

Favorable outcome of abbreviated R-CHOP in patients with primary testicular lymphoma

Diana Al-Sarayfi¹, Johanna Bult¹, Mirian Brink², Ruben A.L. de Groen³, Fleur A. de Groot³, Joost S.P. Vermaat³, Djamilla Issa⁴, Arjan Diepstra¹, Gerwin Huls¹, Mar Bellido¹, Wouter Plattel¹, Marcel Nijland¹

1. Department of hematology, University Medical Center Groningen, Groningen, The Netherlands;
2. Department of Research and Development, Netherlands Comprehensive Cancer Organisation (IKNL), Utrecht, The Netherlands;
3. Department of Hematology, Leiden University Medical Center, Leiden, The Netherlands;
4. Department of hematology, Jeroen Bosch Hospital, 's Hertogenbosch, The Netherlands.

Background

Patients with limited stage primary testicular lymphoma (PTL) receive a multimodality treatment approach including 6 cycles of R-CHOP to prevent relapses. In low-risk limited stage DLBCL, the number of cycles of R-CHOP is nowadays reduced to 4. However, it is unknown whether the reduction of cycles of R-CHOP in patients with PTL is feasible. Therefore, we aimed to investigate whether reduced R-CHOP impacted the outcome in a real-world cohort of PTL patients.

Methods

PTL patients ≥ 18 years, Ann Arbor stage I-II, diagnosed in 2014-2021, who received ≥ 3 cycles of R-CHOP were identified in the Netherlands Cancer Registry, with survival follow-up through 2023. Patients with CNS involvement at diagnosis were excluded. Treatment modalities were categorized as 3 or 6 cycles R-CHOP. The endpoints were progression-free survival (PFS), overall survival (OS) and cumulative incidence function (CIF) of CNS relapse. Uni- and multivariable analyses were conducted, using Cox regression analyses, to establish independent predictors of risk of relapse and mortality among patients who received 3 cycles of R-CHOP versus 6 cycles of R-CHOP.

Results

A total of 140 patients were identified: median age, 70 years (range, 37-86 years); stage I, 69%; IPI 0, 87%. Of these patients, 44 received 3 cycles R-CHOP and 96 received 6 cycles R-CHOP. Patients with stage I disease more commonly received 3 cycles of R-CHOP compared to patients with stage II ($p < 0.01$; Table 1). Of the patients who received 3 cycles R-CHOP, 32% received < 4 MTX IT cycles, compared to 14% in patients who received 6 cycles R-CHOP ($p = 0.01$). The median follow-up from end of treatment was 36 months (inter quartile range [IQR], 12-56 months). Overall response rate (ORR; partial remission or greater) for patients who received 3 cycles R-CHOP and 6 cycles R-CHOP were similar (77% versus 86%, respectively, $p = 0.17$).

The 5-year PFS and OS were 59% and 64%, respectively. Regarding 3 versus 6 R-CHOP, the 5-year PFS and OS were similar, i.e. 61% versus 57% ($p = 0.80$) and 70% versus 58% ($p = 0.44$), respectively (Figure 1). In uni- and multivariable analysis, in addition to the number of cycles, patients older than

60 years negatively impacted the risk of relapse or mortality. The 5-year CIF of CNS was 14%, with a median time from end of treatment to CNS relapse of 25 months. No difference in 5-year CIF of CNS was observed between patients receiving 3 cycles of R-CHOP versus those receiving 6 cycles (17% versus 10% respectively, $p=0.39$).

Conclusion

In this nationwide PTL population, nearly one-third of patients received 3 instead of 6 R-CHOP cycles, with no difference in survival. These data challenge the use of 6 cycles of R-CHOP in limited stage PTL.

Table 1. Characteristics of patients with a primary testicular lymphoma

Characteristics	Total		3 cycles R-CHOP		6 cycles R-CHOP		P
	n	(%)	n	(%)	n	(%)	
Total no. of patients (row %)	140	100	44	31	96	69	
Age, years							
Median (range)	70 (37-86)		69 (41-85)		71 (37-86)		0.77
18-60	24	17	8	18	16	17	
≥61	116	83	36	82	80	83	
WHO performance status							0.53
0, 1, 2	91	65	29	66	62	65	
3, 4	0	0	0	0	0	0	
Unknown	49	35	15	34	34	35	
Ann Arbor stage							<0.01
I	96	69	43	98	53	55	
II	44	31	1	2	43	45	
Elevated LDH							0.88
N	111	79	36	82	75	78	
Yes	25	18	7	16	18	19	
Unknown	4	3	1	2	3	3	
>1 extranodal localizations							1.00
No	140	100	44	100	96	100	
Yes	0	0	0	0	0	0	
IPI score							0.85
Very good 0	122	87	38	86	84	88	
Good 1-2	18	13	6	14	12	13	
Poor 3-5	0	0	0	0	0	0	
Treatment							
Prophylactic treatment							0.29
No MTX	5	4	2	5	3	3	
MTX IT	130	93	42	95	88	92	
HD-MTX	5	4	0	0	5	5	
Number of cycles*							0.01
≥4 MTX cycles	113	81	30	68	83	86	
<4 MTX cycles	27	19	14	32	13	14	
Consolidation							0.58
Radiotherapy	116	83	37	84	79	82	
Orchidectomy	7	5	1	2	6	6	
No consolidation	17	12	6	14	11	11	

*All patients who received HD-MTX were included in the ≥4 MTX cycles group. Patients who did not receive MTX cycles were included in the <4 MTX cycles group.

Figure 1: 5-year progression-free survival in 140 patients with primary testicular lymphoma treated with 3 or 6 cycles of R-CHOP.

