

MATRix and HD-MTX/IFO/DEP treatment and autologous stem cell transplantation in secondary central nervous system lymphoma: a Dutch retrospective analysis

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Supplemental Table 1: details of high-dose methotrexate/ifosfamide/liposomal-cytarabine (HD-MTX/IFO/DEP) and high-dose methotrexate/cytarabine/rituximab/thiotepa (MATRix) induction treatment schemes and prior chemotherapy

- A) Details of HD-MTX/IFO/DEP and MATRix treatment
 B) Chemotherapy pre-treatment before secondary central nervous system diffuse large B-cell lymphoma (SCNS-DLBCL) diagnosis

A

HD-MTX/IFO/DEP part I (total 2 cycles in case of response, 1x per 3 weeks)		
	Dose	Day(s)
Methotrexate	4000 mg/m ²	1
Ifosfamide	2000 mg/m ²	3-5
Liposomal cytarabine	50 mg	6
HD-MTX/IFO/DEP part II (total 2 cycles in case of response, 1x per 3 weeks)		
	Dose	Day(s)
Cytarabine	3000 mg/m ²	1-2
Thiotepa	40 mg/m ²	2
Liposomal cytarabine	50 mg	3
Conditioning with BCNU/thiotepa/etoposide + ASCT		

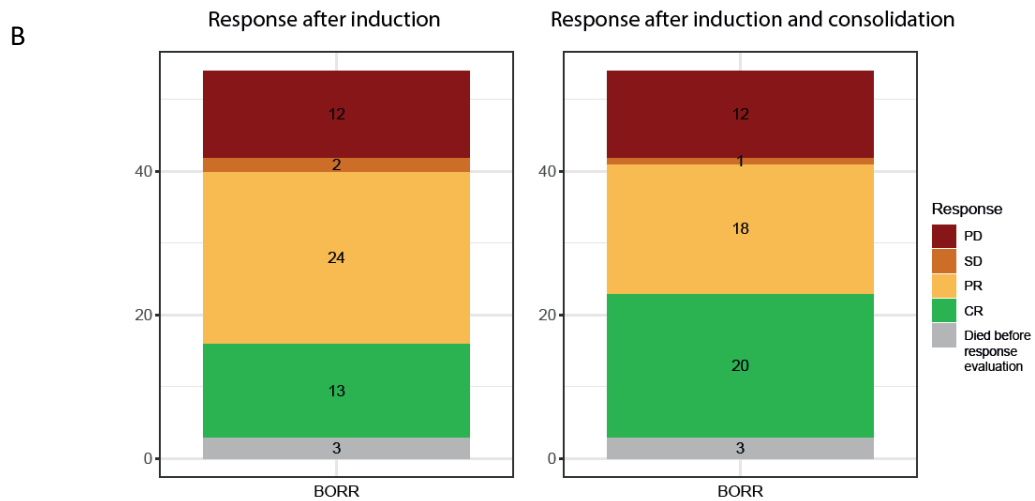
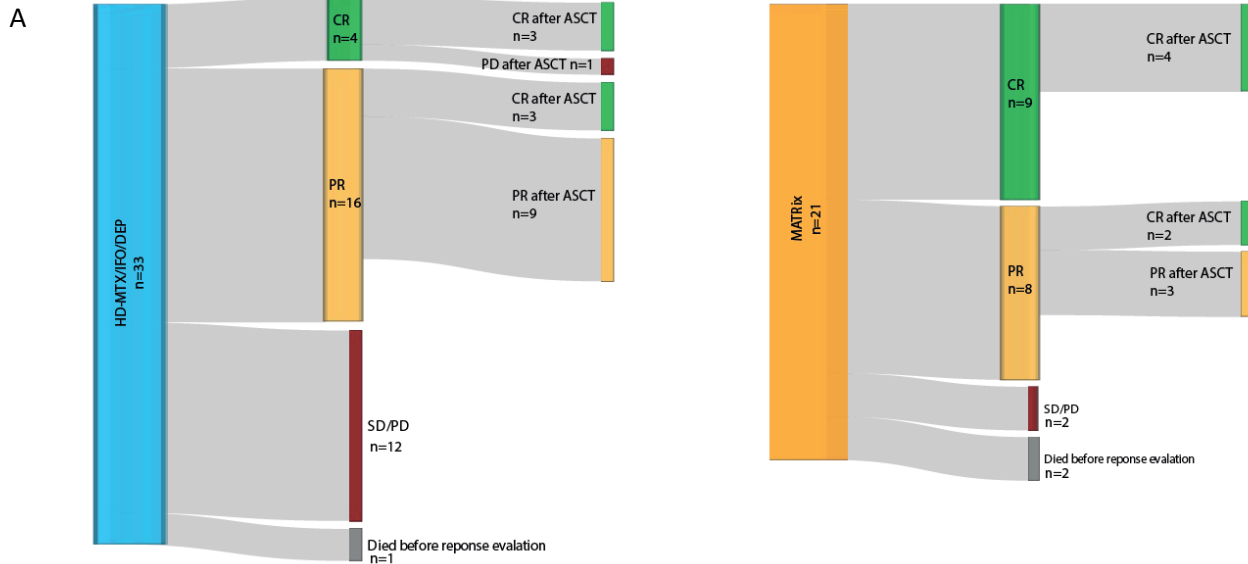
MATRix (total 4 cycles, 1x per 3 weeks)		
	Dose	Day(s)
Rituximab	375 mg/m ²	0
Methotrexate	3500 mg/m ²	1
Cytarabine	2000 mg/m ²	2-3
Thiotepa	30 mg/m ²	4
Conditioning with R-BCNU/thiotepa + ASCT		

B

SCNS-DLBCL treatment	Prior chemotherapy
HD-MTX/IFO/DEP	1x R-CHOP + 5x DA-EPOCH-R
HD-MTX/IFO/DEP	No, treatment naïve SCNS-DLBCL
HD-MTX/IFO/DEP	6x R-CHOP
HD-MTX/IFO/DEP	6x R-CHOP + radiotherapy
HD-MTX/IFO/DEP	6x R-CHOP + 2R + radiotherapy
HD-MTX/IFO/DEP	4x R-CHOP
HD-MTX/IFO/DEP	6x R-CHOP + radiotherapy
HD-MTX/IFO/DEP	6x R-CHOP
HD-MTX/IFO/DEP	6x R-CHOP
HD-MTX/IFO/DEP	4x R-CHOP
HD-MTX/IFO/DEP	4x R-CHOP
HD-MTX/IFO/DEP	3x R-CHOP + radiotherapy
HD-MTX/IFO/DEP	9x R-CHOP + radiotherapy
HD-MTX/IFO/DEP	3x R-CHOP + radiotherapy
HD-MTX/IFO/DEP	6x R-CHOP + radiotherapy
HD-MTX/IFO/DEP	8x R-CHOP
HD-MTX/IFO/DEP	2x R-CHOP + 4x DA-EPOCH-R + BEAM/ASCT
HD-MTX/IFO/DEP	6x R-CHOP
HD-MTX/IFO/DEP	8x R-CHOP
HD-MTX/IFO/DEP	No, treatment naïve SCNS-DLBCL
MATRIX	1x R-CHOP + 1x HD-MTX noted as treatment naïve SCNS-DLBCL
MATRIX	4x R-CHOP
MATRIX	No, treatment naïve SCNS-DLBCL
MATRIX	No, treatment naïve SCNS-DLBCL
MATRIX	Radical orchiectomy, 6x R-CHOP, 6x MTX it + radiotherapy
MATRIX	3x CHVMP/BV + radiotherapy
MATRIX	6x R-CHOP
MATRIX	8x R-CHOP
MATRIX	6x R-CHOP
MATRIX	1x R-CHOP
MATRIX	6x R-CHOP en 3x MTX it
MATRIX	3x R-CHOP + radiotherapy
MATRIX	6x R-CHOP + 3x it MTX
MATRIX	No, treatment naïve SCNS-DLBCL
MATRIX	6x RCHOP + 2R
MATRIX	2x RCHOP
HD-MTX/IFO/DEP	6x RCHOP en 2xR
HD-MTX/IFO/DEP	8x RCVp + 2x DA-EPOCH-R + it MTX, 3x RCHOP + HD-MTX
HD-MTX/IFO/DEP	6x RCHOP + 2R, RGDP, RVIM
HD-MTX/IFO/DEP	R-CHOP
HD-MTX/IFO/DEP	ABVD, DHAP + BEAM/ASCT
HD-MTX/IFO/DEP	2x RCHOP
HD-MTX/IFO/DEP	6x RCHOP + 2xR
HD-MTX/IFO/DEP	6x RCHOP + 2xR, 2x RGDP, ASCT
HD-MTX/IFO/DEP	RCHOP + it MTX
HD-MTX/IFO/DEP	1x RCHOP en 1x DA-EPOCH-R
HD-MTX/IFO/DEP	6x RCHOP+2xR +6xitMTX en RT andere testis
HD-MTX/IFO/DEP	RCHOP + HD-MTX
MATRIX	6x R-CHOP
MATRIX	8x R-CHOP + radiotherapy, 4x MTX it
MATRIX	8x R-CHOP
MATRIX	Only radiotherapy
MATRIX	4x RCHOP

Supplemental Figure 1: Summary of the secondary central nervous system diffuse large B-cell lymphoma (SCNS-DLBCL) cohort (n=54)

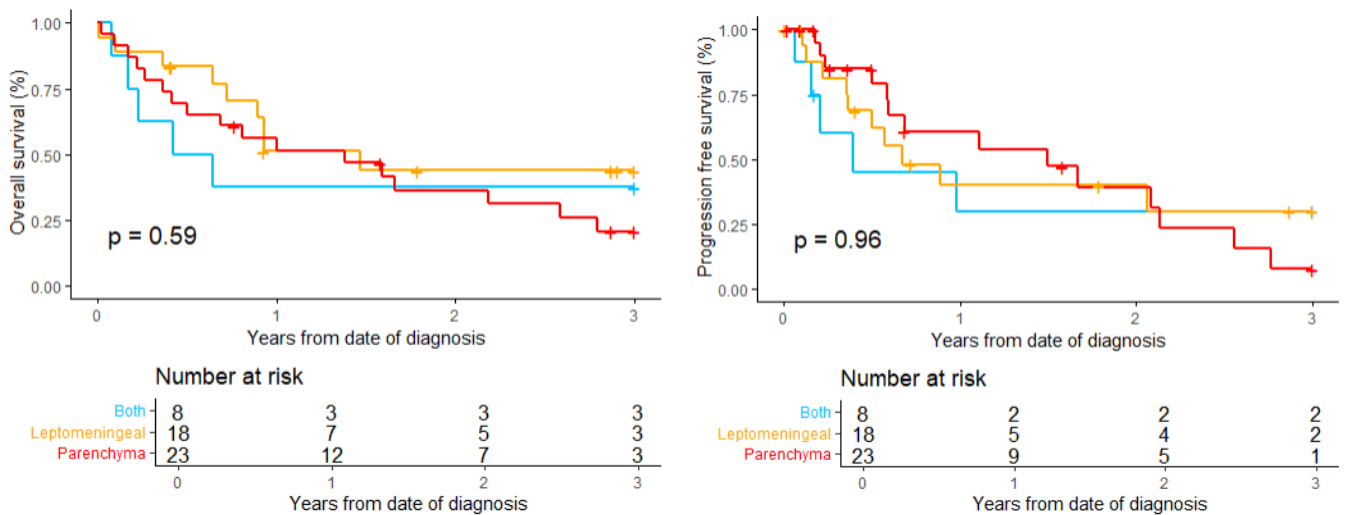
- A) Sankey plots of clinical responses
- B) Barcharts of best overall response rates after induction and after consolidation treatment



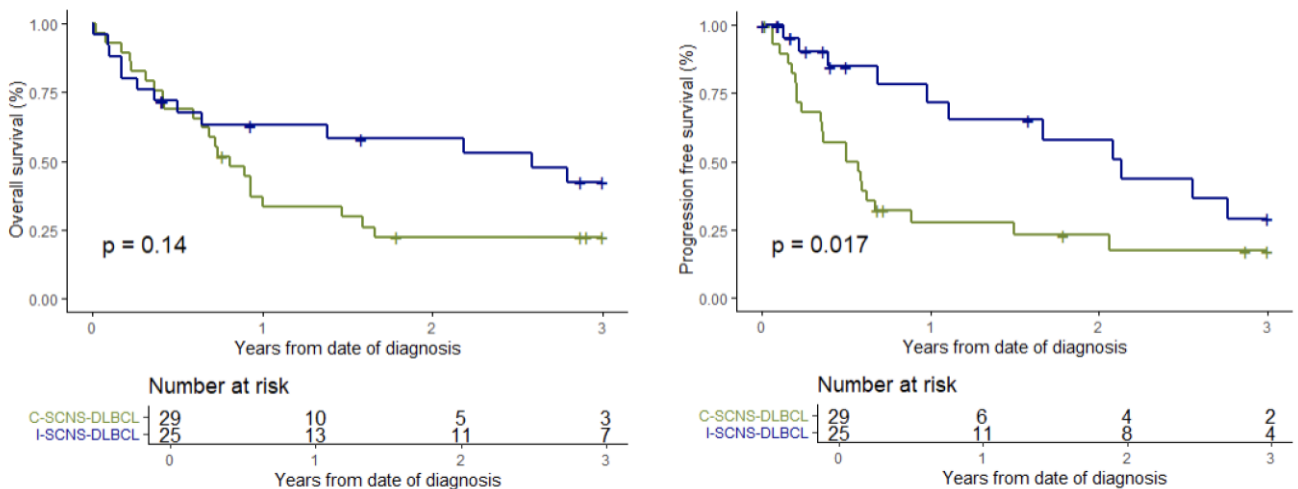
Supplemental Figure 2: Additional survival analyses

- A) Univariable analysis on CNS compartment (brain parenchyma vs leptomeningeal)
- B) Univariable analysis on isolated SCNS-DLBCL vs concomitant SCNS-DLBCL
- C) Multivariable analysis on overall survival and progression-free survival using a Cox proportional hazards model including age, lactate dehydrogenase (LDH) levels at diagnosis, time to relapse, subtype SCNS-DLBCL, induction treatment and autologous stem cell transplantation (ASCT) consolidation

A



B



C

Variable		N	Hazard ratio	Reference	p
>60	no	23	1.00	Reference	
	yes	31	1.68 (0.76, 3.68)		0.20
	Unk	13	0.81 (0.31, 2.09)		0.66
Elevated LDH at SCNSL diagnosis	no	30	1.00	Reference	
	yes	11	2.25 (0.98, 5.20)		0.06
	Unk	13	0.81 (0.31, 2.09)		0.66
Time to relapse	after 12 months	29	1.00	Reference	
	within 12 months	25	1.06 (0.51, 2.17)		0.88
Subtype SCNSL	C-SCNSL	29	1.00	Reference	
	I-SCNSL	25	1.23 (0.53, 2.87)		0.63
Induction treatment	'Korfel'	33	1.00	Reference	
	MATRix	21	0.38 (0.17, 0.84)		0.02
ASCT	no	29	1.00	Reference	
	yes	25	0.34 (0.15, 0.77)		0.01

	Hazard ratio	Reference	p
Overall survival	1.00	Reference	
	0.60 (0.27, 1.33)		0.21
	1.46 (0.59, 3.60)		0.41
Progression free survival	1.00	Reference	
	0.77 (0.29, 2.05)		0.60
	1.10 (0.49, 2.47)		0.83
Overall survival	1.00	Reference	
	0.64 (0.24, 1.69)		0.37
	0.38 (0.16, 0.89)		0.03
Progression free survival	1.00	Reference	
	0.30 (0.12, 0.77)		0.01