EE369

Cost-effectiveness analysis of bireociclib versus abemaciclib in HR+/HER2- advanced or metastatic breast cancer: comparing Matching-Adjusted Indirect Comparison and Simulated Treatment Comparison approaches

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Background and Objective

- Cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitor monotherapy is a recommended option in setting of hormone receptor-positive (HR+) and human epidermal growth factor receptor 2-negative (HER2−) advanced or metastatic breast cancer (ABC/MBC). Bireociclib (BIR) and Abemaciclib (ABE) are both CDK4/6 inhibitors that can be administered as monotherapy and have demonstrated clinical efficacy in their separate randomised clinical trials.
- BIR demonstrated clinically meaningful improvement in progression free survival (PFS) as well as final overall survival (OS) in its single-arm phase II clinical trial BRIGHT-1, with a mPFS of 11 months and a mOS of 29 months.
- MONARCH-1 showed that following treatment with ABE, the mPFS was 6 months and the mOS was 17.7 months.
- In absence of head-to-head data, an population-adjusted indirect treatment comparison is required. Matching-Adjusted Indirect Comparison (MAIC) and simulated treatment comparison (STC) are two well-known methods in the case of no common comparator.
- **Objective**: The objective of this study was to determine the cost effectiveness of BIR versus ABE in patients with HR+/HER2- ABC/MBC who have progressed after endocrine therapies from the Chinese healthcare system perspective, and to compare outcomes generated by two cross-trial adjustment approaches: MAIC and STC.

Methods

➢ **Model structure**

A cohort-based three-state (progression-free, progressed disease, and death) partitioned survival model (shown in Figure 1) was developed with a cycle length of 28-day over a lifetime horizon of 15 years. The discount rate for both effects and costs was 5% per annum.

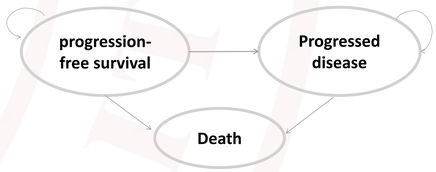

Figure 1. Model structure

➢ **Model inputs**

● **Survival probabilities for BIR and ABE**:

- **Efficiency data source**

  Efficiency data for BIR were obtained from the BRIGHT-1 individual patient data (IPD) supported by *Xuanzhu Biopharm.* For ABE, aggregate data (AGD) were extracted from the MONARCH-1.
- **Indirect treatment comparison**
  - **Scenario 1**: **Unanchored MAIC** were performed. The IPD of BRIGHT-1 were used to align the patient's baseline characteristics with the MONARCH-1. All baseline characteristics were incorporated in the adjustment as detailed in MONARCH-1.
  - **Scenario 2**: **STC** were performed. An outcome model is fitted to IPD, to which the mean relevant characteristics of ABE are applied.
- **Extrapolation of survival outcomes**
  - Parametric distributions, including the Weibull, log-normal, log-logistic, exponential, Gamma, and Gompertz distributions, were used to extrapolate survival outcomes to the lifetime horizon.
  - The goodness of fit of distributions was evaluated using visual inspection and statistical testing (Akaike information criterion and Bayesian information criterion). Since Kaplan-Meier curves for PFS of ABE were not reported in the MONARCH-1, an exponential distribution was used to extrapolate its lifetime PFS outcomes.
  - For ABE, exponential and log-normal were used to explore the impact. For BIR, the best-fitting parametric distributions for the PFS and OS data were log-normal and log-logistic, respectively, in Scenario 1. And both were log-logistic in Scenario 2.
  - The exploration and fitting of PFS and OS are shown in Figures 2. After MAIC, the mPFS and mOS from the fitted curves for BIR were 11.3 and 32.8 months, respectively. After STC the mPFS and mOS were 13.2 and 36.6 months, respectively. In comparison, the results obtained using MAIC was more consistent with the actual survival curves .

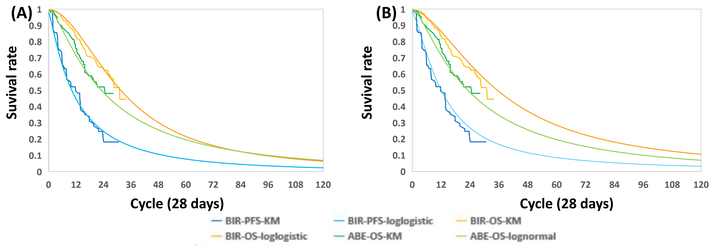

Figure 2. The exploration and fitting of PFS and OS (A: Scenario 1 using MAIC; B: Scenario 2 using STC)

● **Costs, utilities, and mortality data:**

- These data were obtained from literature and national databases, with the price of abemaciclib derived from the latest PharmCube data and that of bireociclib from the 2025 national drug price negotiation.
- Only direct medical costs were estimated, including treatment costs, costs of AE management, costs of subsequent treatment, costs of disease management, follow-up costs, and end-of-life care costs.
- Utility values were assumed similar between treatments (Table 1).

Table 1. Key cost and utility Input

Model parameters	BIR	ABE
Cost （per cycle ）		
PF: Drug acquisition	¥3,377.92	¥5,209.96
PD: Drug acquisition	¥2,207.88	
Follow-up costs	PF:¥811.31; PD:¥840.218	
Utility values		
PF state	0.830（0.747-0.913）	
PD state	0.443（0.399-0.487）	

➢ The primary outcome was the incremental cost-effectiveness ratio (ICER), compared against a willingness-to-pay (WTP) threshold of China's 2024 per-capita GDP (¥95,749).

➢ **Sensitivity analyses**: Deterministic and probabilistic sensitivity analyses were performed to test model robustness.

Results

- **Base case analysis**

In scenario using MAIC-adjusted survival data, bireociclib was the dominant strategy over abemaciclib, providing an additional 0.452 quality-adjusted life-years (QALYs) while saving costs. When applying STC-adjusted data, bireociclib remained cost-effective with an ICER of ¥13,601 per QALY (Tabel 2).

Table 2. Summary of the cost and health outcomes results

Scenario	Treatment	Total cost	Total QALY	Inc. costs*	Inc. QALYs*	ICER
Scenario 1 : MAIC						
	BIR	¥249,895	1.850	-¥9,059	0.452	dominant
	ABE	¥258,954	1.398			
Scenario 2 : STC						
	BIR	285,954	2.099	¥12,605	0.927	¥13,601 /QALY
	ABE	273,349	1.173			

***Inc. Costs, Incremental costs; Inc. QALYs, Incremental quality-adjusted life years**

- **Deterministic sensitivity analyses**

The tornado diagrams of the top 10 most influential key parameters in the two scenarios are presented in Figure 3. According to both scenarios 1 and 2 DSA results, the unit costs of BIR and ABE, the cost of PD, utility of PFS and end-of-life care cost were the main driving parameters .

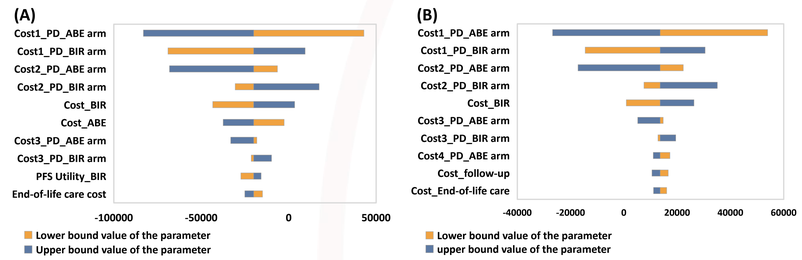

Figure 3. Tornado diagram of ICER in one-way sensitivity analysis (A: Scenario 1; B: Scenario 2)
Cost1_PD, the cost of optimal supportive care during the PD state; Cost2_PD, the cost of chemotherapy during the PD state; Cost3_PD, the cost of other CDK4/6 inhibitors combined with endocrine therapy in the PD state; Cost4_PD, the cost of targeted therapy in the PD state

- **Probabilistic sensitivity analyses**

Probabilistic sensitivity analysis showed that at the WTP threshold, the probability of BIR being cost-effective was 73.9% under the MAIC scenario and 77.4% under the STC scenario (Figure 4).

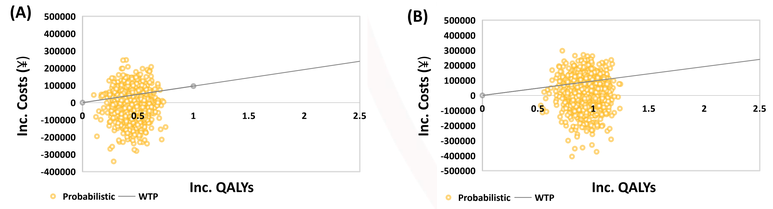

Figure 4. Scatterplot generated in the probabilistic sensitivity analysis (A: Scenario 1; B: Scenario 2)
Inc. Costs, Incremental costs; Inc. QALYs, Incremental quality-adjusted life years;
WTP, willingness-to-pay

Conclusion

Bireociclib was consistently estimated as a cost-effective option compared with abemaciclib in this population. STC showed more positive survival outcomes than MAIC. However, considering the inherent methodological uncertainty in both MAIC and STC, the findings should be interpreted with consideration of these uncertainties, and further validation through head- to- head trials or real- world studies is warranted.

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