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## Supplementary Material

# Long-Term Remissions in Patients with Peripheral T-Cell Lymphoma Following High-Dose Chemotherapy, Autologous Stem Cell Transplantation (ASCT) and Subsequent Radiotherapy

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### ABSTRACT

**Purpose:** The prognosis of patients with peripheral T-cell lymphoma and missing complete remission or relapsing before ASCT is assessed to be unfavourable. The aim of this study is to contribute data to the open question, whether additional radiotherapy improves the outcome.

**Patients and Methods:** Forty-eight patients with peripheral T-cell-lymphoma were treated in our institution with high-dose therapy (usually BEAM protocol) and ASCT (age median 54 years, range 19-77). Twenty-five patients received ASCT in first treatment line, 13 in second line, 10 in third line (all refractory to 2<sup>nd</sup>-line salvage therapy). Seven of these 48 patients received radiotherapy (36-40 Gy, median 36) after ASCT.

**Results:** Five-year overall survival (OS) and progression-free survival (PFS) after 1<sup>st</sup>-line ASCT and 2<sup>nd</sup>-line ASCT were 59% and 50%, respectively, and after 3<sup>rd</sup>-line ASCT significantly lower with 30% and 30%, respectively. Twenty-one patients achieved a sustained complete remission of 2.7 - 22.7 years (median 5.8). No patient relapsed after radiotherapy.

**Conclusion:** Sustained long-term remissions can be achieved in patients with peripheral T-cell lymphoma following ASCT in first, second or third treatment line. Early irradiation after ASCT can possibly consolidate remission in localized residual or refractory disease.

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**TABLE S1:** Relapse areas after ASCT in 21 relapsed patients.

Relapse area	1st-line ASCT	2nd-line ASCT	3rd-line ASCT
Supradiaphragmatic lymph node involvement (n patients)	2 (1 with signs of diss. relapse: increase of Calcium and LDH and ED)	1	
Disseminated lymph node involvement (n)	2	1	
Bone marrow + lymph node involvement (n)	2		1
Lymphoma cells in the blood (n)			2
Liver + disseminated lymph node involvement (n)	1		
Pulmonary + lymph node involvement (n)	1		
Central nervous system involvement (n)	2	1	
Disseminated skin involvement (n)	2		
Unknown		2	1

diss.: disseminated; LDH: lactate dehydrogenase; ED: early death due to a severe infection shortly after ASCT.

**TABLE S2:** Univariate and multivariate analysis of 48 patients with peripheral T-cell lymphoma, per OS and PFS.

OS (N = 48)		N (%)	HR (univariable)	HR (multivariable)
age	< 60 yrs	33 (68.8)	-	-
	>= 60 yrs	15 (31.2)	1.32 (0.59-2.96, p=0.495)	<b>0.13 (0.02-0.66, p=0.014)</b>
gender	F	16 (33.3)	-	-
	M	32 (66.7)	1.64 (0.70-3.84, p=0.255)	1.83 (0.48-6.97, p=0.375)
treatment line	1st-line ASCT	25 (52.1)	-	-
	2nd-line ASCT	13 (27.1)	0.80 (0.30-2.14, p=0.654)	2.04 (0.45-9.35, p=0.358)
	3rd-line ASCT	10 (20.8)	2.92 (1.21-7.03, p=0.017)	<b>64.52 (2.81-1482.61, p=0.009)</b>
histology	ALCL, ALK pos.	7 (14.6)	-	-
	ALCL, ALK neg.	12 (25.0)	2.80 (0.55-14.32, p=0.217)	1.51 (0.25-9.13, p=0.652)
	ALCL, ALK	2 (4.2)	0.89 (0.08-10.07, p=0.927)	11.42 (0.19-681.98, p=0.243)
	unknown			
	PTL	12 (25.0)	3.51 (0.72-17.16, p=0.121)	4.17 (0.54-31.91, p=0.169)
radiation after ASCT	AIL	11 (22.9)	<b>5.66 (1.15-27.94, p=0.033)</b>	<b>46.78 (3.72-587.74, p=0.003)</b>
	other	4 (8.3)	5.60 (0.89-35.39, p=0.067)	<b>17.26 (1.56-190.36, p=0.020)</b>
	yes	7 (14.6)	-	-
	no	41 (85.4)	<b>4.98 (1.14-21.66, p=0.033)</b>	10.15 (0.76-136.23, p=0.080)
HDT regimen	B/TEAM	40 (83.3)	-	-
	TBIC	2 (4.2)	1.50 (0.35-6.52, p=0.587)	0.10 (0.01-1.32, p=0.079)
	M-CHOEP	6 (12.5)	2.33 (0.92-5.89, p=0.075)	<b>7.21 (1.36-38.32, p=0.020)</b>
remission at ASCT	complete	12 (25.0)	-	-
	partial	26 (54.2)	1.66 (0.59-4.70, p=0.336)	2.80 (0.71-11.06, p=0.143)
	other	10 (20.8)	<b>4.08 (1.35-12.32, p=0.013)</b>	0.78 (0.07-8.95, p=0.842)
LDH at ASCT	normal	42 (87.5)	-	-
	elevated	6 (12.5)	1.35 (0.45-4.06, p=0.595)	0.80 (0.08-7.59, p=0.846)
PFS (N = 48)		N (%)	HR (univariable)	HR (multivariable)
age at ASCT	< 60 yrs	33 (68.8)	-	-
	>= 60 yrs	15 (31.2)	1.06 (0.48-2.33, p=0.880)	<b>0.13 (0.03-0.59, p=0.008)</b>
gender	F	16 (33.3)	-	-
	M	32 (66.7)	1.48 (0.66-3.32, p=0.338)	2.04 (0.59-7.00, p=0.259)
treatment line	1st-line ASCT	25 (52.1)	-	-
	2nd-line ASCT	13 (27.1)	0.79 (0.32-1.97, p=0.614)	2.09 (0.56-7.78, p=0.271)
	3rd-line ASCT	10 (20.8)	2.20 (0.95-5.12, p=0.067)	8.70 (0.69-110.46, p=0.095)
histology	ALCL, ALK pos.	7 (14.6)	-	-
	ALCL, ALK neg.	12 (25.0)	3.45 (0.70-16.96, p=0.127)	5.70 (0.94-34.55, p=0.058)
	ALCL, ALK	2 (4.2)	1.04 (0.09-11.72, p=0.974)	26.14 (0.62-1101.75, p=0.087)
	unknown			
	PTL	12 (25.0)	4.52 (0.97-21.14, p=0.055)	<b>10.51 (1.51-73.15, p=0.017)</b>
AIL	11 (22.9)	<b>5.05 (1.05-24.30, p=0.043)</b>	<b>50.04 (4.70-533.01, p=0.001)</b>	

	radiation after	other	4 (8.3)	4.76 (0.77-29.38, p=0.093)	10.49 (1.18-93.52, p=0.035)
		yes	7 (14.6)	-	-
<b>ASCT</b>					
	HDT regimen	no	41 (85.4)	<b>5.70 (1.32-24.71, p=0.020)</b>	<b>17.07 (1.46-198.98, p=0.024)</b>
		B/TEAM	40 (83.3)	-	-
		TBIC	2 (4.2)	1.27 (0.30-5.43, p=0.749)	0.11 (0.01-1.27, p=0.076)
		M-CHOEP	6 (12.5)	<b>2.72 (1.08-6.89, p=0.035)</b>	<b>6.94 (1.67-28.79, p=0.008)</b>
	remission at ASCT	complete	12 (25.0)	-	-
		partial	26 (54.2)	1.81 (0.68-4.78, p=0.234)	1.70 (0.50-5.79, p=0.399)
		other	10 (20.8)	3.32 (1.15-9.63, p=0.027)	1.60 (0.19-13.82, p=0.667)
	LDH at ASCT	normal	42 (87.5)	-	-
		elevated	6 (12.5)	1.28 (0.43-3.79, p=0.653)	2.40 (0.33-17.42, p=0.388)

Statistically significant differences are indicated in bold type.

**TABLE S3:** Characteristics of 7 patients with peripheral T-cell lymphoma and radiotherapy after ASCT.

Patients, n	7
Age (years, median/range)	47 (24-73)
Sex (female/male), n (%)	4 (57) / 3 (43)
Histology: Anaplastic Large-Cell Lymphoma, 3 of whom ALK-, 1 ALK+, 2 ALK not tested, n (%)	6 (86)
Peripheral T-Cell Lymphoma (NOS and similar), n (%)	1 (14)
Stage (Ann Arbor) 1 <sup>st</sup> -line ASCT: I, n (%)	0
II, n (%)	1 (14)
III, n (%)	0
IV, n (%)	1 (14)
IPI at 1 <sup>st</sup> -line chemotherapy: low risk, n (%)	1 (14)
low-intermediate risk, n (%)	1 (14)
high-intermediate risk, n (%)	0
high risk, n (%)	0
Prior treatment with anthracyclines (CHOP or CHOEP), n (%)	7 (100)
High-dose therapy: BEAM	7 (100)
Treatment line: 1 <sup>st</sup> -line ASCT, n (%)	2 (29)
2 <sup>nd</sup> -line ASCT, n (%)	3 (43)
3 <sup>rd</sup> -line ASCT, n (%)	2 (29)
Refractory to 2 <sup>nd</sup> -line chemotherapy, n (%)	2 (29)
Second relapse, n (%)	0
LDH: elevated at 1 <sup>st</sup> -line ASCT, n (%)	0
elevated at 2 <sup>nd</sup> -line ASCT, n (%)	1 (33)
elevated at 3 <sup>rd</sup> -line ASCT, n (%)	0
Remission status: CR/PR/SD/PD at 1st-line ASCT, n	0/2/0/0
CR/PR/SD/PD after 1st-line ASCT, n	0/2/0/0
CR/PR/SD/PD at 2nd-line ASCT, n	3/0/0/0
CR/PR/SD/PD/ED after 2nd-line ASCT, n	3/0/0/0
CR/PR/SD/PD at 3rd-line ASCT, n	0/0/0/2
CR/PR/SD/PD/ED/NI after 3rd-line ASCT, n	2/0/0/0
Allogeneic stem cell transplantation	0

ALK: Anaplastic Lymphoma Kinase; TL: T-cell Lymphoma; NOS: Not Otherwise Specified; IPI: International Prognostic Index; BEAM: High-dose BCNU, Etoposide, Cytarabine, Melphalan; Mega-CHOEP: High-dose Cyclophosphamide, Doxorubicin, Vincristine, Etoposide, Prednisone; TBI: Total Body Irradiation; mo: Months; LDH: Lactic Dehydrogenase; CR: Complete Remission; PR: Partial Remission; SD: Stable Disease; PD: Progressive Disease; ED: Early Death; NI: No Information.