Poster # RWD17

Real-World Treatment Patterns and Overall Survival Among Follicular Lymphoma Patients: A SEER-Medicare Analysis

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OBJECTIVE

To describe clinical characteristics, real-world treatment patterns, and overall survival (OS) in patients with follicular lymphoma (FL)

CONCLUSIONS

Utilization of novel therapy is uncommon among older patients with FL and the most common treatment regimens are anti-CD20 mAb therapy with or without chemotherapy

As patients with FL progress through multiple lines of therapy (LOTs), their survival outcomes decline

Poor prognostic factors for overall survival include older age, late-stage cancer, and disease refractoriness to both anti-CD20 mAb and alkylating therapies

These findings underscore the heterogeneity of FL and highlight the need for novel effective therapies

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Disclosures

Yang, Chawla, Zhang, Rivas, Blaedel, Mutebi: Genmab: Current Employment. **Wang, Yu, Arnette:** AbbVie: Current Employment.

References

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BACKGROUND

- FL is the most common subtype of indolent non-Hodgkin lymphoma (NHL) and accounts for about 22% of all newly diagnosed cases of NHL[1]
- FL is an incurable disease in most cases, and patients usually experience multiple relapses and require multiple LOTs[1,2]
- Treatment options for FL during the study period include chemoimmunotherapy, radiation/radioimmunotherapy, stem cell transplantation, and novel therapies such as PI3K inhibitors, and chimeric antigen receptor T-cell therapy (CAR T)[1]
- Epcoritamab is a subcutaneously administered CD3xCD20 T-cell–engaging bispecific antibody that activates T cells to kill malignant CD20+ B cells and has shown promising efficacy and safety in ongoing trials among patients with relapsed/refractory FL[3]

STUDY DESIGN

- Patients aged ≥65 years with FL as primary cancer (ICD-O-3: 9695/3, 9691/3, 9698/3, 9690/3) between January 1, 2000, and December 31, 2017, were identified from SEER-Medicare
- A new LOT was defined as the initiation of a new antilymphoma regimen or the next antilymphoma regimen (including retreatment with an anti-CD20 mAb) after 180 days from completion of previous treatment
- A sensitivity analysis were conducted that excluded ICD-O-3 code 9690/3 ("*Follicular lymphoma, NOS*" histology) when identifying patients with FL and used a ≤365-day no-treatment gap to define maintenance therapy with an anti-CD20 mAb
- Being refractory to anti-CD20 mAb (or alkylating) therapy was defined as the initiation of a new LOT within 6 months of completing a prior regimen containing anti-CD20 mAb (or alkylating) therapy, and double refractoriness was defined as being refractory to both anti-CD20 mAb and alkylating therapies
- Cox proportional-hazards modeling was conducted to quantify the magnitude of association between prognostic factors and overall survival (OS); double refractoriness was modeled as a time-varying variable

RESULTS

- Overall, 14,077 incident patients with FL were identified (**Table 1**)
  - Median age at diagnosis was 76 years; most were White (94.2%), female (55.2%), had National Cancer Institute Comorbidity Index score >0 (65.4%), and were diagnosed with FL before 2010 (58.7%)
  - Excluding missing data, 74.7% had FL grade 1/2, and 52.4% had Ann Arbor stage III/IV

Table 1. Patient demographic and clinical characteristics at diagnosis

Characteristics, %		Overall N=14,077	LOT 1+ n=8967	LOT 2+ n=3295	LOT 3+ n=1301
Age, y	66–70	23.3	25.8	26.8	28.6
	71–75	24.8	27.1	29.2	31.4
	76–80	22.7	22.9	23.0	21.8
	>80	29.2	24.2	21.0	18.1
Sex	Male	44.8	45.0	45.5	46.9
	Female	55.2	55.0	54.5	53.1
Race	White	94.2	94.5	94.9	95.2
	Black	2.6	2.3	2.2	1.8
	Other[a]	3.2	3.2	3.0	2.9
FL diagnosis year	2000–2004	29.0	30.9	39.8	47.7
	2005–2009	29.7	30.9	33.1	35.3
	2010–2014	25.5	24.3	20.2	14.1
	2015–2017	15.9	13.9	6.9	2.9
FL grade[b]	I or II	48.9	49.1	52.7	54.1
	III	16.6	18.4	15.2	14.8
	Unspecified	34.5	32.6	32.1	31.1
Ann Arbor stage	I	17.9	14.6	13.7	13.1
	II	10.1	11.3	11.3	9.7
	III	14.7	17.3	18.8	20.1
	IV	16.1	19.0	21.9	23.3
	Not applicable/ Unknown	41.2	37.8	34.4	33.8
NCI Comorbidity Index[c]	0	34.6	36.8	39.7	42.1
	0–1	45.0	45.8	45.4	44.6
	1+	20.4	17.4	14.9	13.3

[a]American Indian/Alaska Native, Asian or Pacific Islander, and Unknown. [b]The data source could not distinguish between FL 3a vs 3b. [c]The index includes 16 comorbid conditions, with values weighted according to risk of death. The scale ranges from 0 to 9.
FL, follicular lymphoma; LOT, line of therapy; NCI, National Cancer Institute; y, year.

- Across different LOTs, the most used regimens were rituximab or obinutuzumab (R/O) + chemotherapy followed by R/O monotherapy (**Table 2**)
- As patients progressed to later LOTs, median OS declined (1L 81.9 mo; 2L 49.6 mo; 3L 35.1 mo; 4L 27.1 mo; 5L 22.6 mo) (**Figure 1**)
  - Sensitivity analysis excluding ICD-O-3 code 9690/3 and with ≤365-day gap to define R/O maintenance therapy showed similar results (**Figure 2**)

Table 2. Treatment regimens by LOTs

Regimens, %	LOT 1+ n=8967	LOT 2+ n=3295	LOT 3+ n=1301
R/O + Chemotherapy	**60.0**	**44.6**	**41.9**
R/O + CHOP	22.5	9.3	4.9
R/O + CVP	15.5	10.3	8.8
R/O + bendamustine	14.6	13.1	14.9
R/O + cyclophosphamide	2.3	1.9	2.1
R/O + lenalidomide	0.1	0.5	0.7
R/O + other	5.1	9.3	10.5
R/O Monotherapy	**31.3**	**40.2**	**38.0**
Chemotherapy	**8.5**	**12.3**	**14.1**
CVP	2.5	1.7	1.3
CHOP	2.3	1.2	0.9
Bendamustine	0.1	0.7	1.6
Other	3.6	8.6	10.3
Other Regimens	**0.3**	**2.9**	**6.0**
Ibritumomab + R/O	0.2	2.0	4.1
HSCT[a]	0.1	0.5	0.2
Novel therapy[b]	0.0	0.4	1.7

[a]Including autoSCT and alloSCT. [b]Including CAR T and PI3K inhibitors.
AlloSCT, allogeneic hematopoietic stem cell transplantation; autoSCT, autologous stem cell transplantation; CAR T, chimeric antigen receptor T-cell therapy; CHOP, cyclophosphamide, doxorubicin, vincristine, prednisone; CVP, cyclophosphamide, vincristine sulfate, prednisone; HSCT, hematopoietic stem cell transplantation; LOT, line of therapy; PI3K, phosphatidylinositol 3-kinase; R/O, rituximab or obinutuzumab.

Figure 1. OS by LOTs

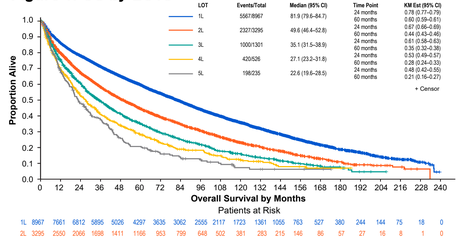
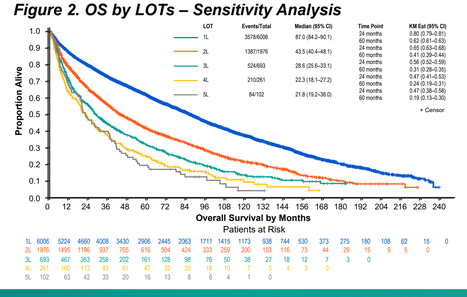


Figure 2. OS by LOTs – Sensitivity Analysis



- **Double-refractory disease was associated with worse OS**
  - The Cox model that adjusted for covariates showed that patients experiencing double-refractory disease had a 151% higher mortality rate compared with those not experiencing double refractoriness (adjusted HR [95% CI]: 2.51 [2.29–2.74]) (**Table 3**)
- **Older age at diagnosis was associated with worsening OS**
  - Median OS from initial diagnosis by age groups: 65–70, 145 mo; 71–75, 110 mo; 76–80, 80 mo; 81+, 40 mo (**Figure 3**)
  - Compared with patients aged 65–70, patients aged 71–75, 76–80, and 81+ were associated with an increased mortality rate by 35%, 95%, and 248%, respectively (**Table 3**)
- **OS worsened with more advanced cancer stage**
  - Median OS from initial diagnosis by Ann Arbor Stage: stage I/II, 89.1 mo; stage III, 78.6 mo; stage IV, 72.1 mo (**Figure 4**)
  - Compared with patients with stage I/II at diagnosis, patients with stage III and stage IV were associated with an increased mortality rate by 26% and 46% (**Table 3**)

Figure 3. OS by Age Groups at Diagnosis

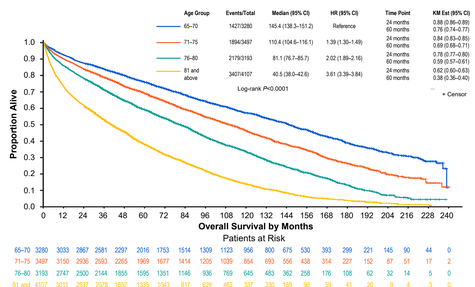


Figure 4. OS by Ann Arbor Stage at Diagnosis

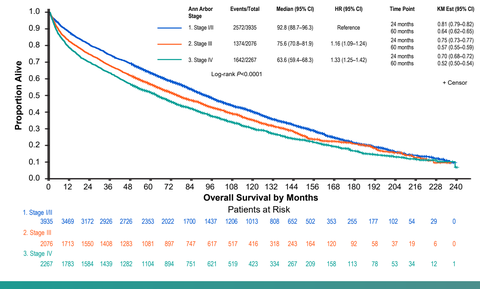


Table 3. Prognostic factors for overall survival in FL patients[a]

Prognostic factors		Adjusted HR (95% CI)
Age group at diagnosis	65–70	Reference
	71–75	1.35 (1.26–1.44)
	76–80	1.94 (1.82–2.08)
	≥81	3.48 (3.27–3.71)
Sex	Male	Reference
	Female	0.79 (0.76–0.83)
Diagnosis year	2000–2004	Reference
	2005–2009	0.84 (0.80–0.88)
	2010–2014	0.72 (0.68–0.76)
	2015–2017	0.64 (0.58–0.70)
FL disease grade at diagnosis	I/II	Reference
	III	1.16 (1.09–1.23)
	Unspecified	1.20 (1.15–1.26)
Ann Arbor stage at diagnosis	Stage I/II	Reference
	Stage III	1.26 (1.18–1.34)
	Stage IV	1.46 (1.37–1.56)
	Unknown	1.13 (1.07–1.21)
NCI Comorbidity Index Score at diagnosis	0	Reference
	0–1	1.29 (1.23–1.36)
	1+	2.16 (2.04–2.29)
Double-refractory disease[b]	No	Reference
	Yes	2.51 (2.29–2.74)

FL, follicular lymphoma; HR, hazard ratio; CI, confidence interval; NCI, National Cancer Institute; OS, overall survival.
[a]Association between factors at diagnosis and OS was modelled among all incident FL patients (N= 14,077), and association between double-refractoriness and OS was modelled among patients who started 1L (N= 8967). [b]Double refractoriness was defined as being refractory to both anti-CD20 mAb and alkylating therapies.

Limitations

- Results from our analyses of Medicare patients may not be generalizable to the younger FL population