LETTER TO THE EDITOR

Leukemic presentation in nodal mantle cell lymphoma is characterized by frequent SOX11 negativity, a poor risk genomic landscape including higher *TP53* alterations, and worse overall survival

Authors

Mingfei Yan,[1] Shenon Sethi,[1] Jyoti Kumar,[1,2°] Anita Kumar,[3] Ahmet Dogan[1] and Pallavi Galera[1]

[1]Hematopathology Service, Department of Pathology and Laboratory Medicine; [2]Diagnostic Molecular Pathology Service, Department of Pathology and Laboratory Medicine and [3]Lymphoma Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA

°Current address: Department of Diagnostic Medicine, Dell Medical School, The University of Texas at Austin, Austin, TX, USA

Correspondence:
P. GALERA - GaleraP@mskcc.org

https://doi.org/10.3324/haematol.2024.287108

Supplemental material

Leukemic presentation in nodal mantle cell lymphoma is characterized by frequent SOX11 negativity, a poor risk genomic landscape including higher *TP53* alterations, and worse overall survival

Mingfei Yan, Shenon Sethi, Jyoti Kumar, Anita Kumar, Ahmet Dogan, Pallavi Galera

Supplemental table 1. Clinicopathological features of mantle cell lymphomas with different disease presentations.

	Disease presentations			p values		
	nMCL (n=193)	**lnMCL (n=29)**	**nnMCL (n=25)**	**nMCL vs lnMCL**	**nMCL vs nnMCL**	**lnMCL vs nnMCL**
Gender % of male/female	71.5% / 28.5%	69% / 31%	64% / 36%	0.827	0.486	0.777
Age median (range)	66 (29 – 96)	69 (48 – 86)	64 (38 – 78)	0.209	0.618	0.123
Aggressive histomorphology [1] positive/total No. (%)	29/191 (15.2%)	4/29 (13.8%)	1/20 (5%)	1	0.320	0.636
CD5-positive positive/total No. (%)	182/191 (95.3%)	27/29 (93.1%)	17/19 (89.5%)	0.642	0.261	0.643
CyclinD1-positive [2] positive/total No. (%)	191/193 (99%)	27/27 (100%)	17/18 (94.4%)	1	0.236	0.4
Bone marrow involvement positive/total No. (%)	90/137 (65.7%)	27/27 (100%)	20/20 (100%)	**<0.001**	**<0.001**	1
Lymphoma % to BM cellularity median (range)	15 (1 – 100)	60 (30 – 85)	55 (5 – 90)	**<0.001**	**<0.001**	0.231
Splenomegaly positive/total No. (%)	71/185 (38.4%)	21/28 (75%)	21/25 (84%)	**<0.001**	**<0.001**	0.509
PB lymphoma cell count ($x10^9$/L) median (range)	0.3 (0.0002 – 4.3)	14.9 (5.3 – 266.6)	17.9 (0.2 – 228.8)	**<0.001**	**<0.001**	0.487
WBC count ($x10^9$/L) [3] median (range)	7.1 (1.8 – 32.2)	23.8 (10.8 - 322)	26.7 (4.2 – 261.2)	**<0.001**	**<0.001**	0.873
Initial active surveillance positive/total No. (%)	35/173 (20.2%)	4/29 (13.8%)	14/24 (58.3%)	0.611	**<0.001**	**0.001**
Median survival (months)	101.9	31.4	Not reached	**<0.001**	0.244	**0.001**

Note 1: Included blastoid and pleomorphic morphology.
Note 2: There were 3 CyclinD1-negative cases and another 9 cases which lacked CyclinD1 immunohistochemistry (IHC). Among them, 10 demonstrated *CCND1* translocation by fluorescence in situ hybridization (FISH), including 1 case with negative CyclinD1 IHC. The remaining 2 CyclinD1-negative cases included one which showed positivity for CyclinD2, CyclinD3, CD5, and SOX11 by IHC but lacked *CCND1* FISH and another one which was negative for *CCND1* translocation but showed two extra copies of *CCND1* by FISH and was positive for CyclinD2 and SOX11 by IHC.
Note 3: Only the white blood cell (WBC) counts for patients with peripheral blood involvement by mantle cell lymphoma confirmed by flow cytometric study were included for analysis.

Bold p values indicate statistical significance.

Supplemental table 2. Comparison of mutational frequencies among patients with different disease presentations.

	Disease presentations			p values		
Genes mutated/tested No. (%)	nMCL (n=182)	lnMCL (n=29)	nnMCL (n=24)	nMCL vs lnMCL	nMCL vs nnMCL	lnMCL vs nnMCL
ATM	88/182 (48.4%)	13/29 (44.8%)	1/25 (4%)	0.842	**<0.001**	**<0.001**
TP53	40/182 (22%)	14/29 (48.3%)	8/25 (32%)	**0.005**	0.312	0.274
KMT2D	47/182 (25.8%)	7/29 (24.1%)	2/25 (8%)	1	0.076	0.153
CCND1	25/182 (13.7%)	3/29 (10.3%)	9/25 (36%)	0.774	**0.009**	**0.046**
UBR5	25/174 (14.4%)	1/28 (3.6%)	0/25 (0%)	0.138	**0.049**	1
NSD2	15/175 (8.6%)	6/29 (20.7%)	1/25 (4%)	0.090	0.699	0.108
SMARCA4	14/182 (7.7%)	3/29 (10.3%)	2/25 (8%)	0.711	1	1
BIRC3	14/182 (7.7%)	4/29 (13.8%)	0/25 (0%)	0.283	0.227	0.115
NOTCH1	13/182 (7.1%)	5/29 (17.2%)	0/25 (0%)	0.081	0.374	0.054
TERT	9/182 (4.9%)	4/29 (13.8%)	2/25 (8%)	0.085	0.626	0.675
CARD11	10/182 (5.5%)	2/29 (6.9%)	0/25 (0%)	0.672	0.613	0.493
SAMHD1	3/174 (1.7%)	3/28 (10.7%)	2/25 (8%)	**0.036**	0.12	1
SP140	10/174 (5.7%)	3/28 (10.7%)	1/25 (4%)	0.397	1	0.613
MEF2B	11/182 (6.0%)	0/29 (0%)	1/25 (4%)	0.368	1	0.463
NOTCH2	3/182 (1.6%)	3/29 (10.3%)	2/25 (8%)	**0.035**	0.112	1
BCOR	9/182 (4.9%)	0/29 (0%)	0/25 (0%)	0.615	0.604	1
FAT1	7/182 (3.8%)	0/29 (0%)	2/25 (8%)	0.597	0.298	0.21
ARID1A	6/182 (3.3%)	1/29 (3.4%)	1/25 (4%)	1	0.6	1
ROBO1	6/174 (3.4%)	0/28 (0%)	1/25 (4%)	1	1	0.472
DNMT3A	6/182 (3.3%)	2/29 (6.9%)	2/25 (8%)	0.303	0.249	1
TET2	5/182 (2.7%)	1/29 (3.4%)	1/25 (4%)	0.593	0.543	1
CXCR4	6/182 (3.3%)	1/29 (3.4%)	1/25 (4%)	1	0.6	1
SF3B1	8/182 (4.4%)	1/29 (3.4%)	0/25 (0%)	1	0.6	1
ARID2	4/182 (2.2%)	1/29 (3.4%)	0/25 (0%)	0.526	1	1
ARID1B	3/182 (1.6%)	0/29 (0%)	2/25 (8%)	1	0.112	0.21
EPHA7	2/182 (1.1%)	0/29 (0%)	0/25 (0%)	1	1	1
SPEN	1/182 (0.5%)	2/29 (6.9%)	1/25 (4%)	0.050	0.228	1
MGA	3/182 (1.6%)	1/29 (3.4%)	0/25 (0%)	0.449	1	1

Bold p values indicate statistical significance.

Supplemental table 3. Comparison of treatments for mantle cell lymphoma patients.

Comparison of treatments for all patients by disease presentations and high-risk features													
	Disease presentations				***TP53* status**			**Ki67 index**			**Histomorphology**		
Treatment patient No. (%)	**nMCL** (n=174)	**lnMCL** (n=29)	**nnMCL** (n=24)	**p value**	**Wild-type** (n=164)	**Mutated** (n=63)	**p value**	**<30%** (n=117)	**>30%** (n=86)	**p value**	**Conventional** (n=187)	**Aggressive** (n=33)	**p value**
R-CHOP/EPOCH	38 (21.9%)	11 (37.9%)	4 (16.7%)	0.135	37 (22.6%)	16 (25.4%)	0.726	25 (21.4%)	26 (30.2%)	0.19	41 (21.9%)	12 (36.4%)	0.081
R-DHAX/DHAP	51 (29.3%)	7 (24.1%)	3 (12.5%)	0.226	47 (28.7%)	14 (22.2%)	0.404	35 (30%)	23 (26.7%)	0.641	51 (27.3%)	9 (27.3%)	1
BR	44 (25.3%)	7 (24.1%)	4 (16.7%)	0.744	39 (23.8%)	16 (25.4%)	0.863	22 (18.8%)	29 (33.7%)	**0.021**	44 (23.5%)	10 (30.3%)	0.39
Cytarabine [1]	72 (41.4%)	14 (48.3%)	6 (25%)	0.204	67 (40.8%)	25 (39.7%)	1	47 (40.2%)	41 (47.7%)	0.317	74 (39.6%)	17 (51.5%)	0.25
BTK inhibitor	62 (35.6%)	20 (69%)	8 (33.3%)	**0.003**	44 (26.8%)	46 (73%)	**<0.001**	32 (27.4%)	50 (58.1%)	**<0.001**	68 (36.4%)	21 (63.6%)	**0.004**
Lenalidomide	21 (12.1%)	5 (17.2%)	2 (8.3%)	0.647	20 (12.2%)	8 (12.7%)	1	15 (12.8%)	12 (14%)	0.837	23 (12.3%)	5 (15.2%)	0.582
Venetoclax	37 (21.3%)	10 (34.5%)	5 (20.8%)	0.288	19 (11.6%)	33 (52.4%)	**<0.001**	15 (12.8%)	34 (39.5%)	**<0.001**	39 (20.9%)	12 (36.4%)	0.072
Autologous transplantation	31 (17.8%)	2 (6.9%)	1 (4.2%)	0.098	31 (18.9%)	3 (4.8%)	**0.006**	20 (17.1%)	13 (15.1%)	0.848	30 (16%)	4 (12.1%)	0.794

Note 1: Included patients treated by both cytarabine monotherapy and combinational therapy with other chemoimmunotherapeutic agents.

Abbreviations: BR: Bendamustine, Rituximab; **BTK**: Bruton tyrosine kinase; **CHOP**: Cyclophosphamide, Doxorubicin hydrochloride, Vincristine sulfate, Prednisone; **DHAP**: Dexamethasone, High-dose cytarabine, Cisplatin; **DHAX**: Dexamethasone, High-dose cytarabine, Oxaliplatin; **EPOCH**: Etoposide Phosphate, Prednisone, Vincristine Sulfate, Cyclophosphamide, Doxorubicin hydrochloride; **R**: Rituximab.

Comparison of selected treatments for only leukemic nodal MCL (lnMCL) patients by high-risk features									
	***TP53* status**			**Ki67 proliferation index**			**Histomorphology**		
Treatment patient No. (%)	**Wild-type** (n=15)	**Mutated** (n=14)	**p value**	**< 30%** (n=6)	**>30%** (n=18)	**p value**	**Conventional** (n=25)	**Aggressive** (n=4)	**p value**
Cytarabine positive/total number (%)	7 (46.7%)	7 (50%)	1	3 (50%)	11 (61.1)	0.665	10 (40%)	4 (100%)	**0.042**
BTK inhibitor positive/total number (%)	7 (46.7%)	13 (92.9%)	**0.014**	2 (33.3%)	15 (83.3%)	**0.038**	16 (64%)	4 (100%)	0.28
Autologous transplantation positive/total number (%)	2 (13.3%)	0	0.483	1 (16.7%)	1 (5.6%)	0.446	2 (8%)	0/4	1

Bold p values indicate statistical significance.