ABCL-101

Cost-effectiveness of polatuzumab vedotin in previously untreated diffuse large B-cell lymphoma

Matthew Matasar,[1] Anthony Masaquel,[2] Rodrigo Ho,[3] Aino Launonen,[3] Carmen Ng,[2] Rongrong Wang,[2] David Fox,[2] Farah Hossain,[2] Jia Li,[2] Joshua A. Roth,[2] **John M. Burke**[4]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Genentech, Inc., South San Francisco, CA, USA; [3]F. Hoffmann-La Roche Ltd., Basel, Switzerland; [4]Rocky Mountain Cancer Centers/US Oncology, Aurora, CO, USA

Summary

POLARIX (NCT03274492) is a Phase III, randomized, double-blind study of Pola-R-CHP vs R-CHOP in patients with previously untreated DLBCL and International Prognostic Index 2–5.[1]

A three-state partitioned survival **cost-effectiveness analysis model** was developed to estimate life years, QALYs, and cost impacts of Pola-R-CHP vs R-CHOP based on the POLARIX trial.

This economic model demonstrates **an improvement of 0.51 QALYs with Pola-R-CHP** vs R-CHOP and savings in costs relating to DLBCL progression.

Pola-R-CHP was projected to be cost-effective (<$150,000/QALY) vs R-CHOP in previously untreated DLBCL.

Background

- Diffuse large B-cell lymphoma (DLBCL) is the most common form of lymphoma;[2] approximately 30–40% of patients relapse or are refractory to rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP), the current standard of care for DLBCL.[3]
- Polatuzumab vedotin in combination with rituximab, cyclophosphamide, doxorubicin, and prednisone (Pola-R-CHP) was evaluated as a frontline (1L) treatment in DLBCL vs R-CHOP in the Phase III, randomized, double-blind POLARIX trial (NCT03274492)[1]
  - Pola-R-CHP significantly increased progression-free survival (PFS) relative to R-CHOP (hazard ratio, 0.73; 95% confidence interval: 0.57–0.95; p=0.02)
  - The safety profile of Pola-R-CHP was similar to that of R-CHOP.

Objective

- To evaluate the cost-effectiveness of Pola-R-CHP vs R-CHOP in previously untreated DLBCL in the US.

Methods

Model structure

- A three-state (PFS, progressive disease [PD], death) partitioned survival model was developed to estimate the life years, quality-adjusted life years (QALY), and cost impacts of Pola-R-CHP vs R-CHOP in patients with previously untreated DLBCL.
- Mixture-cure survival modelling was used, a lifetime horizon (60 years) was assessed, all outcomes were discounted at 3% per year, and payer and societal perspectives were examined
  - A societal perspective included indirect costs, e.g. costs associated with work productivity loss.
- Estimated PFS (**Figure 1A**), estimated overall survival (OS; **Figure 1B**), drug utilization, treatment duration, adverse events (AE), and subsequent treatment inputs were derived from POLARIX
  - Patients had a mean age of 63 years, mean body weight of 75.92kg, and mean body surface area of 1.86m^2 from POLARIX.

Analyses conducted

- One-way and probabilistic sensitivity analyses (PSA) were performed to assess the impact of uncertainty on cost per QALY-gained outcomes.
- A scenario analysis, where chimeric antigen receptor-modified T-cell therapy (CAR-T) use after Pola-R-CHP and R-CHOP increases from base case to 14.78% and 20.00%, respectively, was conducted to assess the future impact of increased second-line CAR-T utilization following progression or relapse subsequent to completing 1L therapy.

Cost estimation

- Costs were adjusted based on consumer price index inflation in 2022, where applicable.
- **Drug treatment** was based on Average Sales Price (ASP; April 2022 drug pricing file) from Centers for Medicare and Medicaid Services (CMS); ASP was calculated by dividing the payment values by 1.06 (**Table 1**).[4]
- **Drug administration** (first hour: $140.16; subsequent hours: $29.76) was based on CMS Physician Fee Schedule.[5]
- **Subsequent treatment** data after 1L treatment with Pola-R-CHP and R-CHOP were derived from the POLARIX trial,[3] including higher utilization of CAR-T and stem-cell transplantation (SCT) in the R-CHOP arm compared with the Pola-R-CHP arm;[6,7] costs for treatment regimens were based on published claims data where available, or ASP (**Table 2**).
- **AEs** (Grade 3–5) with an incidence of >2% in either POLARIX treatment arm were considered; costs were obtained from the Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project database (**Table 3**).[8,9]
- **Routine care** costs were based on non-treatment-related office visits, laboratory tests, and radiology tests.[10] Routine care was estimated to be $960/week in the progression-free state while on treatment only and a one-time cost of $21,362 in the PD state based on a weighted average of costs in second- and third-line treatment.[10]
- **Work productivity** was based on the assumption that patients in the progression-free state miss one day of work during each IV administration and patients in the PD state were assumed to be unable to work. Cost inputs were obtained from the Bureau of Labor Statistics.[11]
- **End-of-life cost** was estimated to be $26,157[8,12] and was applied during the last month of life in the model.

Table 1. Drug costs (USD).*

Drug	Drug cost per mg (USD)
Polatuzumab vedotin	107.14
Rituximab	5.59
Cyclophosphamide	0.23
Doxorubicin	0.28
Vincristine	4.70
Prednisone	0.02

*April 2022 average sales price. Polatuzumab vedotin administration is weight based at 1.8mg/kg (available as 30mg and 140mg vials). Duration of drug treatment was based on time-to-off treatment Kaplan-Meier curves from the POLARIX trial. The model assumed wastage, and an average price was used for rituximab and rituximab biosimilars (TRUXIMA®, RUXIENCE®, and RIABNI™). USD, US dollars.

Table 2. Subsequent treatment after frontline therapy.

Subsequent treatment	Pola-R-CHP N=123*	R-CHOP N=197*
Mean number of subsequent treatments	1.78	1.97
R-ICE (intention to proceed with transplant)	40%	39%
ICE (intention to proceed with transplant)	7%	5%
Bendamustine	9%	10%
Bendamustine + rituximab	34%	27%
Pola-BR	0%	5%
Rituximab monotherapy	2%	3%
CAR-T†	8%	11%
SCT‡	16%	21%

*Treatment level analysis. N represents number of treatments post 1L and not number of patients. R-ICE $20,828; ICE $3,053; Bendamustine $24,913; BR $38,825; Pola-BR $120,375; Rituximab $39,320; CAR-T $433,717; SCT $342,501. †Cost of a CAR-T episode was based on an average from three US claims databases ($433,717).[6] ‡The 1-year cost of SCT was $342,501.[7] BR, bendamustine + rituximab; CAR-T, chimeric antigen receptor T-cell therapy; Pola-BR, polatuzumab + BR; (R)-ICE, (rituximab), ifosfamide, carboplatin, etoposide; SCT, stem-cell transplantation.

Table 3. AE cost calculations.

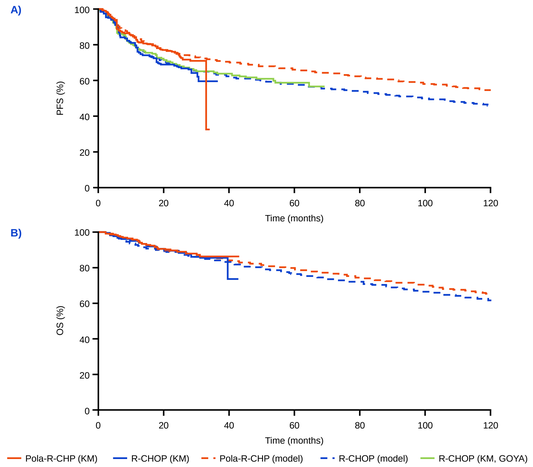
Treatment	Anemia	Diarrhea	Febrile neutropenia		Neutropenia*		Pneumonia
			Gr 3	Gr 4	Gr 3	Gr 4	
Pola-R-CHP, %†	12	4	14	4	10	24	3
R-CHOP, %†	7	1	6	3	13	27	4
Cost of treating AE‡, USD	7,131	7,661	13,451	13,451	13,451	13,451	10,151

*Data are body system-defined neutropenia but potentially include laboratory values for neutrophil count decrease. Gr 3 and 4 neutrophil count decrease were reported in 3% and 8% of Pola-R-CHP recipients, respectively, and 2% and 6% of R-CHOP recipients, respectively, and costs of treating were USD 114 and 114, respectively; †AE incidence rates based on an analysis of patient-level data from the POLARIX study; ‡Costs taken from the Agency for Healthcare Research Quality, Healthcare Utilization Project mean inpatient costs (2018) inflated to 2022 USD. AE, adverse event; Gr, grade; Pola-R-CHP, polatuzumab vedotin plus rituximab, cyclophosphamide, doxorubicin, and prednisone; R-CHOP, rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone; USD, US dollars.

QALY estimation

- A mixture-cure model[13,14] was chosen for long-term extrapolation of PFS and OS curves (OS informed by PFS). Based on POLARIX, long-term remission fractions of 75% (95% confidence interval [CI]: 70–79) and 64% (95% CI: 56–71) were estimated for Pola-R-CHP and R-CHOP, respectively, using a generalized gamma distribution. The long-term remission fraction was also used to extrapolate OS.
- Using mixture-cure methodology, and data from the Phase III GOYA trial in 1L DLBCL (median follow-up: POLARIX, 28.2 months[1] vs GOYA, 47.4 months[15]), the patient-matched PFS curve for R-CHOP from the GOYA trial showed good alignment with that from POLARIX (**Figure 1**).
- Health utilities were based on EQ-5D results from patients matched from the GOYA trial to the POLARIX trial (0.83 in PFS and 0.72 in PD), with US tariffs applied.[15,16]
- Health utilities for the general population were applied for patients with PFS after Year 3 (mean EQ-5D score: 0.86 for patients aged 65–74; 0.84 for patients aged 75–89).[17]

Figure 1. Modelled PFS (A) and OS (B) based on the POLARIX trial.



	Pola-R-CHP	R-CHOP
PFS, %		
24-month	76.6	69.9
60-month	67.9	60.0
OS, %		
24-month	88.9	88.8
60-month	79.9	77.6

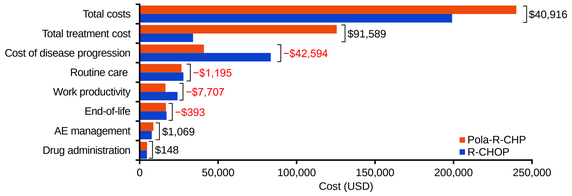
KM, Kaplan-Meier; OS, overall survival; PFS, progression-free survival; Pola-R-CHP, polatuzumab vedotin plus rituximab, cyclophosphamide, doxorubicin, and prednisone; R-CHOP, rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone.

Results

Incremental cost-effectiveness ratio (ICER)

- Differences in incremental costs between Pola-R-CHP and R-CHOP are shown in **Figure 2**.
- The ICER of Pola-R-CHP vs R-CHOP was **$80,444/QALY gained** from a societal perspective, and **$95,597/QALY gained** from a payer perspective (i.e. excluding work productivity cost offsets; **Table 4**).
- From a societal perspective, the total cost of Pola-R-CHP was $40,916 higher than R-CHOP (**Table 4**), primarily due to higher drug costs ($125,623 vs $34,034, respectively)
  - Drug cost offsets for Pola-R-CHP included subsequent treatment costs (−$42,594), routine care (−$1,195), end-of-life care (−$393), and work productivity (−$7,707).
- AE management costs were $1,069 higher with Pola-R-CHP ($8,782) vs R-CHOP ($7,713).
- Pola-R-CHP resulted in an increase of 0.50 life years and 0.51 QALYs vs R-CHOP.

Figure 2. Incremental costs of Pola-R-CHP and R-CHOP.



Differences in net costs between Pola-R-CHP and R-CHOP indicated adjacent to each bar. AE, adverse event; Pola-R-CHP, polatuzumab vedotin plus rituximab, cyclophosphamide, doxorubicin, and prednisone; R-CHOP, rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone; USD, US dollars.

Table 4. Cost-effectiveness summary: societal and payer perspective.

Treatment	Life years	QALYs	Total cost (USD)	Cost per QALY
Societal perspective				
Pola-R-CHP	12.61	10.44	240,031	
R-CHOP	12.11	9.93	199,114	
Difference	0.50	0.51	40,916	$80,444/QALY
Payer perspective				
Pola-R-CHP	12.61	10.44	223,597	
R-CHOP	12.11	9.93	174,973	
Difference	0.50	0.51	48,624	$95,597/QALY

Pola-R-CHP, polatuzumab vedotin plus rituximab, cyclophosphamide, doxorubicin, and prednisone; R-CHOP, rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone; QALY, quality-adjusted life year; USD, US dollars.

Results

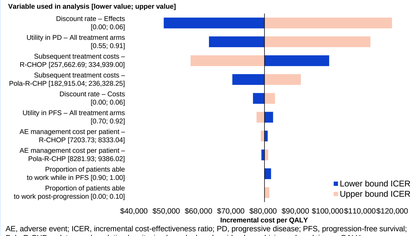
Sensitivity analyses

- The impact of individual variables on the ICER results, using a one-way sensitivity analysis, is shown in **Figure 3**.
- PSA results demonstrated that Pola-R-CHP was cost-effective in 62.2% of simulations at a willingness-to-pay threshold of $150,000/QALY[18] gained from a societal perspective, and 58.5% of simulations from a payer perspective.

Scenario analysis

- In the future CAR-T use scenario (14.7% in Pola R-CHP and 20% R-CHOP), the ICER improved from $80,444/QALY gained to $60,806/QALY gained in the societal perspective.

Figure 3. Incremental cost per QALY



AE, adverse event; ICER, incremental cost-effectiveness ratio; PD, progressive disease; PFS, progression-free survival; Pola-R-CHP, polatuzumab vedotin plus rituximab, cyclophosphamide, doxorubicin, and prednisone; QALY, quality-adjusted life year; R-CHOP, rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone.

Study limitations

- There is some uncertainty around the OS extrapolation used in the model.
- Health utilities from a patient-matched population from the Phase III GOYA trial were applied in the model given the longer follow-up with GOYA.
- Costs were derived from different data sources.

Conclusions

- Pola-R-CHP was projected to be cost-effective (<$150,000/QALY) vs R-CHOP in previously untreated DLBCL, from both a societal and a payer perspective.
- This economic model demonstrates an improvement of 0.51 QALYs with Pola-R-CHP vs R-CHOP and savings in costs relating to DLBCL progression.
- Based on this cost-effectiveness analysis, Pola-R-CHP is a cost-effective treatment and represents good value relative to R-CHOP in previously untreated DLBCL.

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Disclosures

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