Outcomes among North American patients with diffuse large B-cell lymphoma are independent of tumor Epstein-Barr virus positivity or immunosuppression

Sean I. Tracy,¹ Thomas M. Habermann,¹ Andrew L. Feldman,¹ Matthew J. Maurer,¹ Ahmet Dogan,² Usha S. Perepu,³ Sergei Syrbu,³ Stephen M. Ansell,¹ Carrie A. Thompson,¹ George J. Weiner,³ Grzegorz S. Nowakowski,¹ Cristine Allmer,¹ Susan L. Slager,¹ Thomas E. Witzig,¹ James R. Cerhan¹ and Brian K. Link³

¹Mayo Clinic, Rochester, MN; ²Memorial Sloan Kettering Cancer Center, New York, NY and ³University of Iowa, Iowa City, IA, USA

©2017 Ferrata Storti Foundation. This is an open-access paper. doi:10.3324/haematol.2017.176511

Received: July 14, 2017.

Accepted: November 22, 2017.

Pre-published: November 23, 2017.

Correspondence: brian-link@uiowa.edu

<u>Supplemental Table 1:</u> Demographic and clinical characteristics of patients included in the study compared to all patients in the MER.

	MER patients included in study cohort (N=362)	MER patients not included in study cohort (N=719)	Total (N=1,081)	p value
Diagnosis Age		,		0.26
Median	63	64	64	
Q1, Q3	53, 72	54, 73	54, 72	
Range	(20-89)	(18-95)	(18-95)	
Age 51+				0.83
No	68 (18.8%)	139 (19.3%)	207 (19.1%)	
Yes	294 (81.2%)	580 (80.7%)	874 (80.9%)	
Age Group				0.46
<=60	152 (42.0%)	285 (39.6%)	437 (40.4%)	
>60	210 (58.0%)	434 (60.4%)	644 (59.6%)	
Gender				0.43
F	147 (40.6%)	310 (43.1%)	457 (42.3%)	
M	215 (59.4%)	409 (56.9%)	624 (57.7%)	
PS				0.67
Missing	1 (0.3%)	5 (0.7%)	6 (0.6%)	
<2	291 (80.4%)	573 (79.7%)	864 (79.9%)	
>=2	70 (19.3%)	141 (19.6%)	211 (19.5%)	
Ann Arbor Stage				0.04
Missing	3 (0.8%)	12 (1.7%)	15 (1.4%)	
I-II	144 (39.8%)	234 (32.5%)	378 (35.0%)	
III-IV	215 (59.4%)	473 (65.8%)	688 (63.6%)	
Number of Extranodal Sites				0.05
<=1	297 (82.0%)	553 (76.9%)	850 (78.6%)	
>1	65 (18.0%)	166 (23.1%)	231 (21.4%)	
LDH				0.007
Missing	40 (11.0%)	69 (9.6%)	109 (10.1%)	
<=Normal	163 (45.0%)	262 (36.4%)	425 (39.3%)	
>Normal	159 (43.9%)	388 (54.0%)	547 (50.6%)	
IPI Group				0.01

	MER patients included in study	MER patients not included in study		
	cohort	cohort	Total	
	(N=362)	(N=719)	(N=1,081)	p value
0-1 Low	130 (35.9%)	204 (28.4%)	334 (30.9%)	
2 Low Intermediate	109 (30.1%)	215 (29.9%)	324 (30.0%)	
3 High Intermediate	86 (23.8%)	185 (25.7%)	271 (25.1%)	
4-5 High	37 (10.2%)	115 (16.0%)	152 (14.1%)	
Age-adjusted IPI				0.008
Missing	0 (0.0%)	4 (0.6%)	4 (0.4%)	
0	103 (28.5%)	141 (19.6%)	244 (22.6%)	
1	114 (31.5%)	232 (32.3%)	346 (32.0%)	
2	105 (29.0%)	256 (35.6%)	361 (33.4%)	
3	40 (11.0%)	86 (12.0%)	126 (11.7%)	
BM Involvement				0.69
Missing	21 (9 60/)	73 (10.2%)	104 (9.6%)	0.09
Concordant	31 (8.6%) 71 (19.6%)	` ′	206 (19.1%)	
	, ,	135 (18.8%)		
Discordant	260 (71.8%)	511 (71.1%)	771 (71.3%)	
Bulky Disease				0.16
Missing	4 (1.1%)	15 (2.1%)	19 (1.8%)	
Yes	29 (8.0%)	78 (10.8%)	107 (9.9%)	
No	329 (90.9%)	626 (87.1%)	955 (88.3%)	
GCB/non-GCB				<0.001
Missing	75 (20.7%)	378 (52.6%)	453 (41.9%)	
Non-GCB	128 (35.4%)	100 (13.9%)	228 (21.1%)	
GCB	159 (43.9%)	241 (33.5%)	400 (37.0%)	
Composite				<0.001
	296 (81.8%)	632 (87.9%)	928 (85.8%)	<0.001
No Yes	66 (18.2%)	87 (12.1%)	153 (14.2%)	
Immuno-chemo				0.75
No	38 (10.5%)	80 (11.1%)	118 (10.9%)	
Yes	324 (89.5%)	639 (88.9%)	963 (89.1%)	
Radiation Therapy				0.001
No	289 (79.8%)	627 (87.2%)	916 (84.7%)	
Yes	73 (20.2%)	92 (12.8%)	165 (15.3%)	
FU Status				0.10
Alive	243 (67.1%)	446 (62.0%)	689 (63.7%)	0.10
Dead	119 (32.9%)	273 (38.0%)	392 (36.3%)	

	MER patients included in study cohort (N=362)	MER patients not included in study cohort (N=719)	Total (N=1,081)	p value
EFS24				< 0.001
Missing	8 (2.2%)	0 (0.0%)	8 (0.7%)	
Achieved	250 (69.1%)	460 (64.0%)	710 (65.7%)	
Failed	104 (28.7%)	259 (36.0%)	363 (33.6%)	
FU Months				<0.001
Median	59.1	47.2	48.5	
Q1, Q3	32.6, 94.9	21.7, 82.9	24.9, 83.5	
Range	(0.7-155.2)	(0.4-155.2)	(0.4-155.2)	

Supplemental Table 2: Clinical characteristics of immunosuppressed patients.

<u>Patient</u>	Age	EBV	Condition	<u>Immunosuppression</u>
1	42	-	CVID	none
2	42	-	Histiocytosis X	cyclophosphamide, MTX, CS
3	46	-	SLE	mycophenolate, azathioprine, HCQ, CS
4	49	-	RA	MTX
5	51	-	RA	MTX
6	52	-	RA	MTX, HCQ
7	53	-	RA, PMR	infliximab, CS
8	54	-	scleroderma HCV-related	CS
9	56	-	vasculitis	HCQ, CS
10	56	-	RA	infliximab, MTX
			RA, Felty's	
11	56	+	syndrome	MTX, CS
12	57	-	Crohn's disease	mesalamine, sulfasalazine, CS
13	58	-	PMR	CS
14	59	-	SLE	MTX, CS
15	59	-	SLE	HCQ
16	59	-	ulcerative colitis	Sulfasalazine
17	61	-	RA	etanercept, MTX, CS
18	62	-	RA	CS
19	64	-	RA	Etanercept
20	64	-	RA	MTX
21	64	-	RA	MTX
22	65	-	RA	adalimumab, HCQ, MTX, CS
23	66	+	seizure disorder autoimmune	phenytoin, levetiracetam
24	67	-	hepatitis	Azathioprine
25	67	-	MCTD	CS
26	69	-	RA	MTX, infliximab, gold, d-penicillamine
27	69	-	seizure disorder	Carbamazepine
28	71	-	RA	MTX
29	71	+	SLE	HCQ, mycophenolic acid, CS
30	72	-	RA	MTX
31	74	-	RA	MTX
32	74	-	RA	MTX

TRACY et al. SUPPLEMENTAL DLBCL WITH EBV OR IMMUNOSUPPRESSSION

33	75	-	Crohn's disease	Azathioprine
				HCQ, sulfasalazine,
34	75	-	RA	CS
35	76	+	GPA	azathioprine, cyclophosphamide, CS
36	77	-	RA	MTX
37	78	-	RA	MTX
38	78	-	sarcoidosis	carbamazepine, MTX, CS
39	79	-	SLE	HCQ

Abbreviations: $CVID = common\ variable\ immunodeficiency.\ SLE = systemic\ lupus\ erythrematosus.\ RA = rheumatoid\ arthritis,\ PMR = polymyalgia\ rheumatica.\ MCTD = mixed\ connective\ tissue\ disease.\ GPA = granulomatosis\ with\ polyangiitis.\ MTX = methotrexate.\ CS = corticosteroids.\ HCQ = hydroxychloroquine.$