Cost Effectiveness of Trastuzumab for Management of Breast Cancer in India

Nidhi Gupta, MD1; Rohan Kumar Verma, MSc2; Sudeep Gupta, DM3; and Shankar Prinja, MD2

abstract

PURPOSE We undertook this study to evaluate the incremental cost per quality-adjusted life-year (QALY) gained with use of adjuvant trastuzumab as compared with chemotherapy alone among patients with nonmetastatic breast cancer in India.

METHODS We used a Markov model to estimate the incremental cost of using trastuzumab (for 1 year, 6 months, or 9 weeks) as compared with chemotherapy alone using a societal perspective, excluding indirect productivity losses. Although the outcomes (QALYs) in the standard chemotherapy arm were estimated after calibrating the model as per survival data from 2 Indian cancer registries, effectiveness estimates from the HERA trial and a joint analysis of the NSABP B-31 and NCCTG N9831 trials were used to estimate the consequences of 1-year trastuzumab use. The cost of treatment was estimated using national standard treatment guidelines and real-world use estimates for different treatment modalities as per data from Indian cancer registries. Probabilistic sensitivity analysis was undertaken to evaluate parameter uncertainty.

RESULTS For 1 year of trastuzumab use, the incremental benefit per patient, incremental cost per QALY gained, and probability of being cost effective using HERA trial estimates were 1.29 QALYs, 178,877 Indian national rupees (INRs; US$2,558), and 4%, respectively, whereas the corresponding figures using joint analysis estimates were 1.69 QALYs, INR 134,413 (US$1,922), and 57.3%, respectively.

CONCLUSION Use of trastuzumab for 1 year is not cost effective in India at the current price. 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%.

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INTRODUCTION

Breast cancer is the most common cancer among women in India and accounts for 27% of all cancers in that country.1 Overexpression of the oncogene human epidermal growth factor receptor 2 (HER2/neu) is associated with poor prognosis and high risk of recurrence.2-4 Addition of the HER2-targeted monoclonal antibody trastuzumab to chemotherapy in adjuvant treatment has been shown to improve disease-free survival (DFS) by 50% and overall survival (OS) by 30%.5-7 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.8 The low rate of trastuzumab use raises the important question of whether public resources should be used to make this treatment routinely accessible in India. This question is highly relevant because of the recently announced ambitious Indian health insurance program, Ayushman Bharat, which includes coverage of chemotherapy for cancer treatment under the Prime Minister’s Jan Aarogya Yojana (PMJAY) component.9,10 Many cost-effectiveness analyses of trastuzumab have been reported, with variable results.11-19 The variability in findings can be attributed to differences in perspective, modeling method, context, health care delivery structure, price, and other input parameters. 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).7 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.20 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.

METHODS

Model Overview

A Markov model was developed for HER2-positive breast cancer in Indian women (Fig 1). The 5 health states were as follows: disease-free state, locoregional recurrence (LR), metastasis, death resulting from breast cancer, and all-cause mortality. Ten percent of those who developed LR were assumed to revert back to a disease-free state in the subsequent year.21 Thereafter, no remission from LR to back to a disease-free state was possible. Transition probability from LR to metastasis was 3 times that of disease-free state to metastasis.

CONTEXT

Key Objective

Is the use of Trastuzumab cost effective for patients with nonmetastatic breast cancer in low-income countries like India?

Knowledge Generated

Addition of trastuzumab to chemotherapy in the adjuvant setting for 1 year was not cost effective at the current price, but addition of trastuzumab for 9 weeks was cost effective. At the current price, 1-year trastuzumab use has just a 4% to 57% probability of being cost effective. In contrast, 9-week adjuvant trastuzumab therapy incurs an incremental cost per quality-adjusted life-year gained, ranging from 34,268 Indian national rupees (INRs; US$490) to INR 43,264 (US$619).

Relevance

Nine weeks of adjuvant trastuzumab is an efficient option for use in India and other low-income countries where a large majority of patients do not experience the benefits of trastuzumab because of its cost.

We modeled the lifetime 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 from a societal perspective. Both health system costs and out-of-pocket expenditures were estimated. Indirect costs resulting from productivity losses were not included. Outcomes were calculated on the basis of life-years (LYs) and quality-adjusted LYs (QALYs) gained. All future costs and consequences were discounted at 3% considering international best practices, as well as recently published Indian guidelines for economic evaluation.22-24 A cycle length of 1 year was considered appropriate based on available literature.16,18,19,20 Results are reported as incremental cost (Indian national rupee [INR]) per LY and QALY gained with use of trastuzumab. As per guidelines for health technology assessment in India, we used a threshold of per-capita gross domestic product (GDP) in 2019 to evaluate cost effectiveness.23

Intervention and Control

We considered 1 year of trastuzumab along with adjuvant chemotherapy as an intervention and adjuvant chemotherapy (comprising anthracycline and taxane-based drugs) as a counterfactual group in the base case analysis. 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. Three alternative intervention scenarios were considered based on the duration of trastuzumab use: 1 year, 6 months, and 9 weeks, respectively. Patients in a disease-free, LR, or metastatic state were assumed to be managed as per standard international (National Comprehensive Cancer Network) and national (Indian Council of Medical Research) guidelines27,28 (Table 1).

Cost

Trastuzumab infusion at 8 mg/kg for the first cycle and 6 mg/kg for the remaining 16 cycles was considered for all
**TABLE 1.** Clinical Parameters for Assessing Cost Effectiveness of Adjuvant Trastuzumab Versus Chemotherapy

| Parameter                        | Base Value | 95% CI          | Source |
|----------------------------------|------------|-----------------|--------|
| **Utility**                      |            |                 |        |
| Disease free in first year       | 0.749      | 0.579 to 0.919  | 16     |
| Disease free after first year    | 0.847      | 0.703 to 0.991  | 16     |
| LR                               | 0.81       | 0.673 to 0.947  | 16     |
| Metastatic                       | 0.484      | 0.402 to 0.566  | 16     |
| **Transition probability**       |            |                 |        |
| **Standard chemotherapy**        |            |                 |        |
| Disease free to LR               | 0.049      | 0.043 to 0.055  | 42,44  |
| Disease free to metastatic       | 0.084      | 0.074 to 0.094  | 42,44  |
| LR to metastatic                 | 0.231      | 0.205 to 0.258  | 42,44  |
| Metastatic to DC                 | 0.73       | 0.647 to 0.813  | 42,44  |
| Disease free to ACM              | 0.009      | 0.008 to 0.01   | 49     |
| LR to ACM                        | 0.009      | 0.008 to 0.01   | 49     |
| LR to disease free (second year only) | 0.1 | 0.089 to 0.111  | 21     |
| **1-year trastuzumab**           |            |                 |        |
| **Year 1**                       |            |                 |        |
| Disease free to LR               | 0.021      | 0.018 to 0.023  | 47     |
| Disease free to metastatic       | 0.035      | 0.031 to 0.039  | 47     |
| Metastatic to DC                 | 0.73       | 0.647 to 0.813  | 43,44  |
| Disease free to ACM              | 0.009      | 0.008 to 0.01   | 49     |
| LR to ACM                        | 0.009      | 0.008 to 0.01   | 49     |
| LR to metastatic                 | 0.097      | 0.086 to 0.108  | 47     |
| **Year 2**                       |            |                 |        |
| Disease free to LR               | 0.026      | 0.023 to 0.029  | 48     |
| Disease free to metastatic       | 0.045      | 0.039 to 0.05   | 48     |
| Metastatic to DC                 | 0.73       | 0.647 to 0.813  | 43,44  |
| Disease free to ACM              | 0.009      | 0.008 to 0.01   | 49     |
| LR to ACM                        | 0.009      | 0.008 to 0.01   | 49     |
| LR to metastatic                 | 0.123      | 0.109 to 0.137  | 48     |
| LR to DFS                        | 0.053      | 0.047 to 0.059  | 48     |
| **Years 3-15**                   |            |                 |        |
| Disease free to LR               | 0.037      | 0.033 to 0.041  | 7,45,46|
| Disease free to metastatic       | 0.064      | 0.057 to 0.071  | 7,45,46|
| Metastatic to DC                 | 0.73       | 0.647 to 0.813  | 43,44  |
| Disease free to ACM              | 0.009      | 0.008 to 0.01   | 49     |
| LR to ACM                        | 0.009      | 0.008 to 0.01   | 49     |
| LR to metastatic                 | 0.176      | 0.156 to 0.196  | 7,45,46|
| **Years 16-20**                  |            |                 |        |
| Disease free to LR               | 0.049      | 0.043 to 0.055  | 43,44  |
| Disease free to metastatic       | 0.084      | 0.074 to 0.094  | 43,44  |
| Metastatic to DC                 | 0.231      | 0.205 to 0.258  | 43,44  |
| Disease free to ACM              | 0.73       | 0.647 to 0.813  | 49     |
| LR to ACM                        | 0.009      | 0.008 to 0.01   | 49     |
| LR to metastatic                 | 0.009      | 0.008 to 0.01   | 43,44  |

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TABLE 1. Clinical Parameters for Assessing Cost Effectiveness of Adjuvant Trastuzumab Versus Chemotherapy (Continued)

| Parameter                                                                 | Base Value | 95% CI | Source |
|----------------------------------------------------------------------------|------------|--------|--------|
| HR for DFS from HERA trial, year                                          |            |        |        |
| 1                                                                          | 0.42       | 47     |        |
| 2                                                                          | 0.53       | 48     |        |
| 3-4                                                                       | 0.76       | 45     |        |
| 5-8                                                                       | 0.76       | 46     |        |
| 9-15                                                                      | 0.76       | 7      |        |
| HR for DFS from joint analysis of NSABP B-31 and NCCTG N9831 trials       |            |        |        |
| Year 1-15                                                                 | 0.6        | 6      |        |
| Discount rate, %                                                           | 3          | 22-24  |        |
| Proportion of patients requiring management in trastuzumab and SC arms, % |            |        |        |
| LR                                                                        |            |        |        |
| Surgery                                                                   | 88.1       | 31     |        |
| Radiotherapy                                                               | 57.6       | 31     |        |
| Chemotherapy                                                               | 85         | 31     |        |
| Hormone therapy                                                           | 38.4       | 31     |        |
| Tamoxifen                                                                 | 50         |        |        |
| Aromatase inhibitor                                                        | 50         |        |        |
| Metastasis                                                                 |            |        |        |
| Surgery                                                                   | 18.8       | 31     |        |
| Radiotherapy                                                               | 36.1       | 31     |        |
| Chemotherapy                                                               | 85.7       | 31     |        |
| Hormone therapy                                                           | 42.6       | 31     |        |
| Line of therapy                                                           |            |        |        |
| Hormone therapy                                                           | 42.6       | 31     |        |
| First                                                                     | 95         | Expert opinion |
| First and second                                                          | 5          | Expert opinion |
| Chemotherapy                                                               | 85.7       | 31     |        |
| First                                                                     | 75         | Expert opinion |
| First and second                                                          | 20         | Expert opinion |
| First, second, and third                                                  | 5          | Expert opinion |
| Disease free                                                              |            |        |        |
| Hormone therapy                                                           | 50         | Expert opinion |
| Tamoxifen                                                                 | 50         | Expert opinion |
| Aromatase inhibitor                                                        | 50         | Expert opinion |
| Average trastuzumab daily dose in first year, mg/kg                        | 8 for first cycle and 6 for next 16 cycles | 47     |        |
| Survival rate in SC arm, %                                                |            |        |        |
| At 5 years                                                                 | 66.1       | 43     |        |
| At 10 years                                                                | 35         | 44     |        |

Abbreviations: ACM, all-cause mortality; DC, death resulting from breast cancer; DFS, disease-free survival; LR, locoregional recurrence; SC, standard chemotherapy.

patients in the first year in the intervention arm, assuming an average weight of 60 kg. The average weight of women with breast cancer in India was assumed as per findings of previous studies.29,30 The cost for those with a disease-free health state in the intervention arm accounted for outpatient (OPD) oncology and cardiac consultation, electrocardiogram, echocardiography, mammography, and hormone therapy. For those with LR, the cost accounted for...
Valuation of Consequences

Eight studies modeled consequences using effectiveness estimates reported in the HERA trial, whereas 6 used the joint analysis of NSABP B-31 (ClinicalTrials.gov identifier: NCT00004067) and NCCTG N9831 (ClinicalTrials.gov identifier: NCT00898898) trials. The HERA trial reported OS and DFS over a longer follow-up period and reported hazard ratios (HRs) at multiple time points, but this protocol is not commonly practiced in India or elsewhere. Moreover, crossover of patients between study arms was likely to have led to an underestimation of the benefits of adjuvant trastuzumab. The joint analysis reported a greater benefit, with an HR of 0.60, and its protocol is commonly followed in routine practice. Therefore, we used the efficacy data from both analyses to separately report the outcomes and cost effectiveness of 1 year of trastuzumab in 2 separate base case analyses.

The CONCORD study, which used data on survival outcomes from 2 Indian cancer registries, reported 5-year survival of 66.1%. Similarly, another Indian study that reported long-term outcomes found a 35% survival rate at 10 years. We calibrated the model in the control arm (because use of trastuzumab has been reported in India among only 8.6% of eligible patients) so that the survival rates were as reported for the Indian patient population. Furthermore, using the DFS HRs from the HERA trial at each of the 5 different time points, from the first to 11th year, we applied the year-wise HRs to the control arm transition probabilities to arrive at the intervention arm transition probabilities. For the 12th to 15th years, we assumed the same HR reported in the HERA trial for 11th year; beyond year 15, we did not assume any further trastuzumab effectiveness. For computing the transition probability in the intervention arm using the effectiveness estimate of the joint analysis, we used an HR of 0.60 for each year up to 15 years.

Sensitivity Analysis

A probabilistic sensitivity analysis using second-order Monte Carlo simulation was undertaken. The values for transition probability varied by 10%, whereas values for both utility and cost varied by 20% each around the base value. Beta distribution was used to parameterize transition probability and health state utility values. Similarly, gamma distribution was used for cost parameters. The number of iterations was restricted to 1,000.

We undertook a subgroup analysis to assess the cost effectiveness of 6-month and 9-week trastuzumab use compared with standard chemotherapy. The HRs for DFS and cardiac events with 6 versus 12 months of trastuzumab use were derived from estimates reported in 2 trials, PERSEPHONE and PHARE, respectively. Because the estimates of each of the 2 trials were slightly different, the incremental cost-effectiveness ratios (ICERs) were computed separately using the HR for DFS reported in each trial. The HRs for DFS of 1.07 and 1.08 as reported in the PERSEPHONE and PHARE trials, respectively, were applied to the transition probabilities of 1-year trastuzumab use as computed earlier in the base model to derive transition probabilities for 6-month trastuzumab use. The probability of dying with metastasis was similar to that of the base case. Similarly, transition probabilities for 9-week
| Parameter                                                                 | Unit Cost | 95% CI          | Source |
|---------------------------------------------------------------------------|-----------|-----------------|--------|
| **Drug**                                                                  |           |                 |        |
| Annual (lifetime) trastuzumab cost                                         | 241,963   | 173,825 to 275,523 | 35     |
| Daily hormone therapy (tamoxifen)                                          | 0.86      | 0.66 to 1.06    | 35     |
| Daily hormone therapy (letrozole)                                          | 0.58      | 0.41 to 0.72    | 35     |
| Chemotherapy (paclitaxel + docetaxel)                                      | 544       | 436 to 653      | 35     |
| Chemotherapy (zoledronic, 1 vial)                                          | 70        | 54 to 86        | 35     |
| Line therapy, chemotherapy (capecitabine, 1 500-mg tablet)                | 15        | 11 to 18        | 35     |
| Line therapy, chemotherapy (carboplatin + gemcitabine + vinorelbine)      | 2,696     | 2,086 to 3,306  | 35     |
| Line therapy, hormone therapy (fulvestrant)                                | 67,920    | 52,548 to 83,292| 35     |
| **Clinical and radiologic tests**                                          |           |                 |        |
| ECG                                                                        | 18        | 14 to 22        | 33     |
| Echocardiography                                                           | 358       | 277 to 439      | 33     |
| OPD cardiac consultation                                                   | 259       | 109 to 408      | 33     |
| OPD consultation                                                           | 150       | 116 to 184      | 34     |
| Mammography                                                               | 370       | 286 to 454      | 34     |
| Bone scan                                                                 | 3,934     | 3,044 to 4,824  | 34     |
| CBC, BCT, and LFT                                                          | 187       | 84 to 289       | 34     |
| CECT chest                                                                 | 4,500     | 3,482 to 5,518  | 34     |
| CECT abdomen                                                               | 4,500     | 3,482 to 5,518  | 34     |
| Biopsy of recurrence                                                       | 1,257     | 973 to 1,541    | 32     |
| ER, PR, and HER2/neu                                                       | 2,750     | 2,128 to 3,372  | 32     |
| PET scan                                                                  | 14,663    | 11,344 to 17,982| 34     |
| Local mastectomy, simple                                                   | 12,650    | 9,787 to 15,513 | 34     |
| 3D CRT                                                                    | 75,000    | 58,026 to 91,974| 38     |
| Day care                                                                  | 958       | 741 to 1,175    | 32     |
| Chest x-ray                                                               | 60        | 46 to 74        | 34     |
| USG abdomen                                                                | 323       | 250 to 396      | 34     |

NOTE. 1 US$ = INR 69.92.

Abbreviations: BCT, breast-conserving therapy; CBC, complete blood count; CECT, contrast-enhanced computed tomography; CRT, conformal radiation therapy; ER, estrogen receptor; INR, Indian national rupee; LFT, liver function test; OPD, outpatient department; PET, positron emission tomography; PR, progesterone receptor; SC, standard chemotherapy; USG, ultrasound sonography.
trastuzumab use were computed using hazard rates and cardiac events from 9 weeks versus 12 months of trastuzumab separately as reported in the Short HER (HR, 1.13) and FinHER trials.51-53

A threshold analysis was undertaken to ascertain the price at which the ICER value was below the per capita GDP. The threshold was justified based on economic evaluations conducted in India,22 Indian health technology assessment guidelines,23 and a recent oncologic cost-effectiveness analysis conducted in India.54-56

RESULTS

One-Year Trastuzumab: Base Case 1 (HERA trial effectiveness)

The lifetime discounted cost per patient for those receiving 1 year of adjuvant trastuzumab with chemotherapy was found to be INR 341,046 (US$4,878; Table 3). Similarly, patients receiving adjuvant chemotherapy alone incurred a lifetime cost of INR 110,151 (US$1,575). The incremental cost per patient of trastuzumab use was INR 230,895 (US$3,302; Table 3).

The number of QALYs lived per patient among those receiving trastuzumab and chemotherapy alone were 6.6 and 5.3 years, respectively. The incremental health benefits gained per patient after treatment with trastuzumab were 1.48 LYs and 1.29 QALYs.

Overall, our findings show that use of trastuzumab for 1 year would incur an incremental cost of INR 156,291 (US$2,235) per LY gained and INR 178,877 (US$2,558) per QALY gained (Table 3). The value of incremental cost per QALY gained would be more than the per capita GDP of India; therefore, use of trastuzumab for 1 year would not be considered cost effective in the Indian setting.

Subgroup and Sensitivity Analyses

The incremental cost per QALY gained with 6-month trastuzumab use was found to be INR 110,455 (US$1,580) and INR 114,060 (US$1,631) when effectiveness estimates from the PERSEPHONE and PHARE trials, respectively, were used. The incremental cost of 9-week trastuzumab use per QALY gained was found to be INR 43,264 (US$619) and INR 34,268 (US$490) considering the effectiveness reported in the Short HER and FinHER trials, respectively. Each of these ICER estimates falls within the cost-effectiveness threshold of per capita GDP (Table 4).

The findings of cost effectiveness are highly sensitive to the price of trastuzumab, DFS utility after 1 year, and transition probability from a disease-free to metastatic state in the chemotherapy arm. The findings of the probabilistic sensitivity analysis suggest that there is a 4% probability for 1-year trastuzumab use to be cost effective at a willingness-to-pay threshold equal to the per capita GDP (Figs 2 and 3). However, reducing the price by 15% to 35% increases the probability of 1-year trastuzumab use being cost effective to 90% (Fig 3).

| Finding (discounted)          | HERA Trial | Joint Analysis of NSABP B-31 and NCCTG N9831 Trials | SC   |
|-------------------------------|------------|------------------------------------------------------|------|
| Lifetime cost per patient, INR| 341,046    | 337,935                                              | 110,151|
| Health consequences per patient|            |                                                      |      |
| LYs                           | 8.3        | 8.7                                                  | 6.8  |
| QALYs                         | 6.6        | 7.0                                                  | 5.3  |
| Incremental cost, INR          | 230,895    | 227,784                                              |      |
| Incremental benefit            |            |                                                      |      |
| LYs                           | 1.48       | 1.93                                                 |      |
| QALYs                         | 1.29       | 1.69                                                 |      |
| ICER                           |            |                                                      |      |
| INRs per person LY gained      | 156,291    | 118,096                                              |      |
| INRs per person QALY gained    | 178,877    | 134,413                                              |      |

Abbreviations: ICER, incremental cost-effectiveness ratio; INR, Indian national rupee; LY, life-year; QALY, quality-adjusted life-year; SC, standard chemotherapy.
| Source of Effectiveness Data | Cost | QALYs (95% CI) | Cost per QALY Gained | Probability of Cost Effectiveness at per Capita GDP (%) |
|-----------------------------|------|----------------|----------------------|-----------------------------------------------|
|                            | INR  | US$            | Mean INR US$         | 95% CI INR US$                                 |
| 1-year adjuvant trastuzumab use |      |                |                      |                                               |
| HERA trial                  | 133,163 | 1,905          | 1.29 (1.04 to 1.54)  | 104,503 1,495 104,470 to 104,537 1,494 to 1,495 4.0 |
| Joint analysis of NSABP B-31 and NCCTG N9831 trials | 227,915 | 3,260          | 1.69 (1.39 to 1.99)  | 135,713 1,941 135,672 to 135,754 1,940 to 1,942 57.3 |
| 6-month adjuvant trastuzumab use |      |                |                      |                                               |
| PERSEPHONE trial            | 121,331 | 1,735          | 1.09 (0.86 to 1.31)  | 112,957 1,616 112,920 to 112,994 1,615 to 1,616 88.6 |
| PHARE trial                 | 120,954 | 1,730          | 1.06 (0.85 to 1.28)  | 115,282 1,649 115,243 to 115,320 1,648 to 1,649 88.2 |
| 9-week adjuvant trastuzumab use |      |                |                      |                                               |
| Short HER trial             | 39,309 | 562            | 0.91 (0.71 to 1.11)  | 43,702 625 43,684 to 43,719 625 to 625 100.0 |
| FinHER trial                | 64,369 | 921            | 1.88 (1.54 to 2.22)  | 34,600 495 34,588 to 34,612 496 to 495 100.0 |

Abbreviations: GDP, gross domestic product; INR, Indian national rupee; QALY, quality-adjusted life-year.
DISCUSSION

Overall, our findings indicate that trastuzumab use for 1 year is not cost effective at its current price. However, with a 15% to 35% reduction of price, 1-year trastuzumab use would be cost effective. Use of trastuzumab for both 6 months and 9 weeks is cost effective. However, with a statistically similar number of QALYs gained, 9 weeks of trastuzumab use has a lower incremental cost and hence is the most efficient option.

We have presented our results using effectiveness data from a variety of different trials. Second, we used estimates of HRs as reported at different time points (as in the HERA trial) rather than a constant HR, which has been assumed in most of the previous economic evaluations. Third, we calibrated our model for the counterfactual scenario to predict survival based on breast cancer survival from 2 Indian cancer registries. Therefore, our findings are much more pragmatic and representative of the Indian population.

With regard to cost, our parameter values for the cost of management of breast cancer and its complications were obtained from locally published cost studies or reimbursement rates under 1 of India’s largest social insurance programs for provider payments. Similarly, the patterns of treatment use specific to each stage of disease were based on analysis of hospital-based cancer registries. Hence, our cost analysis seems realistic from the national viewpoint.

The incremental gain in LYs has ranged from 0.6 to 2.87 in various studies, whereas QALYs gained have varied from 0.49 to 2.83. We found the incremental health benefit after treatment with trastuzumab to be 1.48 LYs and 1.29 QALYs, both of which are well within the range of values in published evidence.

The incremental cost per QALY gained in terms of purchasing power parity ranges from 4,819 international dollars (Int$) to Int$110,283, with a median value of Int$40,998. Our study finding for an ICER (Int$8,954) fell within this range. The relatively lower ICER for trastuzumab use found in India could be attributable to India’s relatively lower drug prices and differences in health care delivery structure.

Considering the huge disease and economic burden that cancer imposes, several publicly financed health insurance schemes have been implemented in India. The PMJAY, which is the largest tax-funded health insurance scheme for the poor in India, also includes cancer treatment in its benefit package. Given the evidence from our study, it is recommended that insurance schemes provide for 9-week trastuzumab treatment for patients with HER2/neu-positive...
breast cancer. Furthermore, the National Pharmaceutical Pricing Authority should consider reducing the price of trastuzumab by at least 35%, such that 1-year trastuzumab use would also become cost effective. The network of cancer hospitals as part of the National Cancer Grid could develop a mechanism for common procurement of chemotherapy drugs, which would likely bring down prices.20

There has been significant emphasis on the development of standard treatment guidelines based on evidence from health technology assessments.23,61 It is recommended that in addition to clinical evidence on effectiveness, evidence on cost effectiveness be considered while framing clinical guidelines.

Empirically derived evidence on transition probabilities and long-term survival to parameterize such cost-effectiveness models is currently lacking. More research is needed using longitudinal studies. Second, there is a lack of clinical data on quality of life at different stages of cancer survival. In the absence of such a study from India, we had to use a valuation study conducted elsewhere. Finally, we recommend generation of a cost database or reference cost menu that could be used by researchers to populate such economic models. This would help reduce the uncertainty.

In conclusion, our study findings show that 1-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.

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AFFILIATIONS
1Department of Radiation Oncology, Government Medical College and Hospital, Chandigarh, India
2Department of Community Medicine and School of Public Health, Post Graduate Institute of Medical Education and Research, Chandigarh, India
3Tata Memorial Centre and Homi Bhabha National Institute, Mumbai, India

CORRESPONDING AUTHOR
Shankar Prinja, MD, Post Graduate Institute of Medical Education and Research, Sector-12, Chandigarh 160012, India; e-mail: shankarprinja@gmail.com.

AUTHOR CONTRIBUTIONS
Conception and design: Nidhi Gupta, Shankar Prinja
Collection and assembly of data: Nidhi Gupta, Rohan Kumar Verma
Data analysis and interpretation: All authors
Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST
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[References are not displayed here due to the nature of the task. They would typically include a list of scholarly works that have been cited in the text, formatted in a specific academic style.]
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