A cost-effectiveness analysis of Polatuzumab in Combination with Bendamustine and Rituximab in Patients with Relapsed/Refractory Diffuse Large B-Cell Lymphoma not Eligible for Haematopoietic Stem Cell Transplant, in Portugal

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1 – Background and Objectives:

– Diffuse Large B-Cell Lymphoma (DLBCL) is the most common histological subtype of aggressive B-cell non-Hodgkin's lymphoma (NHL), representing about 31% of all NHL cases in Western countries [1].

– In Portugal, according to data from the Registo Oncológico Nacional (RON), in 2010 there were 1,812 new cases of NHL, of which 969 occurred in men (53%) and 843 in women (47%). NHL represented approximately 84% of all lymphoma cases and 4% of all cancer cases diagnosed in Portugal that year.

– Polatuzumab vedotin is an antibody-drug conjugate composed of the anti-mitotic agent monomethyl auristatin E (MMAE) covalently conjugated to a CD79b-directed monoclonal antibody (recombinant humanized immunoglobulin G1 [IgG1].

– The aim of this study is to assess the cost-effectiveness of polatuzumab in combination with bendamustine and rituximab (BR) compared to BR in the treatment of patients with relapsed/refractory (R/R) DLBCL, not eligible for hematopoietic stem cell transplant (HCT), in the Portuguese setting.

2 – Methods

Effectiveness Model:

– A partitioned survival model, developed by Roche (Global Access – HTA Evidence Group) was used to estimated patients' pathway through three mutually exclusive health states: progression-free survival (PFS), post-progression survival (PPS) and death.

– Costs, life years (LYs) and quality-adjusted life years (QALYs) were estimated for both arms.

– The analysis was conducted from the National Health Service perspective, incorporating direct medical costs. A lifetime horizon and a 4% discount rate for both costs and effects are assumed. The model applies weekly cycles with half-cycle correction.

Clinical data:

– Polatuzumab + BR was compared directly to BR in R/R based a randomized cohort of GO29365 study [2]. an ongoing phase Ib/II, international, open-label, multicentre, study that aims to investigate the efficacy and safety of Polatuzumab in NHL.

– Subgroup analysis was done to assess the treatment effect in patients with one prior line and patients with two or more prior lines.

– Parametric functions were chosen to extrapolate overall survival (OS), PFS and time on treatment (TOT) according to goodness-of-fit criteria (AIC and BIC) and clinical plausibility. For time to treatment the KM estimates were used. (Table 1)

Table 1. Summary of modelling options.

Outcome	Hazard proportionality	Parametric Curves		
		ITT	2L	3L+
OS	Yes	Exponential	Exponential	Exponential
PFS	Yes	Weibull	Weibull	Weibull

OS, overall survival; PFS, progression free survival; 2L, second line treatment; 3L+ three or more treatment lines.

Adverse events

– The impact of grade 3 or 4 Serious treatment related adverse events (SAE) was incorporated into the model.

– SAE incidence was obtained from the clinical trial GO29365 [2].

Utilities

– Utility scores were based on a submission to NICE [3], benefiting from the similarities between the cohorts followed in the ZUMA-1 and the GO29365 trials.

– Disutilities due to AE were obtained from the literature.

Table 2. Utility scores per health state.

Health State	Mean value (SE)
PFS	0.72 (0.03)
PPS	0.65 (0.06)

PFS, progression free survival; PPS, post progression survival; SE, standard error.

Costs

– Portuguese-specific disease management resource use was based on a panel of experts and on Portuguese 2017 DRG microdata (ACSS, 2017).

– Resources were valued according to national legislation (Portaria nº 207/2017) and official national drug cost databases (Infomed and ACSS Catalog).

– The average weekly follow-up cost per health state is presented below:

Table 3. Estimated weekly follow-up costs.

Model	Arm	PFS	PPS
ITT	Polatuzumab +BR	222 €	547 €
	BR	259 €	547 €
2L	Polatuzumab +BR	213 €	550 €
	BR	292 €	548 €
3L+	Polatuzumab +BR	229 €	548 €
	BR	250 €	548 €

ITT, intent-to-treat; 2L, second line treatment; 3L+ three or more treatment lines; BR, bendamustine and rituximab; PFS, progression free survival; PPS, post progression survival.

3 – Results

Base case scenario:

– Survival projections indicate that treatment with Polatuzumab + BR prolongs both PFS and OS in patients with R/R DLBCL (Figure 1, 2 and 3).

Figure 1. Modelled curves on the base-case scenario for the ITT population.

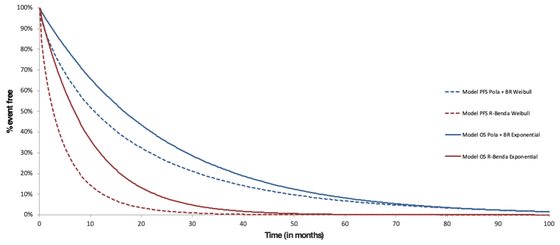


Figure 2. Modelled curves on the base-case scenario for the 2L population.

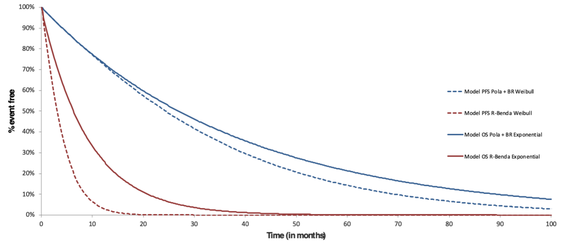
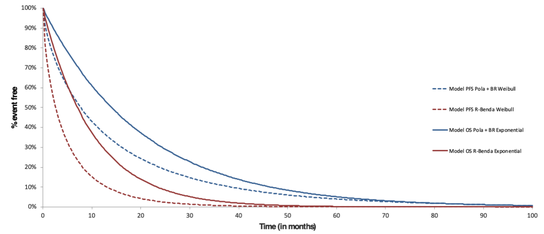


Figure 3. Modelled curves on the base-case scenario for the 3L+ population.



– In ITT population, Polatuzumab+BR is associated with a health benefit of 1.33 QALYs compared to 0.55 in BR arm. In 2L population, Polatuzumab+BR is associated with a health benefit of 2.07 QALYs compared to 0.50 in the comparator arm. In 3L+ population, Polatuzumab+BR is associated with a health benefit of 1.13 QALYs compared to 0.57 in the comparator arm.

– The incremental values Polatuzumab+BR versus BR alone are presented on Table 4.

Table 4. Cost-effectiveness results for the base-case scenario (incremental values).

	ITT	2L	3L+
LY (undiscounted)	1.18	2.48	0.84
LY	1.08	2.18	0.78
QALY	0.78	1.57	0.56
Costs (€)	58,169 €	68,078 €	57,249 €
Treatment	46,966 €	45,328 €	47,856 €
Treatment Administration	434 €	351 €	474 €
Adverse Events	3 €	3 €	3 €
PFS follow-up	12,099 €	22,324 €	8,653 €
PPS follow-up	-1,062 €	631 €	458 €
End of life	-272 €	-559 €	-195 €
ICER (€/LY)	**53,978 €**	**31,231 €**	**73,483 €**
ICUR (€/QALY)	**74,560 €**	**43,408 €**	**101,937 €**

ITT, intent-to-treat; 2L, 2nd line treatment; 3L+, 3rd line treatment or more; LY, life years; PFS, progression free survival; PPS, post progression survival; QALY, quality-adjusted life years.

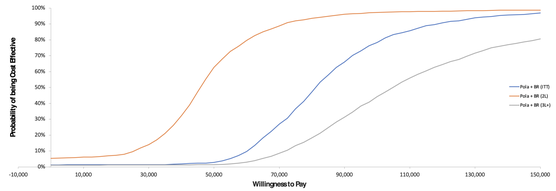
Sensitivity analysis

– Deterministic sensitivity analyses showed that the results were robust to most hypothesis and estimates, except the ones related to vial sharing and parametric extrapolation options.

– Probabilistic sensitivity analysis also shows that results are robust (figures 4, 5 and 6). In ITT population, ICUR ranged between 68,988€/QALY (25% percentile) and 96,743€/QALY (75% percentile). In the 2L population, ICUR ranged between 41,364€/QALY (25% percentile) and 61,518€/QALY (75% percentile). In 3L+ population, ICUR ranged between 94,090€/QALY (25% percentile) and 156,964€/QALY (75% percentile).

– Acceptability curves for each population are displayed on Figure 4.

Figure 4. Cost-effectiveness acceptability curves.



4 – Conclusions:

– Treatment with polatuzumab in combination with BR showed an incremental effectiveness both in terms of LY and QALY compared to BR alone.

– The cost-effectiveness model of polatuzumab in combination with BR in patients with R/R DLBCL, not eligible for HCT, was considered valid to support a reimbursement decision in the Portuguese setting.

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6 – References:

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