The Breast 65 (2022) 91–97

Contents lists available at ScienceDirect

The Breast

journal homepage: www.journals.elsevier.com/the-breast

Cost-effectiveness of trastuzumab biosimilar combination therapy and drug wastage as first-line treatment for HER2-positive metastatic breast cancer

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ARTICLE INFO

Keywords:
Cost-effectiveness analysis
Metastatic breast cancer
Trastuzumab
Docetaxel
ICER

ABSTRACT

Background: The rising cost of cancer drug therapy threatens the long-term sustainability of Taiwan National Health Insurance. Cost savings can be achieved through various strategies, e.g., using smaller vial sizes, sharing vials, weight-based dosing, or switching to biosimilars. Here we aimed to examine the cost-effectiveness of a trastuzumab biosimilar combined with docetaxel (TDbiol) for treatment-naïve HER2$^+$ metastatic breast cancer (MBC), and the financial impact of drug wastage.

Methods: A Markov model with three health states was developed to assess the cost-effectiveness of trastuzumab biosimilars plus docetaxel over a 40-month time horizon in patients with HER2$^+$ MBC. Based on the literature and our expert opinion, we assumed similar efficacy between the trastuzumab biosimilar and its reference product. The primary clinical input for the biosimilar was the same as for the reference product in the Catastrophic Patient Database (HV). Health state utilities were derived from the literature, and direct medical costs were obtained from the National Health Insurance Administration (NHIA).

Results: In the base-case scenario, the incremental cost-effectiveness ratio (ICER) was NTD 811,050 per QALY gained. One-way sensitivity analyses showed that the model was sensitive to utilities and transition probabilities, but not particularly sensitive to the wastage assumption. In scenario analyses, the ICER was higher when applying the price for trastuzumab reference biologic (branded), than for trastuzumab biosimilar.

Conclusion: The trastuzumab biosimilar combination regimen is cost-effective and offers significant drug cost savings in Taiwan.

Sponsorship

No funding or grant to support this study.

1. Introduction

In 2020, breast cancer (BC) was the first leading cause of cancer-related death globally, and fourth in Taiwan [1]. Women with metastatic breast cancer (MBC) have a 5-year survival rate of only 28% [2]. Approximately 25.8% of breast cancers overexpress human epidermal growth factor receptor 2 (HER2), which is associated with aggressive growth [3].

In recent decades, neoadjuvant chemotherapy has been used to treat patients with inoperable breast cancer, increasing the proportion of patients who are eligible for breast-conserving surgery. In several clinical trials, patients with HER2$^+$ primary breast cancer treated with neoadjuvant chemotherapy plus trastuzumab have exhibited improved pathologic complete response (pCR) rates, and significantly increased

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https://doi.org/10.1016/j.breast.2022.07.007
Received 3 December 2021; Received in revised form 2 July 2022; Accepted 11 July 2022
Available online 16 July 2022

event-free survival [4–6]. Clinical trials have also demonstrated that the combination of trastuzumab and other HER2 target inhibitors may exert dual HER2 target inhibition, compared to trastuzumab alone, as an adjunct to taxane-based chemotherapy, yielding higher pCR rates [7,8]. In several recent studies, patients receiving dual HER2 blockade with pertuzumab and trastuzumab combined with any chemotherapy regimen, and specifically with anthracycline-based chemotherapy, showed higher pCR rates and lower rates of symptomatic left ventricular systolic dysfunctions, respectively [9–12]. However, the high cost of these biological treatment options may limit their use, and discourage some practitioners from prescribing these drugs.

The expiration of trastuzumab patents in Western countries has allowed development of several trastuzumab biosimilars [13], which is expected to substantially reduce the cost of these regimens [14]. To date, five trastuzumab biosimilars have been approved by the FDA and the European Medicines Agency. In Taiwan, as healthcare expenditures rise each year, healthcare policymakers have developed strategies to overcome budget deficits, including reimbursement for certain drug programs through weight-based dosing or switching to biosimilars to prevent drug waste. Our NHIA has approved reimbursement for four trastuzumab biosimilars—trastuzumab 420 mg and three trastuzumab 440 mg injections—which cost less than the trastuzumab reference biologic; however, clinical use of these biosimilar products is hindered by low acceptance [15]. Here we aimed to explore the impact of trastuzumab biosimilars on the cost-effectiveness of combination therapy, and to identify drug waste in dosing and cost calculations.

2. Methods

2.1. Data source

Biosimilars are highly similar to their reference products in terms of quality, efficacy, safety, and immunogenicity, and must meet the same criteria as the reference biologics [16,17]. Due to their generally lower development costs, biosimilars usually cost less than their reference products. A hypothetical cohort was generated using the clinical data collected from patients who underwent the trastuzumab biologic regimen, which were obtained from the Longitudinal Health Insurance Database (LHID) and the Catastrophic Illness Dataset (HV) from January 2009 to December 2011. Both are sub-databases of Taiwan's National Health Insurance Research Database (NHIRD). LHID contains all original claims data for 1,000,000 beneficiaries randomly sampled from NHIRD. HV is a subject-specific dataset, with a focus on patients diagnosed with catastrophic diseases, such as cancer. NHIRD contains information about encrypted patient demographics, prescription drug records, inpatient and outpatient claims data, dates of visits, length of stay, and laboratory and diagnostic test data. NHIRD accounts for over 99% of Taiwan's 23 million inhabitants [18].

2.2. Study population

Fig. 1 shows the identification process of our study population. Included patients were female, aged 20 years and older, with an ICD-9 diagnosis code for MBC (ICD-9-CM 174.9) and Her-2/neu Fluorescence In Situ Hybridization (FISH) Positive (+) Claim Code (12xxB). All included patients were treated with trastuzumab (ATC Code L01XC03) plus docetaxel (ATC code L01CD02) or docetaxel alone in a 3-week cycle during 2009–2011 after the index date, which was defined as the date of primary diagnosis of MBC. We also collected data regarding other covariates, including gender, comorbidity, CCI score, and other medications (Table 1). Exclusion criteria included receipt of prior chemotherapy or any prior taxane or anti-HER2 therapy, diagnosis with another cancer during the first year of the study period, not receiving at least one cycle of either regimen, and lack of FISH Test data. The primary outcome was median overall survival.

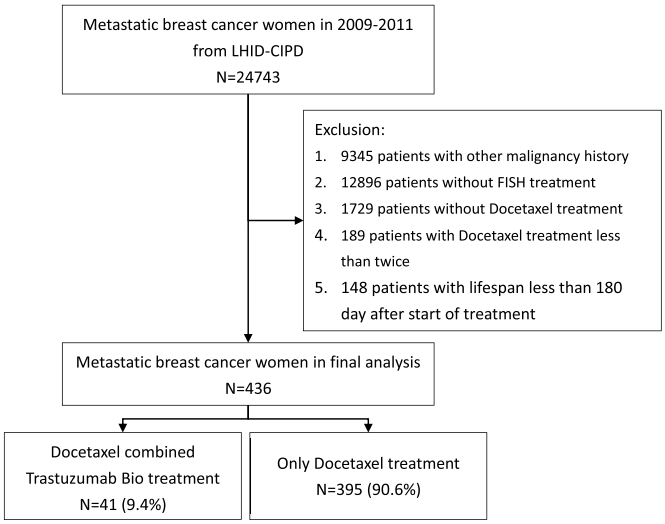

Fig. 1. Study flow chart. LHID-CIPD, Longitudinal Health Insurance Database-Catastrophic Illness Patient Databases.

Table 1
Demographic characteristics between TDbiol vs D.

	T D biol N = 41		Docetaxel alone N = 371		
	n	%	n	%	p-value
Year at diagnosis					0.33
2010	10	24.4	118	31.8	
2011	31	75.6	253	68.2	
Age, year					0.64
<50	17	41.5	167	45.0	
50–64	18	43.9	167	45.0	
65+	6	14.6	37	10.0	
Mean (SD)	52.1	(11.0)	51.6	(9.45)	0.73
CCI score					0.43
0	37	90.2	347	93.5	
1+	4	9.76	24	6.47	
Mean (SD)	0.12	(0.40)	0.07	(0.29)	0.44
Comorbidity					
Hyperlipidemia	10	24.4	89	24.0	0.95
Hypertension	5	12.2	74	20.0	0.23
Sleep disorder	16	39.0	138	37.2	0.82
Anxiety	9	22.0	50	13.5	0.14
Depression	3	7.32	15	4.04	0.41
Obesity	1	2.44	3	0.81	0.34
Alcoholism	0	0.00	0	0.00	
Medication before the end point					
Hormone receptor status	0	0.00	0	0.00	
Prior adjuvant or neoadjuvant chemotherapy					
Cyclophosphamide	36	87.8	346	93.3	0.20
Anthracycline	4	9.76	31	8.36	0.77
Hormone	22	53.7	286	77.1	0.001
Taxane	41	100.0	371	100.0	
Vinorelbine	5	12.2	32	8.63	0.45
Outcomes					
Overall survival, months	18.5		17.8		

Chi-square, Fisher's exact test and *t*-test. TD, trastuzumab biosimilar; D, Docetaxel.

2.3. Markov model

This study followed the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) guidelines for economic evaluation [19]. We created a Markov health-state transition model to simulate cost-effectiveness analysis with TreeAge Pro Suite 2020 software (R1.0 Release; TreeAge Inc., Williamstown, MA) from the perspective of the

Taiwan National Health Insurance Administration (NHIA). Four health states were simulated—stable disease, progressive disease, hospice, and death—according to the experts' opinion and the published literature. The time horizon was 40 months, and three-month cycle lengths were used based on survival data extracted from the HV database. A half-cycle correction was applied for both QALYs and costs. Future costs were discounted at an annual rate of 3% for the relative value of the Taiwan dollar in 2020. The one-time disutility was estimated based on the incidence rate of severe adverse events (SAE), defined as ≥ grade 3, retrieved from the same database. Patients with stable disease were defined as those who received TDbiol until disease progression, unmanageable toxicity, or death. The progression state was defined as patients treated with the next-line regimen until hospice or death and the appearance of adverse events. Following the World Health Organization (WHO) recommendations, the GDP × 3 was used as the willingness-to-pay (WTP) threshold for 2020, which was NTD 2,384,172 (USD 85,149; USD 1 = NTD 28) [20–22].

2.4. Resources usage costs

Resource usage costs—including acquired drug costs, laboratory fees, consultation fees, pharmacy dispensing fees, administrative management fees, nursing care, and other treatment-related fees—were collected in stable state. Estimations of total resource usage costs of salvage chemotherapy and treatment for SAE were collected in the progressive state. The total cost of resource use in the last year of life was retrieved from the HV database, and defined as the cost spent in the hospice state. All costs were presented as NTD in the claim database (Table 2).

In the base case analysis, we calculated the exact drug dose in mg/body weight or body surface area (BSA) as restricted by the reimbursement policy. For example, a vial containing 440 mg of trastuzumab biosimilar is priced at NTD 34,460. We used the mean body weight (58.1 kg) or mean BSA (1.59 m^2) from the Taiwanese female population [23]. For each guideline, the recommended loading dose was 8 mg/kg body weight [24]. Therefore, the total loading dose of trastuzumab biosimilars was calculated as 464.8 mg (equivalent to 1.056 vials). Since the reimbursement unit price of biosimilars was NTD 34,460 per vial, the total cost of trastuzumab biosimilars was NTD 36,390 (USD 1299.6) [15].

Table 2
Direct medical cost imputed in Decision Tree Model.

Parameters	Base-Case Value	Source
Drug Cost	**Unit cost, 2021 NTD**	
Trastuaumab biosimilar 440mg/vial	34,460 (USD1231)	NHI reimbursement price for no dose reduction
Docetaxel 80mg/4mL/vial	11,800 (USD421)	NHI reimbursement price for dose reduction due to SAEs
Administration cost		
Physician OPD visit	356 (USD 13.00)	NHI reimbursement price
Dispensing fee	69 (USD 2.5)	NHI reimbursement price
Follow up monitoring cost		
FISH test	10,400 (USD371)	NHI reimbursement price
Complete blood count	200 (USD 7.00)	NHI reimbursement price
MRI with contrast	13,945 (USD 498)	NHI reimbursement price
Managing grade 3/4 adverse events, **total costs for each patient**		
Anemia	95,309 (USD3404)	Claim data retrieved
Neutropenia	32,964 (USD1177)	Claim data retrieved
Fatigue	47,552 (USD1698)	Claim data retrieved
Diarrhea	2463(USD88)	Claim data retrieved

Remarks: OPD, out-patient department; FISH, Her-2/neu fluorescence in situ hybridization; MRI, magnetic resonance imaging.

2.5. Transition probabilities

We estimated health-state transition probabilities based on the reconstructed individual patient data (IPD) from the Kaplan–Meier (KM) curves according to the algorithm developed by Guyot and colleagues [25–27]. After reconstructing the IPD, the log-normal and gamma distributions were fitted, and the optimal survival function was used to calculate the transition probabilities among health states. The fitting was selected based on the lower value of Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) (Supplementary Table S1 and Fig. S1) [28].

2.6. Effectiveness estimates

Efficacy was defined as QALY, estimated by multiplying the overall survival rate by health state utility [29], as used in previously published cost-effectiveness analyses of trastuzumab [30,31]. Survival rates were obtained from real claims data. For utility values, we considered only severe grade 3–4 toxicities modeled as one-time disutility. Mild grade 1–2 toxicity and chemotherapy toxicity are considered congenital in the metastatic cancer state, and have not been explicitly modeled.

2.7. Sensitivity and scenario analyses

Sensitivity analyses were performed to evaluate the robustness of our model. We assumed the parameter values would change over a range of ±30% based on the values used for the base case (Table 3). One-way sensitivity analysis, presented as a tornado diagram, was performed to identify parameters having the greatest impact on the incremental cost-effectiveness ratio (ICER). Probabilistic sensitivity analysis was simulated by simultaneously varying all parameters with 1000 Monte-Carlo simulations, each run with randomly selected samples from the distributions of model inputs, to assess the impact of uncertainty in the model.

We also performed several scenario analyses to examine how our results were impacted by drug wastage, trastuzumab biosimilar prices, and the addition of pertuzumab to the trastuzumab biosimilar combination regimen. In the first scenario, drug wastage was defined as the difference between the drug amount in the optimal set of vials and the administered amount. Trastuzumab biologic 440 mg/vial/multiple dose (a reconstituted multi-dose solution containing 21 mg/mL trastuzumab) is reimbursed by our NHIA at NTD 43,845/vial (NTD 99.6/mg). To match the reimbursement of the reference brand, we used trastuzumab biosimilar 440 mg/vial/multidose, reimbursed at NTD 34,460/vial (NTD 78.3/mg). The impact of drug waste is shown on a CEA acceptability curve. In the second scenario, we used the price of the trastuzumab biologic instead of the price of the trastuzumab biosimilar, with the same clinical parameter data. In the third scenario, we assumed that pertuzumab was added to a trastuzumab biosimilar combination, based on the doses used in the CLEOPATRA clinical trial [32]. Pertuzumab was given on day 1 of each cycle, starting at a loading dose of 840 mg in the first cycle, and decreasing to a maintenance dose of 420 mg in subsequent cycles, until disease progression or unmanageable toxic effects. The total reimbursement cost for treatment was obtained from the 2021 NHIA reimbursement price list. The utility values and clinical outcomes were assumed to be similar in all scenarios.

3. Results

3.1. Main analysis

In the base-case, the ICER of the TDbiol regimen was NTD 811,050 per QALY gained (USD 28,966; USD 1 = NTD 28), indicating that TDbiol was cost-effective at the WTP threshold of Taiwan.

Table 3
Model parameters values in base case and ranges in sensitivity analyses (±30%).

Parameters	Base estimate	Lower Limit - Upper Limit	Assumed Distribution
Transition Probability			
pStableToProg$_1$ for TD	0.047	0.032–0.061	Gamma
pStableToDead$_1$ for TD	0.046	0.0322–0.0598	Gamma
pStableToHosp1 for TD	0.054	0.0378–0.0702	Gamma
pProgToHospic$_1$ for TD	0.043	0.0301–0.0559	Gamma
pProgToDead1 for TD	0.036	0.0252–0.0468	Gamma
pHospicToDead$_1$ for TD	0.078	0.0546–0.1014	Gamma
pStableToProg for Docetaxel	0.0 43	0.0301–0.0559	LogNormal
pStableToDead for Docetaxel	0.064	0.0448–0.0832	LogNormal
p StableToHospi for Docetaxel	0.052	0.0364–0.0676	LogNormal
pProgToHospi for Docetaxel	0.0595	0.0417–0.077	LogNormal
pProgToDead for Docetaxel	0.073	0.0511–0.0949	LogNormal
pHospicToDead for Docetaxel	0.078	0.0546–0.1014	LogNormal
pStableToStable1 for TD	0.853	0.597–1.1089	Gamma
pProgToProg1 for TD	0.922	0.645–1.1986	Gamma
pHospToHospic1 for TD	0.9215	0.6451–01.198	Gamma
pStableToStable for D	0.841	0.589–1.093	LogNormal
pProgToProg for D	0.867	0.607–1.127	LogNormal
pHospToHospic for D	0.9215	0.6451–01.198	LogNormal
Toxicity grade 3–4			
Trastuzumab + Docetaxel	0.439	0.309–0.569	Beta
Docetaxel	0.466	0.326–0.606	Beta
Effectiveness (e)			
eStable$_1$ for TD	0.635	0.445–0.826	Beta
eStable for Docetaxel	0.590	0.143–0.767	Beta
eProg$_1$ for TD	0.281	0.197–0.365	Beta
eProg for Docetaxel	0.262	0.183–0.341	Beta
eHospice$_1$ for TD	0.469	0.328–0.610	Beta
eHospice for Docetaxel	0.436	0.305–0.567	Beta
Costs (US$=28 NT)at 3% discount, per patient			
cStable$_1$ for TDbiol	253,516	177,461–329,571	PERT
cProg$_1$ for TDbiol	7093	4965–9221	PERT
cHospice$_1$for TDbiol	148,444	103,911–192,977	Normal
cStable for Docetaxel	88,995	62,297–115,694	Normal
cProg for Docetaxel	41,942	29,359–54,525	Normal
cHospice for Docetaxel	82,622	57,835–107,409	Normal
Median overall survival, month			
TDbiol	18.5	13.95–19.06	Beta
Docetaxel	17.8	12.46–23.14	Beta
Total cycle length	40	18–52	Beta

Abbreviations: TDbiol = Trastuzumab biosimilar + Docetaxel; Stable = Progression free survival state; Prog = Progression state; pStableToProg = transition probability from PFS to progression state; pStableToDead = transition probability from PFS to dead state; pProgTo Dead = transition probability from progression to dead state.
Costs are in 2021 dollars 1US = $28 NT).

3.2. Sensitivity and scenario analyses

One-way sensitivity analysis showed that the model was most sensitive to two parameters: the effectiveness of both regimens from steady state to dead state, and the transition probability from stable state to dead state. Two other parameters had a moderate impact on ICER: the transition probability from steady state to dead state, and the total cost of steady state for the TDbiol scheme (Fig. 2). The PSA results demonstrated the robustness of our findings (Fig. 3A).

The wastage assumption in first scenario showed a slight impact on the estimated ICER. Drug wastage was estimated using the loading dose as an example. Based on the loading dose recommendation of 8 mg/kg of body weight, and the average Taiwanese female weight of 58.1 kg, the total loading dose was calculated as 464.8 mg (equivalent to 1.056 vials). Therefore, two vials should be used, and the drug cost for the loading dose would be NTD 68,920 for two vials trastuzumab biosimilar, and NTD 87,690 for two vials trastuzumab biologic. In contrast, if we calculated the loading dose in milligrams, the cost would be NTD 36,394 for biosimilar vs NTD 46,294 for trastuzumab biologic. Therefore, the drug wastage would be about NTD 32,526 when using biosimilar vs NTD 41,396 with trastuzumab biologic. The combination of trastuzumab biosimilar with dose in vial and precise dose in mg/kg had cost-effective acceptability curves of 71% and 76%, respectively (Fig. 3A and B).

The second scenario analysis showed that when using the price of the trastuzumab biologic instead of the price of the trastuzumab biosimilar, the cost would increase by NTD 693,063 (USD 24,752), and ICER would increase approximately NTD 298,724 (USD 10,669) (Table 4). This difference was because the trastuzumab biologic cost approved for reimbursement in 2021 is NTD 43,845, which is 1.27 times that of the trastuzumab biosimilar (TWD 34,460) [31]. Thus, using trastuzumab biosimilars as conventional therapy for first-line treatment of HER2$^+$ metastatic breast cancer would yield an annual cost savings per patient of approximately NTD693,063 (USD 24,752).

The third scenario indicated that adding pertuzumab to either the trastuzumab biologic regimen (PTR) or the biosimilar regimen (PTbiol) was not cost-effective because the ICER (NTD 2,838,560 for PTR vs NTD 2,689,761 for PTbiol) was above the WTP threshold (NTD 2,384,172).

4. Discussion

Our NHIA has approved reimbursement for trastuzumab monotherapy for HER2$^+$ MBC following one or more chemotherapy regimens, or in combination with paclitaxel or docetaxel for naïve HER2$^+$ MBC, or in combination with pertuzumab and docetaxel for HER2$^+$ MBC. A recent study indicates that trastuzumab monotherapy can be considered as an adjuvant therapy for selected older populations [33,34], and it is also approved for the treatment of HER2$^+$ early breast cancer and advanced MBC [35]. However, targeted combination therapies represent a financial burden for healthcare payers because most regimens are not cost-effective. Trastuzumab biosimilars are now available in Taiwan and may be cost-saving, but their clinical use is limited by low acceptability. To our knowledge, this is the first study to evaluate the cost effectiveness of trastuzumab biosimilar combination therapy for HER2$^+$ MBC, and to account for drug wastage.

Our analysis revealed an improved ICER with the trastuzumab biosimilar combination [TWD 811,050 (USD 28,966) per additional QALY], compared to the trastuzumab reference biologic [NTD 1,109,774 (USD 39,635) per additional QALY]. The ICER difference largely resulted from the acquired cost difference incurred in the stable state: NTD 43,845 for trastuzumab reference biologic vs NTD 34,460 for trastuzumab biosimilar. Moreover, the use of trastuzumab biosimilar significantly reduces incremental costs by approximately NTD 693,062 (USD 24,752) (Table 4). When using the HER2-targeted combination, an estimated cost savings of approximately 26.9% per patient was associated with use of trastuzumab biosimilar compared to the trastuzumab reference biologic. These findings were consistent with the results recently published by Sussell et al., which demonstrated that use of a trastuzumab biosimilar led to an approximately 30% reduction in the cost of HER2-targeted therapy compared to a reference trastuzumab [36].

The cost impact of biosimilar switching is particularly important as cancer treatment costs increase due to growing numbers of cancer patients and the high prices of new innovative anticancer biologics. In many countries, Oncology Care Models (OCMs) have been developed to facilitate value-based care planning, to replace fee-for-service reimbursement models, with the ultimate goal of controlling rising cancer treatment costs. However, the prices of newly developed oncology biologics continue to rise, severely impacting the sustainability of national healthcare systems worldwide, especially in countries without universal health care systems and price monitoring policies. Healthcare providers, medical oncologists, and society in general are increasingly concerned about the cost of cancer treatment, drawing attention to the fair pricing of new treatments, which must reflect true benefits to patients, and

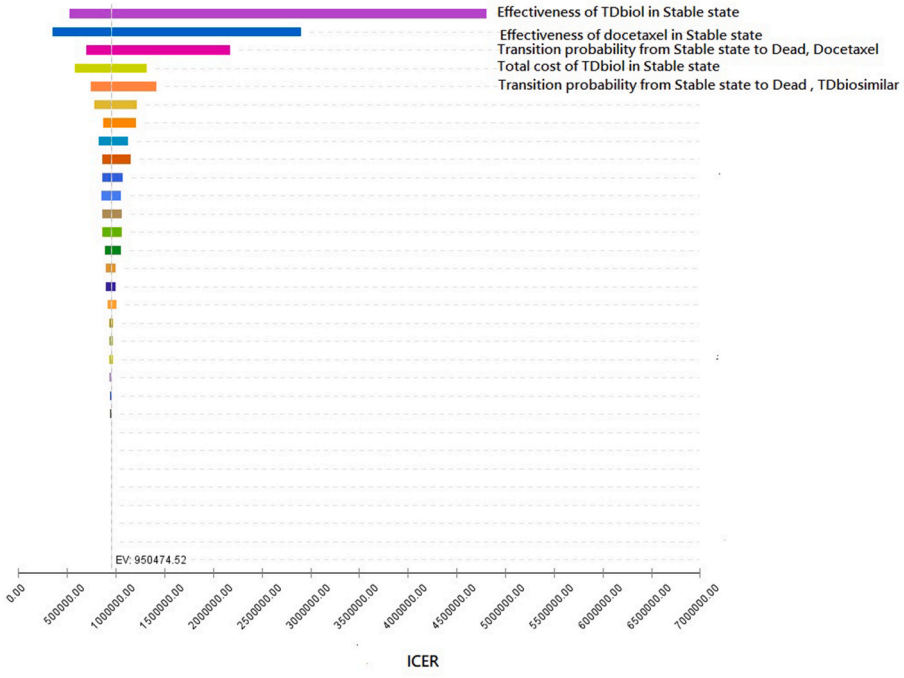

Fig. 2. One - way sensitivity anlysis presented as tornado diagram for TD biosimilar.

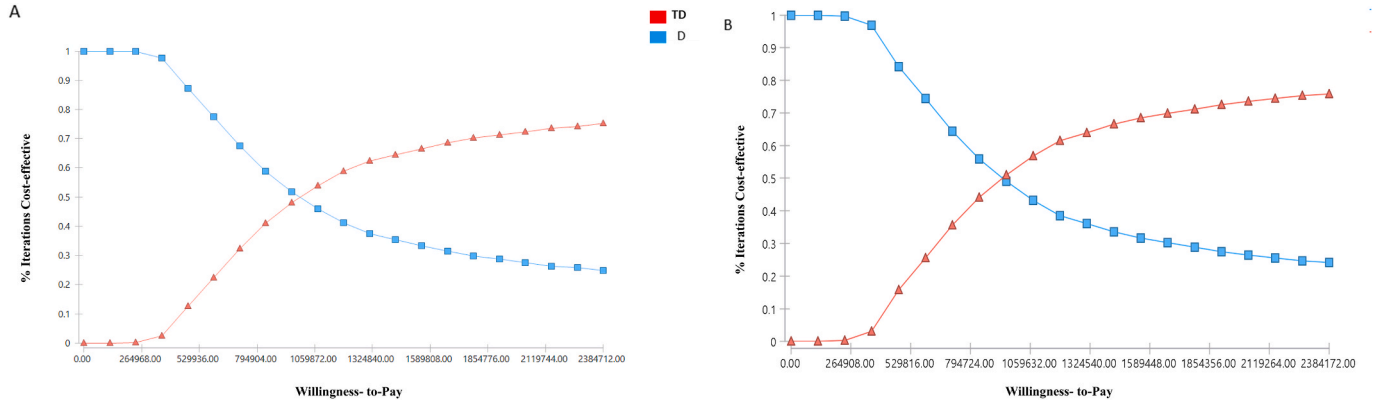

Fig. 3. Acceptability curve for (A)Trastuzumab biosimilar and docetaxel (D) in full unit price/vial, acceptability curve was 71% cost-effective.(B) TD biosimilar (TDbio) in exact amount of mg/kg, acceptability curve was 76% cost-effective at the willingness-today threshold.

Table 4
Cost-effectiveness results comparison for trastuzumab reference and biosimilar in base case scenario.

Strategy	Cost	Cost saving between A and B	Incr Cost	Effectiveness	Incr eff	Incr C/E (ICER)
Docetaxel	1,051,721			6.72		
Trastuzumab reference + D (A)	3,626,484		2,574,763	9.04	2.32	1,109,774
Trastuzumab biosimilar + D (B)	2,933,421	693, 063	1,881,701	9.04	2.32	811,050

Remarks:D,docetaxel; Incr, incremental; eff, effectiveness; Incr C/E, incremental cost/effectiveness; ICER, incremental cost-effectiveness ratio. Cost was calculated in exact dose mg/kg.

societal and patient financial affordability. Therefore, oncology researchers should be encouraged to explore the benefits obtained from the use of biosimilar anticancer drugs rather than reference biologic drugs in the therapeutic cancer setting for different cancer types. Two recent studies reported cost savings and measurable efficacy of switching to biosimilar treatments for several metastatic cancers [37,38]. Furthermore, most available data and post-marketing pharmacovigilance programs support that biosimilar cancer treatments provide direct cost savings, and can also motivate the evaluation and/or clinical use of new treatments and drugs. We believe that these results may encourage oncologists in other countries to adopt biosimilar treatments in their daily clinical practice, particularly to benefit economically disadvantage patients [39].

Our third scenario analysis showed that adding pertuzumab to the PTR or PTbiol combination regimen, which still showed a high ICER, is unlikely to be a cost-effective strategy for HER2^{+} MBC treatment in Taiwan. However, the combination of pertuzumab and trastuzumab biosimilar still provided a cost savings of approximately 5.2% over

pertuzumab combined with the reference trastuzumab biologic. This result is consistent with the previously published CEA studies by Cheng et al. and by Leung et al. They reported that the combination of pertuzumab and the trastuzumab reference biologic regimen was not cost-effective due to high acquired cost of PTR, which should be reduced to a more favorable value below the local consensus WTP threshold [40, 41].

In this study, we also explored drug wastage, as cancer drug waste may be considered a hidden cost adding to the overall cost of cancer care [42]. Our results suggest that the effects of drug wastage may be minimized by using trastuzumab biosimilars and weight-based dosing strategies. The benefit of using weight-based dosing is in line with the recent publication by Jane et al., in which weight-based dosing was promoted as a cost-saving strategies [43].

Our study has several limitations. First, the utilized data were retrieved from a large real-world database, in which patients received a reference brand of trastuzumab (Herceptin). Since trastuzumab biosimilars have only recently been approved by our NHIA, there are currently no clinical trials or studies evaluating the efficacy of trastuzumab biosimilars using real-world claims data. We assumed that the clinical efficacy and safety of trastuzumab biosimilars are very similar to the reference brand, based on extensive bioequivalence studies, which have demonstrated that trastuzumab biosimilars have similar pharmacokinetics, pharmacodynamic properties, clinical efficacy, and safety compared to the original reference biologic [44–46]. Second, we estimated wastage using only the loading dose as an example, based on the unit price per vial or per milligrams multiplied by the exact dose based on body weight. We cannot accurately calculate the amount of medication that is unused after vial-sharing at the end of the day in real daily pharmacist clinical practice. Third, health state utilities were obtained from published literature because no direct utility data were available from local studies. The sensitivity analyses performed in this study might offset the limitations, and thereby ensure the robustness of our study.

5. Conclusions

Here we found that the introduction of a trastuzumab biosimilar and the use of weight-based dosing resulted in significant drug cost savings. We encourage healthcare providers to consider switching to trastuzumab biosimilar combination therapy rather than trastuzumab biologic treatment, especially the very expensive pertuzumab and trastuzumab combination therapy. Moreover, in the near future, it will be critical to develop effective strategies to minimize cancer waste—such as examining the waste of high-cost target drugs, improving waste management practices, and exploring cost-effective dosing regimens—to overcome annual increases of healthcare spending.

Authors' contributions

TYS and WSY contributed to the conceptualization. ALFC contributed to the study design and writing the original draft. HTC provided an expert's opinion. LJH is responsible for the methodology. YHTF contributed to the statistical analyses. All authors were responsible for drafting and revising the manuscript, and have read and approved the final version of manuscript.

Funding

This research received no external funding.

Institutional review board statement

Not applicable.

Informed consent statement

Not applicable.

Data availability statement

Not applicable.

Declaration of competing interest

The authors have indicated that they have no conflicts of interest regarding the content of this article.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.breast.2022.07.007.

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