COST-EFFECTIVENESS AND BUDGET IMPACT ANALYSIS OF DUAL HER2 BLOCKADE IN HIGH-RISK HER2-POSITIVE EARLY BREAST CANCER IN INDONESIAN PERSPECTIVE

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INTRODUCTION

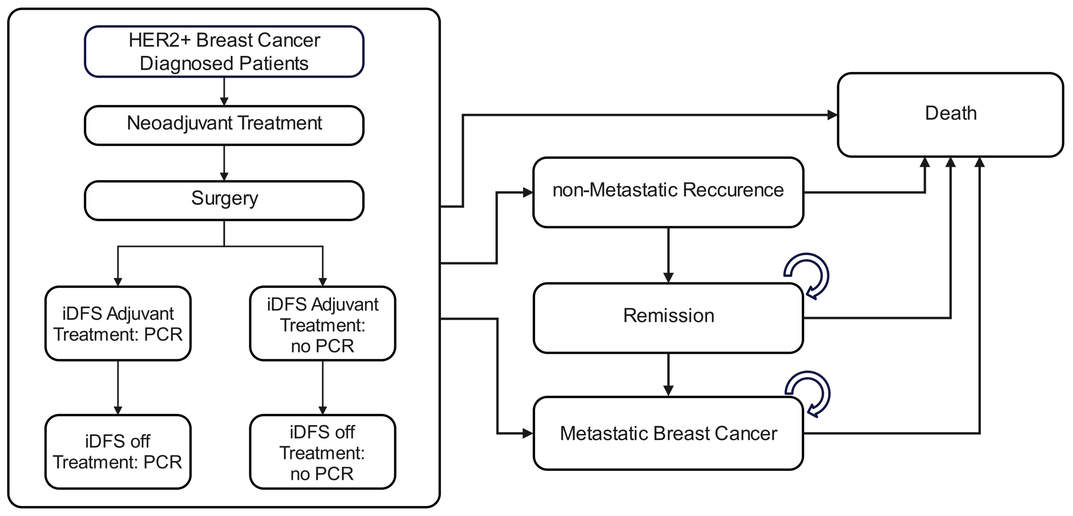
Human epidermal growth factor receptor-2 (HER2) overexpression occurs in 15–20% of breast cancer cases and is associated with more aggressive and poorer clinical outcomes. In Indonesia, the clinical and economic burden of HER2-positive early breast cancer (EBC) remains substantial. While pertuzumab-trastuzumab has demonstrated clinical benefits, its economic value within the Indonesian healthcare system requires further evaluation.

OBJECTIVES

This study evaluates the cost-effectiveness and budget impact of subcutaneous pertuzumab–trastuzumab in combination with chemotherapy in both neoadjuvant and adjuvant settings for patients with HER2-positive early breast cancer in Indonesia.

METHODS

A combined decision tree and cohort-based Markov model (1-month cycle length, 3% annual discount rate for costs and outcomes, lifetime horizon, WTP threshold: 1× 2025 GDP per capita) was developed from the healthcare payer perspective. Patients included were HER2-positive early breast cancer with tumors ≥T2 and node-positive disease. The study assessed the addition of pertuzumab to the standard trastuzumab-chemotherapy regimen in the neoadjuvant setting (6 cycles) and in the adjuvant continuation setting (12 cycles). Patients with residual invasive disease after surgery received standard care. Pooled pCR rates from multiple published sources, including PEONY and APHINITY, informed the decision-tree branches and monthly transition probabilities. A separate 5-year population-based budget impact analysis was conducted.



RESULTS AND DISCUSSION

Cost Utility Analysis

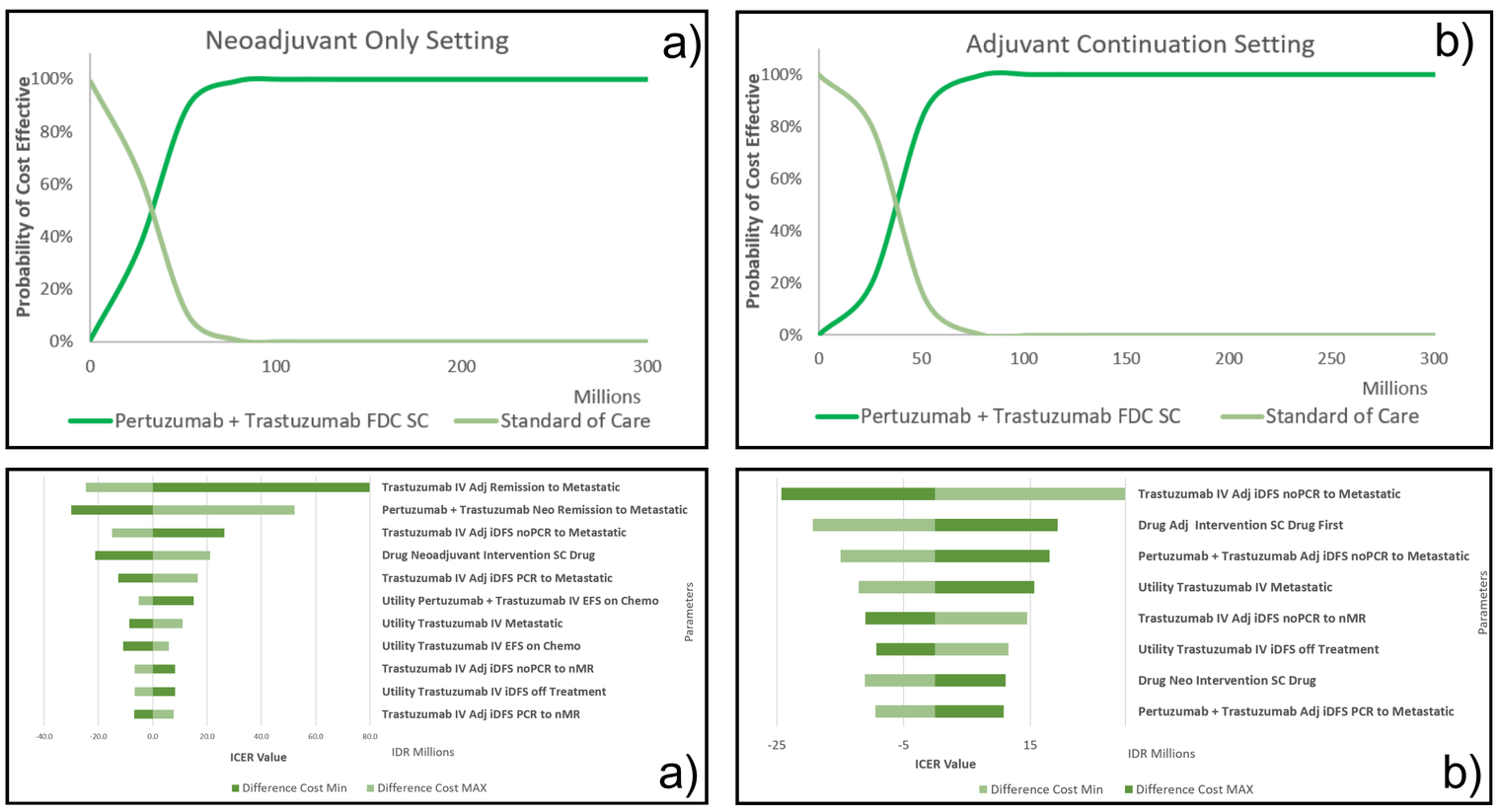
In the neoadjuvant setting, pertuzumab–trastuzumab yielded an ICER of IDR 59,941,272 (USD 3,598) per QALY gained, while in the adjuvant continuation setting the ICER was IDR 77,563,141 (USD 4,652) per QALY gained, with price adjustment of pertuzumab–trastuzumab. The intervention was associated with higher QALYs accompanied by additional costs compared to the comparator, with incremental gains largely attributable to reduced administration time, simplified monitoring, and improved patient convenience

Sensitivity Analysis

Sensitivity analysis indicated that, in the neoadjuvant setting, the most influential variables were transitions from remission to metastatic disease in both the intervention and comparator arms. Within the adjuvant setting, outcomes were primarily driven by the transition of iDFS patients with non-pCR to metastatic disease in the comparator arm, the price of the intervention, and the health-state utility values for metastatic disease and iDFS off-treatment under trastuzumab.

Budget Impact Analysis

Aligned with CEA assumptions, the 5-year budget impact was estimated at IDR 3.8 trillion for Neoadjuvant Only and IDR 8.5 trillion for Adjuvant Continuation, based on eligible population, adoption rates, treatment duration, and e-catalogue drug prices.



Cost Effectiveness Acceptance Curves (CEACs) and One Way Sensitivity Analysis : a) Neoadjuvant; b) Adjuvant Continuation

Both neoadjuvant and adjuvant continuation incurred additional costs but yielded higher QALYs. Pertuzumab-trastuzumab intervention demonstrated a high probability of cost-effectiveness across willingness-to-pay thresholds on the CEAC.

Health and Cost Consequences

Treatment	Incremental Cost vs Standard of Care (IDR 2025)	
	Direct Medical Cost	Direct Non-Medical Cost
Standard of Care	Ref.	Ref.
Neoadjuvant Only	6,015,594	-802,616
Adjuvant Continuation	690,668,620	-11,511,855

*Incremental costs are reported against the Standard of Care.
Direct medical costs: drug acquisition, administration, monitoring, adverse-event management.
Direct non-medical costs: patient/family transport, accommodation, family consumption. Indirect cost were excluded.

The model demonstrates substantial reductions in downstream metastatic-disease-related expenditure, despite higher overall treatment costs. In adjuvant continuation, progression fell from 40% (comparator) to 20% (intervention), yielding a 41.9% cost reduction (IDR 22.9M vs. 13.3M). In the neoadjuvant setting, progression declined from 40% to 30%, lowering metastatic costs by 22.2% (IDR 5.1M) over 5 years.

CONCLUSION

Subcutaneous pertuzumab–trastuzumab fixed-dose combination with chemotherapy demonstrates cost-effectiveness with price adjustment at a willingness-to-pay threshold of one times the 2025 GDP per capita for high-risk HER2-positive early breast cancer in Indonesia, though implementation must consider budget impact and health system affordability

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