

Cost-Effectiveness Analysis of Polatuzumab Vedotin Combined with Chemoimmunotherapy in Untreated Diffuse Large B-cell Lymphoma (DLBCL) in China

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BACKGROUND

- DLBCL is highly aggressive, with short survival and poor prognosis.
- Though conventional treatment regimens like R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) are wildly used in DLBCL clinical practice, there are unmet needs remained.
- Polatuzumab vedotin (pola), the first-in-class antibody drug conjugate (ADC), has launched in China in 2023.
- In the phase 3 POLARIX study, the percentage of patients surviving without progression (PFS) was significantly higher in the pola-R-CHP group than in the R-CHOP group (76.7% vs. 70.2%) at 2 years, and stratified hazard ratio (HR) was 0.73. The efficacy of Asian subgroup was more significant. In the median follow-up 24.2 months, the HR of PFS was 0.64 (95% CI: 0.40-1.03), and the two-year PFS was 74.2% vs. 66.5% (pola-R-CHP group vs. R-CHOP group).

OBJECTIVE

- The aim of the study is to evaluate the cost-effectiveness of pola-R-CHP (pola combined with rituximab, cyclophosphamide, doxorubicin, and prednisone) compared to R-CHOP for untreated DLBCL patients from the perspective of China's healthcare system.

METHODS

- In this study, a cost-effectiveness analysis method was used to simulate the medical costs and health outcomes of patients with previously untreated DLBCL treated with pola-R-CHP regimen and R-CHOP regimen based on the partitioned survival model.

Study population

- The target population of this study was previously untreated DLBCL patients.
- The baseline characteristics of the simulated patients were consistent with Asian subpopulation of an international multicenter, three-phase trial, POLARIX.

Intervention and control groups

- The intervention group: pola-R-CHP. The usage and dosage are consistent with the instructions: 21 days per course; rituximab was used for 2 courses after 6 courses of pola-R-CHP.
- The control group: R-CHOP. The usage and dosage are consistent with the instructions: 21 days per course; rituximab was used for 2 courses after 6 courses of R-CHOP.

Model Structure

- A three health state partitioned survival model was performed((Figure 1):
 - pre-progression survival (PFS)
 - post-progression survival (PD)
 - death.

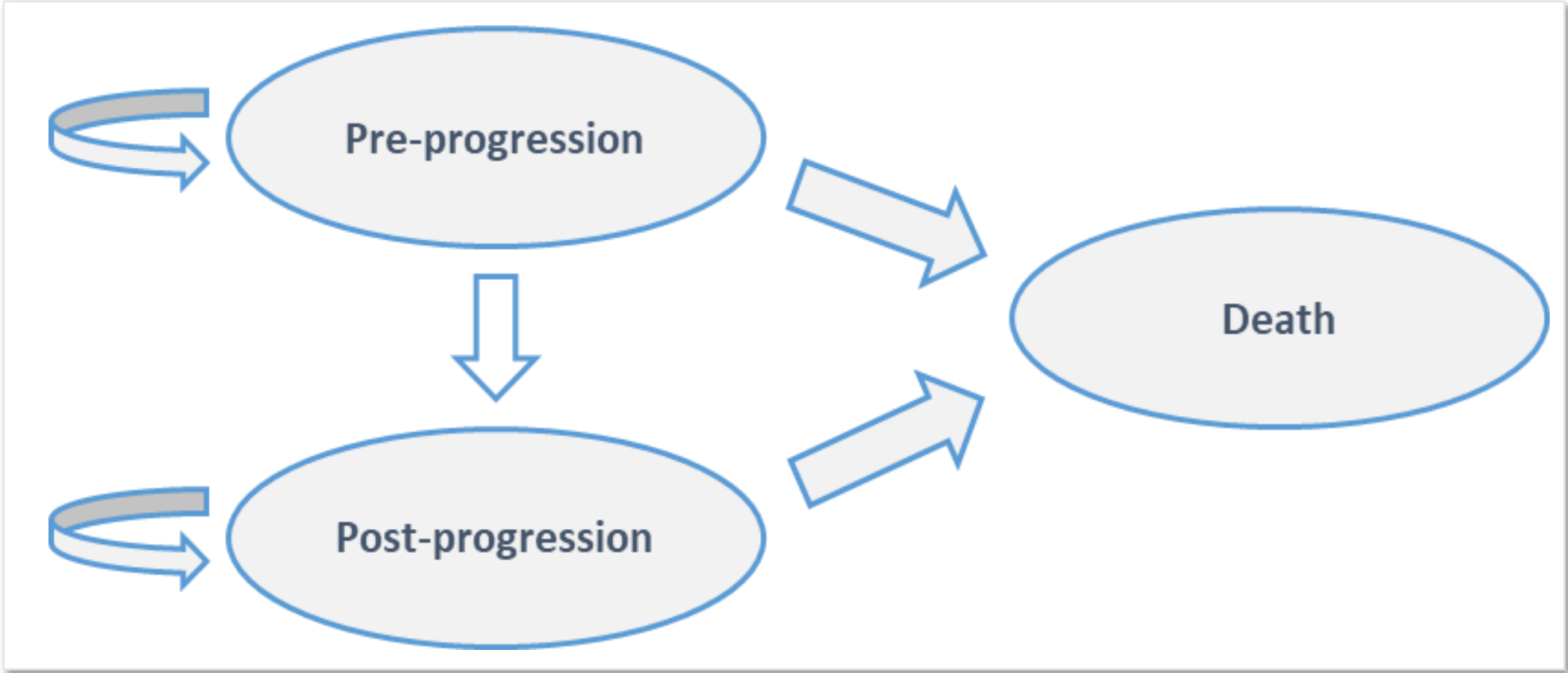


Figure 1. Partitioned Survival Model Structure

Model setting

- Research perspective: China's healthcare system
- Cycle length and time horizon
 - One-week cycles over, and a lifetime horizon
 - The model is corrected by half-cycle correction
- Discount rate: 5%
- Willingness to pay (WTP) threshold: 1.5 times China's per capita GDP (¥128,547/QALY, 2022)
- Assumption: Patients were designated cured if they did not progress by 5 years:
 - No direct medical cost is generated.
 - The utility value is the same as that of general population of the same age.

Input data

- Clinical data (Figure 2-3)
 - Clinical parameters were derived from the Asian subpopulation of the POLARIX trial.
 - Exponential, Weibull, Gompertz, Loglogistic, Lognormal and Generalized Gamma survival distribution functions were used to fit the PFS curve and OS curve of the two groups of patients, respectively.
 - Parametric models were used to fit and extrapolate the survival curves, according to AIC/BIC and the visual judgment.
 - Only AEs with an incidence of $\geq 1\%$ and a grade of ≥ 3 were considered.

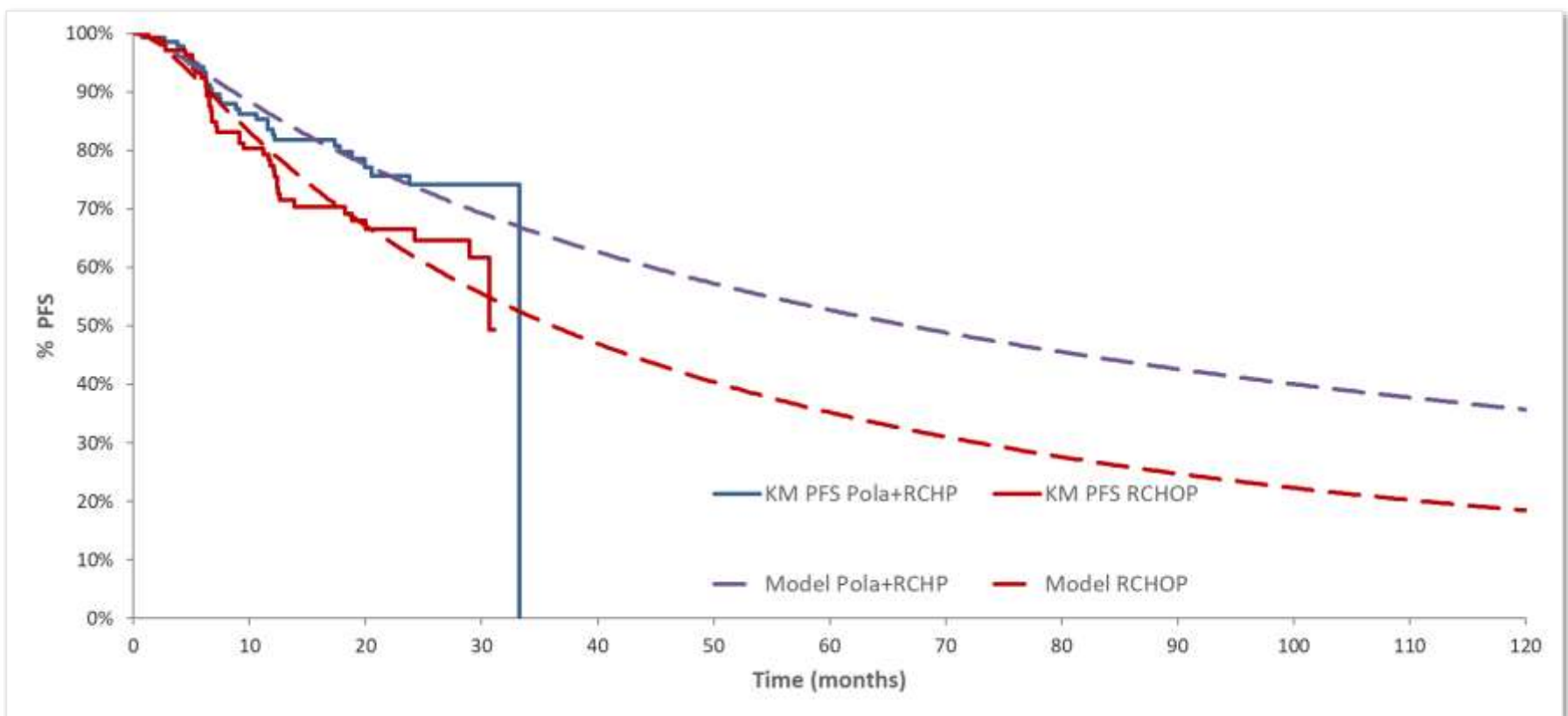


Figure 2. PFS Curves

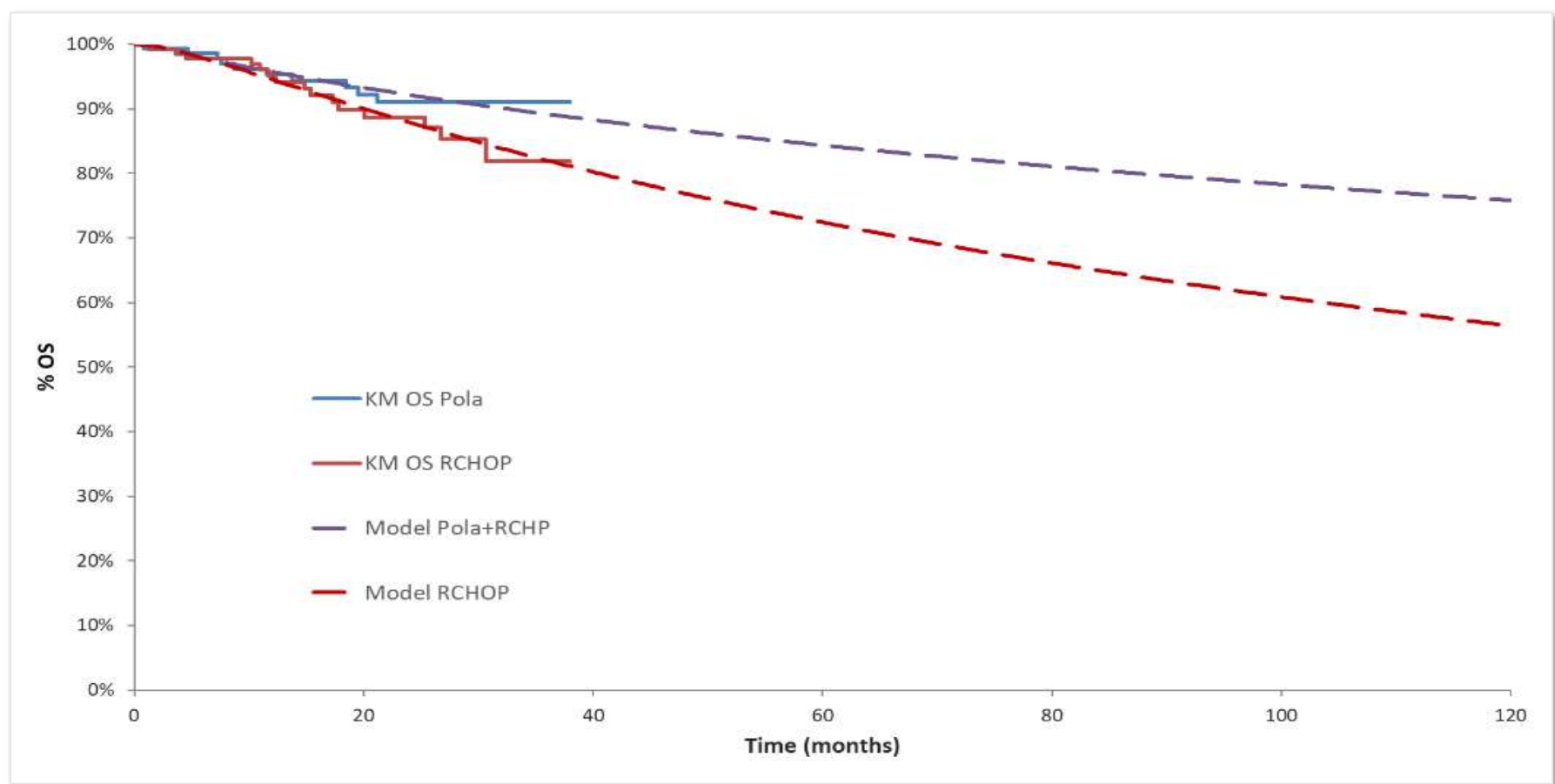


Figure 3. OS Curves

- Costs (Table 2)
 - Under China's health care system, this study only includes direct medical costs.
 - Including: drug costs, administration costs, adverse events manage costs, follow-up treatment costs, hospice care costs and other supportive costs (including inspection, nursing, examination, bed fee).
 - Other drug costs were from the public drug prices in various provinces.
 - Medical resource utilizations and costs were estimated by experienced clinicians via in-depth interviews.
 - The cost of end-of-life care was from published literature.
- Utility values
 - Utility values were sourced from 'White Paper on the Living Conditions of Diffuse Large B Cell Lymphoma Patients in China'.
 - PFS: 0.887; (ii) PD: 0.731; (iii) death: 0
 - It is assumed that the utility values of patients who were still in PFS state after 5 years were the same as that of the general population. (Table 1)

Table 1. Utility values of general population

Age	Male	Female	Age	Male	Female
18-19	0.954	0.957	50-54	0.937	0.957
20-14	0.951	0.948	55-59	0.945	0.930
25-29	0.951	0.946	60-64	0.946	0.929
30-34	0.950	0.952	65-69	0.930	0.924
35-39	0.959	0.965	70-74	0.947	0.887
40-44	0.952	0.955	75-79	0.936	0.926
45-49	0.957	0.958	≥80	0.944	0.776

- Disutility values of AEs were also considered in this study. (Table 2)

Table 2. Disutility values of AEs

AE	Disutility Values	Days
Anemia	0.25	16
Diarrhoea	0.10	2
Febrile neutropenia	0.15	6
Neutropenia	0.09	15
Neutrophil count decreased	0.09	15
pneumonia	0.20	14

RESULTS

Base-case analysis (Table 3)

- The ICER is lower than WTP threshold.

Table 3. Results of base case analysis

Index	Pola-R-CHP	R-CHOP	Incremental
Total cost	¥634,431	¥496,920	¥137,511
Life years	11.73	9.49	2.24
QALYs	9.83	7.78	2.04
ICER	-	-	¥67,333/QALY

Scenario analyses

- Scenario 1 (Table 4)
 - We used the Chinese patients' values collected by the another trial, GOYA, as the utility value of the health status: (i) PFS: 0.926; (ii) PD: 0.772; (iii) death: 0

Table 4. Results of Scenario 1

Index	Pola-R-CHP	R-CHOP	Incremental
Total cost	¥634,431	¥496,920	¥137,511
Life years	11.73	9.49	2.24
QALYs	10.00	7.94	2.06
ICER	-	-	¥66,905/QALY

- Scenario 2 (Table 5)
 - We assumed the patients who were still in PFS state after 2 years as the cure.

Table 5. Results of Scenario 2

Index	Pola-R-CHP	R-CHOP	Incremental
Total cost	¥625,575	¥490,272	¥135,304
Life years	11.73	9.49	2.24
QALYs	9.94	7.89	2.05
ICER	-	-	¥65,905/QALY

Sensitivity analyses

- One-way sensitivity analyses (Figure 4)
 - Top 3 parameters that have the greatest impact on the results are administration cost in subsequent cycle (pola-R-CHP), supportive care cost in PFS (pola-R-CHP), and supportive care cost in PFS (R-CHOP).

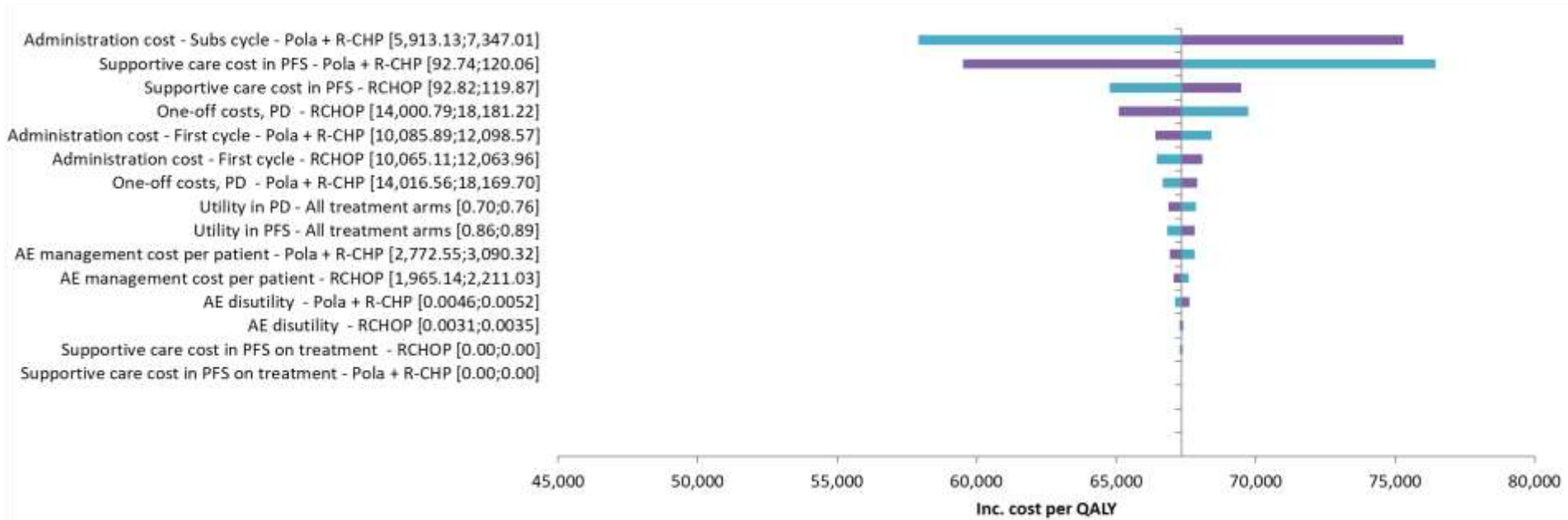


Figure 4. One-way sensitivity analysis

- Probabilistic sensitivity analyses
 - The probability of the pola-R-CHP being cost-effective is 78.6% (Figure 5).

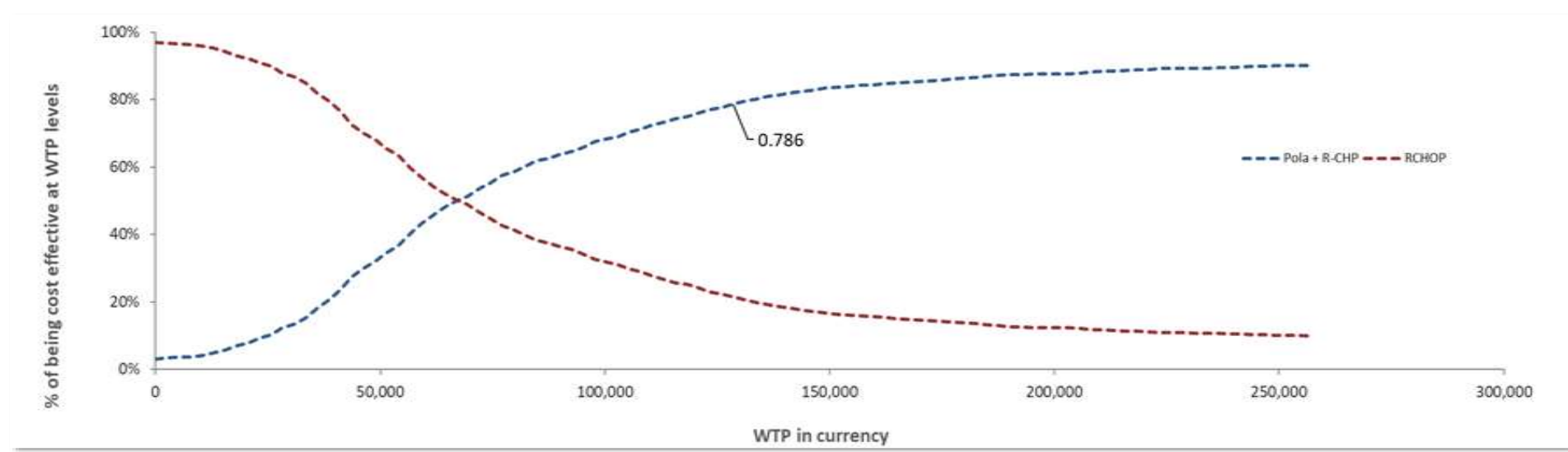


Figure 5. Cost-Effectiveness Acceptability Curve

CONCLUSIONS

- The increased QALYs were 2.04 in the base-case study.
- Pola-R-CHP is cost-effective versus R-CHOP for the treatment of untreated DLBCL in China.

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