

## Supplementary data

**Table S1. Clinical characteristics of 109 patients with primary central nervous system lymphoma**

Variables	HDMTX monotherapy (n = 69)	HDMTX-based polychemotherapies (n = 40)	P value
<b>Age at diagnosis, years‡</b>	64 (39-86)	61 (24-78)	0.061
<b>Sex†</b>			0.746
Male	35 (50.7)	19 (47.5)	
Female	34 (49.3)	21 (52.5)	
<b>Diagnostic strategy†</b>			0.013
Surgical resection	10 (14.5)	14 (35)	
Stereotactic biopsy/CSF analysis	59 (85.5)	26 (65)	
<b>Disease involvement†</b>			0.143
Unifocal	23 (33.3)	19 (47.5)	
Multifocal/primary leptomeningeal	46 (66.7)	21 (52.5)	
<b>Meningeal involvement†</b>			0.006
Present	25 (36.2)	5 (12.5)	
Absent	39 (56.5)	26 (65)	
Unknown	5 (7.3)	9 (22.5)	
<b>Ocular involvement†</b>			<0.001
Present	11 (15.9)	3 (7.5)	
Absent	38 (55.1)	10 (25)	
Unknown	20 (29)	27 (67.5)	
<b>ECOG PS†</b>			0.05
0, 1	18 (26.1)	4 (10)	
≥2	51 (73.9)	36 (90)	
<b>Serum LDH†</b>			0.003
Elevated	9 (13)	15 (27.5)	
Normal	60 (87)	25 (62.5)	
<b>Serum albumin†</b>			0.966
<3.5 g/dL	17 (24.6)	10 (25)	
≥3.5 g/dL	52 (75.4)	30 (75)	
<b>High-risk IELSG score†</b>	19 (27.5)	9 (22.5)	0.562
<b>High-risk MSKCC group†</b>	26 (37.7)	13 (32.5)	0.587
<b>Frontline rituximab†</b>	51 (73.9)	16 (40)	<0.001
<b>Treatment response†</b>			0.192
Overall response	42 (60.9)	25 (62.5)	
CR/CRu	35 (50.7)	21 (52.5)	
PR	7 (10.2)	4 (10)	
SD/PD	24 (34.8)	9 (22.5)	

Not evaluated@

3 (4.3)

6 (15)

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‡ Median (range)

† Number of patients (%)

@ Including four patients with induction death and five patients who were lost to follow up.

Abbreviations: HDMTX, high-dose methotrexate; CSF, cerebrospinal fluid; ECOG PS, Eastern Cooperative Oncology Group Performance Status; LDH, lactate dehydrogenase; IELSG, International Extranodal Lymphoma Study Group; MSKCC, Memorial Sloan Kettering Cancer Center; HDMTX, high-dose methotrexate; CR, complete response; CRu, unconfirmed complete response; PR, partial response; SD, stable disease; PD, progressive disease.

**Table S2. Univariate and multivariate analyses of risk factors for examining overall survival in patients with PCNSL**

Variables	Univariate analysis			Multivariate analysis		
	HR	95% CI	<i>P</i> value	HR	95% CI	<i>P</i> value
Age >60 years	1.36	0.78–2.36	0.282			
Sex (Male vs. Female)	1.45	0.84–2.5	0.186			
Diagnostic strategy@	1.3	0.7–2.41	0.403			
Extent of disease#	1.99	1.08–3.68	0.028*	1.31	0.67–2.58	0.428
Meningeal involvement	1.7	0.94–3.09	0.081			
Ocular involvement	0.63	0.25–1.54	0.306			
ECOG PS (≥2 vs. 0,1)	1.98	0.96–4.09	0.065			
KPS <70	3.92	2.23–6.87	<0.001*			
Serum LDH >1x ULN	5.18	2.75–9.75	<0.001*			
Serum albumin <3.5 g/dL	3.16	1.74–5.75	<0.001*	2.14	1.13–4.04	0.019
High-risk IELSG score	2.14	1.18–3.86	0.012*	1.55	0.83–2.9	0.168
High-risk MSKCC group	3.18	1.84–5.51	<0.001*	2.06	1.15–3.7	0.016
Induction treatment†	1.31	0.73–2.32	0.364			
Frontline rituximab	0.76	0.44–1.31	0.328			
Response to initial therapy‡	3.95	2.27–6.89	<0.001*	3.63	1.96–6.75	< 0.001

@ Surgery resection versus stereotactic biopsy/cerebrospinal fluid analysis.

# Multifocal/primary leptomeningeal disease versus unifocal lesion.

† High-dose methotrexate-based polychemotherapies versus High-dose methotrexate monotherapy.

‡ Stable disease/progressive disease/not evaluable versus complete response/unconfirmed complete response/partial response.

\*All potential prognostic factors for overall survival with a *P* value less than 0.05 in the univariate analysis were selected for multivariate analysis, except for those redundant with IELSG or MSKCC prognostic score.

Abbreviations: PCNSL, primary central nervous system lymphoma; HR, hazard ratio; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group Performance Status; LDH, lactate dehydrogenase; ULN, upper limit of normal; IELSG, International Extranodal Lymphoma Study Group; MSKCC, Memorial Sloan Kettering Cancer Center.

**Table S3. Demographic and clinical characteristics of patients who responded to the induction therapy**

<b>Variables</b>	<b>With consolidation/ maintenance (n = 51)</b>	<b>Without consolidation/ maintenance (n = 16)</b>	<b>P value</b>
<b>Age at diagnosis, years‡</b>	60 (39-84)	63 (24-86)	0.994
<b>Sex†</b>			0.392
Male	27 (52.9)	6 (37.5)	
Female	24 (47.1)	10 (62.5)	
<b>Diagnostic strategy†</b>			0.029
Surgical resection	7 (13.7)	7 (43.7)	
Stereotactic biopsy/CSF analysis	44 (86.3)	9 (56.3)	
<b>Disease involvement†</b>			0.775
Unifocal	22 (43.1)	8 (50)	
Multifocal/primary leptomeningeal	29 (56.9)	8 (50)	
<b>Meningeal involvement†</b>			0.291
Present	12 (23.5)	7 (43.7)	
Absent	34 (66.7)	8 (50)	
Unknown	5 (9.8)	1 (6.3)	
<b>Ocular involvement†</b>			0.169
Present	8 (15.7)	3 (18.7)	
Absent	26 (51)	4 (25)	
Unknown	17 (33.3)	9 (56.3)	
<b>ECOG PS†</b>			0.527
0, 1	15 (39.4)	3 (18.7)	
≥2	36 (70.6)	13 (81.3)	
<b>Serum LDH†</b>			0.05
Elevated	3 (5.9)	4 (25)	
Normal	48 (94.1)	12 (75)	
<b>Serum albumin†</b>			0.716
<3.5 g/dL	8 (15.7)	3 (18.7)	
≥3.5 g/dL	43 (84.3)	13 (81.3)	
<b>High-risk IELSG score†</b>	10 (19.6)	4 (25)	0.73
<b>High-risk MSKCC group†</b>	12 (23.5)	7 (43.7)	0.202
<b>Induction treatment†</b>			0.036
HDMTX monotherapy	36 (70.6)	6 (37.5)	
HDMTX-based polychemotherapy	15 (39.4)	10 (62.5)	
<b>Frontline rituximab†</b>	33 (64.7)	9 (56.3)	0.566
<b>Response to initial therapy†</b>			0.042
CR/CRu	40 (78.4)	16 (100)	
PR	11 (21.6)	0 (0)	

‡ Median (range)

† Number of patients (%)

Abbreviations: CSF, cerebrospinal fluid; ECOG PS, Eastern Cooperative Oncology Group Performance Status; LDH, lactate dehydrogenase; IELSG, International Extranodal Lymphoma Study Group; MSKCC, Memorial Sloan Kettering Cancer Center; HDMTX, high-dose methotrexate; CR, complete response; CRu, unconfirmed complete response; PR, partial response.

## Supplementary figure legends

Fig. S1 Kaplan–Meier curves for (A) overall survival and (B) progression-free survival in patients with primary nervous system lymphoma (PCNSL).

Fig. S2 **Kaplan–Meier survival curves in 18 patients with stable disease/progressive disease who responded to the subsequent salvage therapies, stratified by the adoption of consolidation treatment or not.**

Patients with consolidation treatment had a trend of better overall survival (OS) (A) and progression-free survival (PFS) (B) than those without consolidation treatment. Notably, OS and PFS were calculated from the time of achieving a complete or partial response after salvage treatment.

Fig. S3 **Kaplan–Meier survival curves in patients with primary central nervous system lymphoma who responded to the induction chemotherapy, stratified by the types of induction chemotherapy and the adoption of consolidation/maintenance (cons./main.) treatment or not.**

In the high-dose methotrexate (HDMTX)-monotherapy group (A), the patients with cons./main. treatment had a trend of better overall survival (OS) as compared to those without treatment. Similarly, in the HDMTX-based-polychemotherapy group (B), the patients being treated also had a trend of better OS as compared to the patients without cons./main. treatment. Notably, OS was calculated from

the time of achieving a complete or partial response after induction treatment.

Fig. S1

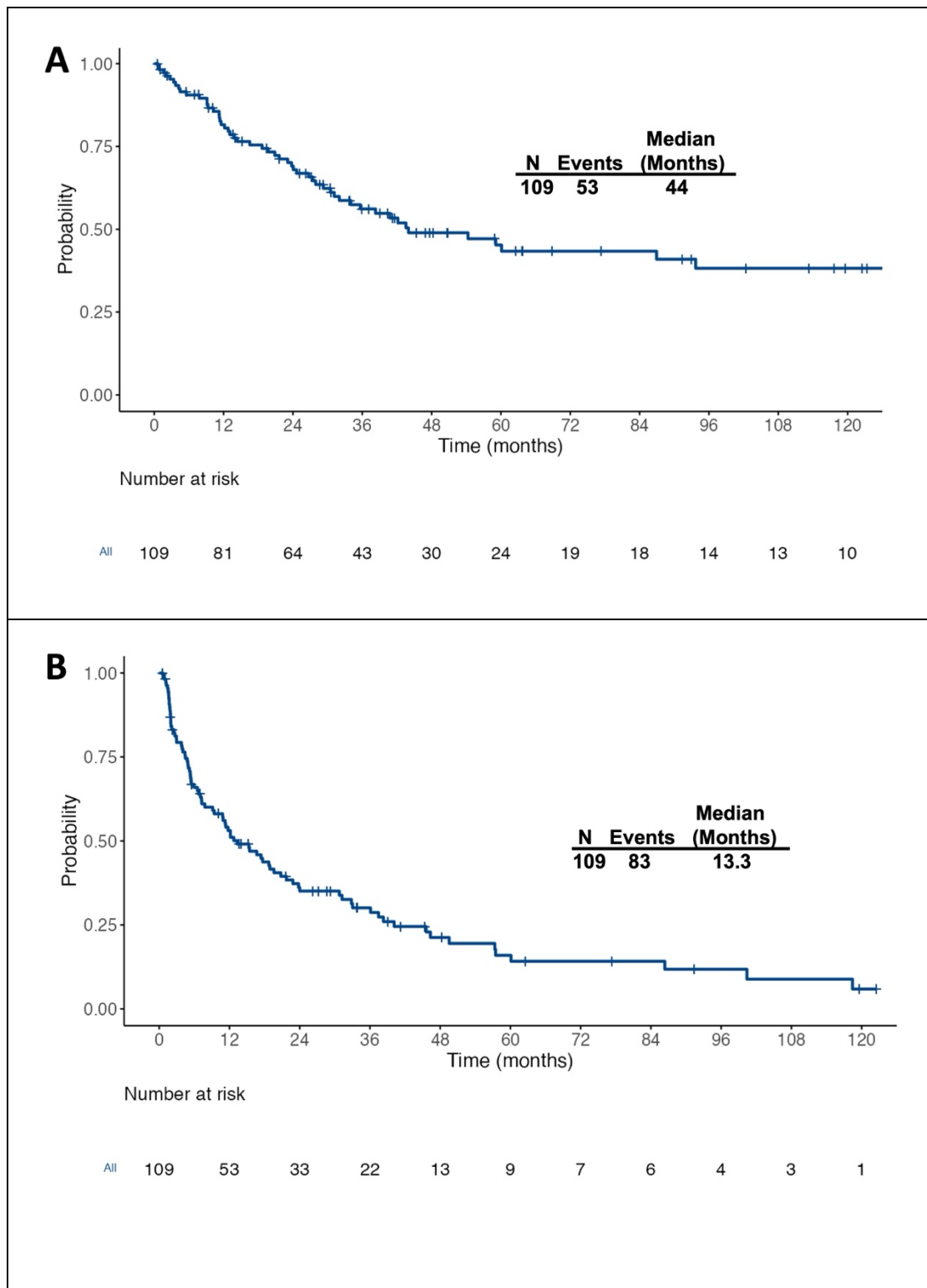




Fig. S2

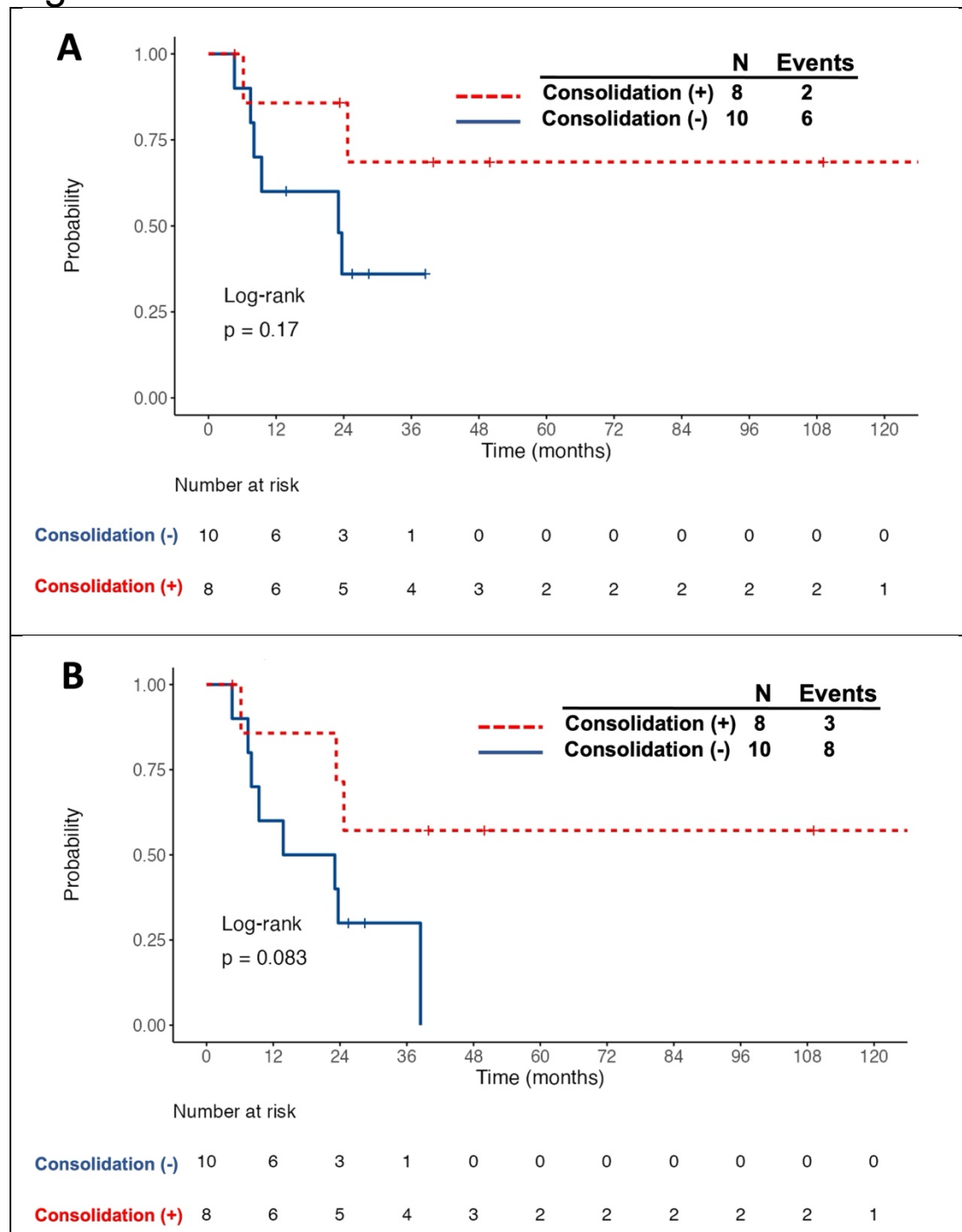


Fig. S3

