

Global Clinical, Economic, and Health-Related Quality of Life Burden and Treatment Outcomes in Follicular Lymphoma: A Systematic Review

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BACKGROUND

- Follicular lymphoma (FL) is the most common indolent non-Hodgkin lymphoma (NHL), accounting for nearly 25% of all NHL cases.¹ FL is heterogenous, with an estimated 20% of patients presenting with aggressive disease, which often becomes relapsed or refractory to current treatments¹

OBJECTIVE

- The objective of this study was to conduct a systematic literature review to understand the reported disease burden of FL and treatment outcomes in relapsed/refractory (R/R) FL

METHODS

- A systematic literature review was conducted to identify studies reporting the disease burden of FL and/or treatment outcomes associated with interventions in patients with R/R FL
 - Disease burden outcomes included incidence, prevalence, 5-year survival rate, 10-year survival rate, economic burden (direct and indirect costs), and health-related quality of life (HRQOL)
 - Treatment outcomes included response (overall response rate [ORR], complete response, partial response, stable disease, progressive disease, and disease control rate), overall survival (OS), progression-free survival (PFS), safety, adherence, costs, healthcare resource utilization (HCRU), and HRQOL
- Only full-text studies were considered in the disease burden screening, except in the evaluation of HRQOL, which included abstracts
- The treatment outcomes search included full text and abstracts of phase 2 or 3 clinical trials and real-world studies
- The search was executed on October 10, 2022, and included PubMed and Embase records from 2017 through the date of the search

RESULTS

- Of the 2768 screened studies, a total of 130 publications²⁻¹³¹ were included (47 disease burden²⁻⁴⁸; 83 treatment outcomes⁴⁹⁻¹³¹)

Disease Burden

- Of the 47 studies²⁻⁴⁸ included in the FL-burden section, 13 studies reported on the incidence and prevalence,²⁻¹⁴ 26 studies reported the 5- or 10-year OS,¹⁴⁻³⁹ 7 studies reported the economic burden,⁴⁰⁻⁴⁶ and 2 studies reported the humanistic burden^{47,48}

Incidence and Prevalence

- Among the 13 incidence and prevalence studies,²⁻¹⁴ 7 reported age-standardized incidence rates (ASIRs)^{2,4-9} and 2 reported crude rates^{3,14} (**Table 1**)

Table 1. Reported Incidence of FL

Study	Country	Data source	Measure	Time period*	Incidence per 100,000		
					Male	Female	All
Radkiewicz et al. 2022	Sweden	Swedish Lymphoma Register	ASIR	2000-2019	3.67	3.39	–
Aladily et al. 2020	Jordan	All academic, public, military, and private medical centers providing diagnosis of lymphoma	ASIR	2014-2019	–	–	0.43
Dinnessen et al. 2020	Netherlands	Netherlands Cancer Registry	ASIR	2009-2016	–	–	2.75
Szamera Ciekiewicz et al. 2020	Poland	Polish National Cancer Registry	ASIR	2000-2014	–	–	0.87
Le et al. 2019	Canada	Canadian Cancer Registry, Registre québécois du cancer, and Canadian Vital Statistics database	ASIR	1992-2010	–	–	3.83
Wu et al. 2019	Taiwan	National Taiwan Cancer Registry	ASIR	2008-2012	0.91	0.81	–
Ye et al. 2017	Canada	Manitoba Cancer Registry	ASIR	2010-2013	6.2	6	–
Weehuizen et al. 2022	Netherlands	RIVM Register	Crude	2002-2017	–	–	2.8
Lech-Marañida et al. 2022	Poland	National Health Fund and Social Insurance Central Registry	Crude	2014	–	–	1.74

ASIR, age-standardized incidence rate; FL, follicular lymphoma; RIVM, National Institute for Public Health and the Environment.
* Most recent time period reported here.

- As shown, the incidence of FL varied by country, with lower ASIRs reported in Jordan, Poland, and Taiwan and higher ASIRs in Canada, the Netherlands, and Sweden, consistent with the published literature
- Three studies^{5,8,9} reported ASIRs over different time periods. In general, the ASIRs increased over time

Survival

- Across all studies with reported data, 5- and 10-year survival rates averaged 81.7% (n=21)^{14-18,21-23,26-29,31-35,37-39} and 75.8% (n=9),^{18-21,26,27,30,36} respectively
- Five-year survival rates were notably higher in the studies of newly diagnosed and treatment-naïve patients compared to the one study of R/R FL patients (**Table 2**)

Table 2. Reported 5-Year Survival in Newly Diagnosed or Treatment-Naïve, R/R FL, and Mixed Populations

Study	Country	Time period	5-Year survival
Newly diagnosed or treatment naïve			
Tobin et al. 2019	Australia, Canada	2005-2017	94%
Ge et al. 2022	China	1/2016-3/2022	92%
Gao et al. 2022	China	3/2002-8/2020	89%
Madsen et al. 2020	Denmark	2000-2015	82%
Masaki et al. 2020	Japan	N/R	79%
Kim et al. 2020	South Korea	2006-2015	79%
Lech-Marañida et al. 2022	Poland	2009-2015	69%
Mozas et al. 2021	Spain	2000-2018	85%
Cheng et al. 2022	Taiwan	2006-2016	86%
Pei et al. 2021	Taiwan	2008-2013	76%
R/R FL			
Selberg et al. 2021	Germany	2004-2018	44%
Mixed population			
Matsuo et al. 2022	Japan	5/2009-7/2019	88%

FL, follicular lymphoma; N/R, not reported; R/R, relapsed/refractory.

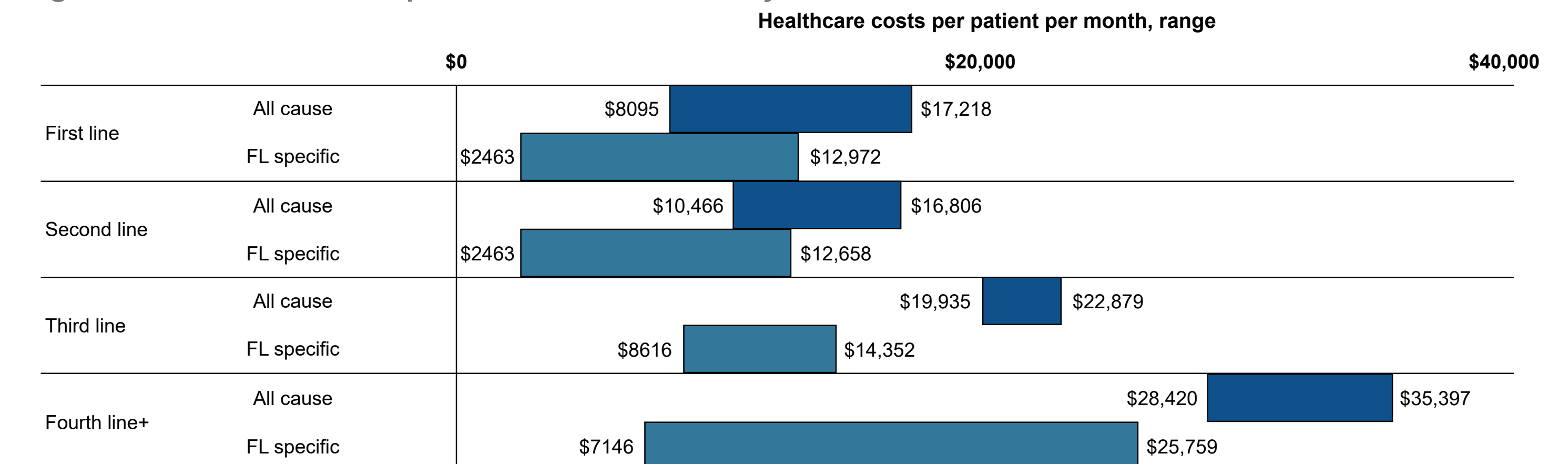
Economic Burden

- Seven studies reported costs associated with patients with FL.⁴⁰⁻⁴⁶ Five of the studies included data from the US,^{40,43-46} and 1 study each included data from France⁴² and Japan⁴¹
- Costs per patient per month (PPPM) generally increased as the line of therapy increased (**Figure 1**). This trend includes both all-cause and FL-specific costs^{40,46}

CONCLUSIONS

- The incidence of FL has been increasing over time, with patients demonstrating prolonged survival requiring several therapies
- The economic/HRQOL burden increases as patients progress through lines of treatment (LOT)
- Evaluations of the effect of interventions on economic/HRQOL outcomes could help comprehensively assess their value to health systems

Figure 1. All-Cause and FL-Specific Healthcare Costs by Treatment Line



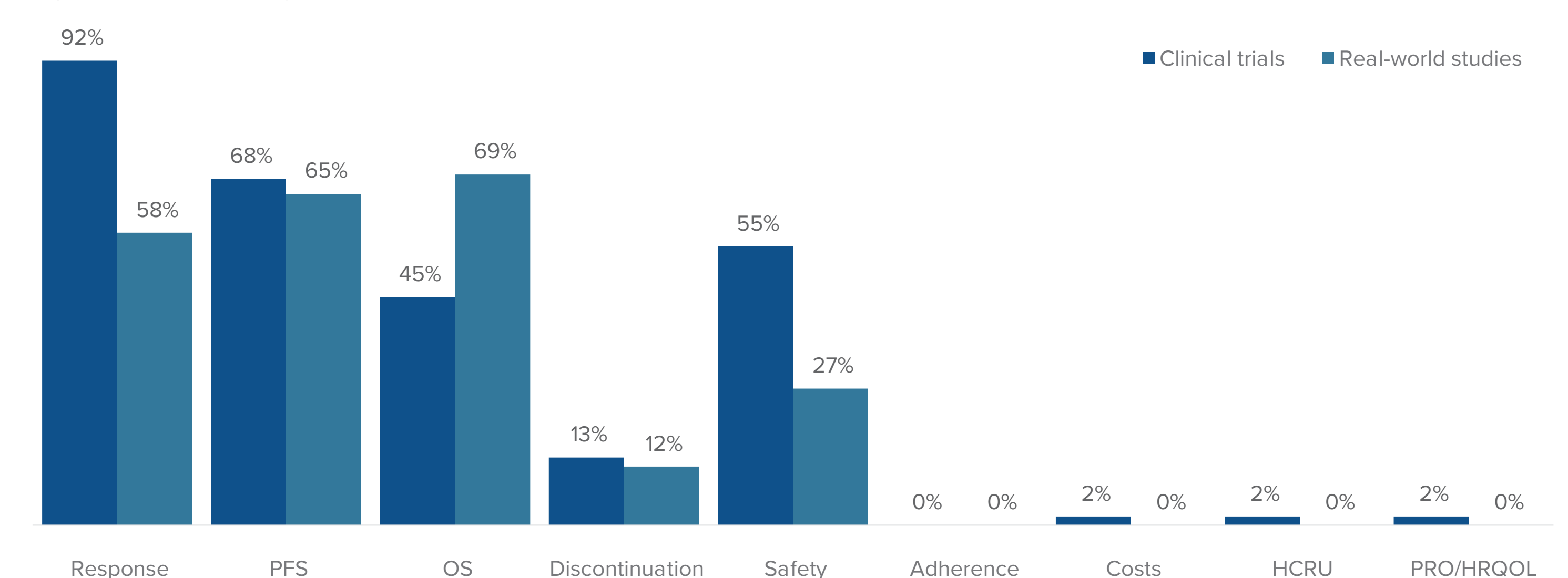
Humanistic Burden

- Studies reporting HRQOL (n=2) showed that physical, role, and social functioning declined as LOT increased, and EQ-5D-5L scores were lower in patients receiving active treatment vs those in remission^{47,48}

Treatment Outcomes

- Among the 83 treatment-outcomes studies,⁴⁹⁻¹³¹ there were 60 clinical trial publications⁴⁹⁻¹⁰⁸ and 26 real-world publications.¹⁰⁶⁻¹³¹ Three publications of clinical trials also included real-world treatment arms¹⁰⁶⁻¹⁰⁸
- The frequency of outcomes measured in the clinical trial and real-world publications is shown in **Figure 2**

Figure 2. Frequency of Outcomes Measured in Publications



* No life table data were available for the UK for 2021.

- Response rates were reported more often in clinical trial publications than real-world studies
- Real-world and trial publications reported PFS at similar rates, but OS was more often reported in real-world publications
- Adherence, costs, HCRU, and HRQOL were not reported in any real-world publications and were reported infrequently in trial publications

Clinical Trial Outcomes

- The 60 clinical trial publications⁴⁹⁻¹³¹ included 39 unique clinical trials
- PI3K ± anti-CD20 was the most common treatment regimen studied (11 unique trials), followed by dual or monotherapy anti-CD20 (5 unique trials), chemoimmunotherapy alone (5 unique trials), and Bruton tyrosine kinase inhibitor ± anti-CD20, chimeric antigen receptor (CAR)-T, and radioimmunotherapy ± chemotherapy/chemoimmunotherapy (3 unique trials each)
- Across all publications, the reported ORR ranged from 11% to 97% and median PFS ranged from 2.2 months to 39.4 months. These wide ranges are primarily due to the large heterogeneity between the patient populations in each of the studies
- Costs/HCRU⁵⁵ and HRQOL⁸⁷ were measured in 1 study each
 - The cost/HCRU study showed higher costs for patients receiving inpatient administration for CAR-T compared to outpatient⁵⁵
 - The PFS benefit was associated with an improvement in HRQOL between the study arms⁸⁷

Real-World Outcomes

- The 26 real-world studies¹⁰⁶⁻¹³¹ included 10 unique classes of treatment regimens. The most frequently used regimens were chemoimmunotherapy (n=8),^{109,117,122,125,126-129} PI3Ks (n=4),^{113,114,119,124} and stem cell transplant (n=4)^{110,112,115,118}
- For chemoimmunotherapy regimens, the ORR ranged from 77.8% to 100% (patients with late relapse) and median PFS from 6.4 months (early relapse) to 6.4 years^{117,125-127,129}
- For PI3Ks, the ORR ranged from 41.7% to 83% and median PFS from 8.4 to 11.5 months¹¹⁴⁻¹²⁴

REFERENCES

Reference list is available through the Quick Response (QR) code

DISCLOSURES

BS: Consulting: Adaptive Biotechnologies, BMS, Novartis, Pfizer, Amgen, Precision Biosciences, Kite, Jazz, Century Therapeutics, Deciphera, Autolus, Lily, Pepromene; Research funding: Incyte, Jazz, Kite, Servier; Travel, accommodations, and expenses: Celgene, Novartis, Pfizer, Janssen, Seagen, AstraZeneca, Stemline Therapeutics, Kite; Honoraria: Pharmacyclics/Janssen, Spectrum/Acrotech, BeiGene, Gilead Sciences. MX: Employment: BeiGene. WF: Employment: Real Chemistry; Stock or other ownership: Real Chemistry. EKS: Employment: BeiGene; Stock or other ownership: BeiGene, Roche. JK, P-YC, MD: Employment: Real Chemistry. KY: Employment: BeiGene; Leadership: BeiGene; Stock or other ownership: BeiGene; Research funding: BeiGene; Travel, accommodations, and expenses: BeiGene.

ACKNOWLEDGMENTS

This study was sponsored by BeiGene, Ltd. Editorial assistance was provided by Nucleus Global, an Inizio Company, and supported by BeiGene.



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