

Xuefei Bai¹, Rongjie Shao¹, Yinyin Jin², Xiao Zhang², Xiaoning He¹

¹ School of Pharmaceutical Science and Technology, Tianjin University, Tianjin, China ² Jiangsu Hengrui Pharmaceuticals Co., Ltd.

BACKGROUND

- Follicular lymphoma (FL) is a kind of normal indolent Non-Hodg-kin's lymphoma (NHL), which accounts for 2.5%~6.0% of NHL in China. The existing standard regimens have limited efficacy on patients with multiple relapses.
- Linperlisib, a highly selective PI3K- δ inhibitor, was firstly approved for patients with relapsed or refractory follicular lymphoma after at least two prior systemic therapies (3L+ FL) with compelling clinical efficacy in China in 2023. And it was recommended by *Chinese Society of Clinical Oncology (CSCO) Guidelines 2023*.

OBJECTIVE

- The first aim is to assess the relative efficacy and safety between linperlisib and duvelisib.
- The second aim is to evaluate the cost-effectiveness of linperlisib compared to duvelisib.

METHODS

A cost-effectiveness analysis method was used to simulate the medical costs and health outcomes of patients with 3L+ FL treated with linperlisib and duvelisib.

Model structure

- A three health state partitioned survival model was performed((Figure 1):

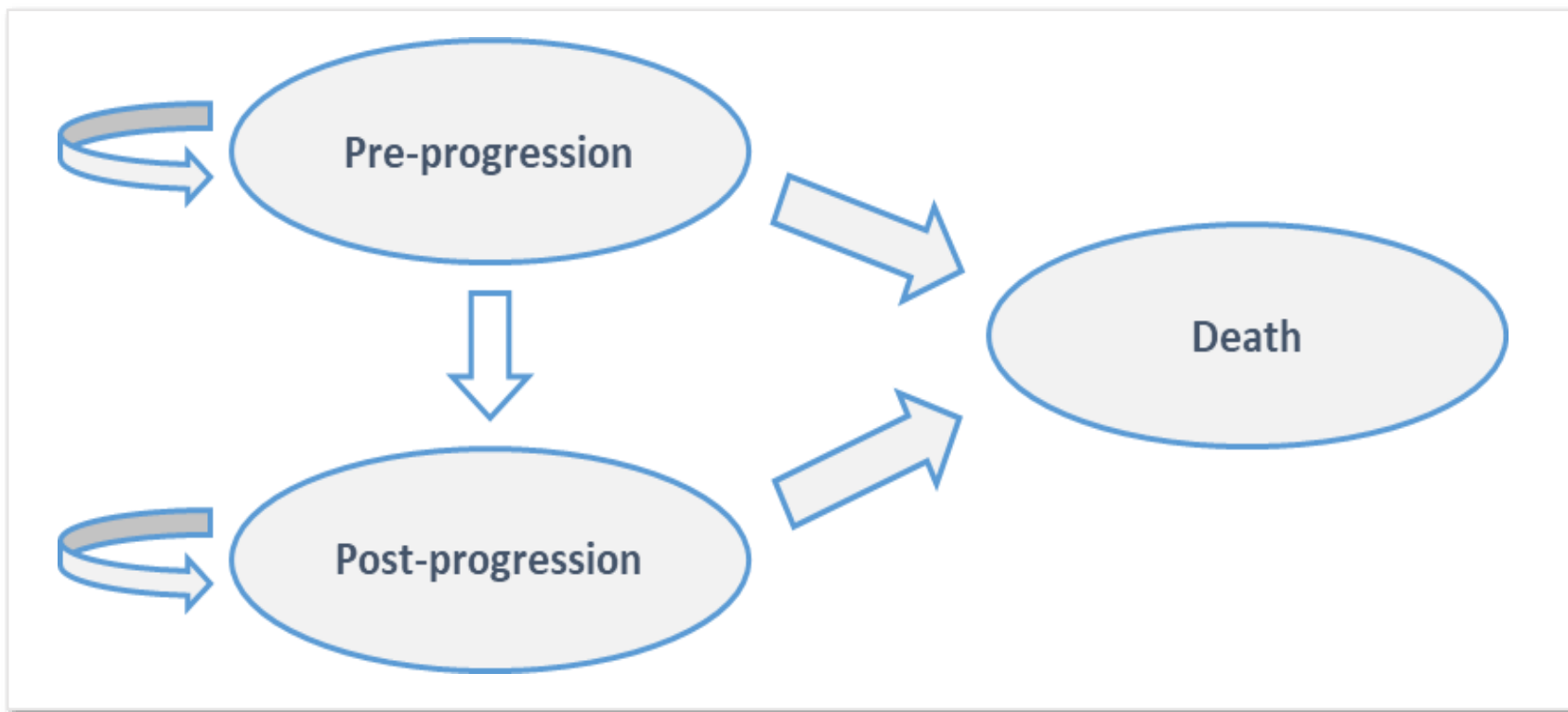


Figure 1. Partitioned Survival Model Structure

Model setting

- Research perspective: China's healthcare system
- Cycle length and time horizon
 - Four-week cycles over, and a lifetime horizon, half-cycle correction
- Discount rate: 5%
- Willingness to pay (WTP) threshold: 1.5 times China's per capita GDP (¥134,037/QALY, 2023).

Model Parameters

- Matching adjusted indirect comparison
 - In the absence of head-to-head clinical trials, matching adjusted indirect comparison (MAIC) was used for survival analyses..
- The individual patient data (IPD) for linperlisib was available from NCT04370405 and the aggregate data (AgD) for duvelisib was from DYNAMO (NCT01882803).
- The baseline characteristics before and after matching are shown in table 1

Table 1. Baseline characteristics for linperlisib versus duvelisib comparison

	Duvelisib (N=129)	Linperlisib	
		Before (N=84)	After (ESS=21)
Age \geq 65 years	50.4%	13.1%	50.4%
Males	68.2%	64.3%	68.2%
Time since diagnosis \geq 54.15 months	50.0%	34.5%	50.0%
Stage at entry I -II	14.7%	6.0%	14.7%
ECOG performance status=0/1	94.6%	97.6%	94.6%
No. of prior anticancer regimens \geq 3	62.8%	77.4%	62.8%

- Parametric models were used to fit and extrapolate the survival curves, according to AIC/BIC and the visual judgment.(Figure 2)
- Only AEs with an incidence of $\geq 3\%$ and a grade of ≥ 3 were considered

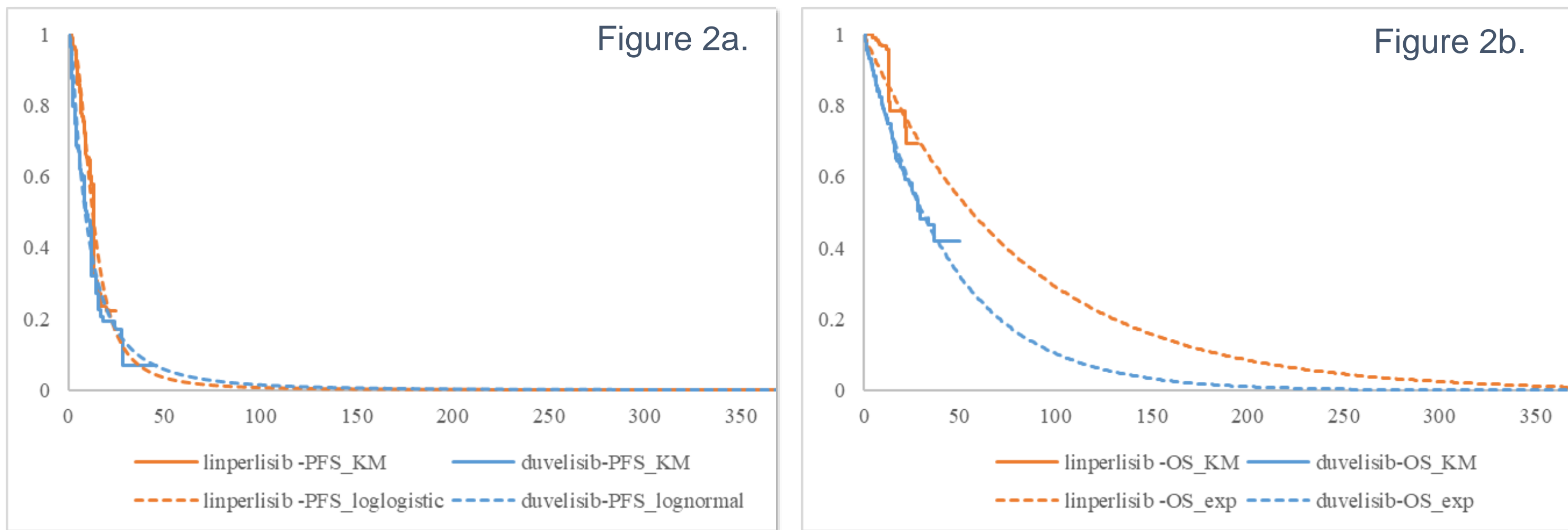


Figure 2. The exploration and fitting of PFS (2a) and OS (2b)

- Costs (Table 2)
 - The prices of linperlisib and duveliser were both determined based on the national drug price negotiation in 2023.
 - Other 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 (Table 2)
 - The utility values of states and disutilities of AEs were from published literature

Table 1. Cost and utility parameters in the model

Parameter	Deterministi c	Low	High	Distributio n
Utility values				
PFS	0.82	0.80	0.84	beta
PD	0.76	0.71	0.81	beta
Costs (¥)				
Administration costs per cycle in PFS	910	7 28	1 092	gamma
AE management costs of linperlisib	1 439	1 151	1 726	gamma
AE management costs of duvelisib	2 597	2 078	3 117	gamma
One-off treatment costs in PD	6 3624	50 899	76 349	gamma
Supportive cost in PD	2 691	2 153	3 230	gamma
Administration costs per cycle in PD	9 21	737	1 106	gamma
End-of-life care cost	1 5098	12 078	18 118	gamma

RESULTS

Base-case analysis (Table 2)

- The ICER is lower than WTP threshold.

Table 2. Results of base case analysis

	linperlisib	duvelisib	Incremental
Costs (¥)			
Total	292 878	184 029	108 849
Drug costs in PFS	153 190	65 683	87 506
Administration costs in PFS	16 459	15 320	1 139
AE management costs	1 439	2 597	-1 159
Treatment costs in PD	61 020	61 129	-109
Supportive cost in PD	2 581	2 586	-5
Administration costs in PD	46 602	23 633	22 969
End-of-life care cost	11 587	13 080	-1 493
QALYs	4.13	2.55	1.58
ICER (¥/QALY)		68 887	

Sensitivity analyses

- One-way sensitivity analyses (Figure 3)

- Top 3 parameters that have the greatest impact on the results: one-off treatment costs in PD of duvelisib, one-off treatment costs in PD of linperlisib, and the utility value in PD state.

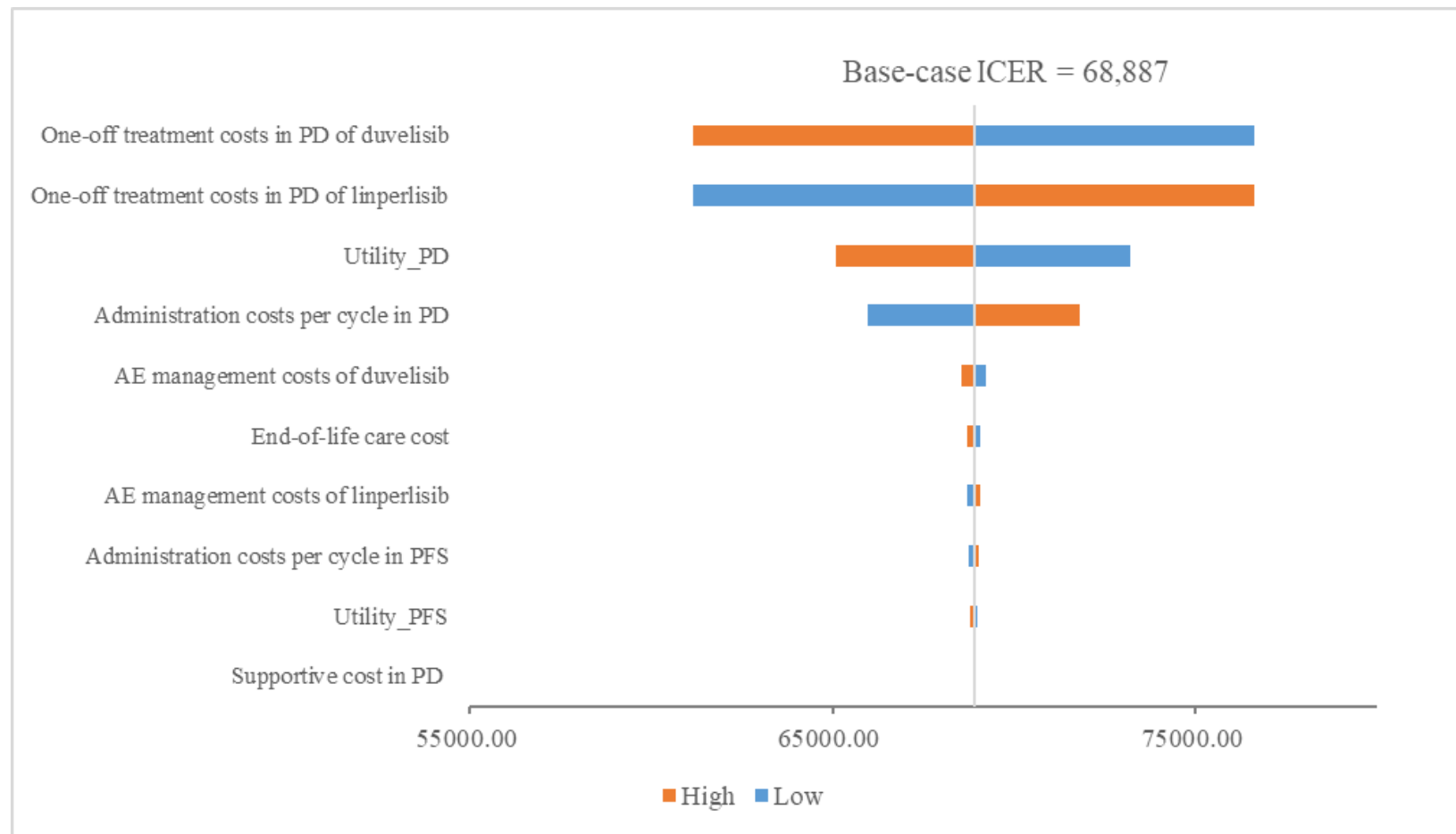


Figure 3. One-way sensitivity analysis

- Probabilistic sensitivity analyses (Figure 4).

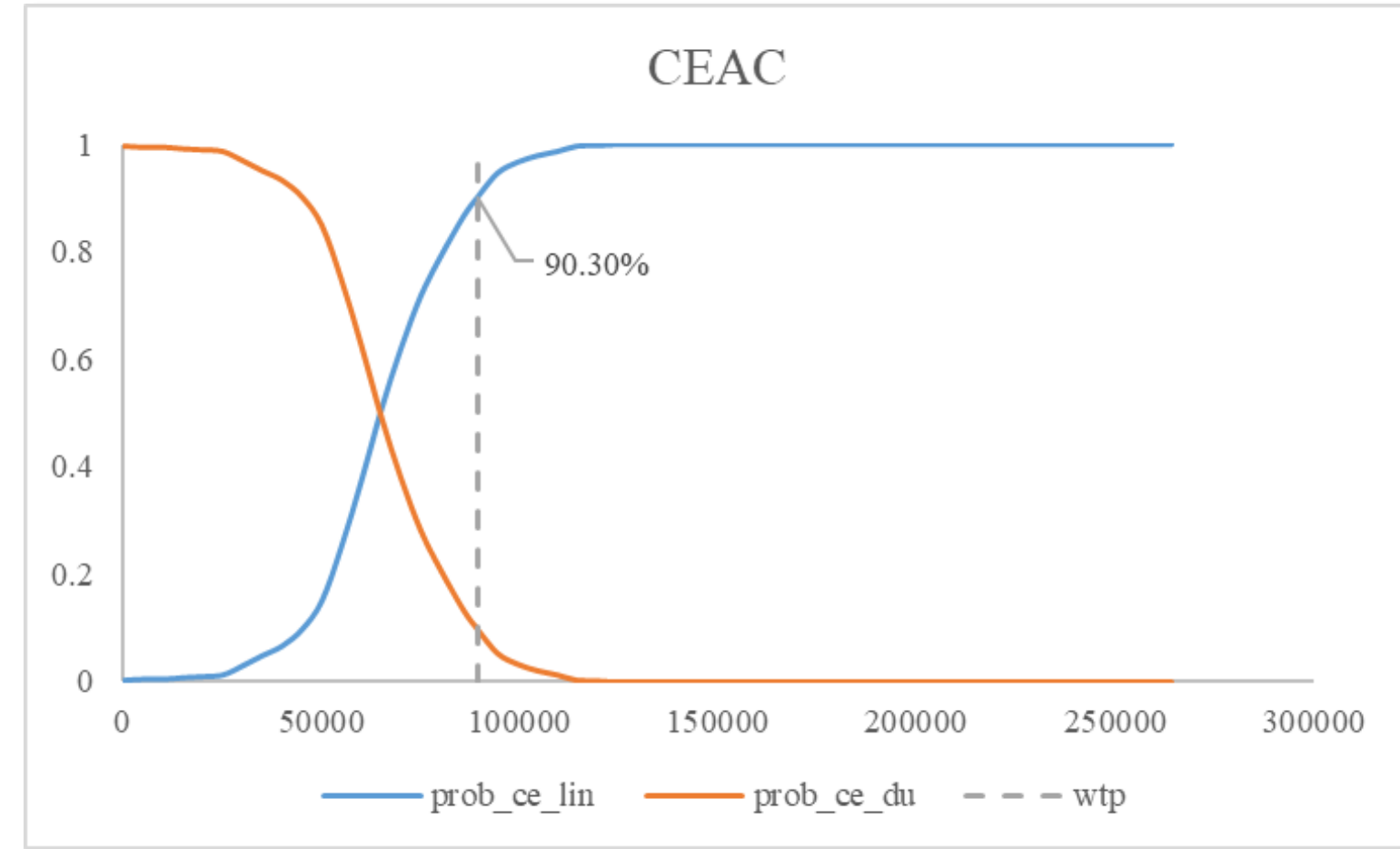


Figure 4. Cost-Effectiveness Acceptability Curve

- The probability of the linperlisib being cost-effective is 90.30%

CONCLUSIONS

- The efficacy of linperlisib is better than duvelisib after matching and adjusted.
- Linperlisib is cost-effective versus duvelisib for the treatment of 3L+ FL in China.

REFERENCES

- GHIONE P, PALOMBA M L, GHESQUIERES H, et al. Treatment patterns and outcomes in relapsed/refractory follicular lymphoma: results from the international SCHOLAR-5 study [J]. Haematologica, 2023, 108(3): 822-32.
- SALLES G, SCHUSTER S J, FISCHER L, et al. A Retrospective Cohort Study of Treatment Outcomes of Adult Patients With Relapsed or Refractory Follicular Lymphoma (ReCORD-FL) [J]. Hemasphere, 2022, 6(7): e745.
- FLINN I W, MILLER C B, ARDESHNA K M, et al. DYNAMO: A Phase II Study of Duvelisib (IPI-145) in Patients With Refractory Indolent Non-Hodgkin Lymphoma [J]. J Clin Oncol, 2019, 37(11): 912-22.
- WANG T, SUN X, QIU L, et al. The Oral PI3K δ Inhibitor Linperlisib for the Treatment of Relapsed and/or Refractory Follicular Lymphoma: A Phase II, Single-Arm, Open-Label Clinical Trial [J]. Clin Cancer Res, 2023, 29(8): 1440-9.