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Cost-effectiveness of sacituzumab govitecan versus single-agent chemotherapy for previously treated metastatic triple-negative breast cancer in Japan

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Research Article

Keywords: Sacituzumab govitecan, Triple-negative breast cancer, Cost-effectiveness analysis, Quality-adjusted life years, Japan

Posted Date: November 18th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11490753/v1

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Abstract

Purpose

Sacituzumab govitecan (SG) improves survival in patients with previously treated metastatic triple-negative breast cancer (mTNBC); however, its high drug cost raises concerns regarding cost-effectiveness. This study evaluated the cost-effectiveness of SG compared with single-agent chemotherapy from the perspective of the Japanese public healthcare payer.

Methods

A partitioned survival analysis model comprising progression-free, progressed disease, and death states was developed using efficacy data from the ASCENT trial. Long-term overall survival and progression-free survival were estimated by fitting parametric survival distributions to reconstructed individual patient data. Direct medical costs were estimated using official drug prices and the JMDC Claims Database, and utility values were obtained from a Japanese study. Costs and quality-adjusted life years (QALYs) were discounted at 2% annually over a lifetime horizon. One-way and probabilistic sensitivity analyses and scenario analyses were performed. Price thresholds for SG corresponding to Japanese cost-effectiveness reference thresholds were also estimated.

Results

SG provided 0.83 QALYs compared with 0.59 QALYs for single-agent chemotherapy, resulting in an incremental gain of 0.24 QALYs. Total healthcare costs were JPY 18,533,967 and JPY 4,700,042, respectively, yielding an incremental cost of JPY 13,833,926. The resulting incremental cost-effectiveness ratio (ICER) was JPY 56,546,430 per QALY, substantially exceeding the Japanese reference threshold of JPY 15 million per QALY. The ICER remained above this threshold in all sensitivity and scenario analyses, and the probability that SG was cost-effective at this threshold was 0%. To achieve ICERs of JPY 15 million, JPY 11.25 million, and JPY 7.5 million per QALY, the SG price would need to be reduced by 76.45%, 83.35%, and 90.25%, respectively.

Conclusion

SG improved survival and QALYs compared with single-agent chemotherapy but was not cost-effective at its current price from the perspective of the Japanese public healthcare payer. Substantial price reductions would be required for SG to meet the reference thresholds used in the Japanese cost-effectiveness evaluation system. These findings provide quantitative evidence to inform pricing, healthcare resource allocation, and decision-making regarding SG in Japan.

Introduction

Breast cancer is the most diagnosed cancer among women in Japan. In 2023, 102,592 women and 832 men were diagnosed with breast cancer, and in 2024, 15,869 women and 136 men died from the disease [1]. According to the National Medical Care Expenditure survey for fiscal year 2023, total healthcare expenditure for malignant neoplasms amounted to JPY 4.5752 trillion, accounting for 13.2% of total national healthcare expenditure. Of this amount, JPY 444.5 billion was attributable to breast cancer, representing 9.7% of total healthcare expenditure for malignant neoplasms [2]. Furthermore, healthcare expenditure associated with breast cancer is expected to continue to increase with population aging and the introduction of novel therapies.

Breast cancer is classified according to the expression of hormone receptors (HRs) and human epidermal growth factor receptor 2 (HER2). Triple-negative breast cancer (TNBC), which accounts for approximately 10–20% of all breast cancers, is characterized by the absence of both HR and HER2 expression [3]. Consequently, patients with TNBC are not candidates for endocrine or anti-HER2 therapies, and chemotherapy has traditionally been the mainstay of systemic treatment [4]. In particular, recurrent or metastatic TNBC (mTNBC) is characterized by rapid disease progression and a poor prognosis. Treatment options remain limited for patients who have received prior therapies, highlighting the need for additional effective treatment strategies. Sacituzumab govitecan (SG) is a Trop-2-directed antibody–drug conjugate (ADC) developed as a treatment option for patients with previously treated mTNBC [4]. The ASCENT trial was a randomized phase III trial comparing SG with single-agent chemotherapy in patients with mTNBC without brain metastases. In the single-agent chemotherapy group, 54% of patients received eribulin, 20% received vinorelbine, 13% received capecitabine, and 12% received gemcitabine [4]. The primary efficacy endpoints included overall survival (OS) and progression-free survival (PFS). Median OS was 12.1 months (95% confidence interval [CI], 10.7–14.0) with SG and 6.7 months (95% CI, 5.8–7.7) with single-agent chemotherapy, demonstrating a significant survival benefit with SG (hazard ratio [HR], 0.48; 95% CI, 0.38–0.59; $P < 0.001$) [4]. Median PFS was also significantly longer with SG than with single-agent chemotherapy (5.6 months [95% CI, 4.3–6.3] vs. 1.7 months [95% CI, 1.5–2.6]; HR, 0.41; 95% CI, 0.32–0.52; $P < 0.001$) [4]. However, grade ≥ 3 treatment-related adverse events occurred in 64% of patients receiving SG compared with 47% of those receiving single-agent chemotherapy.

Despite its substantial clinical efficacy, SG is associated with high drug acquisition costs, making an assessment of its cost-effectiveness important from the perspective of efficient healthcare resource allocation. Several studies in countries including the United States and China have evaluated the cost-effectiveness of SG for patients with mTNBC, providing evidence relevant to healthcare policy and clinical decision-making. However, drug prices, healthcare systems, and the costs of healthcare resources vary considerably across countries, limiting the direct applicability of cost-effectiveness estimates from other countries to the Japanese healthcare setting. Moreover, Japan formally introduced cost-effectiveness evaluation into its drug

pricing system in 2019, further increasing the importance of generating country-specific economic evidence from the perspective of the Japanese public healthcare system.

Therefore, this study aimed to evaluate the cost-effectiveness of SG compared with single-agent chemotherapy for patients with previously treated mTNBC from the perspective of the Japanese public healthcare payer using a model-based cost-effectiveness analysis.

Materials and Methods

Model-based cost-effectiveness analysis

We developed a partitioned survival analysis (PartSA) model to evaluate the cost-effectiveness of SG in previously treated patients with mTNBC without brain metastases from the perspective of the Japanese public healthcare payer. The comparator was physician's choice of single-agent chemotherapy (eribulin, vinorelbine, capecitabine, or gemcitabine), consistent with the comparator used in the ASCENT trial.

The PartSA model comprised three mutually exclusive health states: progression-free (PF), progressed disease (PD), and death (Fig. 1). Healthcare costs and utility values per model cycle were assigned to each health state. Parametric survival functions were fitted to the Kaplan–Meier curves for PFS and OS reported in the ASCENT trial to extrapolate survival beyond the trial follow-up over a lifetime horizon. The proportions of patients in each health state at each time point were derived from the estimated PFS and OS curves. Lifetime healthcare costs and quality-adjusted life years (QALYs) were then estimated by accumulating the costs and utilities associated with each health state over the model time horizon. Cost-effectiveness was evaluated by calculating the incremental cost-effectiveness ratio (ICER) based on the expected costs and QALYs for the SG and single-agent chemotherapy groups. The ICER was calculated as the incremental cost divided by the incremental QALYs and represents the additional cost required to gain one additional QALY. Under the Japanese cost-effectiveness evaluation system, thresholds ranging from JPY 7.5 million to JPY 15 million per QALY are used as reference values for price adjustment in the oncology setting. Therefore, we used JPY 7.5–15 million per QALY as the reference range for assessing the cost-effectiveness of SG [5].

The hypothetical cohort was assumed to reflect the patient population enrolled in the phase III ASCENT trial. Based on the median patient age of 53 years in the ASCENT trial, the model adopted a lifetime horizon of 47 years, corresponding to an age of 100 years. In accordance with the Japanese guidelines for cost-effectiveness evaluation, both costs and health outcomes (QALYs) were discounted at an annual rate of 2% [6]. The model cycle length was 1 month. The model was developed and analyzed using TreeAge Pro Healthcare 2025.

Curve fitting and survival extrapolation

To estimate long-term PFS and OS for each treatment group for the PartSA model, parametric survival functions were fitted to the Kaplan–Meier curves reported in the ASCENT trial (Supplementary Fig. 1). Because individual patient data (IPD) on survival outcomes from clinical trials are generally not publicly available, pseudo-IPD were reconstructed from the published Kaplan–Meier curves and numbers at risk using the method proposed by Guyot et al. [7]. The reconstruction procedure was performed as follows:

1. Data points representing time and cumulative survival probabilities were extracted from the published Kaplan–Meier curves.
2. Pseudo-IPD were reconstructed from the extracted data points and the reported numbers at risk using the algorithm developed by Guyot et al. [7].

Data points were extracted from the Kaplan–Meier curves using WebPlotDigitizer version 4.0, and pseudo-IPD were reconstructed using R version 4.4.0. Six standard parametric survival distributions were fitted to the reconstructed IPD for PFS and OS from the ASCENT trial: exponential, Weibull, Gompertz, log-logistic, log-normal, and generalized gamma distributions. Curve fitting was performed using Stata SE version 17 (StataCorp LLC, College Station, TX, USA). The parametric distributions used in the base-case analysis were selected based on an overall assessment of visual fit to the observed Kaplan–Meier curves, the Akaike information criterion (AIC), the Bayesian information criterion (BIC), and the clinical plausibility of long-term extrapolation (Supplementary Table 1). For the base-case analysis, a Weibull distribution was selected for OS and a log-normal distribution for PFS in the SG group, whereas log-logistic distributions were selected for both OS and PFS in the single-agent chemotherapy group.

Cost

Only direct medical costs were considered in this analysis, consistent with the perspective of the Japanese public healthcare payer. The following cost parameters were incorporated into the model: (1) drug costs before disease progression for each treatment group (JPY/month), (2) other healthcare costs before disease progression for each treatment group (JPY/month), (3) healthcare costs after disease progression for each treatment group (JPY/month), (4) end-of-life healthcare costs (JPY/event), and (5) costs associated with adverse events (AEs) (JPY/event). These cost parameters and their distributions are summarized in Table 1. Drug costs were estimated based on the standard dosing regimens and official drug prices in Japan as of fiscal year 2026 [8]. Patient body weight was estimated using the average body weight of Japanese women in their 50s, based on the median age of 53 years in the ASCENT trial [4].

Table 1
Parameter inputs

Parameter	Estimate	Plausible range		Distribution	Reference
Cost parameter					
Drug cost on PF					
chem group (JPY/month)	362,623	-10%	10%	Triangle	[8]
SG group (JPY/month)	1,622,357	-10%	10%	Triangle	[8]
Other medical cost on PF(JPY/month)	213,359	206,641	220,077	gamma	[JMDC Claims Database]
Medical cost on PD (JPY/month)	237,135	231,425	242,845	gamma	[JMDC Claims Database]
Terminal cost (JPY/event)	1,703,015	1,624,841	1,781,189	gamma	[JMDC Claims Database]
Anemia cost (JPY/event)	2,146,631	1,609,892	2,683,207	gamma	[9]
Diarrhea cost (JPY/event)	633,019	474,682	791,192	gamma	[9]
Nausea /Vomiting cost (JPY/event)	634,656	475,992	711,614	gamma	[9]
utility					
PFS	0.70	0.68	0.73	beta	[10]
PD	0.58	0.55	0.62	beta	[10]
Disutility					
Anemia	0.21	0.18	0.24	beta	[10]
Diarrhea	0.79	0.73	0.85	beta	[10]
Nausea /Vomiting	0.94	0.88	1.00	beta	[10]
Incidence rate of AE (/month)					
Anemia					
chem group	0.00209	0.00088	0.00333	beta	[9]
SG group	0.00338	0.00192	0.00484	beta	[9]
Diarrhea					
chem group	0.00017	0	0.00055	beta	[9]
SG group	0.00461	0.00289	0.00636	beta	[9]
Nausea /Vomiting					
chem group	0.00017	0	0.00055	beta	[9]
SG group	0.00166	0.00063	0.00266	beta	[9]
Discount rate	0.02	0	0.05		[6]

The cost parameters for other healthcare services before disease progression, healthcare services after disease progression, and end-of-life care were estimated using the JMDC Claims Database provided by JMDC Inc. (Table 1). The JMDC Claims Database is a large-scale commercial claims database in Japan that contains health insurance claims for inpatient, outpatient, and pharmacy services, as well as enrollee information and health check-up data. Individuals can be longitudinally followed using anonymized identifiers. However, the database does not include individuals covered by Japan's health insurance system for people aged 75 years or older (the Latter-Stage Elderly Healthcare System).

Data from January 2005 through December 2023 were used in this study. Patients with metastatic breast cancer were identified as those with both a breast cancer-related International Classification of Diseases, 10th Revision (ICD-10) code (C50.0 ~ C50.6, C50.8, or C50.9) and a metastasis-related ICD-10 code (C77 ~ C79). To further identify patients with TNBC, patients who received chemotherapy used for TNBC and had no history of endocrine therapy or anti-HER2 therapy were classified as having TNBC.

Because data on SG were not available in the JMDC Claims Database at the time of this analysis, healthcare costs other than drug costs were assumed to be equivalent between the SG and single-agent chemotherapy groups. Months during which patients received standard chemotherapy were assumed to represent the PF period, and the mean healthcare costs incurred during this period, excluding drug costs, were used to estimate other healthcare costs for the PF period. The period following the discontinuation of standard chemotherapy was defined as the post-progression period, and the mean healthcare costs incurred during this period were used to estimate healthcare costs after disease progression. End-of-life healthcare costs were estimated among patients with breast cancer who died during the observation period and were defined as the total healthcare costs incurred during the

3 months preceding death. Costs associated with AEs were obtained from data used in a previous study [9] and converted to Japanese yen using an exchange rate of USD 1 = JPY 163.74 as of July 28, 2026. All data extraction and statistical analyses were performed using Stata SE version 19 (StataCorp LLC, College Station, TX, USA). Healthcare costs over time by treatment group are shown in Supplementary Fig. 2.

Utility

Baseline utility values for the PF and PD health states were obtained from a Japanese study [10] (Table 1). The baseline utility values for each health state were assumed to be the same between the treatment groups.

For the PF state, temporary reductions in utility associated with AEs were considered. Grade ≥ 3 anemia, diarrhea, and nausea/vomiting were included in the analysis. The disutility associated with each AE was obtained from the same Japanese study [10]. The incidence and associated costs of each AE were obtained from a previous cost-effectiveness study based on the ASCENT trial [9].

Sensitivity analyses

To assess the robustness of the base-case results to parameter uncertainty, one-way sensitivity analysis and probabilistic sensitivity analysis (PSA) were performed.

In the one-way sensitivity analysis, each model parameter was varied individually over its specified range to assess its impact on the ICER. When 95% CIs were available, the lower and upper bounds of the 95% CIs were used as the parameter ranges; otherwise, the ranges were determined based on published literature or assumptions (Table 1).

For the PSA, 1,000 second-order Monte Carlo simulations were performed to account for parameter uncertainty and probabilistically evaluate the cost-effectiveness of SG. Appropriate probability distributions were assigned to model parameters for which distributional information was available (Table 1). In each simulation, parameter values were randomly sampled from the specified probability distributions, and the expected costs, QALYs, and ICER were calculated. Based on the results of the 1,000 simulations, a cost-effectiveness acceptability curve (CEAC) was generated, and the probability that SG was cost-effective was estimated at a willingness-to-pay (WTP) threshold of JPY 15 million per QALY.

Scenario analyses

The results of cost-effectiveness analyses using PartSA models can be sensitive to the parametric distributions used to extrapolate OS and PFS. Therefore, scenario analyses were performed using alternative parametric distributions to assess the uncertainty associated with survival extrapolation.

In addition, the model was used to estimate the SG price thresholds required to achieve ICERs ranging from JPY 7.5 million to JPY 15 million per QALY. The ICER after price adjustment was also estimated assuming that the price of SG was adjusted according to the rules of the Japanese cost-effectiveness evaluation system. Furthermore, changes in the manufacturer-projected peak annual sales were estimated for each of the evaluated SG price scenarios.

Results

Base-case analysis

The changes in the proportions of patients in the PF, PD, and death states over time, as simulated using the PartSA model, are shown in Fig. 2(a) and 2(b). The results of the base-case analysis are presented in Table 2.

Table 2
, Base case

	Cost	Incr Cost	QALY	Incr QALY	ICER	LY (year)	Incr LY (year)	Cost Details				
								Other cost in PFS	Medical cost in PD	Terminal cost	Drug cost in PFS	Cost of AE
chem	4,700,042		0.59			0.99		692,828	1,939,579	1,670,715	381,656	15,264
SG	18,533,967	13,833,926	0.83	0.24	56,546,430	1.32	0.33	1,748,490	1,738,776	1,659,413	13,295,326	91,962

Mean life-years (LYs) were 1.32 years in the SG group and 0.99 years in the single-agent chemotherapy group, resulting in an incremental gain of 0.33 LYs with SG. QALYs were 0.83 and 0.59, respectively, resulting in an incremental gain of 0.24 QALYs with SG. Total healthcare costs were JPY 18,533,967 in the SG group and JPY 4,700,042 in the single-agent chemotherapy group, resulting in an incremental cost of JPY 13,833,926. Of the total costs, drug costs were JPY 13,295,326 and JPY 381,656, respectively, accounting for the majority of the incremental cost. Based on these results, ICER for SG compared with single-agent chemotherapy was estimated at JPY 56,546,430 per QALY.

Sensitivity analyses

The results of the one-way sensitivity analysis are presented in a tornado diagram (Fig. 3). The utility value for the PD state had the greatest impact on the cost-effectiveness of SG. The ICER ranged from JPY 51,442,726 per QALY in the best-case scenario to JPY 62,774,343 per QALY in the worst-case scenario. Even in the best-case scenario, the ICER remained above the threshold of JPY 15 million per QALY.

The results of the PSA and the CEAC are shown in Figs. 4(a) and 4(b), respectively. At a WTP threshold of JPY 15 million per QALY, the probability that SG was cost-effective was 0%.

Scenario analyses

The results of the scenario analyses using alternative parametric distributions for OS and PFS extrapolation are presented in Supplementary Table 2. Because the generalized gamma distribution for PFS in the SG group did not converge, the log-normal distribution used in the base-case analysis was applied to SG PFS in the scenario analysis involving the generalized gamma distribution. The ICER ranged from JPY 25,008,602 to JPY 56,546,430 per QALY across the scenarios and remained above the threshold of JPY 15 million per QALY in all scenarios.

Impact of SG price on cost-effectiveness

The results of the SG price impact analysis are summarized in Table 3. Under the Japanese cost-effectiveness evaluation system, three ICER thresholds of JPY 7.5 million, JPY 11.25 million, and JPY 15 million per QALY are used as reference values for the evaluation and price adjustment of anticancer drugs [5]. We estimated the SG prices and corresponding price reductions required to meet each of these ICER thresholds. We also estimated the adjusted SG price according to the price adjustment rules of the Japanese cost-effectiveness evaluation system. To achieve ICERs of JPY 7.5 million, JPY 11.25 million, and JPY 15 million per QALY, the current SG price would need to be reduced by 90.25%, 83.35%, and 76.45%, respectively. Applying these price reductions to the manufacturer-projected peak annual sales resulted in estimated healthcare cost savings of JPY 8.626 billion, JPY 8.017 billion, and JPY 7.298 billion, respectively.

Table 3
Impact of Alternative Price Scenarios for SG

Scenario	SG price (JPY/vial)	Price reduction (%)	Estimated annual sales at peak, million JPY (change)	ICER (JPY/QALY)
Current price	187,195	-	9,300	56,546,430
SG prices required to meet alternative ICER thresholds				
(a) ICER = JPY 7.5 million/QALY	18,251	90.25%	674 (− 8,626)	7,500,000
(b) ICER = JPY 11.25 million/QALY	31,168	83.35%	1,283 (− 8,017)	11,250,000
(c) ICER = JPY 15.0 million/QALY	44,085	76.45%	2,002 (− 7,298)	15,000,000
Prices after adjustment according to the Japanese cost-effectiveness evaluation system				
(d) Price adjustment coefficient 0.7	171,150	8.570%	8,503 (− 797)	51,888,379
(e) Price adjustment coefficient 0.4	155,105	17.14%	7,706 (− 1,594)	47,230,329
(f) Price adjustment coefficient 0.1	139,059	25.71%	6,909 (− 2,391)	42,571,987
(g) Stop-Loss Price	166,604	11.00%	8,277 (− 1,023)	50,568,623

Because the ICER for SG exceeded JPY 15 million per QALY, a 90% reduction in the premium component (adjustment coefficient, 0.1) would be applied under the Japanese cost-effectiveness evaluation system. This would result in a 25.71% reduction in the SG price and healthcare cost savings of JPY 2.391 billion. However, the system sets a lower limit on price reductions to ensure a stable drug supply [11]. For SG, this rule would limit the price reduction to 11%. At this adjusted price, the ICER for SG was estimated at JPY 50,568,623 per QALY, remaining above the JPY 15 million per QALY threshold.

Discussion

In this study, we evaluated the cost-effectiveness of SG for patients with mTNBC from the perspective of the Japanese public healthcare payer using a PartSA model. Compared with single-agent chemotherapy, SG provided an incremental gain of 0.24 QALYs but increased total healthcare costs by JPY 13,833,926, resulting in an ICER of JPY 56,546,430 per QALY. This ICER exceeded JPY 15 million per QALY, the highest reference threshold for price adjustment under the Japanese cost-effectiveness evaluation system, indicating that SG was not cost-effective compared with single-agent chemotherapy. Sensitivity analyses showed that the utility values had the greatest impact on the ICER; however, the ICER remained above JPY 15 million per QALY across all analyses.

Chen et al. evaluated the cost-effectiveness of SG from the healthcare payer perspectives in China and the United States and reported ICERs of JPY 127,517,120 per QALY in China (CNY 1 = JPY 20) and JPY 80,965,991 per QALY in the United States (USD 1 = JPY 163.74) compared with single-agent chemotherapy [9]. Wang et al. [12] estimated an ICER of JPY 52,986,893 per QALY from the perspective of the Chinese healthcare system, whereas Xie et al. [13] and Lang et al. [14] reported ICERs of JPY 205,050,783 and JPY 127,516,111 per QALY, respectively, from the US healthcare payer perspective. All of these studies concluded that SG was not cost-effective compared with single-agent chemotherapy for mTNBC, consistent with our findings. However, the estimated ICERs differed considerably across studies.

The model structures and approaches used to extrapolate OS and PFS were generally similar between our study and previous studies. However, the discount rates applied to long-term costs and health outcomes differed across studies. In accordance with the Japanese guidelines for cost-effectiveness evaluation [6], we applied an annual discount rate of 2% to both costs and health outcomes. In contrast, two previous studies applied a discount rate of 5%, whereas the other two applied a rate of 3%. Discount rates may vary across countries depending on country-specific guidelines and healthcare decision-making frameworks. These differences in discount rates may have contributed to the differences in the estimated long-term costs, QALYs, and ICERs. Utility values also differed across studies. Unlike previous studies that used utility estimates derived from studies conducted outside Japan, our analysis used utility values derived from a vignette-based study reflecting the preferences of the Japanese general population. These utility values may therefore be more appropriate for informing healthcare resource allocation decisions in Japan. Differences in healthcare costs, particularly drug prices for SG and single-agent chemotherapy, may also have contributed to the variation in ICERs across countries. The price of SG was JPY 936/mg in Japan [8], whereas previous US analyses used prices ranging from JPY 1,834 to JPY 1,988/mg based on Centers for Medicare & Medicaid Services pricing. In the Chinese analyses, because SG was not commercially available in mainland China at the time of the analyses, prices based on those in Hong Kong were used, ranging from JPY 1,185 to JPY 3,850/mg. These SG prices were higher than that used in our analysis. With respect to the prices of single-agent chemotherapy [9], eribulin was less expensive in Japan than in the other countries, whereas vinorelbine and gemcitabine were more expensive in Japan. Given these cross-country variations in the prices of both SG and comparator chemotherapy, their precise contribution to the differences in ICERs is difficult to determine. Nevertheless, higher SG prices or lower chemotherapy prices would be expected to result in higher ICERs.

During the course of this study, the results of Academic Technology Assessment Group (ATAG) for SG under the Japanese cost-effectiveness evaluation system were published. In the ATAG's analysis, the incremental cost and QALYs for SG compared with single-agent chemotherapy were estimated at JPY 13,741,192 and 0.40 QALYs, respectively, resulting in an ICER of JPY 34,735,200 per QALY [15]. Thus, the conclusion that SG was not cost-effective was generally consistent with our findings. However, the ICER estimated in our study (JPY 56,546,430 per QALY) was higher than that reported by the ATAG. This difference may be largely attributable to differences in the estimation of QALYs.

In the ATAG's reanalysis, the impact of AEs was considered to be already reflected in the health-state utility values; therefore, no additional AE-related disutility was applied, and the same utility values were used for both treatment groups. In contrast, our analysis incorporated AE-related disutility separately for each treatment group according to differences in AE incidence. Consequently, the greater incidence of AEs in the SG group resulted in a greater reduction in QALYs, leading to a smaller incremental QALY gain with SG than that estimated in the ATAG's analysis. This may have contributed to the higher ICER observed in our study. Notably, the utility and disutility values used in our analysis were derived from a study reflecting the preferences of the Japanese general population and may therefore be appropriate for estimating QALYs from the perspective of the Japanese public healthcare system.

We used a PartSA model, which is commonly applied in cost-effectiveness analyses of advanced cancers, and constructed the model using standard modeling procedures. To assess the external validity of the model, the long-term survival estimated for the single-agent chemotherapy group was compared with the 5-year survival rate for patients with breast cancer with distant metastases reported by the Foundation for Promotion of Cancer Research in Japan [16]. The reported 5-year survival rate for breast cancer with distant metastases was approximately 40%, whereas the estimated 5-year OS in the chemotherapy group in our analysis was approximately 0%. This difference may be explained by the population evaluated in our study, which was restricted to patients with TNBC, for whom effective subtype-specific therapies such as endocrine therapy and anti-HER2 therapy are not available. Therefore, the poorer long-term survival estimated in our model compared with that reported for the overall population with metastatic breast cancer is clinically plausible, supporting the external validity of the model.

In cost-effectiveness analyses using PartSA models, the methods used to extrapolate OS and PFS can substantially influence the results and are therefore an important source of uncertainty. In our scenario analyses using alternative parametric distributions, the estimated ICERs were lower than that in the base-case analysis across all scenarios. However, all ICERs remained above the threshold of JPY 15 million per QALY. These findings suggest that the conclusion regarding the cost-effectiveness of SG was robust to uncertainty associated with the extrapolation of OS and PFS.

The choice of comparator is another important consideration in cost-effectiveness analyses because it can substantially affect the estimated ICER. The Japanese guidelines for cost-effectiveness evaluation recommend selecting a comparator that is widely used in clinical practice for the target population and is expected to be replaced by the intervention under evaluation, with consideration given to recommendations in clinical practice guidelines. When such a comparator cannot be clearly identified, the guidelines recommend considering comparators used in randomized controlled trials [6]. In our analysis, physician's choice of four single-agent chemotherapies—eribulin, vinorelbine, capecitabine, or gemcitabine—was selected as the comparator based on the ASCENT trial [4]. According to the clinical practice guidelines, platinum-based chemotherapy improves PFS and objective response rate (ORR) in TNBC; however, the evidence is heterogeneous and the recommendation remains weak [17]. Furthermore, the specific patient populations suitable for platinum-based chemotherapy and the preferred treatment regimens have not been clearly established. Therefore, it was difficult to identify a single chemotherapy regimen that is both widely used and clearly preferred for TNBC in Japanese clinical practice. Accordingly, consistent with the Japanese guidelines for cost-effectiveness evaluation, we selected physician's choice of the four chemotherapy regimens used as comparators in the

ASCENT trial. Further studies are needed to evaluate the relative cost-effectiveness of SG and other treatment options, including emerging therapies for TNBC in Japan.

This is the first cost-effectiveness analysis of SG for TNBC from the perspective of the Japanese public healthcare payer. During the course of this study, SG was evaluated under the Japanese cost-effectiveness evaluation system. In August 2026, the Central Social Insurance Medical Council approved an 11.0% price reduction, with the revised price scheduled to take effect in November 2026 [18]. In contrast, our price threshold analysis estimated that reductions of 76.45%, 83.35%, and 90.25% from the current SG price would be required to achieve ICERs of JPY 15 million, JPY 11.25 million, and JPY 7.5 million per QALY, respectively. With the approved 11.0% price reduction, the estimated ICER would decrease from JPY 56,546,430 to JPY 50,568,623 per QALY but would remain substantially above JPY 15 million per QALY. These findings suggest a substantial gap between the price resulting from the current price adjustment system and the price required to meet the specified ICER thresholds.

In Japan, cost-effectiveness evaluation is primarily used for post-reimbursement price adjustment. In contrast, in the United Kingdom, NICE uses cost-effectiveness assessments to inform reimbursement decisions and recommendations on the use of health technologies within the NHS [5]. If cost-effectiveness evaluation in Japan were expanded to reimbursement and treatment-use decisions, our estimated price thresholds could help balance the clinical value of SG against its financial impact. Our findings may therefore provide useful evidence for considering how cost-effectiveness evaluations could be used in healthcare policy decision-making in Japan.

Furthermore, the relevance of our findings may extend beyond healthcare policy to clinical decision-making. The Minds Manual for Clinical Practice Guideline Development 2020 introduced a framework for incorporating health economic evidence, including cost-effectiveness, into the development of clinical practice guidelines [19]. Reflecting this growing emphasis, a new section on health economic evaluation has also been included in the 2026 Japanese Breast Cancer Society Clinical Practice Guidelines for Breast Cancer [20]. In the future, cost-effectiveness may become increasingly important alongside efficacy and safety when making clinical decisions under limited healthcare resources. Our study provides quantitative evidence on the cost-effectiveness of SG for patients with mTNBC in Japan and may contribute to informed decision-making in clinical practice.

There are several limitations to this study. First, although the JMDC Claims Database captures real-world healthcare resource use in Japan, it does not include individuals covered by the Late-stage Medical Care System for the Elderly. This may limit the generalizability of our healthcare cost estimates. Future analyses using the National Database of Health Insurance Claims and Specific Health Checkups of Japan could provide more generalizable cost estimates. In addition, because data on SG were not available in the JMDC Claims Database, healthcare costs other than drug costs were assumed to be equivalent between the SG and single-agent chemotherapy groups, and the estimates for the chemotherapy group were applied to both groups. Second, the generalizability of the treatment effect of SG observed in the ASCENT trial to Japanese patients remains uncertain. The Pharmaceuticals and Medical Devices Agency (PMDA) acknowledged limitations in the evaluation of SG in Japanese patients but concluded that efficacy could be expected based, at least in part, on the observed improvement in response rate [21]. Furthermore, subgroup analyses of the ASCENT trial showed no apparent heterogeneity in the HRs for OS or PFS across racial groups. These findings suggest that the treatment effect of SG observed in the ASCENT trial may be generalizable to Japanese patients. Nevertheless, further clinical studies evaluating the real-world effectiveness of SG in Japan are needed.

This study evaluated the cost-effectiveness of SG for previously treated patients with mTNBC from the perspective of the Japanese public healthcare payer. Although SG improved survival and QALYs compared with single-agent chemotherapy, the substantial incremental cost resulted in an ICER well above the thresholds used in the Japanese cost-effectiveness evaluation system. This finding was consistent across sensitivity and scenario analyses, suggesting that SG is not cost-effective at its current price. Nevertheless, SG remains an important treatment option for previously treated mTNBC. Appropriate pricing and healthcare resource allocation should therefore be considered to balance its clinical value with its financial impact. This study provides quantitative evidence on the cost-effectiveness of SG in Japan and may help inform future healthcare policy and clinical decision-making.

Declarations

Acknowledgments

Not applicable.

Compliance with Ethical Standards

Disclosure of potential conflicts of interest

Tsuguo Iwatani has received honoraria for lectures, presentations, and educational activities from Eisai Co., Ltd., Eli Lilly Japan K.K., and Chugai Pharmaceutical Co., Ltd. The other authors declare that they have no conflicts of interest.

Research involving Human Participants and/or Animals

This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent

Informed consent was not required for this study.

Funding

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Author Contributions

The first draft of the manuscript was written by Mao Yamaguchi-Naruoka, and all authors commented on previous versions of the manuscript.

Data Availability

The data that support the findings of this study are not publicly available because the JMDC Claims Database is a commercially available database provided by JMDC Inc.

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Figures

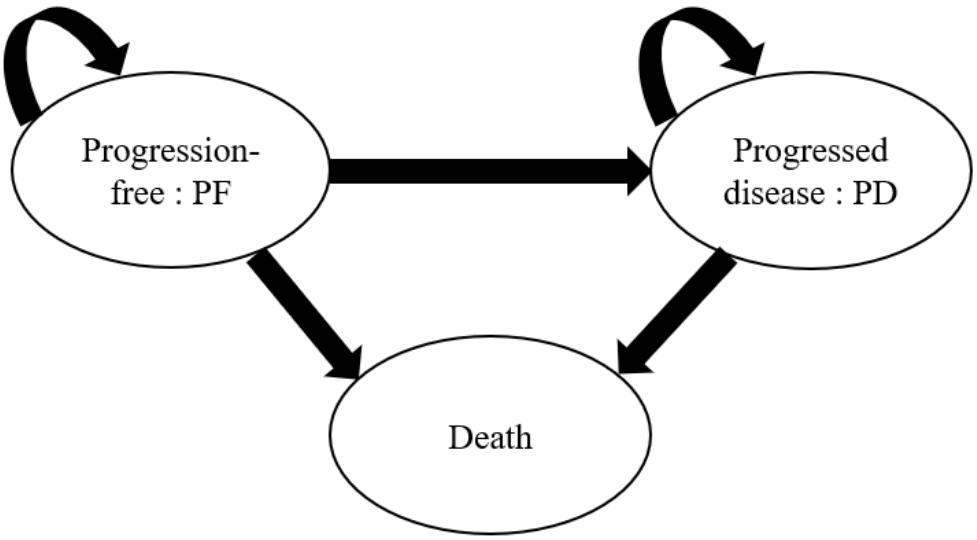


Figure 1

Structure of the partitioned survival analysis model

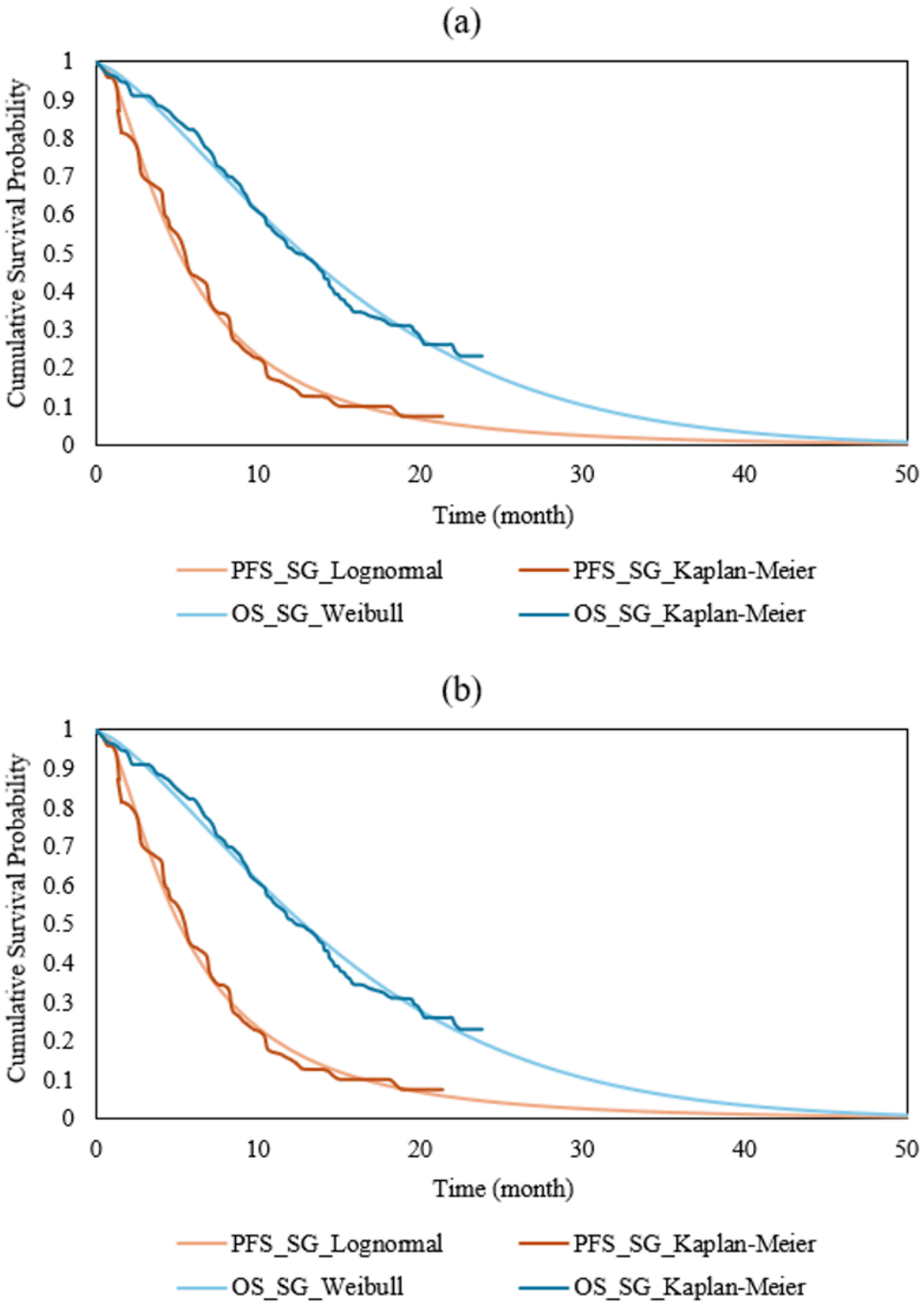


Figure 2

Kaplan–Meier and fitted parametric survival curves for PFS and OS. (a) SG group. (b) Single-agent chemotherapy group.

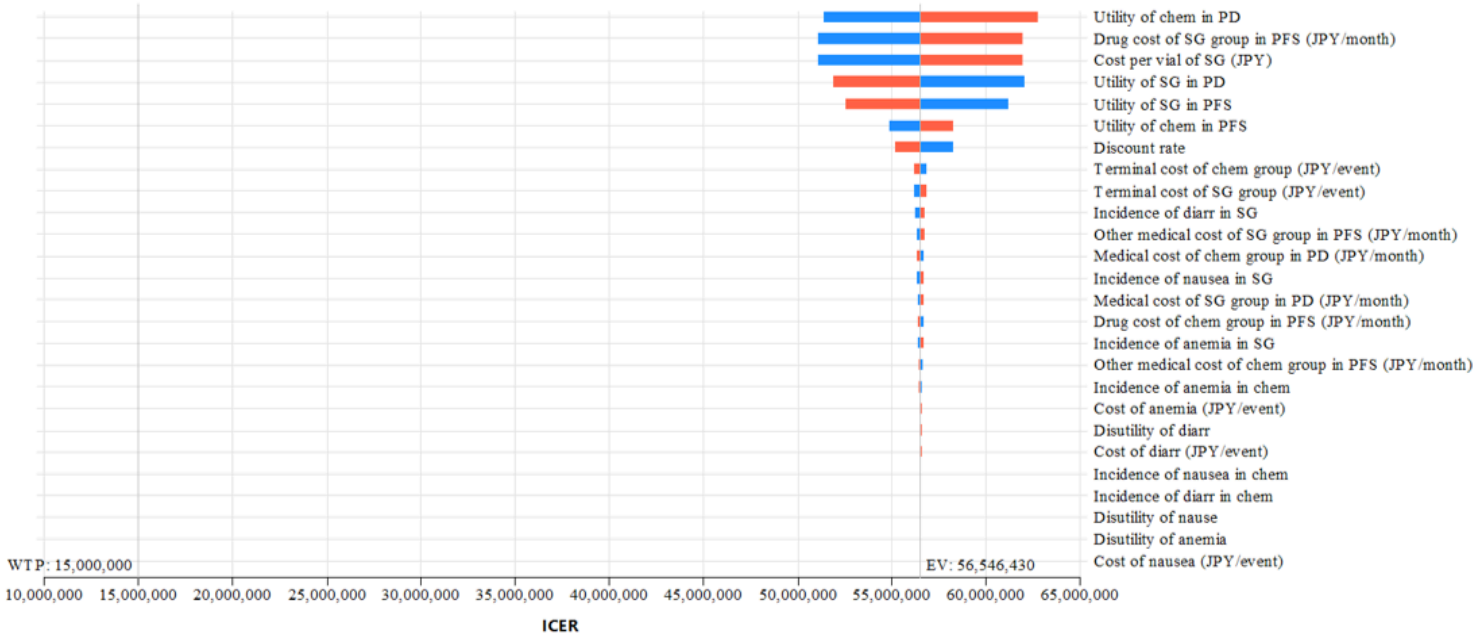


Figure 3

Tornado diagram of the one-way sensitivity analysis

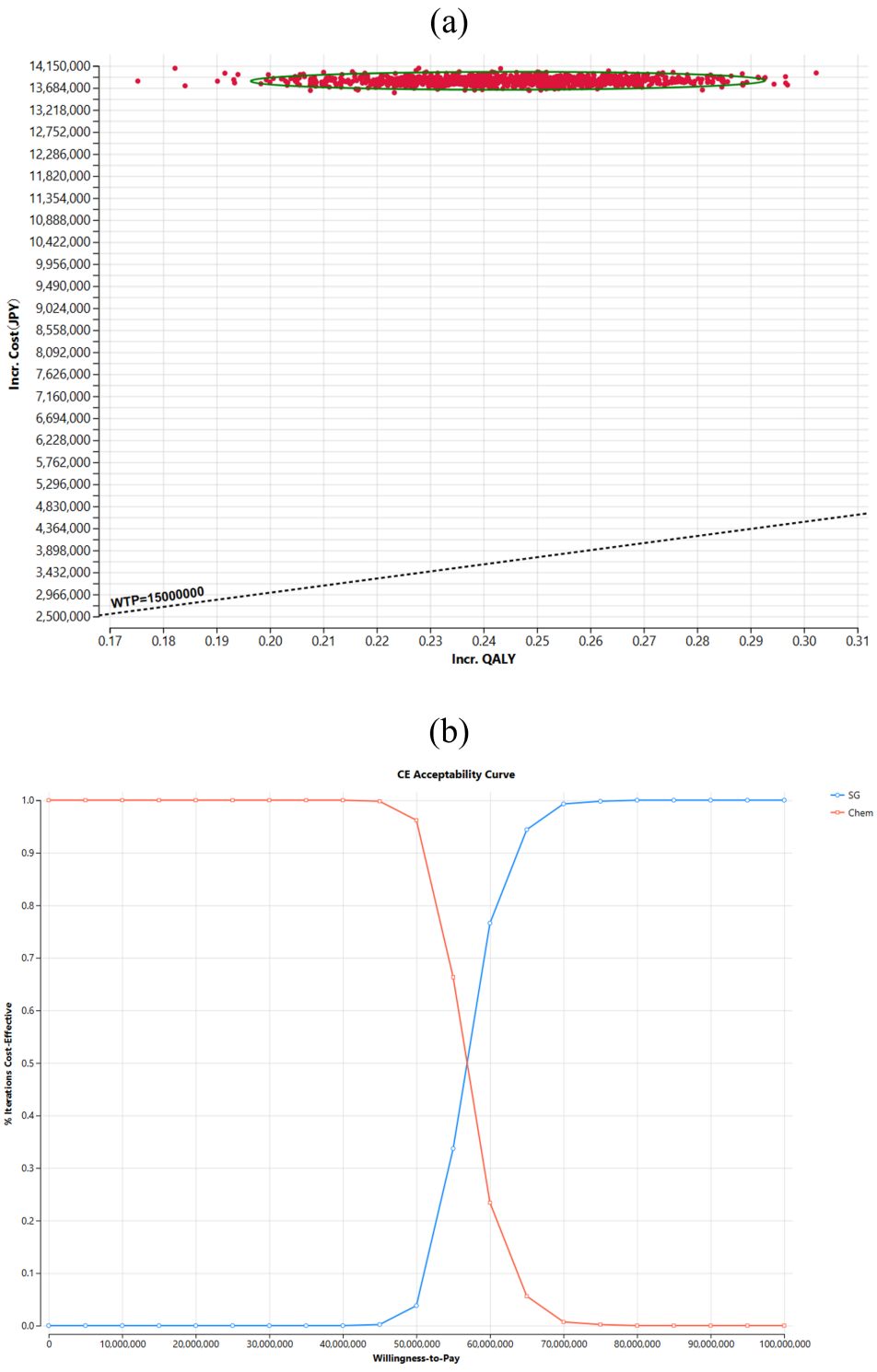


Figure 4

Results of the probabilistic sensitivity analysis. (a) Cost-effectiveness plane. (b) Cost-effectiveness acceptability curve.

Supplementary Files

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