

Successful change of treatment strategy in elderly patients with primary central nervous system lymphoma by de-escalating induction and introducing temozolomide maintenance: results from a phase II study by The Nordic Lymphoma Group

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Supplemental data:

Online Supplementary Table S1:

Chemotherapy schedule. Patients aged 18-65 years. Interval between cycles: 3 weeks.

	Cycle 1 (A1)	Cycle 2 (B1)	Cycle 3 (C1)	Cycle 4 (A2)	Cycle 5 (B2)	Cycle 6 (C2)
Rituximab	375/m ² iv day 1					
Methotrexate	5 g/m ² iv day 1	5 g/m ² iv day 1		5 g/m ² iv day 1	5 g/m ² iv day 1	
Ifosfamide	800 mg/m ² iv day 2-5			800 mg/m ² iv day 2-5		
Dexa- methasone	10 mg /m ² po day 2-5	10 mg /m ² po day 2-5	20 mg/m ² po day 3-7	10 mg /m ² po day 2-5	10 mg /m ² po day 2-5	20 mg/m ² po day 3-7
Vincristine		2 mg iv day 1			2 mg iv day 1	
Depocyte	50 mg isp day 2	50 mg isp day 2		50 mg isp day 2	50 mg isp day 2	
Cyclophos- phamide		200 mg/m ² iv day 2-5			200 mg/m ² iv day 2-5	
Cytarabine			1.5 g/m ² x 2 iv day 1-2			1.5 g/m ² x 2 iv day 1-2
Vindesine			5 mg iv day 1			5 mg iv day 1

Abbreviations: iv intravenously. Po perorally. Isp intraspinally

Online Supplementary Table S2:

Chemotherapy schedule. Patients aged 66-75 years. Interval between cycles: 3 weeks.

	Cycle 1 (A1)	Cycle 2 (B1)	Cycle 3 (C1)	Cycle 4 (A2)	Cycle 5 (B2)	Cycle 6 (C2)
Rituximab	375/m ² iv day 1					
Methotrexate	3 g/m ² iv day 1	3 g/m ² iv day 1		3 g/m ² iv day 1	3 g/m ² iv day 1	

Ifosfamide	800 mg/m ² iv day 2-5					
Dexamethasone	10 mg /m ² po day 2-5	10 mg /m ² po day 2-5	20 mg/m ² po day 3-7	10 mg /m ² po day 2-5	10 mg /m ² po day 2-5	20 mg/m ² po day 3-7
Depocyte	50 mg isp day 2	50 mg isp day 2		50 mg isp day 2	50 mg isp day 2	
Temozolomide		150/m ² mg po day 2-6		150/m ² mg po day 2-6	150/m ² mg po day 2-6	
Cytarabine			1 g/m ² x 2 iv day 1-2			1 g/m ² x 2 iv day 1-2
Vindesine			5 mg iv day 1			5 mg iv day 1

Abbreviations: iv intravenously. Po perorally. Isp intraspinally

Online Supplementary Table S3: Reasons for chemotherapy discontinuation.

No. of patients	No. of chemotherapy courses delivered	Reason for discontinuation of chemotherapy in patients aged 18-65 y	Reason for discontinuation of chemotherapy in patients aged 66-75 y
42 (63.6%)	6		
3 (4.5%)	5	Impaired kidney function in 1 pt**	Poor performance in 2 pts*
6 (9.1%)	4	Early progression in 2 pts. No response to the 3 rd and 4 th cycle in 1 pt*** Poor performance in 1 pt**	Early progression in 1 pt. Neurotoxicity in 1 pt.***
8 (12.1%)	3	Early progression in 1 pt Treatment related death in 1pt	Treatment related death in 3 pts Poor performance in 1 pt*** Toxicity in 1 pt* Impaired kidney function in 1 pt***
3 (4.5%)	2	Early progression in 1 pt.	Poor performance in 1 pt.*** Toxicity in 1pt.***
4 (6.1%)	1	Early progression in 1 pt	Early progression in 1 pt Early progression and impaired kidney function in 1 pt

			Poor performance in 1 pt. ***
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*went on to maintenance therapy. **went on to follow-up. ***went off study

Online Supplementary Table S4. Onset and duration of neurotoxicity symptoms during therapy.

Pt	Trtm phase	Medication before onset of symptoms	Day of onset	Dur. of sympt. (days)	Recovery +/-	Symptoms	CNS lymphoma Present Yes/No	Liposomal Cytarabine suspected Yes/No
Event 1 (pt 13) Age 66 y	A1	Rituximab d. 1 HD-MTX d.1 Ifosfamide d. 2-5 Dexamethasone d. 2-5 Liposom. cytarabine d. 2	15	5	+	Progressive sensory loss of the legs, arachnoiditis suspected	Yes	Yes
Event 2 (pt 14) Age 75 y	A1	Rituximab d. 1 HD-MTX d.1 Ifosfamide d. 2-5 Dexamethasone d. 2-5 Liposom. cytarabine d. 2	3	unresolved	-	Ataxia, somnolence, urinary and bowel incontinence. Cauda equina syndrome and brain dysfunction suspected	Yes	Yes
Event 3 (pt 16) Age 64 y	A1	Rituximab d. 1 HD-MTX d.1 Ifosfamide d. 2-5 Dexamethasone d. 2-5 Liposom. cytarabine d. 2	3	3	+	Headache, nausea, fever, photophobia, stiffness of the back. Arachnoiditis suspected	Yes	Yes
Event 4 (pt 21) Age 52 y	A2	HD-MTX d.1 Ifosfamide d. 2-5 Dexamethasone d. 2-5 Liposom. cytarabine d. 2	7	3	+	Headache, nausea, vomiting, not able to eat or drink. ECOG 4. Arachnoiditis suspected	No	Yes
Event 5 (pt 31) Age 70 y	A1	Rituximab d. 1 HD-MTX d.1 Ifosfamide d. 2-5 Dexamethasone d. 2-5 Liposom. cytarabine d. 2	4	1	+	Fever, clinical signs of meningitis. Arachnoiditis suspected	Yes	Yes
Event 6 (pt 55) Age 49 y	A1	Rituximab d. 1 HD-MTX d.1 Ifosfamide d. 2-5 Dexamethasone d. 2-5	3	Day of recovery not reported	+	Nausea, fever and severe headache. Arachnoiditis suspected	Yes	Yes

		Liposom. cytarabine d. 2						
Event 7 (pt 56) Age 55 y	A1	Rituximab d. 1 HD-MTX d.1 Ifosfamide d. 2-5 Dexamethasone d. 2-5 Liposom. cytarabine d. 2	3	4	+	Headache, fever, vomiting, leg pain, arachnoiditis, pleocytosis in the spinal fluid	yes	Yes
Event 8 (pt 59) Age 65 y	A1	Rituximab d. 1 HD-MTX d.1 Ifosfamide d. 2-5 Dexamethasone d. 2-5 Liposom. cytarabine d. 2	4	4	+	Fever, headache, somnolence, dyspneau. Arachnoiditis and brain dysfunction suspected	Yes	Yes
Event 9 (pt 60) Age 50 y	A1	Rituximab d. 1 HD-MTX d.1 Ifosfamide d. 2-5 Dexamethasone d. 2-5 Liposom. cytarabine d. 2	3	3	+	Photophobia, headache and tremor. Arachnoiditis suspected	Yes	Yes
Event 10 (pt 61) Age 40 y	A1	Rituximab d. 1 HD-MTX d.1 Ifosfamide d. 2-5 Dexamethasone d. 2-5 Liposom. cytarabine d. 2	3	4	+	Fever and headache. Arachnoiditis suspected	Yes	Yes
Event 11 (pt 69) Age 66 y	A2	HD-MTX d. 1 Temozolomide d. 2-6 Dexamethasone d. 2-5 Liposom. Cytarabine d. 2	15	2	+	Sudden dysfunction and loss of sensibility of the left leg. Not able to stand or walk. Arachnoiditis suspected	Yes	No
Event 12 (pt 69) Age 66 y	B2	HD-MTX d.1 Temozolomide d. 2-6 Dexamethasone d. 2-5	3	43	+	Sudden dysfunction and loss of sensibility of the left leg. Not able to stand or walk. Cognitive impairment. Arachnoiditis and brain dysfunction suspected	Yes	No
Event 13 (pt 5) Age 51 y	A1	Rituximab d1 HD-MTX d1 Ifosfamide d.2 Dexamethasone d. 2	2	73	+	Ataxia and somnolence increasing to coma. Brain dysfunction suspected	Yes	No
Event 14 (pt 47) Age 75 y	C1	Cytarabine d. 1-2 Dexamethasone d. 3-7 Vindesine d. 1	7	unresolved	-	Fatigue and confusion Brain dysfunction suspected	Not known	No
Event 15	Mainten	Temozolomide d. 1-5	24	unresolved	-	Hemiparesis	No	No

(pt 34) Age 66 y	ance					Brain dysfunction suspected		
Event 16 (pt 68) Age 67 y	Mainten ance	Temozolomide d. 1-5	3	20	+	Taste disturbances Dysfunction of brain or sensory nerves suspected	No	No