Economic evaluation of trastuzumab in HER2-positive early breast cancer in Indonesia: a cost-effectiveness analysis

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Introduction

- Trastuzumab has significantly enhanced the survival and prognosis of individuals diagnosed with human epidermal growth factor receptor 2 (HER2)-positive early breast cancer[1-3].
- The final analysis of the HERceptin Adjuvant (HERA) trial, with a median follow-up of 11 years, suggested that the administration of trastuzumab for a one-year duration following chemotherapy in individuals diagnosed with HER2-positive early breast cancer demonstrated a significant improvement in long-term disease-free survival (DFS)[3].
- Since tumours in younger women diagnosed with breast cancer often exhibit a higher likelihood of being hereditary, bigger sized and higher graded, often lacking estrogen receptor and progesterone receptor expression, which is related to an unfavourable distant recurrence and overall survival (OS)[4], it is also essential to consider heterogeneity in terms of age at diagnosis.
- A joint analysis NSABP B-31 and NCCTG N9831 evaluating the efficacy and safety of trastuzumab by age group found that patients receiving trastuzumab plus chemotherapy under 40 years old have better DFS and OS compared to the older subgroups[1].
- Considering the potentially conceived high acquisition costs of trastuzumab, evaluating its economic consequences and health benefits is crucial.
- Most economic studies assessing the use of trastuzumab have been conducted in Western countries[5-7], but the evidence in Asian regions is still limited.

Objective

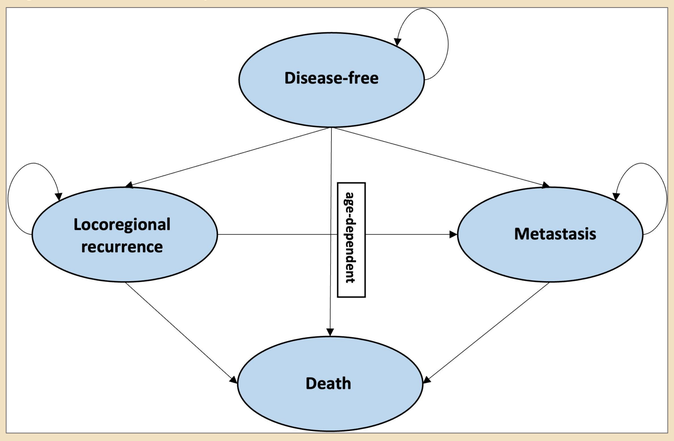
To examine the cost-effectiveness of trastuzumab plus chemotherapy compared with chemotherapy alone for HER-positive early breast cancer in Indonesia from a healthcare payer's perspective. Additionally, we aimed to conduct subgroup analysis based on age at diagnosis to inform clinical decision-making.

Methods

Model structure

- Comparator : taxane-based chemotherapy regimen
- Time horizon : 50 years (lifetime)
- Perspective : healthcare payer

Figure 1. Schematic representation of the Markov model



Patient population

- Baseline characteristics of the hypothetical cohort were based on the pivotal HERA trial which the cohort consisted of women with the median of age 49 years with HER2-positive early breast cancer.

Transition probabilities

- Transition probabilities and treatment effect were based on HERA trial with 11-years follow-up[3].
- Age-dependent transition probabilities were considered for the transition from disease-free to death using the mortality rate in Indonesia reported by the WHO.

Utilities and costs

- Utilities values for each health state were based on a published study from Thailand.
- The cost of trastuzumab per vial (US$ 384/440mg vial) was derived from e-katalog provided by the National Public Procurement Agency (NPPA) Indonesia.
- Costs for health states including costs for disease management and chemotherapy were calculated from verified BPJS Kesehatan reimbursement data from 2020.
- Only direct medical costs were considered since the analysis was conducted from a healthcare payer's perspective.
- The duration of trastuzumab treatment in the disease-free state was one year.
- The Gross Domestic Product (GDP) deflator was used to adjust for inflation.
- All the cost were converted to 2023 US$.

Scenario analysis

- A scenario analysis was conducted based on a joint analysis from NSABP B-31 and NCCTG N9831[1].
- The use of this joint analysis allowed for four different scenarios based on age at diagnosis: <40, 40-49, 50-59, and ≥60 years old.
- The calculation of the scenario analysis was conducted by incorporating the treatment effect (transition probabilities and HRs) for the total study population and each age at diagnosis category into the base-case model.

Model outcomes

- Total lifetime costs, life years, and quality-adjusted life years (QALYs)
- Trastuzumab was considered cost-effective when the ICER fell below 3 times the per-capita GDP (the per-capita GDP for Indonesia was US$4,788).
- Half-cycle correction was applied.
- Costs and utilities were discounted by 3%.

Sensitivity analysis

- A one-way sensitivity analysis and a probabilistic sensitivity analysis (PSA) were performed to evaluate the robustness of the model outcomes.
- Results of the one-way sensitivity analysis were presented in a tornado diagram.
- Results from the PSA were presented in cost-effectiveness planes and cost-effectiveness acceptability curves (CEAC).

Results

Base-case analysis

- The base-case results, using a lifetime horizon, showed total discounted incremental savings of US$11,024 per patient.
- Trastuzumab plus chemotherapy is associated with higher total discounted health benefits of 2.00 LYG and 1.61 QALYs.
- This resulted in an ICER of US$5,510 per LYG and US$6,842 per QALY, which is below the 3 times of WTP threshold (Table 1).

Table 1. Deterministic result of the base-case analysis

	Cost (US$)	LYG	QALY	ICER	
				US$/LYG	US$/QALY
Chemotherapy alone	22,720	8.09	6.48		
Trastuzumab plus chemotherapy	33,744	10.10	8.10		
Difference	11,024	2.00	1.61	5,510	6,842

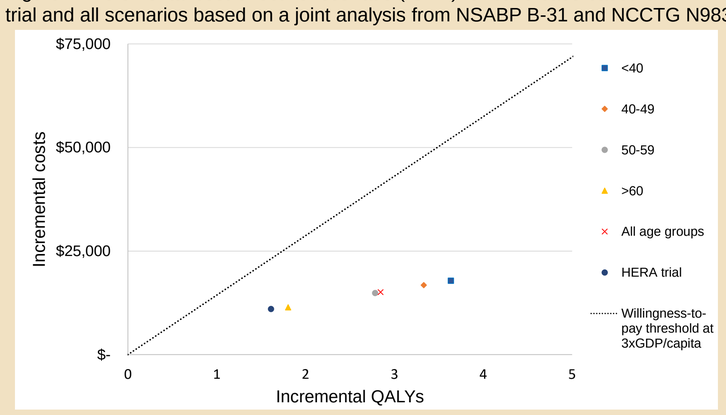
Scenario analysis

- Scenario analysis showed that trastuzumab is most cost-effective in the age at diagnosis below 40 years with an ICER closely approaching the per-capita GDP (Table 2, Figure 2).

Table 2. Deterministic results for the scenario analysis based on a joint analysis from NSABP B-31 and NCCTG N9831

Intervention	Cost (US$)	Life years	QALY	ICER	
				US$/LYG	US$/QALY
Scenario 1 (total population included in the joint analysis)					
Chemotherapy	22,720	8.09	6.48		
Trastuzumab plus chemotherapy	37,913	11.60	9.33		
Difference	11,024	3.51	2.84	4,310	5,309
Scenario 2 (age at diagnosis <40)					
Chemotherapy	22,720	8.09	6.48		
Trastuzumab with chemotherapy	40,573	12.58	10.12		
Difference	17,853	4.49	3.63	3,982	4,912
Scenario 3 (age at diagnosis 40-49)					
Chemotherapy	22,720	8.09	6.48		
Trastuzumab with chemotherapy	39,513	12.20	9.81		
Difference	39,513	4.11	3.33	4,098	5,043
Scenario 4 (age at diagnosis 50-59)					
Chemotherapy	22,720	8.09	6.48		
Trastuzumab with chemotherapy	37,599	11.52	9.27		
Difference	14,879	3.43	2.78	4,342	5,347
Scenario 5 (age at diagnosis >60)					
Chemotherapy	22,720	8.09	6.48		
Trastuzumab with chemotherapy	34,172	10.31	8.29		
Difference	11,453	2.21	1.80	5,174	6,348

Figure 2. Incremental cost-effectiveness ratio (ICER) for base-case based on HERA trial and all scenarios based on a joint analysis from NSABP B-31 and NCCTG N9831



Sensitivity analysis

- The discount rate for utilities emerged as the most influential parameter in the model, followed by the discount rate for costs and the HR for DFS being subsequent in terms of their impact (Figure 3).
- The CEAC illustrates that there was a 96% probability of trastuzumab plus chemotherapy being cost-effective compared to chemotherapy alone from the healthcare payer's perspective (Figure 4—5).
- With 94%, the scenario for women aged 40 or younger showed the highest probability of being cost-effective (Figure 6).
- The scenarios for age at diagnosis of 40-49 and 50-59 years, had lower probabilities of being cost-effective (93% and 91%, respectively).
- The scenario for women above 60 years old had the lowest probability of being cost-effective (82%).

Figure 3. Tornado diagram of one-way sensitivity analysis for the base case

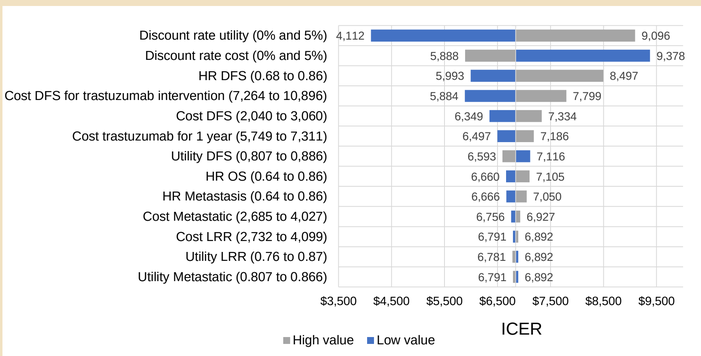


Figure 4. Cost-effectiveness plane from the probabilistic sensitivity analysis based on 1,000 simulations

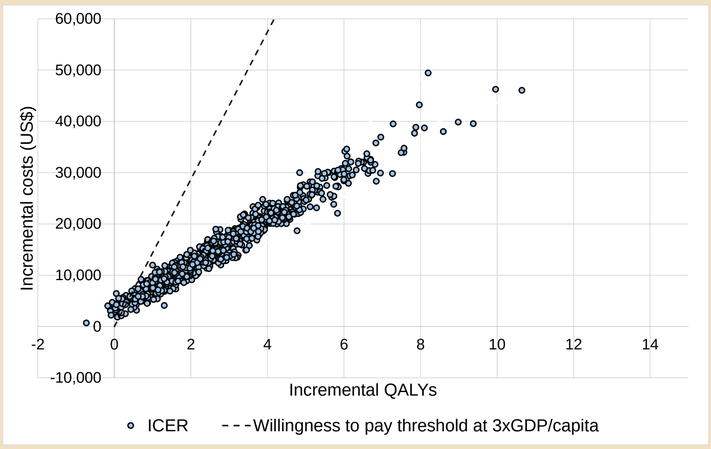


Figure 5. Cost-effectiveness acceptability curve for the base-case analysis

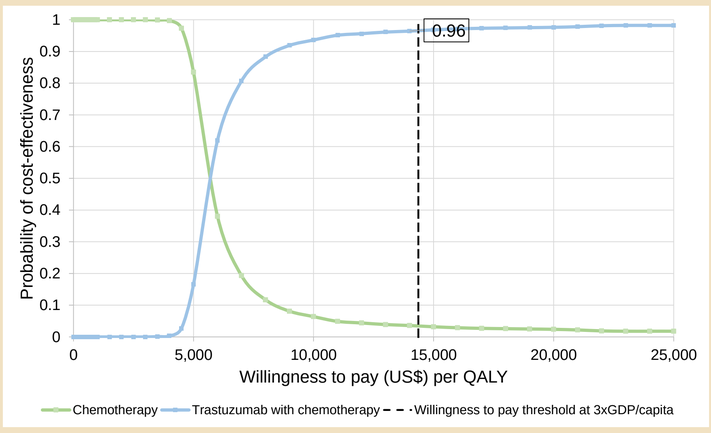
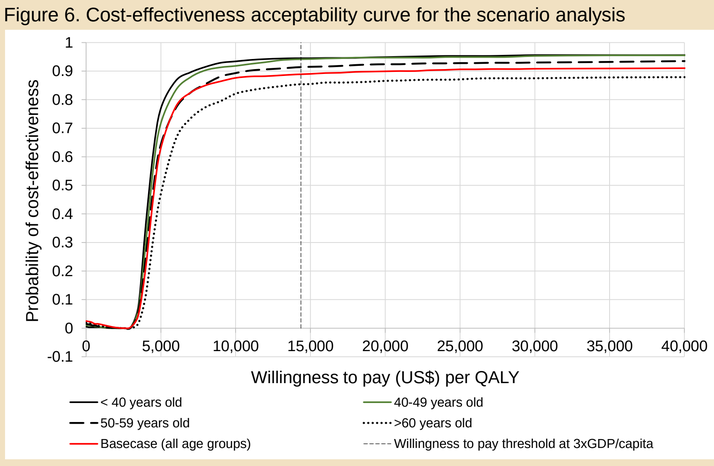


Figure 6. Cost-effectiveness acceptability curve for the scenario analysis



Discussion and conclusion

- One-year of trastuzumab combined with chemotherapy in the HER2-positive early breast cancer treatment is a cost-effective intervention from an Indonesian healthcare payer's perspective at a WTP threshold of 3 times GDP per capita. Sensitivity analysis showed a high probability of being cost-effective (96%). Scenario analysis showed that trastuzumab is most cost-effective in the age at diagnosis below 40 years with an ICER closely approaching the per-capita GDP

Strengths

- The utilization of clinical data derived from comprehensive 11-year analyses of the HERA trials.
- Occupied a time-dependent Markov model to conduct the analysis, incorporating considerations for patient age heterogeneity using the data provided by the trial

Limitations

- Since no clinical trials were conducted in Indonesia, no data were available regarding the drug's efficacy within the Indonesian population
- This analysis does not consider the societal perspective.
- The exclusion of trastuzumab-related cardiotoxicity from the model; however, due to its low incidence rate and based on the sensitivity analyses conducted in prior economic evaluations, it is expected to have only a small impact on the overall cost-effectiveness outcomes.

Conclusion

- Trastuzumab plus chemotherapy can be considered cost-effective in Indonesian breast cancer patients compared with standard chemotherapy alone at three-times GDP and is likely most cost-effective in women <40 years of age, given its substantial impact on long-term clinical outcomes in this age group.

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