Targeted Literature Review of Cost-Effectiveness Models in Relapsed/Refractory Follicular Lymphoma

Poster EE290

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INTRODUCTION

- Follicular lymphoma (FL) is a type of non-Hodgkin lymphoma (NHL; roughly 20-30% of NHL cases) that is slow-growing and affects the lymphoid tissue (begins in B lymphocytes)[1]
- Approximately 20% of patients with FL experience disease relapse within 2 years of treatment. As the disease progresses, it tends to become increasingly refractory with each successive line of therapy[2]
- A significant economic and health burden is related to high rates of relapsed/refractory (R/R) disease,[3] and thus it is important to understand the current literature and health technology assessment (HTA) reports on the cost-effectiveness of treatments for patients with R/R FL
- The objective of this study was to identify cost-effectiveness models (CEMs) in R/R FL, including published studies and recent HTA reports

METHODS

Data Sources

- Bibliographic databases (PubMed and Embase) were searched to retrieve literature published between Jan 1, 2018, and Sep 1, 2023
  - An initial search was carried out from 2018 to 2022, which was then updated to include studies up to Sep 1, 2023
- Prominent HTA databases (Canadian Agency for Drugs and Technologies in Health [CADTH], National Institute for Health and Care Excellence [NICE], Scottish Medicines Consortium [SMC], and Pharmaceutical Benefits Advisory Committee [PBAC]) were searched to retrieve relevant submissions for the same time frame
  - A restriction of 2016 to 2023 was applied to CADTH and SMC to include models of obinutuzumab in R/R FL for completeness, as it is a key treatment for R/R FL

Inclusion Criteria

- Adults diagnosed with R/R FL
- Cost-effectiveness studies on treatments for R/R FL

Search Terms

- Searches were conducted using the keywords *cost effectiveness*, *cost-utility*, *follicular lymphoma*, *relapse*, *refractory*, and *non-Hodgkin lymphoma*

Study Measures

- Data on the indication, intervention(s), comparator(s), key model features (model structure, time horizon, cycle length, and health states), cost-effectiveness results (ie, incremental cost-effectiveness ratio per life-years/quality-adjusted life-years gained), and model limitations (in published journal articles) or HTA agency critiques and company responses (in CADTH, NICE, PBAC, and SMC reports) were extracted (**Table 1**; **Table 2**)

RESULTS

- Seventeen studies (5 globally published studies [**Table 2**], 4 NICE technology appraisals, 4 CADTH reports, 3 SMC reports, and 1 PBAC report) were included in the review (total of 18 CEMs, as one of the NICE TA604 reports included 2 CEMs)
- CEMs were classified as either partitioned survival models (n=12 [67%]) or Markov models (n=6 [33%]) (**Figure 1**) and employed a lifetime time horizon ranging from 20 to 50 years
- Reported cycle lengths (n=14) were 1 week (n=5 [36%]), 28 days (n=5 [36%]), 1 month (n=3 [21%]), and 3 months (n=1 [7%])
- Commonly used health states were progression free, progressive disease, and death (n=13 [76%])
- Of the 12 HTA agency reports, 6 (50%) did not recommend the treatment evaluated, and 6 (50%) recommended the evaluated treatments (with or without conditions)

Table 1. Summary of HTA Reports in R/R FL

HTA Report (year)	Indication	HTA Decision	Intervention	Comparator	ICER
England					
NICE—TA604 (2019)[4]	FL refractory to 2 prior lines of therapy	Not recommended	Idelalisib	Chemotherapy: cyclophosphamide- or fludarabine-containing regimen, bendamustine, chlorambucil	**Company submitted:** £26,076 **ERG corrected:** £32,882
				Best supportive care	**Company submitted:** £25,272 **ERG corrected:** £29,639
NICE—TA629 (2020)[5]	Adults with FL that is refractory to induction with rituximab in combination with chemotherapy or who experienced relapse early during rituximab maintenance	Recommended, under commercial agreement	Obinutuzumab + bendamustine, followed by obinutuzumab monotherapy	Bendamustine	**Company submitted:** £17,408 **ERG corrected:** £15,054
NICE—TA894 (2023)[6]	Received ≥3 prior lines of therapy	Not recommended	Axicabtagene ciloleucel	Rituximab monotherapy and best supportive care	**Company submitted:** £48,272 **ERG corrected:** NA
NICE—TA892 (2023)[7]	Adult patients with R/R FL who had received ≥2 prior systemic therapies	Not recommended	Mosunetuzumab	Rituximab + lenalidomide	**Company submitted:** £16,103
				Rituximab + bendamustine	**Company submitted:** £51,148
				Obinutuzumab + bendamustine	**Company submitted:** £10,397
Canada					
CADTH—PC0075 (2016)[8]	Received ≥2 prior systemic therapies and are refractory to both rituximab and an alkylating agent	Not recommended	Idelalisib	Best supportive care	**Sponsor's results:** CA$130,435 **EGP reanalysis:** CA$231,012
CADTH—PC0091 (2016)[9]	Refractory to a rituximab-containing regimen	Recommended under conditions	Obinutuzumab + bendamustine, followed by obinutuzumab maintenance	Bendamustine	**Sponsor's results:** CA$62,833 **EGP reanalysis:** CA$84,510
CADTH—PG0306 (2022)[10]	R/R grade 1, 2, or 3a FL after ≥2 lines of systemic therapy	Recommended under conditions	Tisagenlecleucel	Axicabtagene ciloleucel	**Sponsor's results:** Tisagenlecleucel was dominant over axicabtagene **CADTH reanalysis:** excluded axicabtagene ciloleucel as a comparator
				Standard of care	**Sponsor's results:** CA$95,025 **CADTH reanalysis A[a]:** CA$193,516 **CADTH reanalysis B[b]:** CA$434,036
CADTH—PG0314 (2023)[11]	Relapsed or refractory grade 1, 2, or 3a FL after ≥2 lines of systemic therapy	Recommended under conditions	Axicabtagene ciloleucel	Standard of care	**Sponsor's results:** CA$115,543 **CADTH reanalysis A[c]:** CA$544,875 **CADTH reanalysis B[d]:** CA$243,879
Scotland					
SMC—1219 (2017)[12]	Patients who did not respond to or had progression during or up to 6 months after treatment with rituximab or a rituximab-containing regimen	Recommended	Obinutuzumab + bendamustine, followed by obinutuzumab maintenance	Rituximab + chemotherapy	**Company submitted:** £27,988
				Bendamustine	**Company submitted:** £34,245
SMC—2281 (2020)[13]	Adult patients with previously treated FL (grade 1-3a)	Recommended	Lenalidomide + rituximab	Rituximab + CVP	**Company submitted:** £19,694
				Rituximab + CHOP	**Company submitted:** £13,561
				Rituximab + bendamustine	**Company submitted:** £20,826
SMC—2542 (2023)[14]	Patients with R/R FL (grade 1-3a) who had received ≥2 prior systemic therapies	Not recommended	Mosunetuzumab	Rituximab + lenalidomide	**Company submitted:** Mosunetuzumab was dominant over rituximab + lenalidomide
				Rituximab + bendamustine	**Company submitted:** £37,821
Australia					
PBAC (2018)[15]	Patients with previously untreated advanced FL	Not recommended	Obinutuzumab + chemotherapy (CHOP, CVP, or bendamustine), followed by obinutuzumab monotherapy	Rituximab + chemotherapy, followed by rituximab monotherapy	AU$15,000-AU$45,000[e]

CADTH, Canadian Agency for Drugs and Technologies in Health; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; CVP, cyclophosphamide, vincristine, and prednisone; EGP, economic guidance panel; ERG, evidence review group; FL, follicular lymphoma; HTA, health and technology assessment; ICER, incremental cost-effectiveness ratio; NA, not available; NICE, National Institute for Health and Care Excellence; OS, overall survival; PBAC, Pharmaceutical Benefits Advisory Committee; R/R, relapsed/refractory; SMC, Scottish Medicines Consortium.
[a] Tisagenlecleucel's OS modeled using exponential distribution. [b] Tisagenlecleucel's OS modeled using log-normal distribution. [c] Assuming exponential distribution for OS. [d] Assuming log distribution for OS. [e] Since results are highly uncertain due to issues in the economic model, a possible range is provided.

CONCLUSIONS

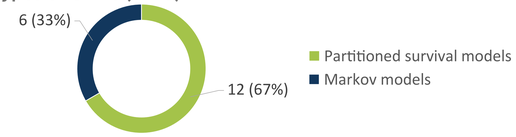
- This review synthesizes the existing CEM literature and highlights the need for robust future economic evaluations in R/R FL
- Key findings underscore the necessity of incorporating robust model validation and relevant comparators to enhance decision-making

Table 2. Summary of Published Studies in R/R FL

County	Study (year) Indication	Intervention and Comparator	ICER/Results and Author-reported WTP
US	Guzauskas et al (2018)[16] Patients with FL who had relapse after or are refractory to a rituximab-containing regimen	**Intervention:** obinutuzumab + bendamustine **Comparator:** bendamustine monotherapy	**Base case:** US$47,016/QALY The ICER falls under the reported WTP threshold (US$100,000/QALY)
Turkey	Erdogan-Ciftci et al (2019)[17] Patients with FL who did not respond to or had progression within 6 months after rituximab or a rituximab-containing regimen	**Intervention:** obinutuzumab + bendamustine **Comparator:** bendamustine monotherapy	**Base case:** • 76,427 TRY/QALY gained • 61,476 TRY/life-year gained The ICER falls under the reported WTP threshold (170,000 TRY)
Netherlands	Thielen et al (2021)[18] Patients with previously treated FL from a societal perspective	**Intervention:** lenalidomide + rituximab **Comparator:** rituximab monotherapy	**Base case:** €40,493/QALY The ICER falls under the reported threshold (€50,000/QALY)
Canada	Vijenthira et al (2021)[19] Transplant-eligible patients with early relapse of FL	**Intervention:** alloSCT and ASCT **Comparator:** obinutuzumab + CHOP	**Life-years/QALY:** ASCT: 10.2 life-years, 7.5 QALYs AlloSCT: 9.9 life-years, 6.6 QALYs Obinutuzumab + CHOP: 10.0 life-years, 7.4 QALYs ASCT was the dominant strategy at a WTP threshold of CA$50,000
US	Potnis et al (2023)[3] Adult patients with R/R FL	**Intervention:** CAR T-cell therapy (axicabtagene ciloleucel) **Comparator:** best supportive care	**Base case:** US$182,127/QALY The ICER does not fall under the reported WTP threshold (US$150,000/QALY)

AlloSCT, allogeneic stem cell transplant; ASCT, autologous stem cell transplant; CAR, chimeric antigen receptor; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; FL, follicular lymphoma; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year; R/R, relapsed/refractory; TRY, Turkish lira; WTP, willingness to pay.

Figure 1. Types of CEMs (N=18)



CEM, cost-effectiveness model

DISCUSSION

- Key HTA recommendations on CEMs included incorporating relevant comparators (n=2), conducting robust model validation (n=4), using utility data from trials and validating them with general population utility and the literature (n=3), appropriately modeling treatment effect duration (n=2), and systematically choosing parametric distributions for long-term extrapolation and presenting various scenarios (n=5)
- Other reported critiques were suggestions regarding the cycle correction and uncertainty regarding the cost calculations

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