

Data supplement

Time to treatment is an independent prognostic factor in aggressive non-Hodgkin lymphomas

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Table S1. Characteristics of **Burkitt lymphoma** patients, stratified by time from diagnosis to start of chemotherapy.

	All patients	Time from diagnosis to chemotherapy			
		0-7 days	8-14 days	15-30 days	>30 days
<i>N</i>	4,552	1,502	1,131	1,237	682
Age, median (IQR)	54 (38-66)	52 (35-64)	54 (38-67)	54 (39-66)	57 (42-69)
Sex, <i>N</i> (%)					
Male	3,136 (69)	1,050 (70)	758 (67)	860 (70)	468 (69)
Female	1,416 (31)	452 (30)	373 (33)	377 (31)	214 (31)
Race/ethnicity, <i>N</i> (%)					
White non-Hispanic	3,625 (80)	1,204 (80)	910 (81)	981 (79)	530 (78)
White Hispanic	403 (9)	132 (9)	95 (8)	109 (9)	67 (10)
Black	265 (6)	93 (6)	53 (5)	70 (6)	49 (7)
Asian/Other	215 (5)	64 (4)	57 (5)	64 (5)	30 (4)
Unrecorded	44 (1)	9 (1)	16 (1)	13 (1)	6 (1)
Stage, <i>N</i> (%)					
1	822 (18)	148 (10)	189 (17)	302 (24)	183 (27)
2	701 (15)	154 (10)	174 (15)	223 (18)	150 (22)
3	519 (11)	153 (10)	141 (13)	139 (11)	86 (13)
4	2,424 (53)	1,021 (68)	610 (54)	548 (44)	245 (36)
Unrecorded	86 (2)	26 (2)	17 (2)	25 (2)	18 (3)
B symptoms, <i>N</i> (%)					
Absent	2,501 (55)	709 (47)	631 (56)	757 (61)	404 (59)
Present	1,523 (34)	630 (42)	386 (34)	344 (28)	163 (24)
Unrecorded	528 (12)	163 (11)	114 (10)	136 (11)	115 (17)
Primary site, <i>N</i> (%) ^a					
Nodal	3,229 (71)	1,157 (77)	835 (74)	813 (66)	424 (62)
Extranodal high risk	828 (18)	219 (15)	185 (16)	248 (20)	176 (26)
Extranodal, other	495 (11)	126 (8)	111 (10)	176 (14)	82 (12)
Comorbidity index, <i>N</i> (%)					
0	3,607 (79)	1,181 (79)	901 (80)	987 (80)	538 (79)
1	693 (15)	240 (16)	167 (15)	186 (15)	100 (15)
2	157 (3)	53 (4)	44 (4)	36 (3)	24 (4)
≥3	95 (2)	28 (2)	19 (2)	28 (2)	20 (3)
Prognostic index, <i>N</i> (%) ^b					
Low	967 (21)	222 (15)	226 (20)	333 (27)	186 (27)
Low-Intermediate	1,150 (25)	368 (25)	295 (26)	300 (24)	187 (27)
High-Intermediate	1,072 (24)	436 (29)	245 (22)	274 (22)	117 (17)
High	1,363 (30)	476 (32)	365 (32)	330 (27)	192 (28)

^a High-risk sites included central nervous system, lung, liver, pancreas, gastrointestinal tract, and bone marrow

^b Burkitt lymphoma-specific, population-based prognostic index according to Castillo et al., Cancer. 2013;119(20):3672-3679.

Table S2. Characteristics of mantle cell lymphoma patients, stratified by time from diagnosis to start of chemotherapy.

	All patients	Time from diagnosis to chemotherapy			
		0-7 days	8-14 days	15-30 days	>30 days
<i>N</i>	11,723	1,431	1,578	3,602	5,112
Age, median (IQR)	65 (58-73)	65 (58-74)	66 (58-74)	65 (58-74)	65 (57-73)
Sex, <i>N</i> (%)					
Male	8,599 (73)	1,058 (74)	1,156 (73)	2,683 (75)	3,702 (72)
Female	3,124 (27)	373 (26)	422 (27)	919 (26)	1,410 (28)
Race / ethnicity, <i>N</i> (%)					
White non-Hispanic	10,405 (89)	1,232 (86)	1,419 (90)	3,261 (91)	4,493 (88)
White Hispanic	518 (4)	95 (7)	66 (4)	136 (4)	221 (4)
Black	482 (4)	70 (5)	55 (4)	116 (3)	241 (5)
Asian/Other	229 (2)	22 (2)	31 (2)	62 (2)	114 (2)
Unrecorded	89 (1)	12 (1)	7 (0)	27 (1)	43 (1)
Ann Arbor stage, <i>N</i> (%)					
1	678 (6)	51 (4)	68 (4)	191 (5)	368 (7)
2	780 (7)	64 (5)	84 (5)	255 (7)	377 (7)
3	1,648 (14)	168 (12)	203 (13)	540 (15)	737 (14)
4	8,455 (72)	1,116 (78)	1,205 (76)	2,566 (71)	3,568 (70)
Unrecorded	162 (1)	32 (2)	18 (1)	50 (1)	62 (1)
B symptoms, <i>N</i> (%)					
Absent	6,929 (59)	651 (46)	800 (51)	2,075 (58)	3,403 (67)
Present	3,479 (30)	622 (44)	623 (40)	1,112 (31)	1,122 (22)
Unrecorded	1,315 (11)	158 (11)	155 (10)	415 (12)	587 (12)
Primary site, <i>N</i> (%) ^a					
Nodal	9,873 (84)	1,230 (86)	1,371 (87)	3,081 (86)	4,191 (82)
Extranodal high risk	1,023 (9)	155 (11)	136 (9)	269 (8)	463 (9)
Extranodal, other	827 (7)	46 (3)	71 (5)	252 (7)	458 (9)
Comorbidity index, <i>N</i> (%)					
0	9,281 (79)	1,040 (73)	1,210 (77)	2,904 (81)	4,127 (81)
1	1,853 (16)	275 (19)	273 (17)	522 (15)	783 (15)
2	438 (4)	81 (6)	69 (4)	130 (4)	158 (3)
≥3	151 (1)	35 (2)	26 (2)	46 (1)	44 (1)
IPI, <i>N</i> (%)					
Low	300 (18)	16 (9)	18 (8)	96 (19)	170 (24)
Low-Intermediate	499 (31)	46 (26)	64 (27)	144 (29)	245 (34)
High-Intermediate	434 (27)	44 (25)	64 (27)	140 (28)	186 (26)
High	405 (25)	71 (40)	91 (38)	121 (24)	122 (17)

^a High-risk sites included central nervous system, lung, liver, pancreas, gastrointestinal tract, and bone marrow
IPI: International prognostic index

Table S3. Characteristics of **peripheral T-cell lymphoma** patients, stratified by time from diagnosis to start of chemotherapy.

	All patients	Time from diagnosis to chemotherapy			
		0-7 days	8-14 days	15-30 days	>30 days
<i>N</i>	9,809	1,402	1,826	3,130	3,451
Age, median (IQR)	61 (49-71)	59 (44-70)	60 (48-71)	61 (49-71)	62 (51-71)
Sex, <i>N</i> (%)					
Male	5,939 (61)	881 (63)	1,122 (61)	1,850 (59)	2,086 (60)
Female	3,870 (40)	521 (37)	704 (39)	1,280 (41)	1,365 (40)
Race / ethnicity, <i>N</i> (%)					
White non-Hispanic	7,274 (74)	1,009 (72)	1,323 (73)	2,416 (77)	2,526 (73)
White Hispanic	593 (6)	99 (7)	122 (7)	159 (5)	213 (6)
Black	1,404 (14)	209 (15)	266 (15)	395 (13)	534 (16)
Asian/Other	430 (4)	68 (5)	93 (5)	130 (4)	139 (4)
Unrecorded	108 (1)	17 (1)	22 (1)	30 (1)	39 (1)
Ann Arbor stage, <i>N</i> (%)					
1	1,311 (13)	95 (7)	155 (9)	398 (13)	663 (19)
2	1,451 (15)	147 (11)	196 (11)	486 (16)	622 (18)
3	2,667 (27)	337 (24)	518 (28)	916 (29)	896 (26)
4	4,225 (43)	802 (57)	929 (51)	1,288 (41)	1,206 (35)
Unrecorded	155 (2)	21 (2)	28 (2)	42 (1)	64 (2)
B symptoms, <i>N</i> (%)					
Absent	4,770 (49)	522 (37)	698 (38)	1,500 (48)	2,050 (59)
Present	4,136 (42)	757 (54)	977 (54)	1,342 (43)	1,060 (31)
Unrecorded	903 (9)	123 (9)	151 (8)	288 (9)	341 (10)
Primary site, <i>N</i> (%) ^a					
Nodal	8,138 (83)	1,217 (87)	1,600 (88)	2,652 (85)	2,669 (77)
Extranodal, high risk	689 (7)	112 (8)	119 (7)	188 (6)	270 (8)
Extranodal, other	982 (10)	73 (5)	107 (6)	290 (9)	512 (15)
Comorbidity index, <i>N</i> (%)					
0	7,735 (79)	1,069 (76)	1,408 (77)	2,498 (80)	2,760 (80)
1	1,574 (16)	252 (18)	317 (17)	494 (16)	511 (15)
2	370 (4)	58 (4)	66 (4)	109 (4)	137 (4)
≥3	130 (1)	23 (2)	35 (2)	29 (1)	43 (1)
IPI, <i>N</i> (%)					
Low	442 (29)	30 (14)	57 (23)	152 (30)	203 (37)
Low-Intermediate	384 (25)	47 (22)	55 (22)	124 (25)	158 (29)
High-Intermediate	328 (22)	65 (30)	55 (22)	105 (21)	103 (19)
High	364 (24)	74 (34)	84 (34)	119 (24)	87 (16)
Histology, <i>N</i> (%)					
PTCL, NOS	4,660 (48)	646 (46)	779 (43)	1,419 (45)	1,816 (53)
Angioimmunoblastic	1,930 (20)	254 (18)	413 (23)	663 (21)	600 (17)
Anaplastic large cell	3,219 (33)	502 (36)	634 (35)	1,048 (34)	1,035 (30)

^a High-risk sites included central nervous system, lung, liver, pancreas, gastrointestinal tract, and bone marrow
IPI: International prognostic index; PTCL, NOS: peripheral T-cell lymphoma, not otherwise specified

Table S4. Overall survival estimates in aggressive non-Hodgkin lymphomas, stratified by time from diagnosis to start of chemotherapy.

Lymphoma / Time to treatment	Overall survival at 3 years		Median survival	
	%	95%CI	Years	95%CI
DLBCL				
0-14 days	58.9	58.4-59.4	6.2	5.9-6.5
>14 days	72.2	71.9-72.6	9.7	9.5-9.9
All	67.8	67.5-68.1	8.7	8.6-8.9
BL				
0-14 days	59.0	57.1-60.9	8.6	7.4-NR
>14 days	68.5	66.3-70.6	NR	
All	63.0	61.6-64.4	NR	
MCL				
0-14 days	50.3	48.4-52.2	3.0	2.8-3.3
>14 days	70.7	69.7-71.7	7.2	6.9-7.6
All	65.5	64.5-66.4	5.9	5.6-6.1
PTCL				
0-14 days	41.1	39.3-42.8	1.2	1.1-1.4
>14 days	51.7	50.4-53.0	3.4	3.1-3.7
All	48.2	47.2-49.2	2.6	2.4-2.8

BL: Burkitt lymphoma; DLBCL: diffuse large B-cell lymphoma; MCL: mantle cell lymphoma; NR: not reached; PTCL: peripheral T-cell lymphoma;

Table S5. Sensitivity analysis: survival outcomes of patients with aggressive non-Hodgkin lymphomas who survived at least 4 months from diagnosis, stratified by histology and time from diagnosis to start of chemotherapy.

Lymphoma, time to treatment	Models stratified by IPI^a		Multivariable models^b	
	HR	95% CI	HR	95% CI
DLBCL				
0-7 days	1.26	(1.15-1.37)	1.49	(1.44-1.55)
8-14 days	1.10	(1.02-1.20)	1.34	(1.29-1.38)
15-30 days	1.04	(0.97-1.12)	1.12	(1.08-1.15)
>30 days	Ref.		Ref.	
BL				
0-7 days	1.41	(1.16-1.71)	1.45	(1.19-1.76)
8-14 days	1.23	(1.01-1.51)	1.25	(1.02-1.54)
15-30 days	1.10	(0.90-1.34)	1.10	(0.90-1.35)
>30 days	Ref.		Ref.	
MCL				
0-7 days	2.02	(1.57-2.59)	2.08	(1.89-2.28)
8-14 days	1.56	(1.24-1.96)	1.61	(1.47-1.77)
15-30 days	1.21	(1.00-1.46)	1.24	(1.15-1.34)
>30 days	Ref.		Ref.	
PTCL				
0-7 days	1.33	(1.03-1.72)	1.51	(1.36-1.68)
8-14 days	1.25	(0.99-1.59)	1.21	(1.10-1.34)
15-30 days	1.19	(0.97-1.45)	1.19	(1.10-1.29)
>30 days	Ref.		Ref.	

^a IPI for DLBCL, MCL, and PTCL, population-based prognostic index for Burkitt lymphoma

^b Model adjusting for age, sex, race/ethnicity, stage, presence of B-symptoms, primary site, comorbidity index, and median income in the county of residence

BL: Burkitt lymphoma; CI: confidence interval; DLBCL: diffuse large B-cell lymphoma; HR: hazard ratio; IPI: international prognostic index; MCL: mantle cell lymphoma; OS: overall survival; PTCL: peripheral T-cell lymphoma; Ref.: reference level.

Figure S1. Overall survival of patients with aggressive non-Hodgkin lymphomas who had available International Prognostic Index (or population-based prognostic index for Burkitt lymphoma), stratified by time from diagnosis to start of chemotherapy: (A) diffuse large B-cell lymphoma (DLBCL), (B) Burkitt lymphoma (BL), (C) mantle cell lymphoma (MCL), and (D) peripheral T-cell lymphoma (PTCL).

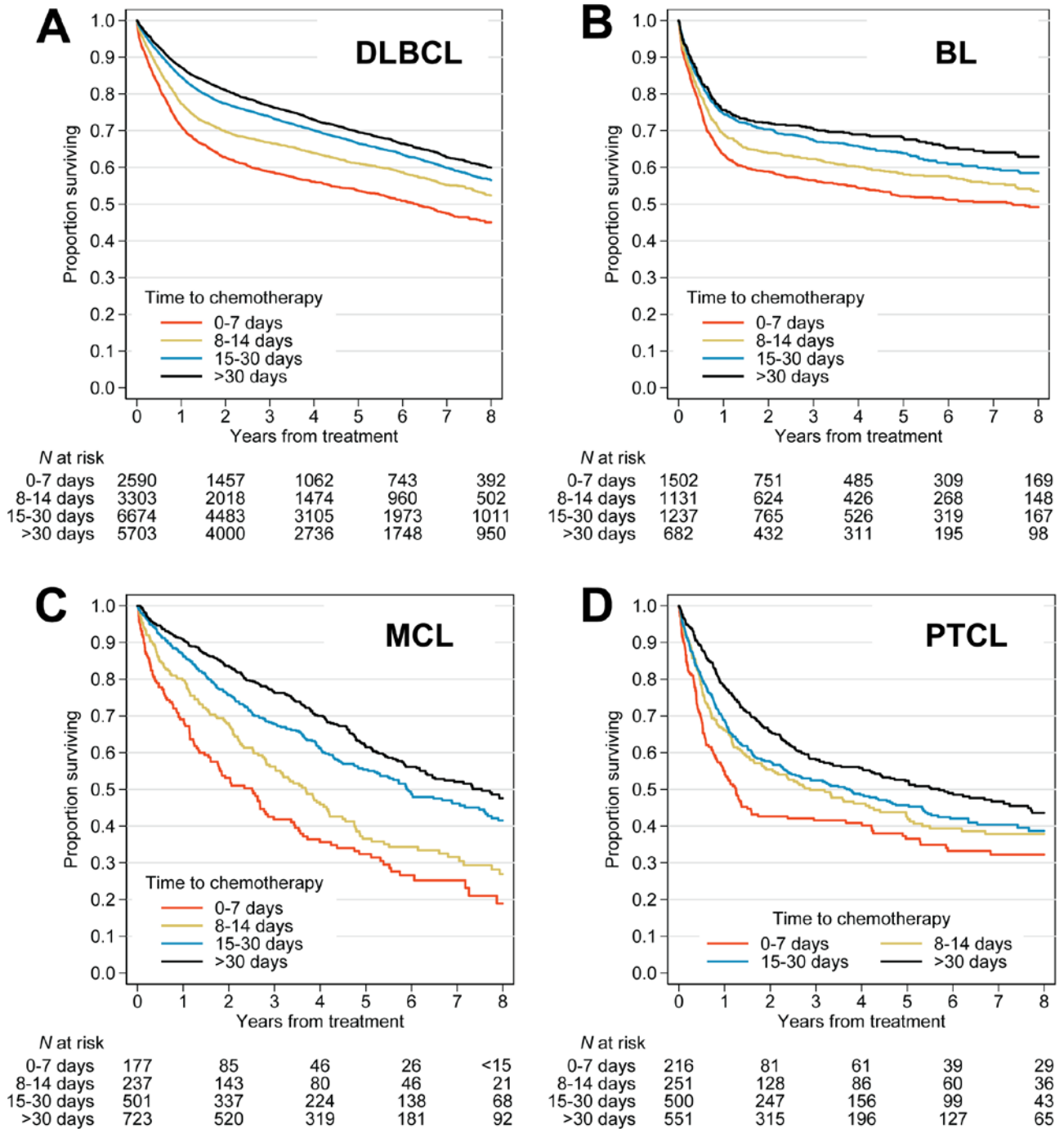


Figure S2. Overall survival of patients aggressive non-Hodgkin lymphomas, stratified by time from diagnosis to start of chemotherapy, and by prognostic index grouping: low/low-intermediate (Low/Low-Int) or high-intermediate/high risk (High-Int/High, defined as International Prognostic Index ≥ 3 , or Burkitt lymphoma population-based index >3): (A) diffuse large B-cell lymphoma (DLBCL), (B) Burkitt lymphoma (BL), (C) mantle cell lymphoma (MCL), and (D) peripheral T-cell lymphoma (PTCL).

