Cost analysis of Polatuzumab vedotin in combination with Rituximab, Cyclophosphamide, Doxorubicin, and Prednisone in the treatment of adult patients with previously untreated Diffuse Large B-Cell Lymphoma

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1 – Background and objective

- Diffuse Large B-Cell Lymphoma (DLBCL) is the most common 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 2021 there were 2.239 new cases of NHL, representing 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 conjugated to a CD79b-directed monoclonal antibody.
- This study aims to assess the potential clinical and economic impact of Polatuzumab + R-CHP *vs.* Rituximab, Cyclophosphamide, Doxorubicin, Vincristine and Prednisone (R-CHOP) in the treatment of adults with DLBCL without previous treatment, in the Portuguese setting, based on a cost-effectiveness model.

2 – Methods

Cost-Effectiveness Model:

- A partitioned survival model, developed by Roche (Global Access – HTA Evidence Group), was used to estimate patients' pathway through 3 exclusive health states: progression-free survival (PFS), post-progression survival (PPS) and death. The model was considered valid to support the reimbursement decision in the Portuguese setting.
- Costs and life years (LYs) were estimated for both arms of the clinical trial.
- The analysis was conducted from the National Health Service perspective. A lifetime horizon and a 4% discount rate are assumed for costs and effects, in accordance with Portuguese guidelines [2]. The model applies weekly cycles with half-cycle correction.
- Given the difference between the clinical trial follow-up period and the time horizon for an economic evaluation study, and evidence of long-term remission in some patients, a mixture cure model was used to extrapolate PFS and overall survival (OS) data.

Clinical Data:

- Polatuzumab + R-CHP was compared with R-CHOP based on POLARIX study [3], a phase III, multicenter, randomized, double-blind, placebo-controlled clinical trial conducted in previously untreated patients with DLBCL. To increase the accuracy of the estimates, PFS data were extended using external matched R-CHOP data from the finalized GOYA study [4] (open-label, phase III, multicenter, randomized clinical trial that compared obinutuzumab + R-CHP *vs*. R-CHOP in previously untreated patients with DLBCL).
- The modelling uses Kaplan-Meier (KM) estimates up to month 42 and an extrapolation tail with a mixture-cure model (generalized gamma distribution). It was assumed the same treatment effect beyond month 42 for both treatment arms (equal to R-CHOP risk).
- All patients in the POLARIX trial completed their treatment or discontinued at the last data cut. This allowed the use of KM estimates directly without the need for extrapolation to estimate treatment duration.

Adverse Events:

- The model considers adverse events (AE) of grade 3 or higher, with an incidence of at least 2% in either treatment arm. The frequencies were obtained from the POLARIX trial [3].

Costs:

- Portuguese-specific disease management resource use was based on an expert panel and on Portuguese 2018 diagnostic-related group microdata (*Administração Central do Sistema de Saúde, ACSS*, 2018). The panel, conducted in 2023, was composed of 5 experts from 5 reference centers for clinical hematology.
- Resources were valued according to national legislation (*Portaria* nº 207/2017 and *Despacho* n. º 7215/2015) and official drug cost databases (*Infomed* and *ACSS* catalog).
- The average weekly follow-up cost per health state is presented below:

Table 1. Estimated weekly follow-up costs (€)

	Polatuzumab + R-CHP	R-CHOP
PFS		
In active treatment	177.26	177.26
After active treatment (1st and 2nd years)	7.00	7.00
After active treatment (3rd year)	3.40	3.40
After active treatment (4th and 5th years)	2.59	2.59
PPS	346.88	344.24

PFS: Progession-free survival; PPS: Post-progression survival; R-CHOP: Rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone; R-CHP: Rituximab, cyclophosphamide, doxorubicin and prednisone.

- The follow-up costs include: disease-related hospitalizations, urgency without admission/ unscheduled consultations, supplementary means of diagnosis and treatment, consultations and ambulatory therapy
- The costs of subsequent therapy (including stem cell transplant) are presented below:

Table 2. One-off cost of treatment in subsequent lines (€)

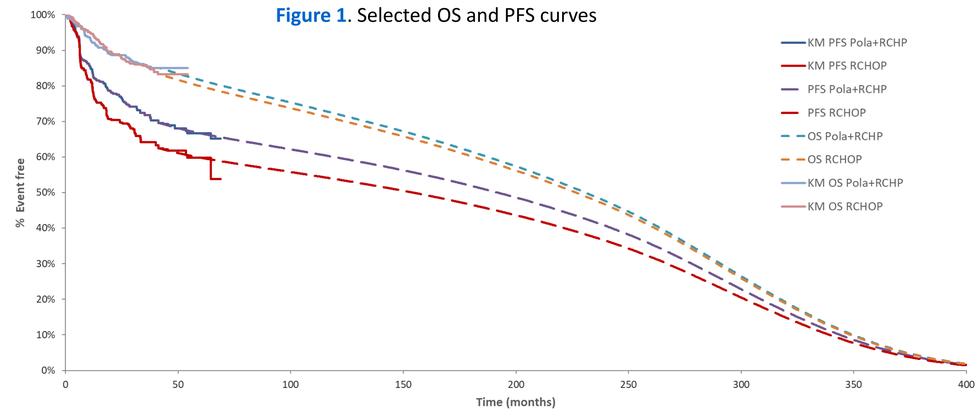
Polatuzumab + R-CHP	19,395.48
R-CHOP	20,773.38

R-CHOP: Rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone; R-CHP, Rituximab, cyclophosphamide, doxorubicin and prednisone.

3 – Results

- Survival projections indicate that treatment with Polatuzumab + R-CHP prolongs both PFS and OS in patients with DLBCL (Figure 1).

Figure 1. Selected OS and PFS curves



PFS: Progession-free survival; OS: overall survival; R-CHOP: Rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone; R-CHP, Rituximab, cyclophosphamide, doxorubicin and prednisone; Pola: Polatuzumab; KM: Kaplan-Meier.

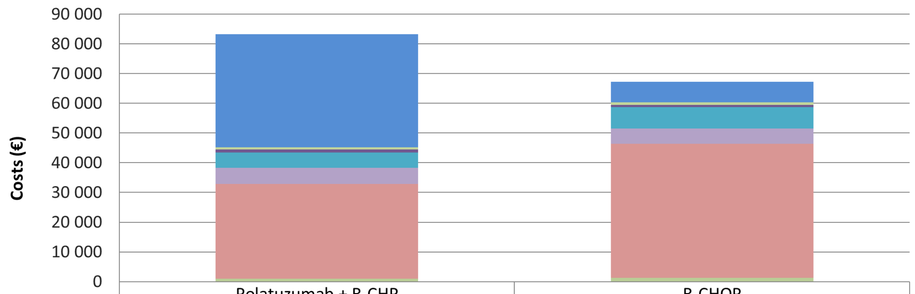
- The estimated cure fractions were 73% for Polatuzumab and 64% for R-CHOP.
- Higher costs of Polatuzumab + R-CHP option are mainly due to higher treatment costs. However, Polatuzumab + R-CHP is associated with a reduction of PPS, resulting in cost savings related to progressive disease states (which reflect in both treatment and follow-up costs (Table 3).

Table 3. Cost-effectiveness results of polatuzumab + R-CHP versus R-CHOP

	Polatuzumab + R-CHP	R-CHOP	Incremental
LY	11.69	11.51	0.18
PFS	9.93	9.01	0.92
PD	1.76	2.51	-0.74
Total costs (€)	83,210	67,216	15,994
Total costs PFS (€)	45,256	13,729	31,527
Polatuzumab (€)	30,972	0	30,972
R-CHP (€)	6,989	0	181
R-CHOP (€)	0	6,948	41
Administration costs (€)	789	769	20
AE costs (€)	1,036	788	248
Follow-up costs (€)	5,470	5,223	246
Total costs PD (€)	36,974	52,177	-15,203
Treatment costs (€)	5,060	7,171	-2,111
Follow-up costs (€)	31,914	45,006	-13,092
End of life costs (€)	980	1,310	-330

PFS: Progession-free survival; PD: progressive disease; R-CHOP: Rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone; R-CHP: Rituximab, cyclophosphamide, doxorubicin and prednisone; AE: Adverse event.

Figure 2. Breakdown of mean total costs of Polatuzumab + R-CHP versus R-CHOP



	Polatuzumab + R-CHP	R-CHOP
Drug acquisition	37 961	6 948
Administration	789	769
AE	1 036	788
Subsequent therapy	5 060	7 171
PFS follow-up	5 470	5 223
PPS follow-up	31 914	45 006
End of life	980	1 310

R-CHOP: Rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone; R-CHP: Rituximab, cyclophosphamide, doxorubicin and prednisone; AE: Adverse event.

4 – Conclusion

- Treatment with Polatuzumab + R- CHP resulted in increased PFS, compared to R-CHOP.
- Although Polatuzumab is associated with higher PFS costs, it contributes to cost savings in the post-progression stage. This is primarily due to the higher cure fraction of Polatuzumab, reducing time in PPS, which leads to lower subsequent therapy costs, reduced PPS follow-up costs and decreased end-of-life costs.

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