

Comparative effectiveness of immunotherapy alone or with chemotherapy as first-line treatment for marginal zone lymphoma

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Data supplement

Outcomes of immunotherapy or combination immunochemotherapy in first-line treatment of marginal zone lymphoma

Table of contents:

Supplemental Table S1. Specification of variables derived from the NCDB 2022 Participant User File and the MZL-RWD datasets. The detailed specification of all NCDB variables is provided at: https://www.facs.org/media/fowa425u/2022-data-dictionary.pdf	2
Supplemental Table S2. Characteristics of patients with MZL in the NCDB dataset according to first-line therapy administered.	4
Supplemental Table S3. Characteristics of patients with MZL in the RWD-MZL dataset according to first-line rituximab or BR therapy administered.	5

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Dataset / Variable	Specification
NCDB	
Patient characteristics	
Age	Per year, capped at 90 per the NCDB policy. Specified using a restricted cubic spline.
Sex	Patient's sex
Race / ethnicity	Combines the NCDB "Race" variable (as recorded by the registry using the hospital record) and "Spanish Origin". Reclassified as White (non-Hispanic), Hispanic (of any race), Black, Asian/Other, and Unrecorded.
Comorbidity index	Using the Charlson Comorbidity Index as recorded in the NCDB. Classified as 0, 1, 2, or ≥ 3 .
Year of diagnosis	2013 to 2018
Health insurance	As recorded by the NCDB, classified as private insurance, Medicaid, Medicare, other government-sponsored, uninsured, or unknown status.
Income	Median household income for each patient's area of residence is estimated by matching the zip code of the patient recorded at the time of diagnosis against files derived from the 2012 American Community Survey data, spanning years 2008-2012 and adjusted for 2012 inflation; Household income is categorized as quartiles based on equally proportioned income ranges among all US zip codes.
Urban / rural status	Indicator derived from the patient's county code recorded at the time of diagnosis, based on the 2013 designation by the US Department of Agriculture Economic Research Service
Disease characteristics	
MZL histology	Determined using the ICD-O-3 histology code and the primary anatomical site code.
Prior malignancy	Derived from the registry "sequence number", which indicates whether the MZL record is the first or subsequent malignancy for the patient.
EMZL primary site	ICD-O-3 primary site code
Ann Arbor stage	As recorded by the NCDB, classified as 1, 2, 3, 4, or unrecorded.
B symptoms	As recorded by the NCDB, classified as present, absent, or unrecorded.
Treatment characteristics	
Diagnosis-to-treatment interval	In days. Specified using a restricted cubic spline.
Surgery prior to systemic therapy	As recorded in the NCDB, for patients whose MZL may have been treated with excision prior to systemic therapy
Radiation therapy prior to systemic therapy	As recorded in the NCDB, for patients whose MZL may have been treated with excision prior to systemic therapy
Facility characteristics	
Academic or community	According to the Commission on Cancer (CoC) designation, based on the type of facility, program structure, services provided, and the number of cases accessioned each year.

	Of the n=1038 facilities included in this analysis, 202 (19.4%) were designated as academic
Facility volume	Calculated for each facility as the total number of MZL cases reported to NCDB divided by the number of calendar years included. Categorized as average \leq or >5 cases per year. Median volume was 1.7 (interquartile range, 0.9 to 3.0), and 119 (11.5%) of facilities were classified as higher volume.
MZL-RWD	
Patient characteristics	
Age	Per year, specified as a restricted cubic spline
Sex	Patient's sex
Performance status	According to the Eastern Cooperative Oncology Group (ECOG) scale, classified as good (0-1) or poor (2-4).
Disease characteristics	
MZL histology	Classified as EMZL, NMZL, or SMZL according to the WHO diagnosis on the pathology report and clinical assessment of the investigator.
Stage	Derived from the medical record, classified as early (1/2) or advanced (3/4).
B symptoms	Present or absent, derived from the medical record.
Bone marrow involvement	Derived from the medical record, when a staging bone marrow biopsy was performed.
Lactate dehydrogenase (LDH)	Serum LDH recorded at diagnosis.
Monoclonal paraprotein	Present or absent/unrecorded.
Albumin	Classified as normal or low according to the institutional reference range.
Hemoglobin	In g/dL (continuous variable) at the time of diagnosis
Ki-67 staining	Classified as $<$ or $\geq 20\%$, when staining performed on the diagnostic biopsy
Complex cytogenetics	When recorded at the time of initial diagnosis
Large cell tumor content	Presence of increased or prominent large cells recorded on the initial diagnostic biopsy by the pathologist.
CD5 expression	Positive or negative, as recorded on the initial diagnostic biopsy or flow cytometry.

Supplemental Table S2. Characteristics of patients with MZL in the NCDB dataset according to first-line therapy administered.

	Immunotherapy N = 4,728 (58.3%)	Immunochemotherapy N = 3,382 (41.7%)	Total N = 8,110	P
Age at diagnosis, median (range)	69 (19-90)	65 (20-90)	67 (19-90)	<0.001
Sex, N (%)				
Male	2,002 (42.3%)	1,601 (47.3%)	3,603 (44.4%)	<0.001
Female	2,726 (57.7%)	1,781 (52.7%)	4,507 (55.6%)	
Race/ethnicity, N (%) ^a				
White non-Hispanic	3,945 (83.4%)	2,720 (80.4%)	6,665 (82.2%)	<0.001
Hispanic	246 (5.2%)	203 (6.0%)	449 (5.5%)	
Black	349 (7.4%)	316 (9.3%)	665 (8.2%)	
Asian/other	148 (3.1%)	128 (3.8%)	276 (3.4%)	
Unknown	40 (0.8%)	15 (0.4%)	55 (0.7%)	
Charlson-Deyo comorbidity index ^a				
0	3,586 (75.8%)	2,626 (77.6%)	6,212 (76.6%)	0.309
1	749 (15.8%)	497 (14.7%)	1,246 (15.4%)	
2	233 (4.9%)	155 (4.6%)	388 (4.8%)	
≥3	160 (3.4%)	104 (3.1%)	264 (3.3%)	
Median income quartiles, N (%) ^a				
< \$38,000	532 (11.3%)	426 (12.6%)	958 (11.8%)	0.029
\$38,000 - \$47,999	834 (17.6%)	628 (18.6%)	1,462 (18.0%)	
\$48,000 - \$62,999	1,115 (23.6%)	823 (24.3%)	1,938 (23.9%)	
\$63,000 +	1,582 (33.5%)	1,023 (30.2%)	2,605 (32.1%)	
Unrecorded	665 (14.1%)	482 (14.3%)	1,147 (14.1%)	
Health insurance, N (%) ^a				
Uninsured	68 (1.4%)	87 (2.6%)	155 (1.9%)	<0.001
Private	4,026 (85.2%)	2,721 (80.5%)	6,747 (83.2%)	
Medicaid	207 (4.4%)	207 (6.1%)	414 (5.1%)	
Medicare	323 (6.8%)	260 (7.7%)	583 (7.2%)	
Other government	46 (1.0%)	35 (1.0%)	81 (1.0%)	
Unknown	58 (1.2%)	72 (2.1%)	130 (1.6%)	
MZL subtype, N (%)				
SMZL	1,103 (23.3%)	328 (9.7%)	1,431 (17.6%)	<0.001
NMZL	1,508 (31.9%)	1,845 (54.6%)	3,353 (41.3%)	
EMZL	2,117 (44.8%)	1,209 (35.7%)	3,326 (41.0%)	
Stage, N (%) ^a				
1/2	1,661 (35.1%)	814 (24.1%)	2,475 (30.5%)	<0.001
3/4	2,626 (55.5%)	2,370 (70.1%)	4,996 (61.6%)	
Unrecorded	441 (9.3%)	198 (5.9%)	639 (7.9%)	
B symptoms, N (%) ^a				
No B-symptoms	3,395 (71.8%)	2,140 (63.3%)	5,535 (68.2%)	<0.001
B-symptoms	887 (18.8%)	904 (26.7%)	1,791 (22.1%)	
Unknown	446 (9.4%)	338 (10.0%)	784 (9.7%)	
Prior malignancy, N (%)				
No	3,743 (79.2%)	2,791 (82.5%)	6,534 (80.6%)	<0.001
Yes	985 (20.8%)	591 (17.5%)	1,576 (19.4%)	
Diagnosis-to-treatment interval in days, median (range) ^a	45 (0-1375)	39 (0-728)	42 (0-1375)	<0.001
Prior radiation, N (%)				
No	4,568 (96.6%)	3,331 (98.5%)	7,899 (97.4%)	<0.001
Yes	160 (3.4%)	51 (1.5%)	211 (2.6%)	
Prior surgery, N (%)				
No	4,049 (85.6%)	2,902 (85.8%)	6,951 (85.7%)	0.831
Yes	679 (14.4%)	480 (14.2%)	1,159 (14.3%)	

^a see Table S1 for details of the specification.

Supplemental Table S3. Characteristics of patients with MZL in the RWD-MZL dataset according to first-line rituximab or BR therapy administered.

	Rituximab N = 355 (65.6%)	BR N = 186 (34.4%)	Total N = 541 (100.0%)	P^b
Age, median (range)	65 (19-96)	61 (35-91)	64 (19-96)	0.001
Sex, N (%)				
Male	174 (49.0%)	91 (48.9%)	265 (49.0%)	0.99
Female	181 (51.0%)	95 (51.1%)	276 (51.0%)	
Poor performance status, N (%) ^a				
No	284 (80.0%)	151 (81.2%)	435 (80.4%)	0.59
Yes	27 (7.6%)	11 (5.9%)	38 (7.0%)	
Missing	44 (12.4%)	24 (12.9%)	68 (12.6%)	
MZL subtype, N (%)				
SMZL	102 (28.7%)	36 (19.4%)	138 (25.5%)	<0.001
NMZL	70 (19.7%)	66 (35.5%)	136 (25.1%)	
EMZL	183 (51.5%)	84 (45.2%)	267 (49.4%)	
Stage, N (%)				
1/2	119 (33.5%)	29 (15.6%)	148 (27.4%)	<0.001
3/4	236 (66.5%)	157 (84.4%)	393 (72.6%)	
B symptoms, N (%)				
No	274 (77.2%)	148 (79.6%)	422 (78.0%)	0.90
Yes	60 (16.9%)	34 (18.3%)	94 (17.4%)	
Missing	21 (5.9%)	4 (2.2%)	25 (4.6%)	
Bone marrow involvement, N (%)				
No	130 (36.6%)	53 (28.5%)	183 (33.8%)	0.023
Yes	141 (39.7%)	94 (50.5%)	235 (43.4%)	
Not tested	84 (23.7%)	39 (21.0%)	123 (22.7%)	
LDH elevated, N (%) ^a				
No	218 (61.4%)	133 (71.5%)	351 (64.9%)	0.027
Yes	88 (24.8%)	32 (17.2%)	120 (22.2%)	
Missing	49 (13.8%)	21 (11.3%)	70 (12.9%)	
Serum M-protein, N (%) ^a				
Absent	99 (27.9%)	60 (32.3%)	159 (29.4%)	0.46
Present	70 (19.7%)	51 (27.4%)	121 (22.4%)	
Missing	186 (52.4%)	75 (40.3%)	261 (48.2%)	
Serum albumin, N (%) ^a				
Normal	280 (78.9%)	145 (78.0%)	425 (78.6%)	0.56
Low	37 (10.4%)	23 (12.4%)	60 (11.1%)	
Missing	38 (10.7%)	18 (9.7%)	56 (10.4%)	
Hemoglobin, g/dL, median (range)	12.6 (3.7-18.9)	12.3 (3.7-16.6)	12.5 (3.7-18.9)	0.53
Ki67 expression >20%, N (%) ^a				
<20%	128 (36.1%)	78 (41.9%)	206 (38.1%)	0.99
≥20%	38 (10.7%)	23 (12.4%)	61 (11.3%)	
Not tested	189 (53.2%)	85 (45.7%)	274 (50.6%)	
Large cells present, N (%) ^a				
No	275 (77.5%)	149 (80.1%)	424 (78.4%)	0.43
Yes	29 (8.2%)	20 (10.8%)	49 (9.1%)	
Not reported	51 (14.4%)	17 (9.1%)	68 (12.6%)	
CD5 expression, N (%) ^a				
No	268 (75.5%)	148 (79.6%)	416 (76.9%)	0.88
Yes	36 (10.1%)	18 (9.7%)	54 (10.0%)	
Not tested	51 (14.4%)	20 (10.8%)	71 (13.1%)	
Complex cytogenetics				
No	174 (49.0%)	80 (43.0%)	254 (47.0%)	0.87
Yes	16 (4.5%)	6 (3.2%)	22 (4.1%)	
Not tested	165 (46.5%)	100 (53.8%)	265 (49.0%)	

^a see Table S1 for details of the specification.

^b statistical tests compare only groups with non-missing values.