

Policy Brief

Executive Summary:

- Breast cancer is the most common cancer among women in India and accounts for 27% of all cancers in that country. Addition of the HER2-targeted mono-clonal antibody trastuzumab to chemotherapy in adjuvant treatment has shown to improve disease-free survival (DFS) by 50% and overall survival (OS) by 30% among human epidermal growth factor receptor (HER)-2 positive early and advanced breast cancers.
- However, trastuzumab is an expensive drug. It was reported to have been used in only 8.6% of eligible patients, half of whom were enrolled in a clinical trial. The low rate of trastuzumab demands evidence on whether public resources should be used to make this treatment routinely accessible in India.
- We used a Markov model to estimate the incremental cost and benefits of using trastuzumab (for 1 year, 6 months, or 9 weeks) as compared to with chemotherapy alone using a societal perspective



Image source: <https://pixels.com/featured/3-human-breast-cancer-sebastian-kaulitzki.html>

- Use of trastuzumab for 1 year is not cost effective in India at the current price. At the current price, 1-year trastuzumab use has just a 4% to 57% probability of being cost-effective.
- However, trastuzumab use for 9 weeks is cost effective and should be included in clinical guidelines and reimbursement policies. A price reduction of 15% to 35% increases the probability of 1-year trastuzumab use being cost effective, to 90%.

Policy

Recommendations:

- One-year use of trastuzumab is not cost effective, or there is significant uncertainty around its cost effectiveness.
- Reducing the price of the drug by 35% would make 1-year trastuzumab use cost effective.
- In the current scenario, use of trastuzumab for 9 weeks is the most efficient option.
- The clinical guidelines and provider payments for cancer treatment under health insurance schemes should be accordingly revised.

Background and Gap in Literature:

Addition of the HER2-targeted mono-clonal antibody trastuzumab to chemotherapy in adjuvant treatment has been shown to improve disease-free survival (DFS) by 50% and overall survival (OS) by 30% [1-3]. However, trastuzumab is an expensive drug. It was reported to have been used in only 8.6% of eligible patients, half of whom were enrolled in a clinical trial [4]. Many cost-effectiveness analyses of trastuzumab have been reported, with variable results [5-13]. A major limitation of the existing literature is that a majority of these model-based cost-effectiveness analyses have based their outcome valuation on the interim results of clinical trials with relatively short follow-up. No cost-effectiveness analysis has yet been published taking into account the long-term clinical benefits based on the Herceptin Adjuvant (HERA) trial (ClinicalTrials.gov identifier: [NCT00045032](https://clinicaltrials.gov/ct2/show/study/NCT00045032)) [3]. Moreover, although a majority of previous economic evaluations have used effectiveness estimates from the HERA trial, the HERA trial protocol is not commonly followed in routine clinical practice by oncologists in India [14].

We undertook this cost-effectiveness analysis of adjuvant trastuzumab in combination with standard chemotherapy compared with chemotherapy alone in the Indian context. The base case presents the analysis for 1-year use of trastuzumab, which is standard practice. Detailed subgroup analyses were also undertaken, and we present cost-effectiveness findings for 6-month and 9-week trastuzumab use.

Aims and Objective

This policy brief addressed the policy question of the cost-effectiveness of adjuvant trastuzumab in combination with standard chemotherapy compared with chemotherapy alone in the Indian context. The study was conducted by the HTAIn Resource center at PGIMER, Chandigarh.

Intervention and control arms:

1. Trastuzumab infusion at 8 mg/kg for the first cycle and 6 mg/kg for the remaining 16 cycles was considered for all patients in the first year.
2. Adjuvant chemotherapy (comprising anthracycline and taxane-based drugs).

Methods and Approach

We undertook this cost-effectiveness analysis (CEA) using a societal perspective, which accounted for both health system and patients' costs. We developed a Markov model and compared the costs and consequences of treating a cohort of patients with surgically resected HER2-positive breast cancer at age ≥ 50 years with adjuvant chemotherapy or adjuvant chemotherapy plus trastuzumab. Our methodological principles are consistent with the Indian reference case for conducting economic evaluations used by the agency for Health Technology Assessment in India (HTAIIn).

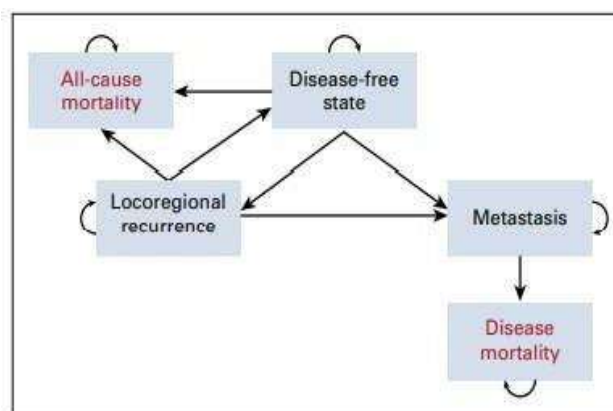


Figure 1: Model schematic

The analysis was performed under the following components:

1. A Markov model with 5 health states—disease-free state, locoregional recurrence (LR), metastasis, death resulting from breast cancer, and all- cause mortality—was developed. Patients with surgically resected HER-2-positive breast cancer entered the model at the age of 50 years.
2. A cycle length of 1 year was considered appropriate based on the available literature. Lifetime horizon was considered in the model.
3. The base case analysis is presented in 2 scenarios. In base case 1, we used the effectiveness evidence from the HERA trial, whereas in base case 2, the effect size of the joint analysis was used; everything else remained constant.
4. The cost of treatment was estimated by using rates of use of various treatment options among patients in different health states, as reported in the pooled data from Indian cancer registries [15]
5. To elicit the unit costs of various diagnostic and therapeutic services provided to these patients, locally published studies [16,17] and provider payment rates under the national social insurance scheme for central government employees [18] were used. Medicine process were obtained from procurement rates of the medical service corporation in Tamil Nadu state [19].

Results:

- The incremental cost per QALY gained was INR 178,877 (HERA trial) and INR 1,34,413 (Joint Analysis of NSABP B-31 and NCCTG N9831 Trials)
- Use of trastuzumab for 1 year is not cost effective in India at the current price. At the current price, 1-year trastuzumab use has just a 4% to 57% probability of being cost-effective.
- However, trastuzumab use for 9 weeks is cost effective and should be included in clinical guidelines and reimbursement policies. A price reduction of 15% to 35% increases the probability of 1-year trastuzumab use being cost effective, to 90%.

	1 Year Trastuzumab Use		
Finding (discounted)	HERA Trial	Joint Analysis of NSABP B-31 and NCCTG N9831 Trials	SC
Lifetime cost per patient, INR	3,41,046	3,37,935	1,10,151
Health consequences per patient			
LYs	8.3	8.7	6.8
QALYs	6.6	7	5.3
Incremental cost, INR	2,30,895	2,27,784	
Incremental benefit			
LYs	1.48	1.93	
QALYs	1.29	1.69	
ICER			
INRs per person LY gained	1,56,291	1,18,096	
INRs per person QALY gained	1,78,877	1,34,413	

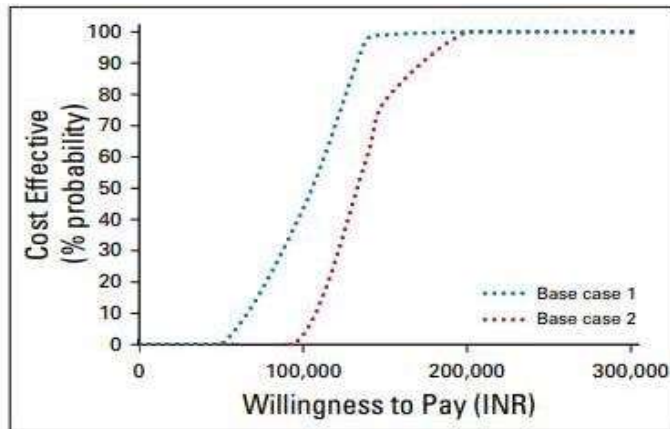


Figure 2: Probability of 1-year trastuzumab use being cost effective at varying willingness-to-pay thresholds. INR, Indian national rupees

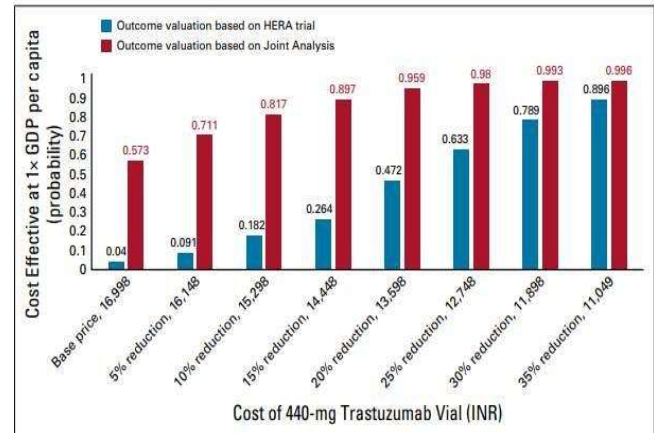


Figure 3 Price sensitivity analyses for cost-effectiveness of 1-year trastuzumab use. GDP, gross domestic product; INR, Indian National Rupee

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