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COST-UTILITY ANALYSES OF GLOFITAMAB FOR THE TREATMENT OF PATIENTS WITH RELAPSED/REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA AFTER TWO OR MORE LINES OF SYSTEMIC THERAPY IN ITALY

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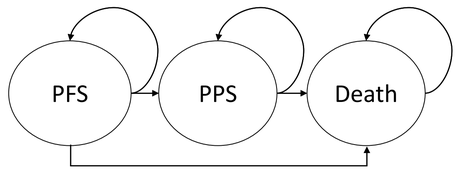
Objective

- Patients with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL) have a extremely poor prognosis, with low response rates to the currently available advanced-line treatments.
- Glofitamab is a humanized anti-CD20/anti-CD3 bispecific monoclonal antibody produced in Chinese hamster ovary cells by recombinant DNA technology. The benefits of glofitamab were evaluated in a study involving adults with DLBCL or a related lymphoma whose cancer had returned or was not responding after at least two other therapies.
- This study aims to assess cost-utility of glofitamab for the treatment, as monotherapy, of adult patients with R/R DLBCL after two or more lines of systemic therapy, from the Italian Health Service perspective.

Methods

- A partitioned survival model of three mutually exclusive health-states – progression-free survival (PFS), post-progression survival (PPS) and death (Figure 1) – was developed to compare lifetime clinical outcomes and costs of patients treated with glofitamab and his main comparators (Table 1).

Figure 1. Model structure



- Clinical inputs were derived from clinical trials (Table 1). Given the lack of head-to-head studies, PFS and OS were modelled independently for glofitamab and comparators using parametric survival curves obtained from inverse probability of treatment weighting (IPTW) (vs. Pola-BR) or matching-adjusted indirect comparisons (MAIC) (vs. the other comparators).
- Data on treatment discontinuation (TD) were derived from clinical trials for glofitamab and Pola-BR (Table 2). In case of missing TD information (Tafa+Len), TD was modelled using the selected parametric distribution for PFS, while, for one-off treatment such as the CAR-T cell therapies, the duration on treatment was assumed to last for a single model cycle.
- Health utility values (for PFS on- and off-treatment and PPS) were obtained by mapping EORTC QLQ-C30 questionnaire scores (NP30179) to EQ-5D-3L values [1], applying Italian tariffs [2].
- Direct healthcare costs, including drug acquisition and administration, disease monitoring, adverse event (AE) management, and post-progression therapy (PPT), were collected from Italian sources (Table 2).
- Costs, updated to 2022 value, and health gains were discounted at an annual 3% rate. A half-cycle correction was applied in the model.
- For cases where a new treatment was lower in cost and less efficacious, the net monetary benefit (NMB) was calculated.
- Probabilistic sensitivity (PSA) and scenario analysis were carried out to evaluate parameter uncertainties.

Table 1 – Glofitamab comparators and clinical input source

Treatment	Population	Source/clinical trials
Glofitamab vs.		NP30179 (NCT03075696)
Polatuzumab vedotin with rituximab and bendamustina (Pola-BR)	Patients non-eligible for chimeric antigen receptor T cell (CAR-T)	GO29365 (NCT02257567)
Tafasitamab plus lenalidomide (Tafa+Len)		L-MIND (NCT02399085)
Tisagenlecleucel (Kym)	Patients eligible for CAR-T	JULIET (NCT02445248)
Axicabtagene ciloleucel (Yesc)		ZUMA-1 (NCT02348216)

Table 2 – Unit costs (€)

Treatment	Drug cost*	AE
Glofitamab	361.00 €/mg	55.83 €/week
Polatuzumab vedotin	79.29 €/mg	179.28 €/week
Rituximab	2.00 €/mg	
Tafasitamab (+len)	3.53 €/mg	27.83 €/week
Tisagenlecleucel	288,800.00 €/unit	1,494.22 €/patient
Axicabtagene ciloleucel	295,117.50 €/unit	4,367.50 €/patient

* Ex-factory prices net of mandatory discount.

Disease monitoring	Weekly cost (€)
PFS on treatment	113.16
PFS off treatment	89.31
PPS	121.63
One-off progression cost	29.94

Administration

The cost of IV administration was estimated in €37.1 based on the corresponding national DRG tariff (DRG 410) reduced by 90% [3]. An additional cost was applied to patients who experienced cytokine release syndrome with glofitamab (17.5% observed rate in NP30179 trial), set at twice the administration cost to cover monitoring resources. CAR-T administration cost (€ 60,428) was computed as a weighted average of the costs of leukapheresis [3], bridging chemotherapy [3,4], and CAR-T cell injection [3], with percentage frequencies retrieved from CAR-T clinical trials.

Disease monitoring and AE management

Annual frequency of health resources consumption and AEs were derived from NICE guidelines [5] or pivotal trials (table 1), respectively. Unit costs were taken from literature [6] or national DRG tariff [3].

Post-progression therapy

PPT shares and treatment duration for glofitamab and comparators were sourced from the NP30179 trial. PPT cost was calculated using mean duration and weekly cost estimates [3], resulting in a cost of €35.050 per week (including anti-CD20 based therapies, SCT, CAR-T).

Results

- Glofitamab generated additional QALYs at a **lower cost** when compared with Pola-BR (0.048; -€6,878), Tafa+Len (0.829; -€386,565) and Kym (0.311; -€294,949), resulting **economically dominant** (Table 2 and Figure 3).
- Instead, when comparing glofitamab with Yesc, the incremental net monetary benefit was estimated in €202,829, proving that glofitamab was a **cost-effective option** at willingness-to-pay threshold of €40,000 per QALY (Table 2).
- Model results were generally robust across scenario (Figure 4) and sensitivity analyses tested (supplementary material). However, there are some areas of uncertainty relating to the limited follow up of glofitamab clinical trial, utility values and residual bias from the ITCs.

Table 2 – Summary results

Comparators	Δ LY	Δ QALY	Δ Cost (€)	ICER/ICUR
Tafa+Len	0.84	0.83	-386,565	Dominant
Pola-BR	0.00	0.05	-6,878	Dominant
Kym	0.31	0.31	-294,949	Dominant
Yesc	-3.30	-2.80	-316,399	Cost-effective at WTP of € 40,000

Figure 3 – Cost breakdown (€). Weighted population for glofitamab.

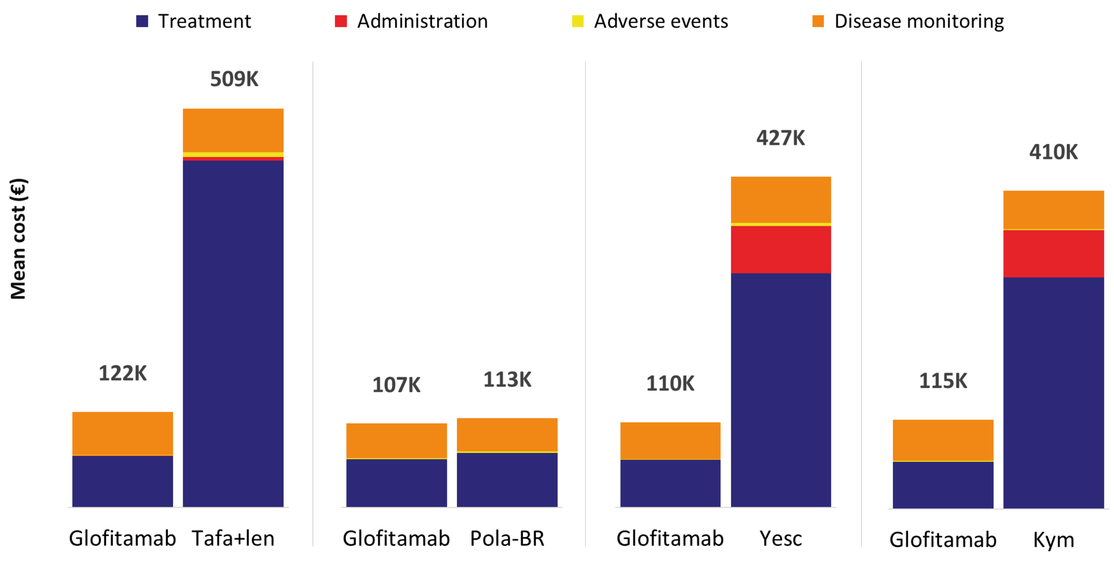
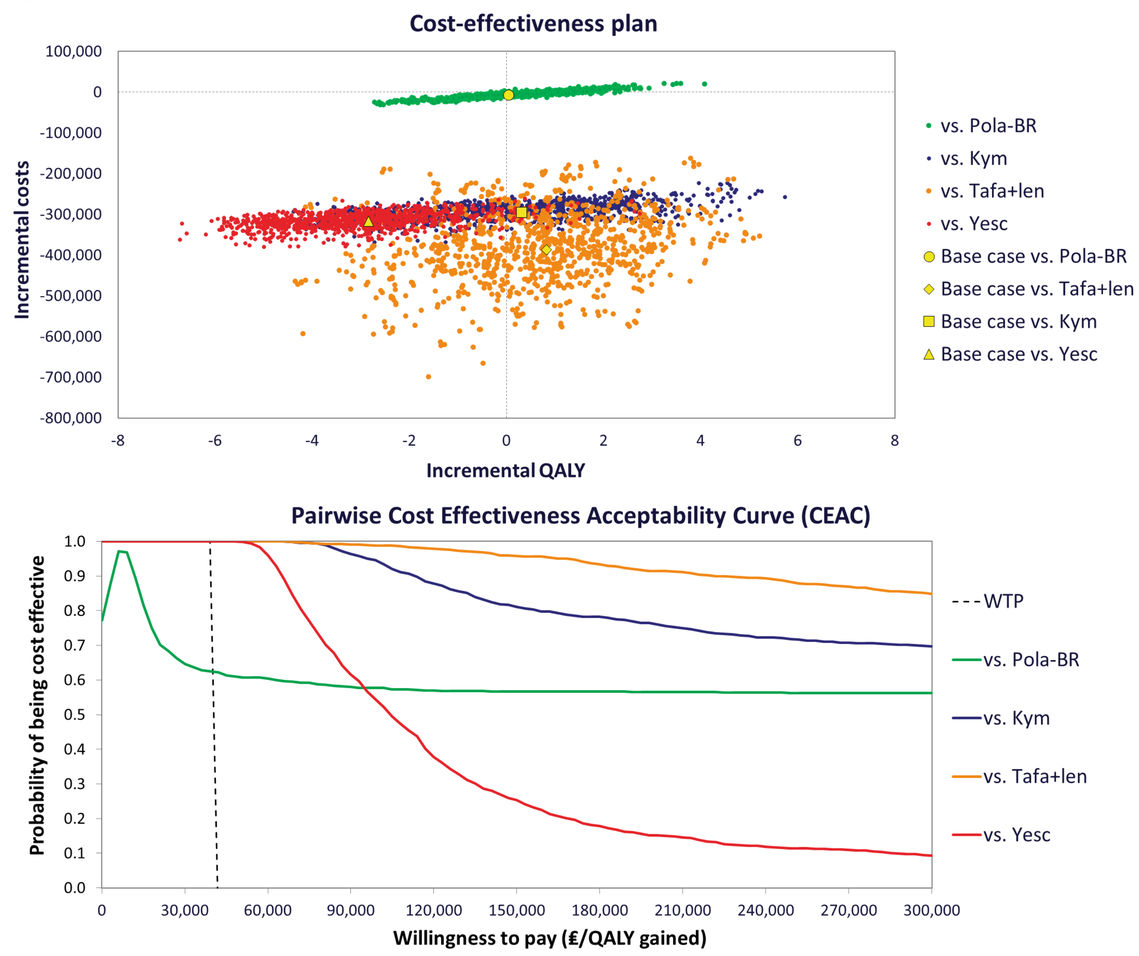


Figure 4 – PSA results



Conclusions

Glofitamab can be considered a **cost-effective option** for Italian patients with 3L+ DBLCL, particularly for those who have exhausted currently available valid alternatives.

References

1. Longworth L et al. *Health Technol Assess.* 2014;18(9):1-224; **2.** Scalone L et al. *Value Health.* 2013;16(5):814-22; **3.** Decreto 10/2012 in GU Serie Generale n.23 del 28-1-2013 (Tariff and DRG); **4.** Regione Lombardia, Deliberazione n° IX / 2946 del 2012 (MAC tariff); **5.** NICE 2020. TA649; **6.** Lazzaro C et al. *Clinicoecon Outcomes Res*. 2013;5:125-135.

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