

Treatment Patterns Among Patients With Relapsed Follicular Lymphoma

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BACKGROUND

- Follicular lymphoma (FL) is the second most common form of non-Hodgkin lymphoma, accounting for about 35% of cases in the USA^{1,2}
- Despite a high 5-year survival rate (53–91%), FL is considered incurable with cycles of relapse and remission occurring frequently^{3,4}
- Treatment may involve radiation or chemoimmunotherapy (drug treatment) according to disease stage; however, standard guidelines recommend a number of options for both first- (1L) and second-line (2L) therapy with no dominant choice for clinical decision makers

OBJECTIVE

- To examine real-world 2L-treatment patterns among patients with relapsed FL

METHODS

Study Design and Data Source

- Retrospective cohort analysis of 2007–2014 Surveillance, Epidemiology, and End Results (SEER)-Medicare data
 - The SEER registry collects clinical, demographic, and cause of death information for persons with cancer residing in SEER regions; cancer diagnoses are confirmed through pathology reports and medical records
 - Medicare claims cover healthcare services received by beneficiaries in the US from the time of Medicare eligibility until death

Patient Population and Time Frame

- Patients with FL identified on the basis of International Classification of Diseases for Oncology, 3rd edition codes 9690–9691, 9695, and 9698, and initiating a target 1L FL treatment during the identification period January 1, 2008–December 31, 2012
- Date of diagnosis occurred on or before the first claim date for 1L treatment (index date)
 - Patients using any FL drug treatment before the index date were excluded
- Patients were followed for ≥ 1 year until death, disenrollment (from Medicare fee-for-service Part A/B or Part D), or study end
- Target 1L-treatments identified by presence of ≥ 1 claim for all agents (except prednisone):
 - Rituximab monotherapy (R-mono)
 - Bendamustine and rituximab (BR)
 - Rituximab, cyclophosphamide, vincristine, and prednisone (R-CVP)
 - Rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP)
 - As clinicians may modify the mix of “CHOP” agents, this study focused on R-CHOP-like regimens in which patients were not on R-CVP and received rituximab and ≥ 1 agent of cyclophosphamide, doxorubicin, and vincristine

METHODS (cont.)

Measures

- Outcomes included:
 - 1L-treatment patterns: regimen count and completion
 - Patients initiating 2L therapy after ≥ 4 cycles of 1L therapy and remission of ≥ 90 days (≥ 180 days for R-mono) were considered to have relapsed FL
 - New drug therapy received before completing all cycles and achieving full remission was considered part of the previous line of therapy
 - 2L-treatment patterns: regimen type and frequency

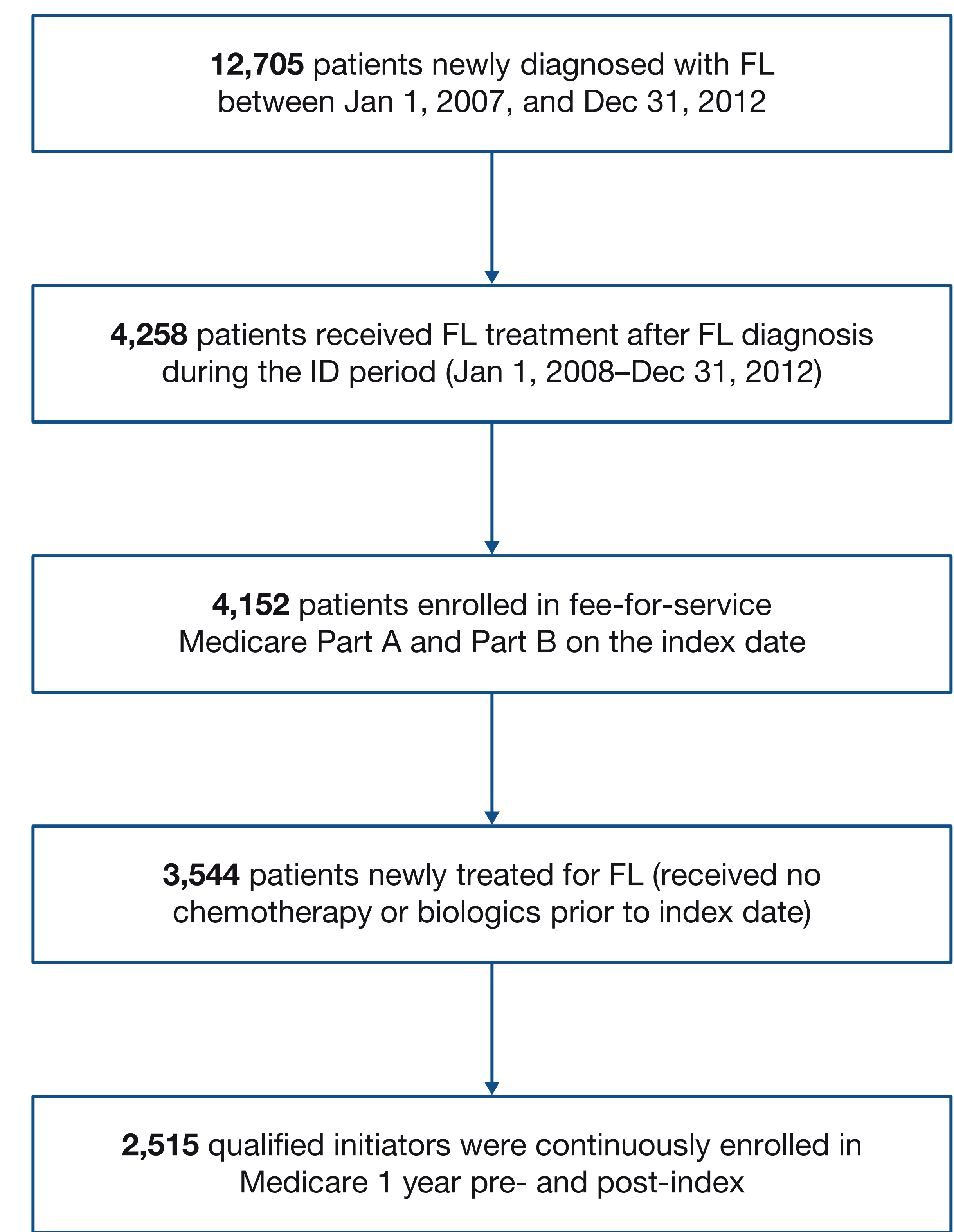
Statistical Analysis

- Descriptive analyses are presented for the cohort overall and stratified by treatment regimen

RESULTS

- 2,515 patients were identified who initiated 1L therapy for FL and met all selection criteria (Figure 1)

Figure 1. Patient Identification Flowchart



Patients receiving rituximab and ibrutinomab tixetan were excluded.
FL, follicular lymphoma; ID, identification.

RESULTS (cont.)

- Overall mean age (standard deviation [SD]) was 74.1 (8.2) years, 87.2% were white, and 53.8% were female (Table 1)
- All disease stages were represented: Ann Arbor stage III (28.4%), IV (26.8%), I (20.8%), II (17.1%), and unknown (6.8%; Table 1)
- Overall mean (SD) number of chronic conditions was 6.9 (2.1; Table 1)
- Two-thirds of patients (66.4%) completed 1L therapy and entered remission during follow-up (Table 2)

Table 1. Demographic and Clinical Characteristics						
Characteristic	Index Treatment Regimen				All (N = 2,515)	P Value
	R-mono (n = 1,124)	R-CHOP-like (n = 888)	R-CVP (n = 229)	BR (n = 274)		
Age at index, mean (SD), years	75.6 (8.8)	72.6 (7.5)	73.9 (7.7)	73.1 (6.8)	74.1 (8.2)	< 0.001
Female, n (%)	641 (57.0)	443 (49.9)	121 (52.8)	149 (54.4)	1,354 (53.8)	0.016
Race/ethnicity, n (%)						
White	989 (88.0)	778 (87.6)	192 (83.8)	235 (85.8)	2,194 (87.2)	0.227
Black	33 (2.9)	37 (4.2)	— ^a	— ^a	86 (3.4)	
Hispanic	67 (6.0)	53 (6.0)	17 (7.4)	18 (6.6)	155 (6.2)	
Other	35 (3.1)	20 (2.3)	11 (4.8)	14 (5.1)	80 (3.2)	
US region, n (%)						
Midwest	117 (10.4)	115 (13.0)	27 (11.8)	36 (13.1)	295 (11.7)	< 0.001
Northeast	230 (20.5)	191 (21.5)	32 (14.0)	50 (18.2)	503 (20.0)	
South	297 (26.4)	268 (30.2)	72 (31.4)	55 (20.1)	692 (27.5)	
West	480 (42.7)	314 (35.4)	98 (42.8)	133 (48.5)	1,025 (40.8)	
FL histologic grade, n (%)						
Grade I: 0–5 centroblasts/HPF	287 (25.5)	110 (12.4)	44 (19.2)	55 (20.1)	496 (19.7)	< 0.001
Grade II: 6–15 centroblasts/HPF	316 (28.1)	176 (19.8)	74 (32.3)	90 (32.8)	656 (26.1)	
Grade III: > 15 centroblasts/HPF	112 (10.0)	292 (32.9)	33 (14.4)	45 (16.4)	482 (19.2)	
NOS	409 (36.4)	310 (34.9)	78 (34.1)	84 (30.7)	881 (35.0)	
Ann Arbor staging, n (%)						
Stage I	254 (22.6)	181 (20.4)	51 (22.3)	37 (13.5)	523 (20.8)	< 0.001
Stage II	204 (18.1)	144 (16.2)	39 (17.0)	44 (16.1)	431 (17.1)	
Stage III	307 (27.3)	266 (30.0)	61 (26.6)	81 (29.6)	715 (28.4)	
Stage IV	264 (23.5)	247 (27.8)	69 (30.1)	95 (34.7)	675 (26.8)	
Unknown	95 (8.5)	50 (5.6)	— ^a	— ^a	171 (6.8)	
Number of chronic conditions, mean (SD)	6.8 (2.1)	6.9 (2.1)	6.8 (2.1)	6.8 (2.1)	6.9 (2.1)	0.717

^a Reported per SEER-Medicare cell size suppression policy. BR, bendamustine and rituximab; FL, follicular lymphoma; HPF, high-power field; NOS, not otherwise specified; R-CHOP-like, regimens in which patients were not on R-CVP and received rituximab and ≥ 1 agent of cyclophosphamide, doxorubicin, and vincristine; R-CVP, rituximab, cyclophosphamide, vincristine, and prednisone; R-mono, rituximab monotherapy; SD, standard deviation; SEER, Surveillance, Epidemiology, and End Results.

Table 2. 1L and 2L Therapies: Number of Regimens Received and Relapse Status					
	Index Treatment Regimen				All (N = 2,515)
	R-mono (n = 1,124)	R-CHOP-like (n = 888)	R-CVP (n = 229)	BR (n = 274)	
1L therapy					
Patients who completed 1L therapy (reached a full course of treatment and entered remission), n (%)	613 (54.5)	674 (75.9)	168 (73.4)	214 (78.1)	1,669 (66.4)
Patients with relapse after completing 1L therapy, n (%)	187 (30.5)	164 (24.3)	47 (28.0)	42 (19.6)	440 (26.4)
2L therapy					
Treatment regimens received during 2L therapy until reaching a full course of treatment or end of follow-up, n (%)					
1	158 (84.5)	134 (81.7)	40 (85.1)	32 (76.2)	364 (82.7)
2	18 (9.6)	23 (14.0)	— ^a	— ^a	54 (12.3)
3	— ^a	— ^a	— ^a	— ^a	12 (2.7)
≥ 4	— ^a	— ^a	— ^a	— ^a	— ^a
Patients who completed 2L therapy (reached a full course of treatment and entered remission), n (%)	95 (50.8)	71 (43.3)	28 (59.6)	12 (28.6)	206 (46.8)
Patients with relapse after completing 2L therapy, n (%)	29 (30.5)	20 (28.2)	— ^a	— ^a	57 (27.7)

^a Reported per SEER-Medicare cell size suppression policy.
1L, first-line; 2L, second-line; BR, bendamustine and rituximab; R-CHOP-like, regimens in which patients were not on R-CVP and received rituximab and ≥ 1 agent of cyclophosphamide, doxorubicin, and vincristine; R-CVP, rituximab, cyclophosphamide, vincristine, and prednisone; R-mono, rituximab monotherapy; SEER, Surveillance, Epidemiology, and End Results.

^a Reported per SEER-Medicare cell size suppression policy. 1L, first-line; 2L, second-line; BR, bendamustine and rituximab; R-CHOP-like, regimens in which patients were not on R-CVP and received rituximab and ≥ 1 agent of cyclophosphamide, doxorubicin, and vincristine; R-CVP, rituximab, cyclophosphamide, vincristine, and prednisone; R-mono, rituximab monotherapy; SEER, Surveillance, Epidemiology, and End Results.

Table 3. Treatment Regimens Received During 1L and 2L Therapy			
1L Therapy (n = 2,515)	Frequency, n (%)	2L Therapy (n = 440)	Frequency, n (%)
R-mono	782 (31.09)	R-mono	232 (52.73)
R-CHOP-like	445 (17.69)	BR	70 (15.91)
R-CHOP-like/r	299 (11.89)	BR/r	21 (4.77)
BR/r	132 (5.25)	R-CHOP-like	20 (4.55)
BR	105 (4.17)	R-mono & BR	12 (2.73)
R-CVP/r	79 (3.14)	Others	85 ^a (19.32)
R-mono & R-mono	69 (2.74)		
R-CVP	69 (2.74)		
R-mono & R-CHOP-like	56 (2.23)		
R-mono & R-CHOP-like/r	42 (1.67)		
R-mono & BR	31 (1.23)		
R-mono & BR/r	25 (0.99)		
R-CHOP-like & R-CVP/r	24 (0.95)		
R-mono & R-CVP	15 (0.60)		
R-CHOP-like & R-CVP	15 (0.60)		
R-CVP & R-CHOP-like	14 (0.56)		
R-mono & R-CVP/r	12 (0.48)		
R-CHOP-like/r & R-CHOP-like/r	12 (0.48)		
Others	289 ^a (11.49)		

^a Treatment patterns with frequencies of < 11; reported per SEER-Medicare cell size suppression policy. 1L, first-line; 2L, second-line; BR, bendamustine and rituximab; r, rituximab maintenance therapy given within 180 days after the primary regimen; R-CHOP-like, regimens in which patients were not on R-CVP and received rituximab and ≥ 1 agent of cyclophosphamide, doxorubicin, and vincristine; R-CVP, rituximab, cyclophosphamide, vincristine, and prednisone; R-mono, rituximab monotherapy; SEER, Surveillance, Epidemiology, and End Results.

RESULTS (cont.)

- Among the 1,669 patients who completed 1L therapy, 26.4% (n = 440) experienced a relapse and began 2L therapy (Table 2)
- R-mono, R-CHOP-like, R-CVP, and BR were most commonly initiated as 2L therapy (97.2%; result not shown)
- Many patients moved on to receive a second (12.3%) or third or more (5.0%) regimen as 2L therapy until completing a full course of therapy or reaching study end (Table 2)
- Considerable heterogeneity was observed in 2L regimens (Table 3)
 - In addition, treatment failure was somewhat common; among the 206 patients who completed 2L therapy and entered remission, 27.7% (n = 57) experienced relapse and began third-line therapy (Table 2)

CONCLUSIONS

- Many patients with FL who receive 1L therapy experience relapse and move on to subsequent lines of therapy
- Regimens received as 1L and as 2L therapy are heterogeneous
- More than a quarter of 2L regimens completed result in failure, suggesting an unmet need for alternative treatment options to treat patients with relapsed FL

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