EE320

COST-EFFECTIVENESS OF GLOFITAMAB VS CHEMOIMMUNOTHERAPY REGIMENS FOR PATIENTS WITH RELAPSED/REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA (rrDLBCL) AFTER AT LEAST TWO LINES OF SYSTEMIC THERAPY IN THE CZECH REPUBLIC

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OBJECTIVES:

As patients with diffuse large B-cell lymphoma (DLBCL) who have failed two or more prior lines of systemic therapy (3+L) continue to have a poor prognosis, there is a high unmet need for new therapeutic options for such patients. In 2023, glofitamab, a new innovative therapy gained a conditional EMA approval based on results of a single-arm phase I/II study (NCT03075696[1]) for treatment of these patients. Glofitamab is a T-cell engaging bispecific monoclonal antibody, which simultaneously binds to CD20 on the surface of malignant B-cells and CD3 on the surface of T-cells in unique 2:1 format, resulting in direct activation of the T-cell response and lysis of CD20-expressing B-cells. In the Czech Republic, patients with DLBCL can be treated in 3+L by modern therapies such as CAR-Ts or polatuzumab vedotin + bendamustine + rituximab (Pola-BR). However, there is a significant number of patients who are CAR-T ineligible or progressed after CAR-T and also those who are unable to receive bendamustine. For these patients, reduced platinum-based chemotherapy regimens or gemcitabine-based regimens usually combined with rituximab or R-CEOP (rituximab, cyclophosphamide, etoposide, vincristine and prednisone) regimen remain main options. We aimed here to evaluate cost-effectiveness of glofitamab compared to R-CEOP and R-GD (rituximab, gemcitabine, dexamethasone) regimens for patients with rrDLBCL after at least two lines of systemic therapy from payers' perspective in the Czech Republic. This analysis was submitted as a part of a reimbursement application for glofitamab in 3+L DLBCL in the Czech Republic.

METHODS:

A global three-health states partitioned survival pharmacoeconomic model (Figure 1) was used for calculation of incremental costs and QALYs. Progression-free survival (PFS) and overall survival (OS) curves determined the patient proportions in each health state. We used BR regimen as a proxy for clinical efficacy of R-CEOP and R-GD as there was no appropriate efficacy data for these regimens available in 3+L setting for indirect treatment comparison against glofitamab. Therefore, a matching-adjusted indirect comparison (MAIC) vs rituximab and bendamustine regimen (BR) was conducted using data from Hong 2018[2]. Results in Hong 2018 included patients pretreated by at least one line of therapy (LOT) and patients with ECOG performance status > 1, whereas glofitamab trial was designed only for patients pretreated by at least 2 LOTs and with ECOG PS 0-1 (Table 1). As it was impossible to adjust MAIC for these imbalances, an additional adjustment for these factors was performed using hazard ratios (HRs) calculated from RWD[3] (Table 2). A correction factor for number of prior LOTs was calculated as a weighted average of respective HRs and proportions of patients in glofitamab trial (after MAIC weighting) with given number of previous LOTs. These correction factors where then applied as HRs on modelled PFS and OS curves. To model PFS and OS states, standard parametric functions were fitted on PFS and OS Kaplan-Meier curves. Based on AIC, BIC and clinical plausibility, generalized gamma was chosen for both PFS and OS extrapolations (Figure 2). Utilities were based on EORTC-QLQ-C30 data collected in NCT03075696 glofitamab trial. Costs for management of adverse events in the comparative arm were conservatively omitted. Direct medicinal costs were adapted according to the published local costs of 2024.

Table 1. Patient characteristics from glofitamab and BR trials

characteristic	glofitamab[1] (n=154)	BR[2] (n=58)
Median age (years)	66	69
Males (%)	65	57
Ann Arbor Stage I–II (%)	23	26
Ann Arbor Stage III–IV (%)	75	74
ECOG PS 0-1 (%)	100	78
ECOG PS 2-4 (%)	0	22
Primary refractory (%)	58	10
1 prior LOT (%)	0	29
>2 prior LOTs (%)	60	40
Prior SCT (%)	18	22

RESULTS:

Over a time horizon of 37 years with 3% discount rates, treatment with glofitamab generated 2.80 incremental QALYs compared to R-CEOP or R-GD, and incremental costs of 61,266 EUR vs R-CEOP and 61,446 EUR vs R-GD resulting in ICER 21,882 EUR/QALY or 21,946 EUR/QALY, respectively (Table 3). A scenario without RWD[3] correction factors resulted in a total QALY gain in the glofitamab arm of 3.14 QALYs (2.22 in PFS and 0.91 in PD) with incremental QALYs decreased to 2.32. Change in total costs was negligible. This scenario led to an ICER increase of 21%.

Figure 1. Model scheme

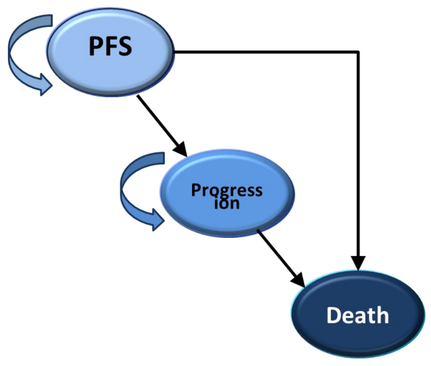


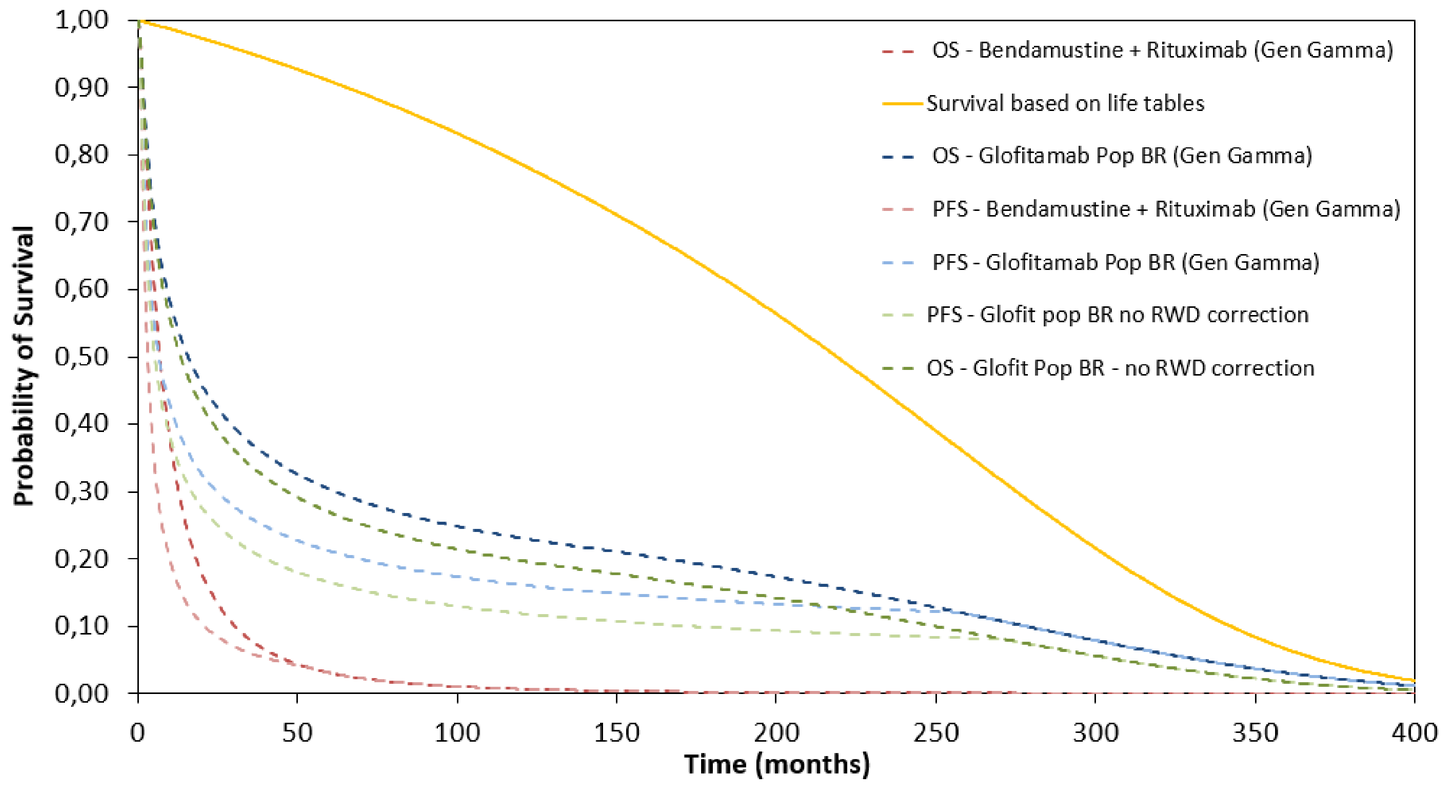
Table 2. Association between number of prior LOTs, ECOG PS and clinical outcomes[3]

	PFS				OS			
	HR	Lower CI	Upper CI	P-value	HR	Lower CI	Upper CI	P-value
No. of prior LOTs, 2 vs 1	1.40	0.94	2.08	0.098	1.45	1.12	1.87	0.005
No.of prior LOTs, 3 vs 1	1.98	1.06	3.67	0.032	1.73	1.19	2.52	0.005
No. of prior LOTs, 4+ vs 1	2.35	1.20	4.60	0.013	1.70	1.14	2.55	0.010
ECOG PS 2 vs 0	1.05	0.68	1.63	0.818	1.17	0.85	1.60	0.344

Table 3. Deterministic results of cost-effectiveness analysis (base-case)

	glofit	R-CEOP	R-GD	glofit vs R-CEOP	glofit vs R-GD
QALYs in PFS	2.83	0.60	0.60	2.23	2.23
QALYs in PD	0.79	0.22	0.22	0.57	0.57
Total QALYs	**3.62**	**0.82**	**0.82**	**2.80**	**2.80**
Treatment cost (EUR)	63,575	3,283	3,366	60,293	60,209
Drug administration cost (EUR)	541	794	531	-253	10
Adverse event cost (EUR)	905	0	0	905	905
Supportive care cost in PFS (EUR)	359	102	102	256	256
Supportive care cost in PD (EUR)	338	92	92	246	246
Terminal care cost (EUR)	1,375	1,555	1,555	-181	-181
Total costs (EUR)	**67,092**	**5,826**	**5,647**	**61,266**	**61,446**
ICER (EUR/QALY)				**21,882**	**21,946**

Figure 2. Modelation of PFS and OS curves with (base-case) or without RWD correction



CONCLUSION:

Czech HTA body accepted efficacy of BR regimen as a proxy for R-CEOP and R-GD regimens. This assumption could by applicable also to some other chemotherapy regimens combined with rituximab. The costs for R-CEOP and R-GD regimens were very similar. Our cost-effectiveness analysis showed a substantial gain in QALYs with acceptable incremental costs. Additional adjustment of PFS and OS using HRs based on RWD[3] helped us to address bias underestimating glofitamab results in a presence of high heterogeneity between two studies which could not be sufficiently reduced by MAIC. This approach had a positive impact on cost-effectiveness.

1. Dickinson et al. 2022; Glofitamab for Relapsed or Refractory Diffuse Large B-Cell Lymphoma. NEJM, 387(24), 2220–2231.
2. Hong et al. 2018; Bendamustine plus rituximab for relapsed or refractory diffuse large B cell lymphoma: a multicenter retrospective analysis. Ann Hematol. , 97(8), 1437-43.
3. Ip et al. 2022; Real-World Outcomes in Patients With Relapsed or Refractory Diffuse Large B-Cell Lymphoma Treated With Standard of Care: A COTA Database Analysis. Presented at the 64th American Society of Hematology Annual Meeting and Exposition. New Orleans