no	no	7.96	
50	no	no	/	no	no	no	2.60	
51	no	no	/	no	no	panhypopituitarism	3.53	
52	no	no	/	no	no	osteonecrosis	5.62	
53	no	no	/	massive visual deficit on the left side	no	no	0.19	
54	yes	yes	relapse / neurological disorder	no	no	no	/	
55	no	no	/	no	no	no	1.92	
56	no	no	/	no	no	no	0.87	
57	no	no	/	photophobia, chronic headaches, polyneuropathy	no	no	4.96	
58	no	no	/	no	no	no	0.87	
59	no	no	/	no	no	no	2.27	
60	no	no	/	no	no	no	1.52	
61	no	no	/	no	no	no	0.68	
62	yes	no	/	no	no	no	7.50	
63	yes	no	/	diminished cognitive function	no	no	10.41	
64	no	no	/	epilepsy	no	no	6.83	
65	no	no	/	no	no	no	0.85	
66	yes	no	/	no	no	no	1.84	
67	no	no	/	facial nerve palsy	no	no	0.99	
68	no	no	/	no	no	no	9.00	
69	no	no	/	no	no	no	0.69	
70	no	no	/	no	no	no	2.16	
71	no	no	/	bilateral hearing loss	no	no	CMV retinitis, chronic GvHD	2.41
72	no	no	/	no	no	no	4.14	
73	no	no	/	no	no	no	9.02	
74	no	no	/	epilepsy	no	no	5.01	
75	yes	no	/	no	no	no	3.39	

Abbreviations: No., number; TRM, treatment-related mortality; PCNSL, primary central nervous system lymphoma; CMV, cytomegalovirus; GvHD, graft-versus-host disease; y, years.

Supplemental Table 4A: Univariate analysis for event-free survival

Variables	Estimate	Std Err	ChiSq	p-value	Hazard Ratio	HR Lower CL	HR Upper CL
Pre-existing disease: no vs. yes	-0.974	0.470	4.302	0.027	0.377	0.150	0.948
HD-MTX used: yes vs. no	-1.707	0.520	10.756	0.0002	0.181	0.065	0.503
HD-ARA-C used: yes vs. no	-1.077	0.451	5.712	0.012	0.341	0.141	0.824
Alkylators used: yes vs. no	-1.034	0.519	3.971	0.033	0.356	0.129	0.983
Anthracyclines used: yes vs. no	-0.415	0.518	0.643	0.423	0.660	0.239	1.821
Intrathecal therapies: yes vs. no	-0.652	0.750	0.755	0.385	0.521	0.120	2.267
Rituximab used: yes vs. no	0.112	0.565	0.039	0.843	1.118	0.370	3.382
Radiotherapy: yes vs. no	0.540	0.448	1.452	0.228	1.716	0.713	4.127
Chemo + RT vs. chemo alone	0.820	0.559	2.156	0.142	2.271	0.760	6.788
Ritux. + chemo vs. chemo alone	0.704	0.677	1.082	0.298	2.021	0.537	7.610
Other therapy* vs. chemo alone	1.888	0.842	5.021	0.025	6.604	1.267	34.425
Age group: ≥15 vs. <15 years	0.416	0.490	0.722	0.396	1.516	0.581	3.956
Lansky 20-39% vs. <20%	-0.834	0.872	0.915	0.339	0.434	0.079	2.398
Lansky 40-59% vs. <20%	-1.098	0.822	1.786	0.181	0.334	0.067	1.669
Lansky 60-79% vs. <20%	-1.921	1.003	3.665	0.056	0.146	0.020	1.047
Lansky ≥80% vs. <20%	-2.410	1.004	5.763	0.003	0.090	0.013	0.643
Gender: female vs. male	0.094	0.457	0.042	0.837	1.098	0.449	2.689
B-symptoms: yes vs. no	-0.210	0.753	0.078	0.781	0.811	0.186	3.544
ALCL vs. DLBCL	0.511	0.495	1.067	0.302	1.667	0.632	4.398
Burkitt's lymphoma vs. DLBCL	-0.794	1.050	0.571	0.450	0.452	0.058	3.540
Mature B-NHL NOS vs. DLBCL	NA	NA	NA	NA	NA	NA	NA
Other NHL vs. DLBCL	0.058	0.775	0.006	0.940	1.060	0.232	4.842
Number of lesions: ≥2 vs. 1	0.913	0.548	2.776	0.085	2.493	0.851	7.300
Pediatric NHL protocol: yes vs. no	-0.784	0.470	2.783	0.095	0.457	0.182	1.147

Abbreviations: Std Err, standard error; ChiSq, Chi square test; HR, hazard ratio; CL, confidence limit; HD-MTX, high-dose-methotrexate; HD-ARA-C, high-dose-cytarabine; Chemo, chemotherapy; RT, radiotherapy. Ritux., rituximab; ALCL, anaplastic large cell lymphoma; DLBCL, diffuse large B-cell lymphoma; NOS, not otherwise specified; NHL, non-Hodgkin's lymphoma; NA, not applicable.

* n=3 (no initial therapy due to logistic reasons, n=1; without any initial therapy, n=1; wait-and-see strategy after total resection, n=1)

Supplemental Table 4B: Univariate analysis for overall survival

Variables	Estimate	Std Err	ChiSq	p-value	Hazard Ratio	HR Lower CL	HR Upper CL
Pre-existing disease: no vs. yes	-1.683	0.581	8.403	0.001	0.186	0.060	0.580
HD-MTX used: yes vs. no	-1.411	0.674	4.386	0.023	0.244	0.065	0.913
HD-ARA-C used: yes vs. no	-0.427	0.615	0.482	0.488	0.653	0.196	2.177
Alkylators used: yes vs. no	-0.276	0.777	0.126	0.723	0.759	0.165	3.480
Anthracyclines used: yes vs. no	0.246	0.777	0.100	0.752	1.278	0.279	5.861
Intrathecal therapies: yes vs. no	-0.388	1.051	0.136	0.712	0.679	0.087	5.322
Rituximab used: yes vs. no	-0.058	0.781	0.006	0.941	0.944	0.204	4.365
Radiotherapy: yes vs. no	0.074	0.588	0.016	0.900	1.077	0.340	3.408
Chemo + RT vs. chemo alone	0.348	0.673	0.267	0.605	1.416	0.379	5.291
Ritux. + chemo vs. chemo alone	0.224	0.872	0.066	0.797	1.251	0.227	6.906
Other therapy* vs. chemo alone	1.156	1.124	1.057	0.304	3.177	0.351	28.764
Age group: ≥15 vs. <15 years	-0.462	0.776	0.354	0.552	0.630	0.138	2.884
Lansky 20-39% vs. <20%	-1.152	1.010	1.301	0.254	0.316	0.044	2.288
Lansky 40-59% vs. <20%	-1.502	0.915	2.692	0.101	0.223	0.037	1.339
Lansky 60-79% vs. <20%	-1.550	1.001	2.396	0.122	0.212	0.030	1.511
Lansky ≥80% vs. <20%	-2.033	1.003	4.109	0.018	0.131	0.018	0.935
Gender: female vs. male	0.159	0.586	0.073	0.787	1.172	0.372	3.696
B-symptoms: yes vs. no	0.569	0.797	0.509	0.476	1.766	0.370	8.425
ALCL vs. DLBCL	0.330	0.633	0.271	0.602	1.391	0.402	4.808
Burkitt's lymphoma vs. DLBCL	-0.286	1.073	0.071	0.790	0.751	0.092	6.158
Mature B-NHL NOS vs. DLBCL	NA	NA	NA	NA	NA	NA	NA
Other NHL vs. DLBCL	NA	NA	NA	NA	NA	NA	NA
Number of lesions: ≥2 vs. 1	1.487	0.802	3.433	0.043	4.423	0.918	21.319
Pediatric NHL protocol: yes vs. no	0.384	0.776	0.245	0.621	1.468	0.321	6.712

Abbreviations: Std Err, standard error; ChiSq, Chi square test; HR, hazard ratio; CL, confidence limit; HD-MTX, high-dose-methotrexate; HD-ARA-C, high-dose-cytarabine; Chemo, chemotherapy; RT, radiotherapy. Ritux., rituximab; ALCL, anaplastic large cell lymphoma; DLBCL, diffuse large B-cell lymphoma; NOS, not otherwise specified; NHL, non-Hodgkin's lymphoma; NA, not applicable.

* n=3 (no initial therapy due to logistic reasons, n=1; without any initial therapy, n=1; wait-and-see strategy after total resection, n=1)

Multivariate analyses for event-free and overall survival

In multivariate analyses, only usage of high-dose methotrexate retained significance for event-free survival (hazard ratio: 0.195, 95% confidence limits: 0.070–0.540, p-value: 0.002) and only pre-existing disorders (hazard ratio: 0.172, 95% confidence limits: 0.041–0.716, p-value: 0.016) for overall survival.