Cost-effectiveness of trastuzumab rezetecan versus trastuzumab deruxtecan for the subsequent-line treatment of advanced HER2-mutant non-small-cell lung cancer: application of a matching-adjusted indirect comparison

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BACKGROUND

- HER2 mutations occur in 2–4% of NSCLC globally and 3.8–5.6% in Chinese patients, with poor prognosis under conventional therapy (median OS <15 months in real-world cohorts).
- Two HER2-directed antibody-drug conjugates (ADCs) are now available in China:
  - Trastuzumab deruxtecan (T-DXd) – global Phase II evidence (DESTINY-Lung02/05); NCCN & CSCO recommended.
  - Trastuzumab rezetecan (SHR-A1811) – domestically developed; included in China's National Reimbursement Drug List (NRDL) following 2025 price negotiation.
- No head-to-head RCT exists between the two ADCs. Existing CEA only compared T-DXd with chemotherapy/TKIs over a 5-year horizon — outdated and limited.

OBJECTIVES

- **To evaluate the cost-effectiveness of SHR-A1811 versus T-Dxd for the subsequent-line treatment of advanced HER2-mutant NSCLC from the perspective of the Chinese healthcare system.**

METHODS

A cost-utility analysis method was used to simulate the medical costs and health outcomes of patients with advanced HER2-mutant NSCLC with SHR-A1811 and T-DXd .

Study population

- The target population was patients with advanced HER2-mutant NSCLC who had received at least one prior systemic therapy.
- Intervention: trastuzumab rezetecan(SHR-A1811) Control: trastuzumab deruxtecan(T-DXd)

Model structure

- Three states were incorporated into the partitioned survival model (PSM) : progression-free survival (PFS), progressive disease (PD), and death.

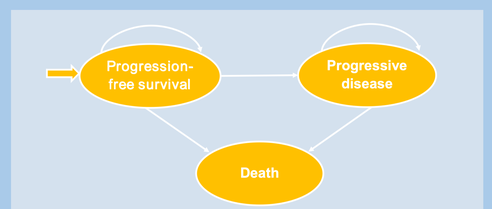

Figure 1. Model structure

Model setting

Table 1. Model setting

Item	Specification
Perspective	Chinese healthcare system (direct medical costs only)
Cycle length	3 weeks (21 days), half-cycle correction
Time horizon	Lifetime
Discount rate	4.5% (annual, costs and outcomes)
Outcomes	Total costs, LYs, QALYs, ICER
WTP threshold	CNY 191,498/QALY (2 × China per-capita GDP, 2024)

Clinical parameters

- **Matching-adjusted indirect comparison**
  - In the absence of head-to-head clinical trials, an unanchored MAIC was used to assess relative efficacy.
  - Individual patient data (IPD) for SHR-A1811: HORIZON-Lung (NCT04818333), N=94.
  - Aggregate data (AgD) for T-Dxd: DESTINY-Lung05 (NCT05246514), N=72.
  - Effective sample size (ESS): 94 → 70 (25.5% reduction).
  - The efficacy of SHR-A1811 was better than T-DXd after matching and adjustment, with PFS benefit (HR 0.89, p=0.588) and statistically significant OS benefit (HR 0.57, p=0.030).
- **Survival functions fitting and extrapolation**
  - Parametric models were used to fit and extrapolate the survival curves, according to AIC/BIC and visual judgment (Figure 2). The Log-normal distribution was selected for T-DXd PFS, the Weibull for T-DXd OS, and the Log-logistic for trastuzumab rezetecan PFS. Trastuzumab rezetecan OS was derived by applying the MAIC-adjusted HR to the T-DXd OS curve, since the proportional hazards assumption held.

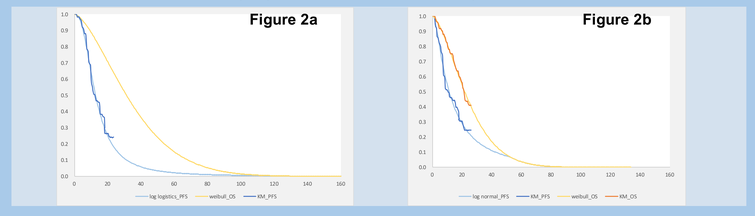

Figure 2. The extrapolating and fitting of SHR-A1811 (2a) and T-DXd (2b)

Utility values

- Utility values were sourced from CheckMate 078 (EQ-5D-3L, Chinese value set).

Table 2. Utility parameters

Utility	Value (range)	distribution
Health state utility		
PFS state	0.82 (0.79,0.85)	beta
PD state	0.76 (0.74,0.79)	beta
AEs disutility		
Grade ≥3 drug-related adverse events	-0.20	Not varied
Grade ≥1 interstitial lung disease	-0.19	Not varied

Cost parameters

- The unit price of drugs is based on the latest negotiated price of medical insurance and the average bid price of each province in the past year. The use and cost data of other medical resources came from the clinical expert consultations of five provinces and cities in China.

Table 3. Cost parameters

Cost	Value（range）
PFS state	
price of SHR-A1811 (per cycle)	9522 (8570,9522)
price of T-DXd	3480 (3132,3480)
follow-up examination of PFS state (per cycle)	1439 (1151,1726)
AEs management cost of SHR-A1811 (one-off cost)	2693(2154,3232)
AEs management cost of T-DXd (one-off cost)	2822(2257,3386)
PD state	
cost of SHR-A1811 in PD state	25441 (20353,30529)
cost of T-DXd in PD state	25441 (20353,30529)
follow-up examination of PD state (per cycle)	1506 (1205,1807)
Death state	
Terminal care cost	6524(5219,7828)

RESULTS

Base case results

- SHR-A1811 was a dominant strategy — yielding both lower total costs and greater quality-adjusted survival than trastuzumab deruxtecan over a lifetime horizon.

Table 4. Base case results

Outcomes	SHR-A1811	T-DXd	Incremental
Total cost (CNY)	333,584	407,247	-73,663
Drug costs in PFS	229,410	323,360	-93,950
Follow-up costs in PFS	34,662	35,554	-892
AE management costs	2,693	2,822	-128
Drug costs in PD	24,273	24,086	187
Follow-up costs in PD	36,792	15,433	21,359
Death costs	5,753	5,992	-239
Total LYs	2.79	2.01	0.78
Total QALYs	2.21	1.61	0.59
ICER(CNY/QALY)	SHR-A1811 dominant		

Scenario analysis results

Table 5. Scenario analysis results

Scenarios	Treatment plan	Costs /CNY	QALYs	ΔCosts	ΔQALY	ICER (CNY/QALY)
Comparing SHR-A1811 against T-DXd using efficacy data from the global DESTINY-Lung02 trial	SHR-A1811	337,069	3.31	-96,636	1.36	SHR-A1811 dominant
	T-DXd	433,705	1.95			

Sensitivity analysis results

- OWSA (Figure 3); Probabilistic sensitivity analysis (Figure 4).

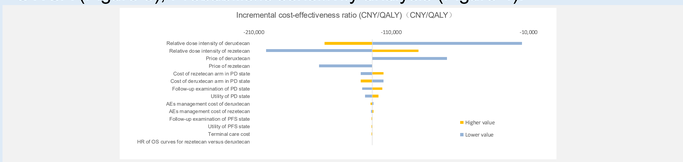

Figure 3. Tornado diagram for base case analysis

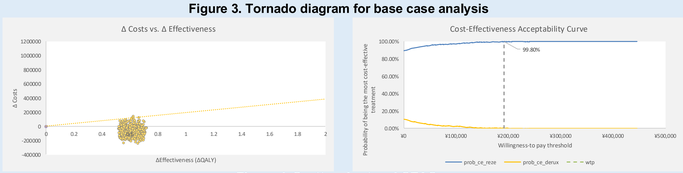

Figure 4. Scatter chart and CEAC

CONCLUSION

- The efficacy of SHR-A1811 was better than T-DXd after matching and adjustment, with statistically significant OS benefit (HR 0.57, p=0.030).
- SHR-A1811 was a dominant strategy versus T-Dxd for the subsequent-line treatment of advanced HER2-mutant NSCLC in China, yielding lower costs and greater QALYs over a lifetime horizon. The result was robust across all sensitivity and scenario analyses.

References

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