

Cost-Effectiveness of Sacituzumab Tirumotecan vs Chemotherapy for EGFR- TKI–Resistant NSCLC: Evidence to Inform Drug Pricing in the U.S. and China

Yulong He

Nanxishan Hospital of Guangxi Zhuang Autonomous Region

Qinling Jiang

Nanxishan Hospital of Guangxi Zhuang Autonomous Region

Qi Ai

Nanxishan Hospital of Guangxi Zhuang Autonomous Region

Xianling Zhao

Nanxishan Hospital of Guangxi Zhuang Autonomous Region

Huiqing Jiang

Nanxishan Hospital of Guangxi Zhuang Autonomous Region

Liang Xiao

Nanxishan Hospital of Guangxi Zhuang Autonomous Region

Wenwang Lang

290702062@qq.com

Nanxishan Hospital of Guangxi Zhuang Autonomous Region

Research Article

Keywords: Cost-effectiveness, non–small-cell lung cancer, sacituzumab tirumotecan, ADC, Markov model, EGFR-TKI–resistant

Posted Date: June 25th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-9881354/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Additional Declarations: No competing interests reported.

Cost-Effectiveness of Sacituzumab Tirumotecan vs Chemotherapy for EGFR-TKI-Resistant NSCLC: Evidence to Inform Drug Pricing in the U.S. and China

Yulong He¹, Qinling Jiang¹, Qi Ai¹, Xianling Zhao¹, Huiqing Jiang¹, Liang Xiao¹, Wenwang Lang^{2,3}

1 Department of Oncology, Nanxishan Hospital of Guangxi Zhuang Autonomous Region, Guilin, China

2 Department of Pharmacy, Nanxishan Hospital of Guangxi Zhuang Autonomous Region, Guilin, China

3 Correspondence: 290702062@qq.com 541002

Abstract

Background

Sacituzumab tirumotecan (sac-TMT) is a Trop-2-targeted antibody–drug conjugate (ADC) that has demonstrated clinically meaningful improvements in progression-free survival (PFS) and overall survival (OS) compared to standard platinum-based chemotherapy in patients with advanced non-small-cell lung cancer (NSCLC) harboring epidermal growth factor receptor (EGFR) mutations who have developed resistance to EGFR tyrosine kinase inhibitors (TKIs). To date, no economic evaluation has systematically assessed the cost-effectiveness of sac-TMT from the U.S. payer and Chinese healthcare system perspectives.

Method

A Markov state-transition model was used for the economic evaluation, reflecting the perspectives of both the U.S. payer and the Chinese healthcare system. Baseline patient demographics and vital clinical data were obtained from the OptiTROP-Lung04 trial. Costs and utilities were obtained from open-access databases and the published literature. The primary outcomes included quality-adjusted life years (QALYs), incremental cost-effectiveness ratio (ICER), incremental net health benefit (INHB), and incremental net monetary benefit (INMB). To address the inherent uncertainties in the model parameters, we conducted a one-way sensitivity analysis (OWSA), probabilistic sensitivity analysis (PSA), price simulation, and scenario analysis.

Results

In the base-case analysis, sac-TMT was associated with a gain of 0.84 QALYs at an incremental cost of \$33,751.50, resulting in an ICER of \$40,116.07/QALY. This ICER value was marginally below China's willingness-to-pay (WTP) threshold of \$41,910.00 per QALY, with an INHB of 0.036 QALYs and an INMB of \$1,509.31, indicating marginal cost-effectiveness in the Chinese healthcare setting. In contrast, from the U.S. payer perspective, sac-TMT yielded an additional 0.91 QALYs but incurred an incremental cost of \$399,471.55, leading to an ICER of

\$438,507.95 per QALY, substantially exceeding the US WTP threshold of \$150,000.00 per QALY. Price simulation analyses revealed that sac-TMT would need to be priced below \$3,333.75 per treatment cycle in the U.S. to achieve cost-effectiveness at the established WTP threshold.

Conclusion

Sacituzumab tirumotecan may be cost-effective for Chinese patients with EGFR-TKI-resistant, EGFR-mutated advanced NSCLC, whereas it is not cost-effective for their U.S. counterparts under current pricing strategies. Substantial price reductions are required to improve the cost-effectiveness of sac-TMT and expand its accessibility among U.S. patients.

Keywords

Cost-effectiveness, non-small-cell lung cancer, sacituzumab tirumotecan, ADC, Markov model, EGFR-TKI-resistant

Introduction

Non-small cell lung cancer (NSCLC) is the most common cause of cancer-related deaths worldwide[1]. It accounts for nearly 85% of all lung cancer cases and is responsible for more than 1.8 million deaths annually[1-3]. Among patients with NSCLC, mutations in the epidermal growth factor receptor (EGFR) gene define a clinically important molecular subtype of

63 NSCLC[4]. These mutations occur in approximately 15%–20% of patients
64 in Western populations and up to 50% of patients in Asian populations.
65 Owing to their distinct biological characteristics and treatment responses,
66 EGFR-mutated tumors require targeted therapeutic approaches[5]. For
67 individuals with advanced EGFR-mutated NSCLC who are not candidates
68 for curative surgery or definitive chemoradiotherapy, third-generation
69 EGFR tyrosine kinase inhibitors (TKIs), particularly osimertinib, are
70 currently recommended as first-line therapy owing to their improved
71 efficacy and tolerability compared with traditional cytotoxic
72 chemotherapy[6]. However, resistance to EGFR-targeted therapies almost
73 invariably develops[7]. Most patients experience disease progression
74 within 1–2 years of treatment initiation, leaving few effective therapeutic
75 alternatives and contributing to unfavorable long-term survival
76 outcomes[8].

77 To address treatment failure following EGFR-TKI therapy, recent
78 research in precision oncology has explored a range of novel therapeutic
79 strategies for EGFR-TKI-resistant NSCLC. These approaches include
80 combination regimens that integrate chemotherapy with immune
81 checkpoint inhibitors, antiangiogenic therapies, or bispecific antibodies.
82 However, despite the encouraging mechanistic rationale, several large

clinical trials, including HARMONi-A, ORIENT-31, MARIPOSA-2, and HERTHENALung02, have not demonstrated statistically significant improvements in overall survival (OS)[9-12]. Given that OS remains the most definitive endpoint for evaluating therapeutic benefits in advanced malignancies, the lack of survival improvement highlights the ongoing unmet clinical need for more effective treatment options in this patient population.

Trophoblast cell surface antigen 2 (Trop-2) has recently emerged as a promising molecular target for developing antibody–drug conjugates (ADCs). Trop-2 is a transmembrane glycoprotein frequently overexpressed in EGFR-mutated NSCLC and is associated with resistance to EGFR-TKI therapy[13]. Sacituzumab tirumotecan (sac-TMT) is a novel Trop-2–directed ADC consisting of a humanized monoclonal antibody targeting Trop-2 linked to SN-38, a potent topoisomerase I inhibitor derived from belotecan[14].

The clinical efficacy of sac-TMT was recently evaluated in the phase 3 OptiTROP-Lung04 trial, a randomized, open-label, multicenter study comparing sac-TMT with platinum-based chemotherapy in patients with EGFR-mutated advanced NSCLC who experienced disease progression after EGFR-TKI therapy[15]. The trial demonstrated clear therapeutic

advantages for sac-TMT, including a significant improvement in progression-free survival (PFS) (8.3 vs. 4.3 months; hazard ratio [HR] = 0.49; $P < 0.001$) as well as a statistically significant benefit in OS (HR = 0.60; two-sided $P = 0.001$). These findings position sac-TMT as a promising treatment option for this patient population, particularly given that other Trop-2-targeted ADCs—such as datopotamab deruxtecan and sacituzumab govitecan—have not achieved comparable survival benefits in clinical trials[16, 17]. Despite these favorable clinical outcomes, the high acquisition cost of sac-TMT raises concerns regarding its affordability and economic value, especially in healthcare systems with constrained resources. As sac-TMT continues to advance through global clinical development across multiple malignancies[18-20], evaluating its economic impact has become increasingly important. Accordingly, the present study aimed to assess the cost-effectiveness of sac-TMT compared with standard chemotherapy from both the U.S. payer perspective and the Chinese healthcare system perspective, thereby providing evidence to support pricing strategies, reimbursement decisions, and optimal allocation of healthcare resources.

Methods

Model Structure

This cost-effectiveness analysis was performed in accordance with the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) guidelines to ensure transparency and robustness of the methodology[21]. The economic model was developed using TreeAge Pro 2023 (TreeAge Software, Williamstown, MA, USA) and further analyzed and validated using R software (version 4.2.3; R Foundation for Statistical Computing, Vienna, Austria). A state-transition Markov framework with three mutually exclusive health states was constructed to represent the disease trajectory of patients with EGFR-mutated advanced NSCLC who developed resistance to EGFR-TKI therapy. The defined health states included PFS, progressive disease (PD), and death (D)(**Figure 1**). At model initiation, all simulated patients were assumed to begin in the PFS state after receiving either sac-TMT or standard chemotherapy. Transitions among health states occurred according to the progression and mortality probabilities estimated from clinical trial outcomes. The analytic time horizon was set at 10 years, which allowed the model to capture more than 99% of the expected mortality events across both treatment strategies, thereby reflecting the full long-term economic consequences of the interventions. The analysis was conducted from two perspectives: the U.S. payer perspective, which considered only direct medical expenditures, and

the Chinese healthcare system perspective, which incorporated all healthcare-related costs in accordance with the national pharmacoeconomic evaluation recommendations in China.

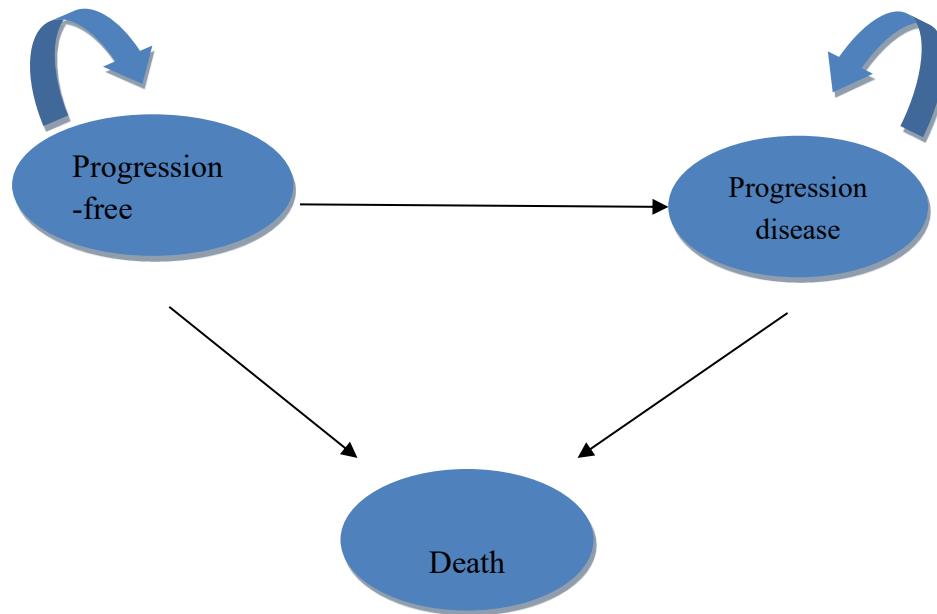


Figure 1. Markov model structure

Patients and Interventions

The modeled cohort was designed to reflect the eligibility criteria of the OptiTROP-Lung04 clinical trial. Eligible participants were adults aged $\geq$ 18 years with histologically or cytologically confirmed nonsquamous NSCLC that was either locally advanced (stage IIIB–IIIC) or metastatic (stage IV) and not suitable for curative surgical resection or definitive chemoradiotherapy. All included patients harbored activating EGFR

166 mutations, specifically exon 19 deletions or exon 21 L858R substitutions.
167 In addition, patients were required to have experienced disease progression
168 after treatment with EGFR-TKIs. This included individuals who
169 progressed after first- or second-generation EGFR-TKIs with confirmed
170 T790M-negative status, as well as those whose disease progressed after
171 third-generation EGFR-TKI therapy, regardless of T790M mutation status.
172 Baseline demographic and clinical characteristics, such as age distribution,
173 sex, smoking history, and disease stage, were aligned with those reported
174 in the OptiTROP-Lung04 trial to maintain consistency with the trial
175 population and enhance the external validity of the model.

176 In the intervention arm, sac-TMT was administered intravenously at a
177 dose of 5 mg/kg on days 1 and 15 of each 28-day treatment cycle. The
178 comparator regimen consisted of pemetrexed (500 mg/m²) combined with
179 either carboplatin (target area under the concentration–time curve of 5
180 mg/mL/min) or cisplatin (75 mg/m²) according to the investigator's
181 discretion. These agents were administered on day 1 of a 21-day cycle for
182 a maximum of four cycles, after which the patients could continue with
183 pemetrexed as maintenance therapy.

184 Following progression on first-line therapy, subsequent treatments
185 were administered to 72.30% of patients in the sac-TMT group and 85.50%

of those in the chemotherapy group. Post-progression treatment strategies followed recommendations from the National Comprehensive Cancer Network (NCCN) and the Chinese Society of Clinical Oncology (CSCO) guidelines for NSCLC[22, 23], consistent with the treatment pathways applied in the OptiTROP-Lung04 trial. Assumptions regarding physiological parameters, including body surface area and creatinine clearance, were derived from previous studies. Radiological tumor evaluations were performed at baseline, every 6 weeks during the first 48 weeks of treatment, and every 12 weeks thereafter. For the economic analysis of adverse events (AEs), only grade 3 or 4 serious adverse events (SAEs) occurring at an incidence greater than 3% in either treatment arm, as reported in the OptiTROP-Lung04 trial, were incorporated into the model. To simplify the analysis, the associated management costs and disutility values were applied during the first treatment cycle, reflecting the clinical observation that the most severe toxicities arise early in the treatment course (**Tables 1-2**).

Table 1. Key clinical input data(China)

Parameters	Baseline value	Range		Distribution	Reference
		Minimum	Maximum		
Survival model for OS					
Sacituzumab Tirumotecan group	Meanlog=3.39			Lognormal	[15]

		Sdlog=1.21				
Chemotherapy group		Shape=1.60 Scale=22.10			Weibull	[15]
<i>Survival model for PFS</i>						
Sacituzumab Tirumotecan group		Meanlog=2.04 Sdlog=1.01			Lognormal	[15]
Chemotherapy group		Shape=2.41 Scale=4.60			Loglogistic	[15]
<i>Drug cost, \$/per cycle</i>						
Cost of Sacituzumab Tirumotecan		1011.7	809.36	1214.04	Gamma	[24]
Cost of Pemetrexed		98.28	78.62	117.94	Gamma	[24]
Cost of Carboplatin		50.57	40.46	60.68	Gamma	[24]
Cost of Cisplatin		34.55	27.64	41.46	Gamma	[24]
Cost of Docetaxel		75.60	60.48	90.72	Gamma	[24]
Cost of Bevacizumab		700.00	560.00	840.00	Gamma	[24]
Cost of the laboratory test		92.99	74.39	111.59	Gamma	[25]
Enhanced CT		171.03	136.82	205.24	Gamma	Local charge
Cost of end-of-life		1839.00	1471.20	2206.80	Gamma	[26, 27]
Best supportive care		345.60	276.48	414.72	Gamma	[26]
Cost of drug administration per unit	Preventive medication per intravenous administration	93.93	75.14	112.72	Gamma	[26, 27]
	Infusion fee per intravenous administration	1.86	1.49	2.23	Gamma	[26, 27]

	Preventive medication	39.14	31.31	46.97	Gamma	[26, 27]
<i>Proportion of receiving subsequent treatment</i>						
Sacituzumab Tirumotecan group		72.30%	57.84%	86.76%	Beta	[15]
Chemotherapy group		85.50%	68.40%	100.00%	Beta	[15]
<i>Cost of AEs, \$</i>						
Anaemia		138.75	111.00	166.50	Gamma	[25]
Decreased platelet count		1505.92	1204.74	1807.10	Gamma	[25]
Decreased white blood cell count		454.26	363.41	545.11	Gamma	[25]
Stomatitis		200.00	160.00	240.00	Gamma	[28]
Fatigue		19.84	15.87	23.81	Gamma	[29]
Hypokalemia		3000.00	2400.00	3600.00	Gamma	[30]
Pneumonia		1625.16	1300.13	1950.19	Gamma	[29]
<i>Utilities</i>						
Utility of PFS		0.69	0.55	0.83	Beta	[31]
Utility of PD		0.60	0.48	0.72	Beta	[31]
<i>Disutility estimates</i>						
Anemia		0.07	0.06	0.08	Beta	[25]
Decreased platelet count		0.20	0.16	0.24	Beta	[25]
Decreased white blood cell count		0.20	0.16	0.24	Beta	[25]
Stomatitis		0.22	0.18	0.26	Beta	[28]
Fatigue		0.07	0.06	0.08	Beta	[29]
Hypokalemia		0.04	0.03	0.05	Beta	[30]
Pneumonia		0.17	0.14	0.20	Beta	[29]
<i>Risk for main AEs in Sacituzumab Tirumotecan group</i>						
Anemia		11.70%	9.36%	14.04%	Beta	[15]

Thrombocytopenia	2.13%	1.70%	2.56%	Beta	[15]
Decreased white blood cell count	39.89%	31.91%	47.87%	Beta	[15]
Stomatitis	4.79%	3.83%	5.75%	Beta	[15]
Fatigue	3.72%	2.98%	4.46%	Beta	[15]
Hypokalemia	2.13%	1.70%	2.56%	Beta	[15]
Pneumonia	6.38%	5.10%	7.66%	Beta	[15]
<i>Risk for main AEs in Chemotherapy group</i>					
Anemia	14.29%	11.43%	17.15%	Beta	[15]
Thrombocytopenia	16.48%	13.18%	19.78%	Beta	[15]
Decreased white blood cell count	32.97%	26.38%	39.56%	Beta	[15]
Fatigue	2.75%	2.20%	3.30%	Beta	[15]
Hypokalemia	5.49%	4.39%	6.59%	Beta	[15]
Pneumonia	3.85%	3.08%	4.62%	Beta	[15]
Discount rate(China)	5.00%	4.00%	6.00%	Beta	
BMI/m ²	1.72				
Weight/kg	65				
\$1 = ¥7.1429	41,910.00				

OS: overall survival, PFS: progression-free survival, PD: progression disease, AE: adverse event, BMI: body mass index.

Table 2. Key clinical input data (US)

Parameters	Baseline value	Range		Distribut ion	Reference
		Minimum	Maximum		
<i>Drug cost, \$/per cycle</i>					
Cost of Sacituzumab Tirumotecan	16269.67	13015.74	19523.60	Gamma	Estimated
Cost of Pemetrexed	7977.4	6381.92	9572.88	Gamma	[32]

Cost of Carboplatin	54.54	43.63	65.45	Gamma	[32]
Cost of Cisplatin	37.62	30.10	45.14	Gamma	[32]
Cost of Docetaxel	100.56	80.45	120.67	Gamma	[32]
Cost of Bevacizumab	8270.47	6616.38	9924.56	Gamma	[32]
Cost of the laboratory test	373.00	298.40	447.60	Gamma	[32]
Enhanced CT	711.00	568.80	853.20	Gamma	[32]
Cost of end-of-life	21603.00	17282.40	25923.60	Gamma	[33]
Best supportive care	1447.79	1158.23	1737.35	Gamma	[33]
Cost of drug administration first hour	142.55	114.04	171.06	Gamma	[32]
Administration intravenous, additional hour	30.68	24.54	36.82	Gamma	[32]
<i>Cost of AEs, \$</i>					
Anemia	20620.00	16496.00	24744.00	Gamma	[34]
Decreased platelet count	22698.00	18158.40	27237.60	Gamma	[34]
Decreased neutrophil count	17181.00	13744.80	20617.20	Gamma	[34]
Stomatitis	18515.00	14812.00	22218.00	Gamma	[34]
Fatigue	20620.00	16496.00	24744.00	Gamma	[34]
Hypokalemia	25326.00	20260.80	30391.20	Gamma	[34]
Pneumonia	21929.00	17543.20	26314.80	Gamma	[34]
Discount rate	3.00%	2.40%	3.60%	Beta	
BMI/m ²	1.79				
Weight/kg	75				

207 AE: adverse event, BMI: body mass index.

208

209 ***Base-Case Analysis***

The primary outcomes of the economic evaluation included overall survival expressed in life-years, quality-adjusted life-years (QALYs), incremental cost-effectiveness ratio (ICER), incremental net health benefit (INHB), and incremental net monetary benefit (INMB). Future costs and health outcomes were discounted to present values to reflect time preferences. Consistent with national pharmacoeconomic guidelines, an annual discount rate of 3% was applied for the U.S. analysis and 5% for the Chinese analysis[35, 36]. For the Chinese setting, all cost estimates were first adjusted to 2025 price levels using the national consumer price index and subsequently converted to US dollars at an exchange rate of \$1 = ¥7.1429.

The willingness-to-pay (WTP) threshold for each country was defined as three times the national per capita gross domestic product (GDP) for 2025, following recommendations commonly used in economic evaluations in middle- and high-income settings. Based on this approach, the WTP threshold was estimated at \$41,910.00 per QALY for China and \$150,000.00 per QALY for the U.S[37, 38]. To further quantify the economic value of sac-TMT relative to chemotherapy, INHB and INMB were calculated using standard pharmacoeconomic equations. Specifically, INHB was estimated as: $INHB(\lambda) = (\mu E1 - \mu E0) - (\mu C1 - \mu C0) / \lambda = \Delta E -$

$\Delta C / \lambda$ and INMB was calculated as: $INMB(\lambda) = (\mu E1 - \mu E0) \times \lambda - (\mu C1 - \mu C0) = \Delta E \times \lambda - \Delta C$, where μC_i and μE_i represent the mean costs and health outcomes for the sac-TMT group ($i = 1$) and the chemotherapy group ($i = 0$), respectively, and λ denotes the selected WTP threshold.

Clinical Data Inputs

Survival probabilities for OS and PFS were derived from the Kaplan–Meier curves reported in the OptiTROP-Lung04 trial. Graphical data were digitized using GetData Graph Digitizer software (<http://getdata-graph-digitizer.com>), and individual patient-level data were reconstructed following the algorithm proposed by Guyot et al[37].

Because the duration of follow-up in the clinical trial was insufficient to cover the entire analytic time horizon, survival extrapolation was necessary to estimate the long-term outcomes[39]. The reconstructed time-to-event data were fitted using several candidate parametric survival distributions, including exponential, Weibull, Gompertz, gamma, log-logistic, log-normal, and generalized gamma models.

The selection of the optimal survival function was based on multiple criteria. These included statistical goodness-of-fit evaluated using the Akaike information criterion (AIC), likelihood-based comparison through

log-likelihood statistics (LogLik), and visual examination of fitted survival curves against observed Kaplan–Meier data (**Table 3**).

Prior to estimating the hazard ratios (HRs) for OS and PFS using the Cox proportional hazards (PH) model, the validity of the proportional hazards’ assumption, an essential requirement for appropriate model interpretation, was assessed using two complementary approaches. First, a graphical evaluation of the log–log survival plots was performed. Second, Schoenfeld residuals were analyzed to provide quantitative assessments[40, 41] (**Figures 2-3**).

Although statistical testing yielded p-values greater than 0.05 for both OS and PFS, suggesting no significant violation of the PH assumption, two additional observations raised these concerns. Specifically, the cumulative hazard curves between the treatment and comparator groups appeared to cross, and the smoothed Schoenfeld residuals demonstrated a non-horizontal pattern over time (**Figures 4-5**). These patterns were documented as potential limitations of the proportional hazards assumption and were acknowledged in the interpretation of the modeling results of this study.

Table 3. The Akaike information criteria (AIC) and Bayesian information criteria (BIC)

Type of	Sacituzumab Tirum otecan (OS)	Chemotherapy (OS)	Sacituzumab Tirum otecan (PFS)	Chemotherapy (PFS)
------------	----------------------------------	----------------------	-----------------------------------	-----------------------

distrib ution	AIC	BIC	Log Lik	AIC	BIC	Log Lik	AIC	BIC	Log Lik	AIC	BIC	Log Lik
Expon ential	643. 1530	646. 3895	320. 5765	866. 1284	869. 3649	432. 0642	983. 8194	987. 0558	490. 9097	892. 6093	895. 8458	445. 3047
Weib ull	638. 2849	644. 7578	317. 1425	845. 2212	851. 6941	420. 6106	975. 1846	981. 6575	485. 5923	857. 6488	864. 1216	426. 8244
Gam ma	637. 6461	644. 1190	316. 8231	845. 7552	852. 2281	420. 8776	973. 0825	979. 5554	484. 5413	846. 8228	853. 2957	421. 4114
Gener alised gamm a	638. 7236	648. 4329	316. 3618	847. 0957	856. 8051	420. 5479	972. 2344	981. 9437	483. 1172	841. 2113	850. 9207	417. 6057
Gomp ertz	641. 7907	648. 2636	318. 8954	847. 8134	854. 2863	421. 9067	981. 7390	988. 2118	488. 8695	884. 3369	890. 8098	440. 1685
Logno rmal	637. 1281	643. 6010	316. 5640	527. 0768	532. 5840	261. 5384	971. 4021	977. 8750	483. 7011	839. 6874	846. 1603	417. 8437
Log- logisti c	637. 1685	643. 6414	316. 5843	529. 9545	535. 4617	262. 9773	972. 9121	979. 3850	484. 4560	836. 8792	843. 3521	416. 4396

268 OS: overall survival, PFS: progression-free survival, AIC: Akaike information
269 criterion, BIC: Bayesian information criterion, LogLik: Log likelihood.

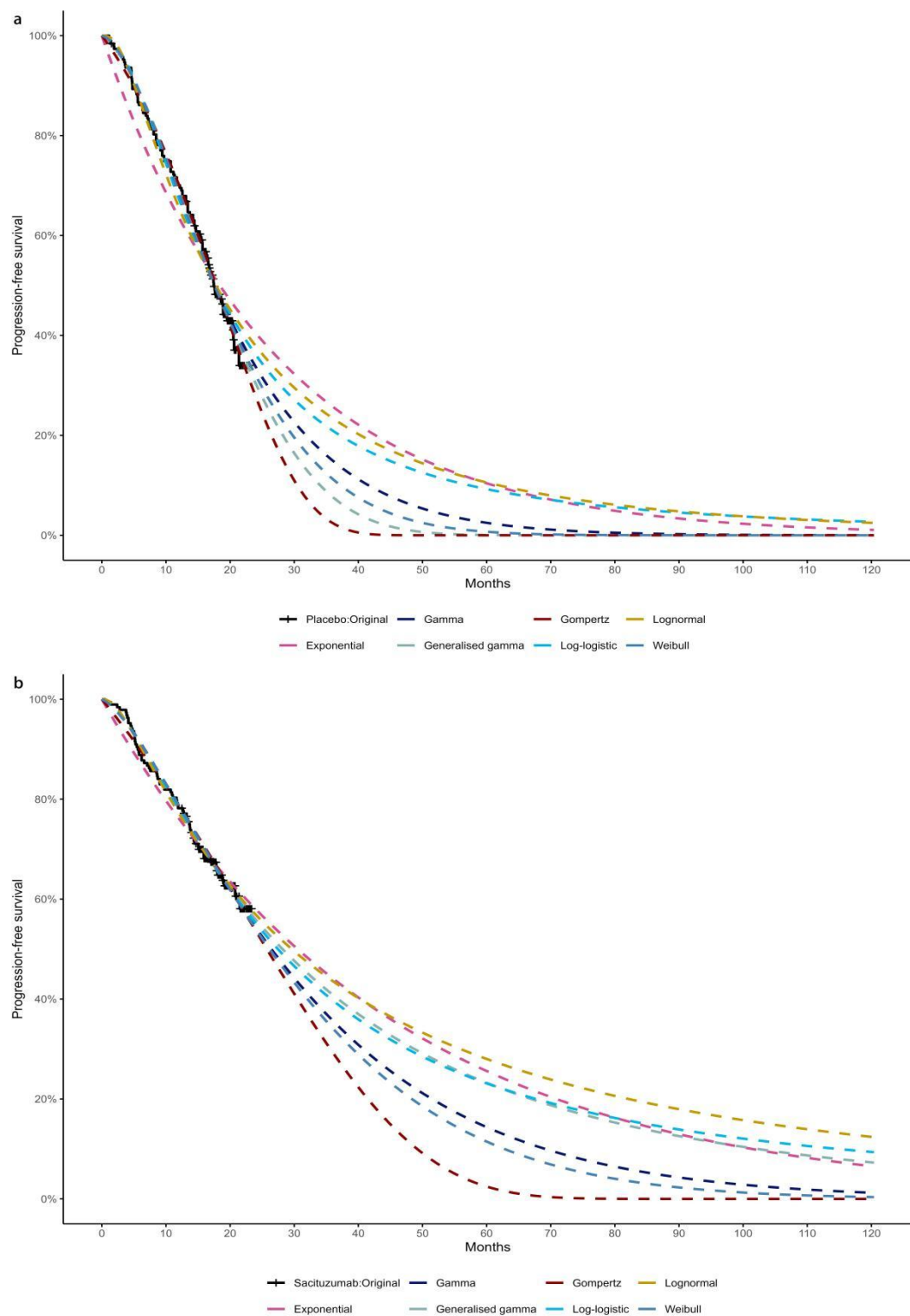


Figure 2. The Kaplan-Meier:(a) overall survival curves of Chemotherapy group, (b) overall survival curves of Sacituzumab Tirumotecan group.

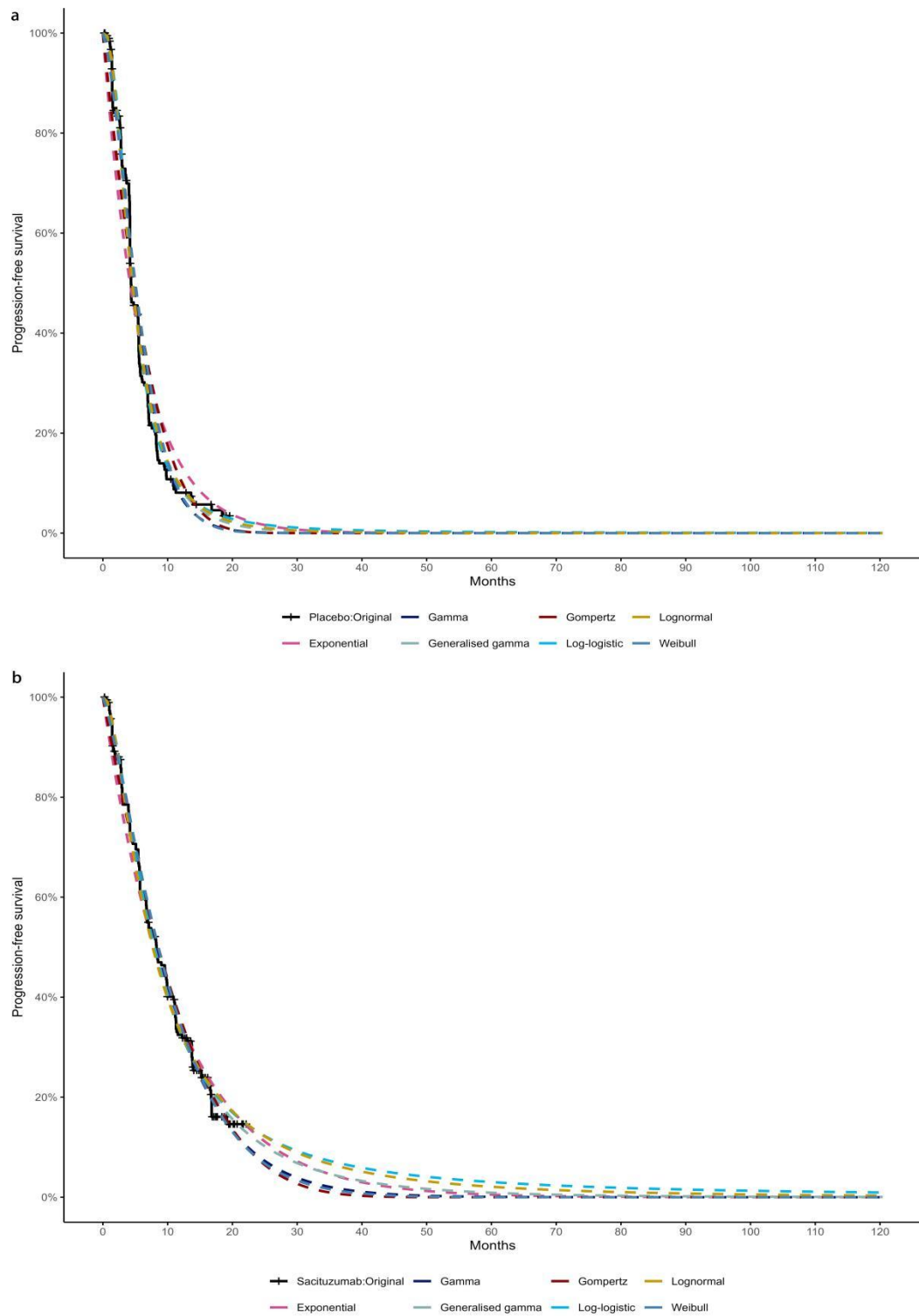


Figure 3. The Kaplan-Meier:(a) progression-free survival curves of Chemotherapy group, (b) progression-free survival curves of Sacituzumab Tirumotecan group.

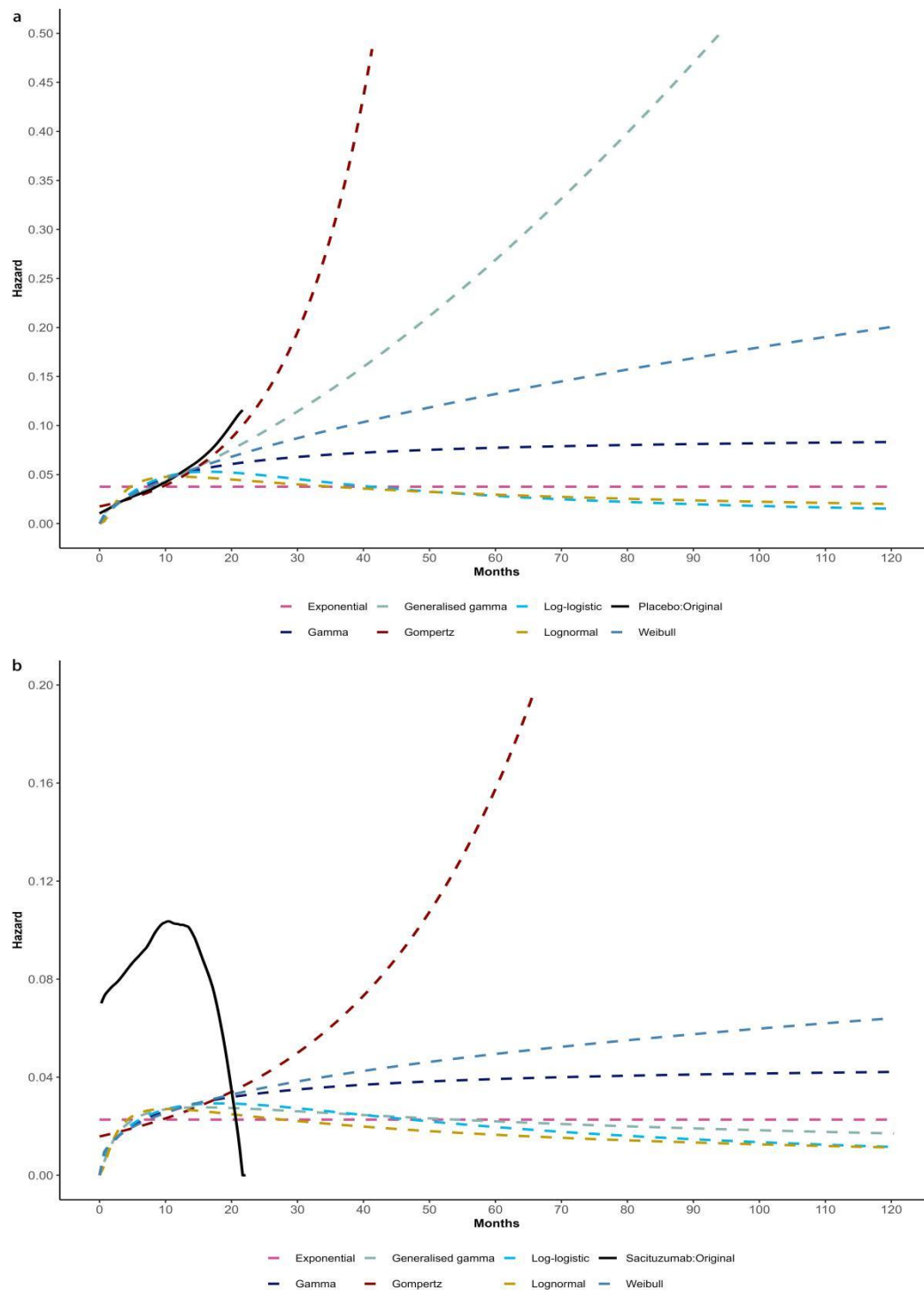
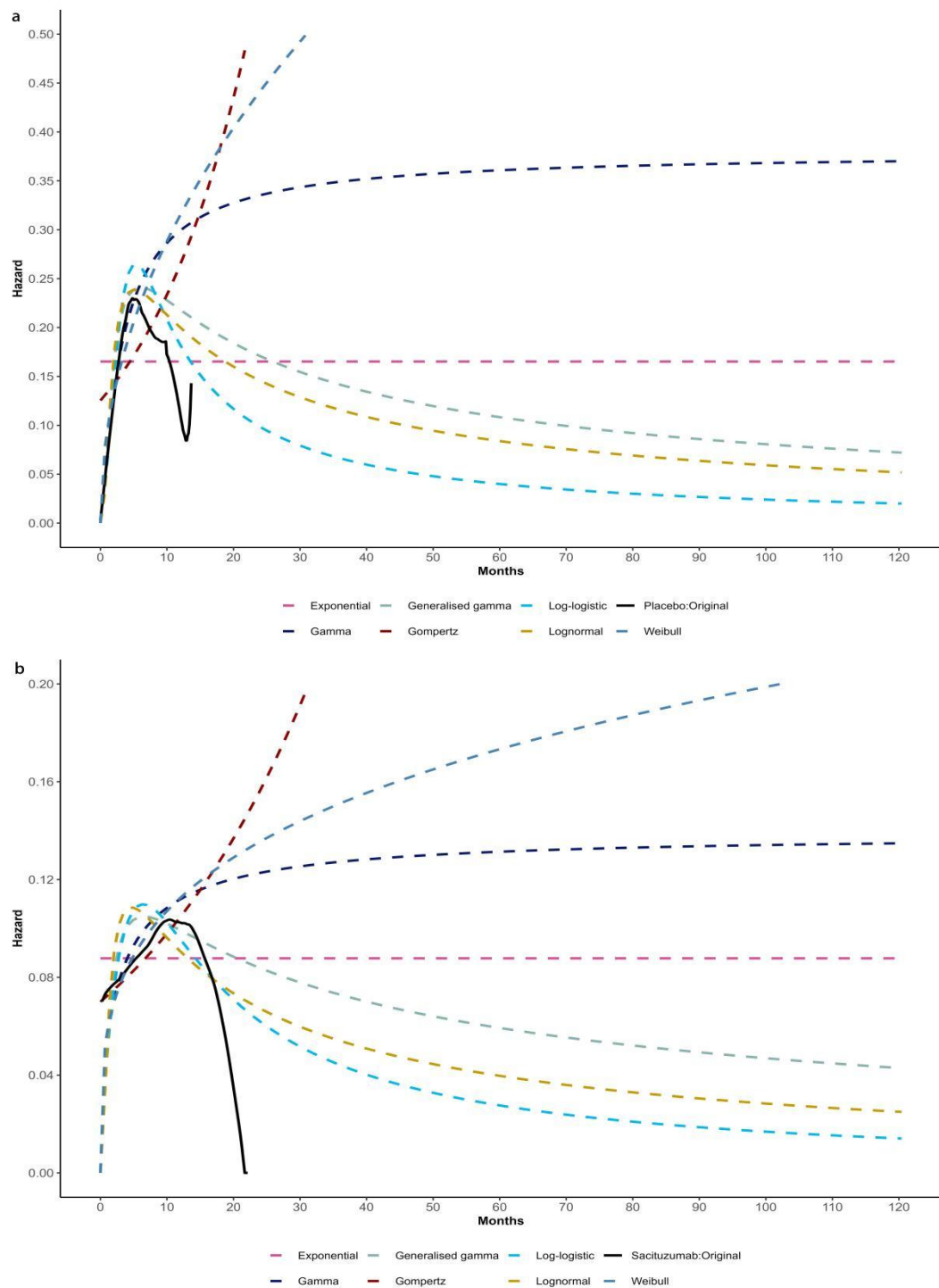


Figure 4. Comparison of Fitted Proportional Hazards Survival Models With Observed Kaplan–Meier Curves of overall survival curves:(a) Chemotherapy group, (b) Sacituzumab Tirumotecan group.



280

281 **Figure 5.** Comparison of Fitted Proportional Hazards Survival Models With Observed
 282 Kaplan–Meier Curves of progression-free survival curves:(a) Chemotherapy group, (b)
 283 Sacituzumab Tirumotecan group.

Cost Input

The analysis incorporated a range of direct medical costs associated with the treatment and disease management. These included medication acquisition costs, laboratory testing, contrast-enhanced computed tomography (CT) imaging, prophylactic medications required for intravenous infusion, drug administration expenses, best supportive care, end-of-life care, costs of subsequent therapies following disease progression, and expenditures related to the management of grade 3–4 AEs[24-30, 32-34] (**Tables 1-2**). Because official pricing data for sac-TMT were unavailable in the U.S. at the time of the analysis, an estimated price was derived using datopotamab deruxtecan—a comparable Trop-2–targeted antibody–drug conjugate—as a reference[42]. This surrogate estimate was adjusted to account for differences in the dosing schedules and therapeutic efficacy between the two agents. The drug dosing schedules were consistent with the OptiTROP-Lung04 trial protocol, and the cost per treatment cycle was calculated using country-specific pricing sources.

Utility Inputs

Health utility values were incorporated to reflect the quality of life (QoL) of patients associated with different disease states. The utility scores ranged

from 0, representing death or the poorest health status, to 1, indicating perfect health. In the present model, the mean utility values for PFS and PD health states were set at 0.69 and 0.60, respectively, based on previously published studies[31] (**Table 1**). In addition, the disutility associated with severe treatment-related AEs (grade ≥ 3) was incorporated into the model to capture the negative impact of these complications on the patient's QoL [25, 28-30].

Scenario and Subgroup Analyses

Scenario analyses were performed to explore the uncertainty surrounding the price of sac-TMT in the U.S., given the absence of directly reported pricing data. Using a price index approach and referencing the market price of sacituzumab govitecan, the estimated US price of sacituzumab tirumotecan (400 mg) was calculated as \$16,269.67. To evaluate the potential economic value of sac-TMT across a range of possible pricing scenarios, the drug cost varied between \$0 and \$20,000 per 400 mg dose and was assessed against the U.S. WTP threshold of \$150,000/QALY.

In addition, exploratory subgroup analyses were conducted to investigate the cost-effectiveness of sac-TMT across predefined patient subgroups reported in the OptiTROP-Lung04 trial. These subgroups included sex, age (≤ 65 vs. > 65 years), smoking history (never vs. ever),

EGFR mutation subtype (exon 19 deletion vs. L858R mutation), T790M mutation status (positive, negative, or unknown), treatment line (first/second vs. later lines), and presence of brain or liver metastases. Subgroup-specific treatment effects were incorporated by adjusting the HRs for OS and PFS. Survival functions were estimated using the *flexsurv* package in R, and economic simulations were implemented using TreeAge Pro 2023.

Sensitivity Analysis

Sensitivity analyses were performed to evaluate the robustness of the model and examine how uncertainty in key parameters might influence economic outcomes. Deterministic one-way sensitivity analyses (OWSA) were conducted by varying individual model parameters across a range of $\pm 20\%$ around their base-case estimates, allowing assessment of the relative influence of each parameter on ICER.

In addition, probabilistic sensitivity analyses (PSA) were performed using a Monte Carlo simulation with 10,000 iterations. In these simulations, all input parameters were simultaneously varied according to their predefined probability distributions to account for the joint parameter uncertainty. The PSA results were summarized using cost-effectiveness acceptability curves (CEACs), which depict the likelihood that sac-TMT

would be considered the most cost-effective treatment option across a range of WTP thresholds.

Results

Base-Case Analysis

Across the 10-year analytic horizon, the base-case model estimated that treatment with sac-TMT generated an average of 1.57 QALYs at a total cost of \$49,559.94. In comparison, the chemotherapy strategy produced 0.73 QALYs with an overall cost of \$15,808.44. Relative to chemotherapy, sac-TMT resulted in an additional 0.84 QALYs but required an incremental expenditure of \$33,751.50, corresponding to an ICER of \$40,116.07/QALY(**Table 4**).

When evaluated against the Chinese WTP threshold of \$41,910.00 per QALY, sac-TMT was considered borderline cost-effective. The INHB was estimated at 0.04 QALYs, while the INMB reached \$1,509.31, suggesting a modest economic advantage in the Chinese healthcare setting.

However, the findings differed substantially when examined from a US payer perspective. In this scenario, sac-TMT provided an incremental benefit of 0.91 QALYs but required an additional cost of \$399,471.55 compared with chemotherapy. This resulted in an ICER of \$438,507.95 per

QALY, far exceeding the commonly accepted US WTP threshold of \$150,000.00 per QALY. Correspondingly, the estimated INHB was -1.75 QALYs and, the INMB was -\$262,824.70, indicating that sac-TMT would not be considered a cost-effective option in the U.S. under current pricing conditions.

Table 4. The base case analysis

Treatment	Cost	QALY	Incremental cost	Incremental QALY	INHB	INMB	ICER
Sacituzumab Tirumotecan(China)	49559.94	1.57	33751.50	0.84	0.04	1509.31	40116.072
Chemotherapy(China)	15808.44	0.73					
Sacituzumab Tirumotecan(US)	602030.96	1.65	399471.55	0.91	-1.75	-262824.70	438507.95
Chemotherapy(US)	202559.41	0.74					

QALY: Quality-adjusted life year, ICER: Incremental cost-effectiveness ratio, INMB : the incremental net monetary benefits, INHB: the incremental net health benefits.

Price Simulation

The U.S. price simulation analysis demonstrated a clear positive relationship between the sac-TMT price and the ICER value. As the assumed price of sac-TMT increased from \$0 to \$20,000.00 per 400 mg dose, the ICER rose proportionally. The analysis indicated that sac-TMT

would only meet the cost-effectiveness criterion in the U.S. (ICER $\leq$ \$150,000.00 per QALY) if the drug price were reduced to below \$3,333.75 per 400 mg. These findings emphasize the substantial influence of drug pricing on the economic value of sac-TMT in the U.S. healthcare system (Figure 6).

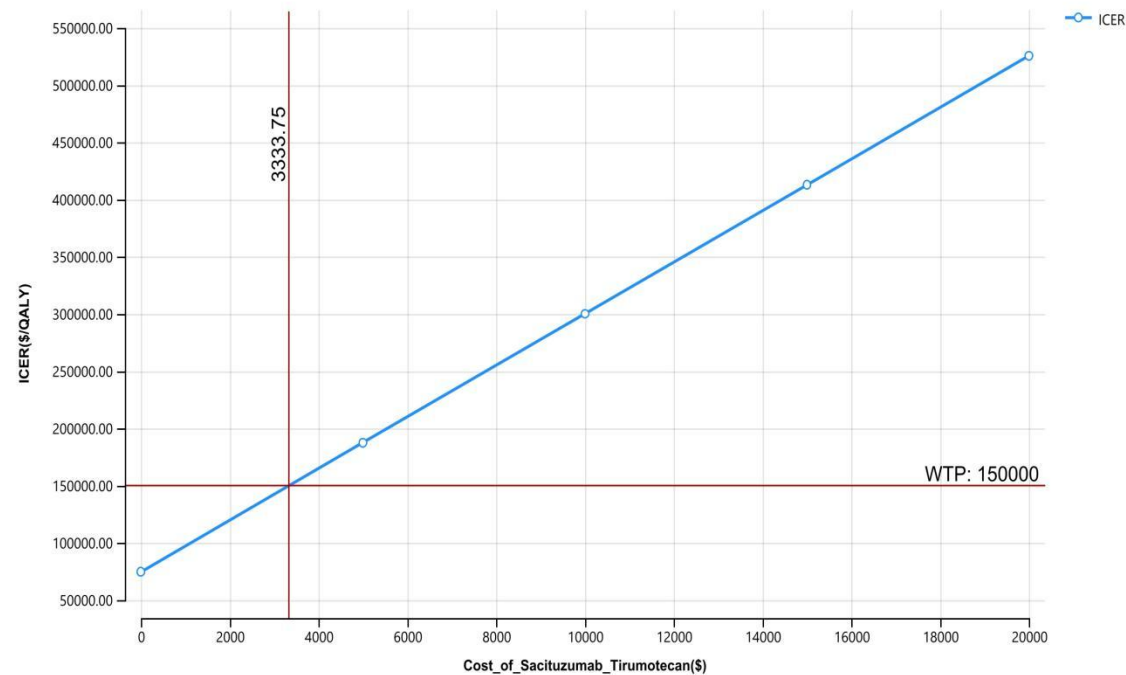


Figure 6. Price Simulation of the U.S.

Subgroup Analyses

Exploratory subgroup analyses suggested that sac-TMT could be considered cost-effective in China for several clinically relevant patient groups. These included female patients, individuals aged ≤ 65 years, never-smokers, patients harboring EGFR exon 19 deletions, individuals with

T790M-positive tumors, patients receiving sac-TMT as first- or second-line therapy, and those with or without brain or liver metastases(**Figure 7**).

Among these subgroups, the most favorable economic outcomes were observed in patients with T790M-positive disease, who demonstrated the highest INHB (0.37; 95% CI: -0.06 to 0.69). This result is likely attributable to the longer OS observed in this subgroup, which may reflect the availability of more effective targeted treatment options following disease progression.

In contrast, all evaluated patient subgroups in the U.S. yielded negative INHB values, indicating that sac-TMT would not be considered cost-effective in any subgroup under current pricing conditions, regardless of demographic or clinical characteristics (**Figure 8**).

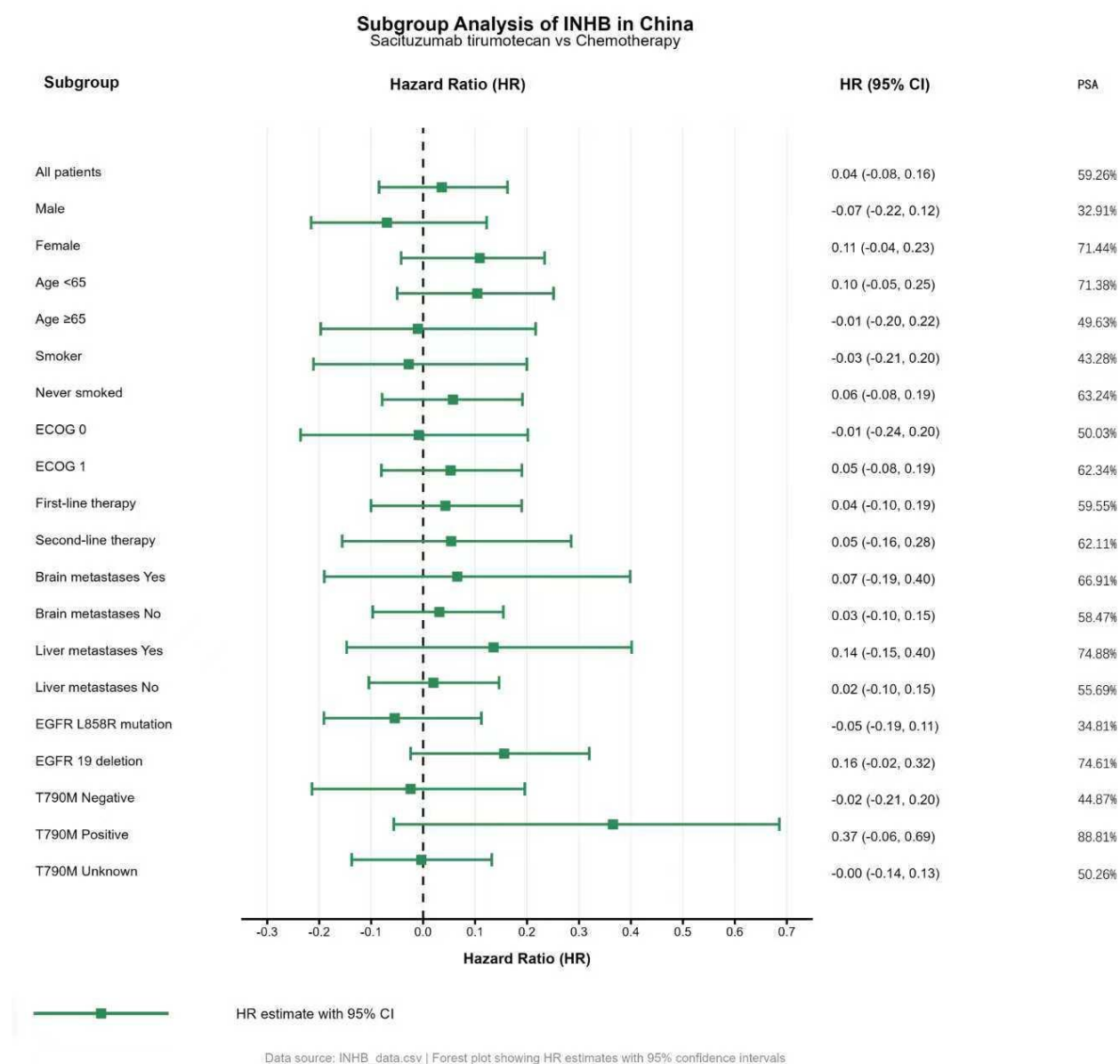


Figure 7. Subgroup analysis results in China.

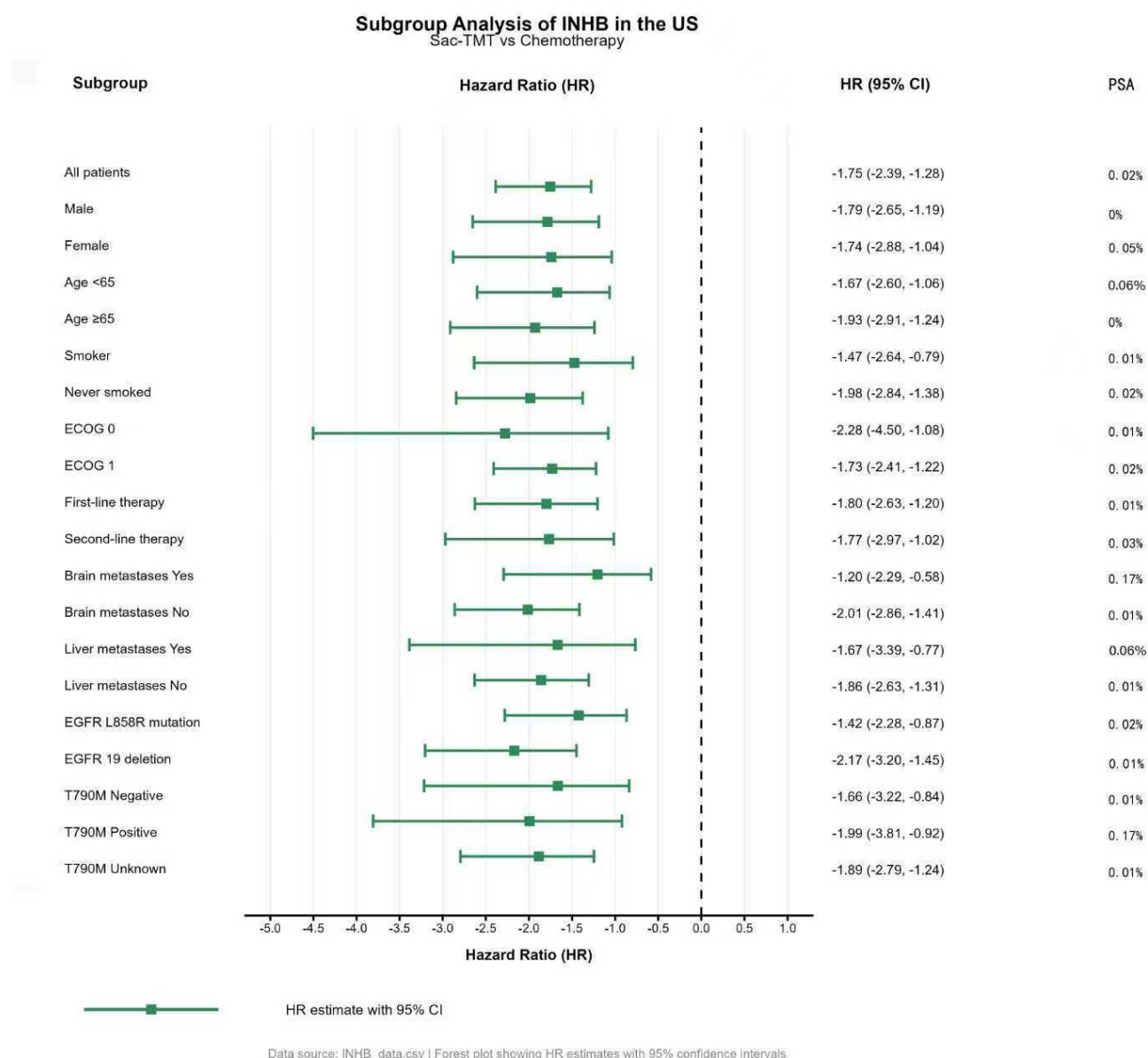


Figure 8. Subgroup analysis results in the U.S.

Sensitivity Analyses

The OWSA, summarized using tornado diagrams, identified several parameters that exerted the greatest influence on the ICER estimates in both China and the U.S. The most influential variables included the utility

values assigned to the PFS and PD health states, acquisition costs of sac-TMT and bevacizumab, and the proportion of patients receiving subsequent therapies following disease progression (**Figure 9**).

In the Chinese healthcare setting, variations in these parameters—particularly the utilities of PFS and PD, the cost of sac-TMT, the cost of bevacizumab, and the proportion of patients receiving subsequent treatment in the sac-TMT arm—were the only factors that could alter the overall conclusion regarding cost-effectiveness. This finding suggests that the base case results are relatively robust within the plausible parameter ranges.

PSA results, illustrated through CEAC and probabilistic scatter plots (**Figures 10–11**), further quantified the uncertainty associated with this model. In China, the probability that sac-TMT would be considered cost-effective at the WTP threshold of \$41,910.00 per QALY was estimated at 59.26%, indicating a moderate level of confidence in the base-case findings. By contrast, in the U.S., the probability of sac-TMT being cost-effective at the \$150,000.00 per QALY threshold was only 0.03%, reinforcing the conclusion that sac-TMT is highly unlikely to represent a cost-effective intervention in the U.S. healthcare system at its current price.



Figure 9. The tornado diagram of one-way sensitivity analysis: (a) China, (b) The U.S.

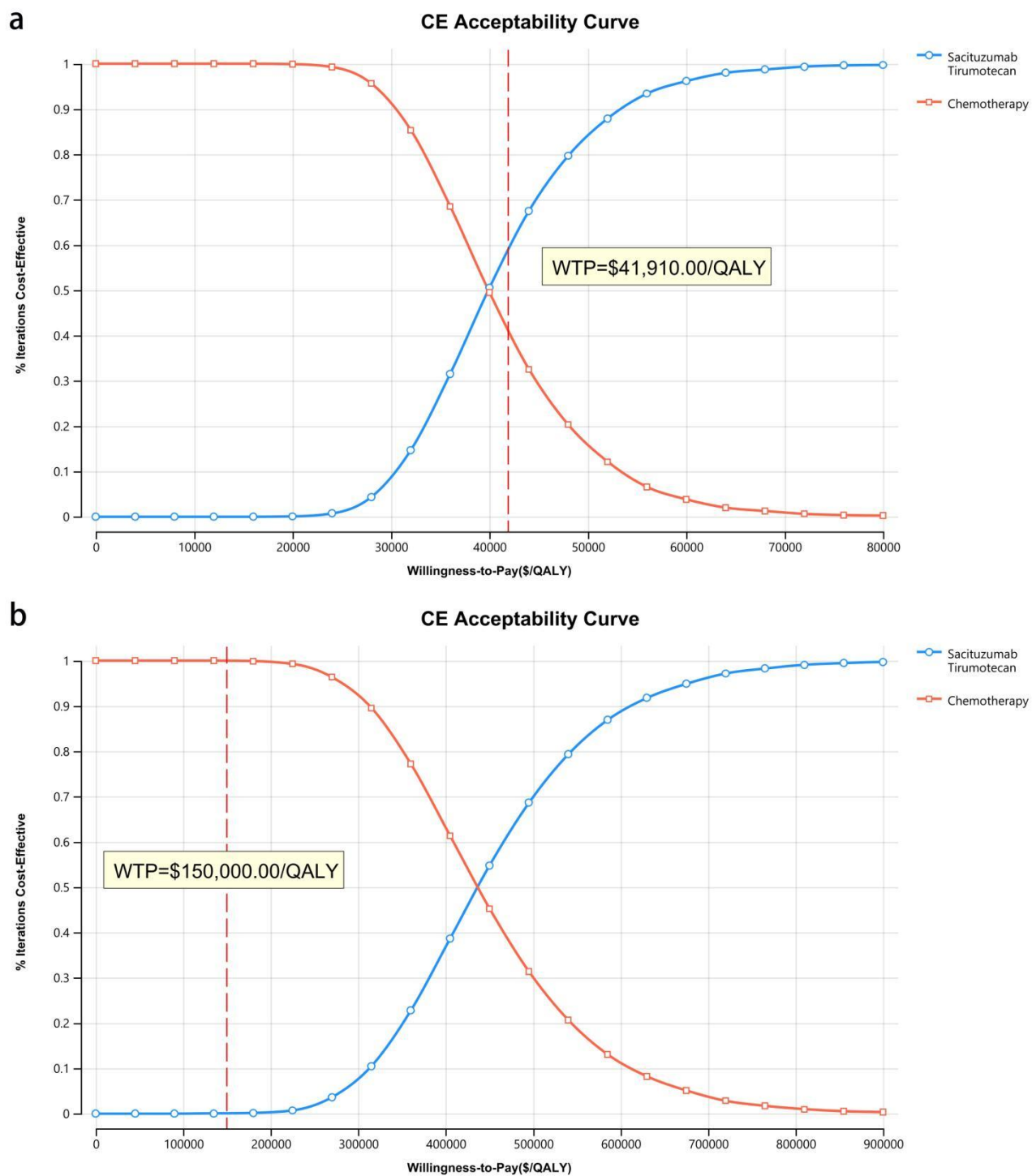


Figure 10. The cost-effectiveness acceptability curve: (a) China, (b) The U.S.

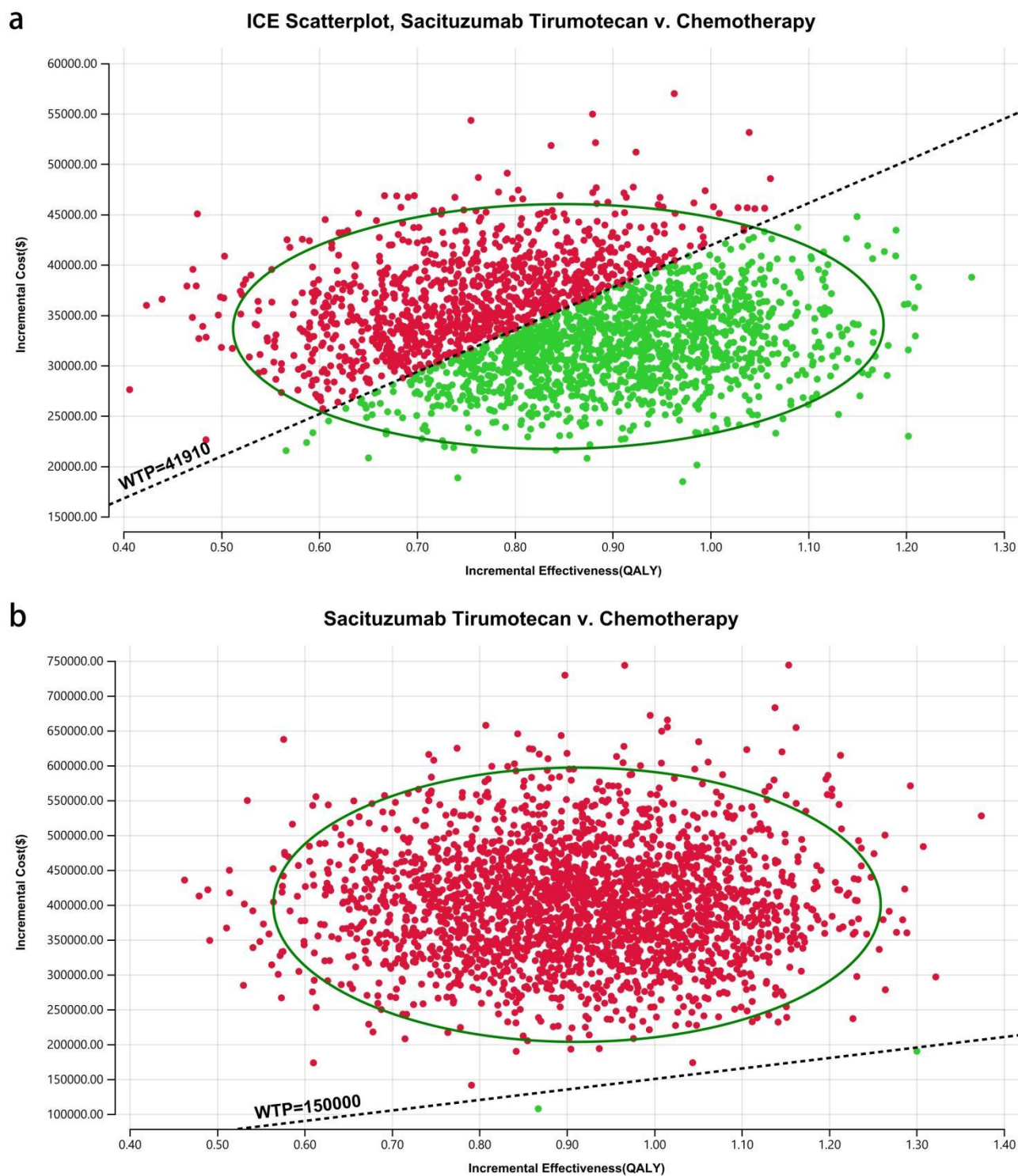


Figure 11. The cost-effectiveness probabilistic scatter plot: (a) China, (b) The U.S.

Discussion

Following the emergence of resistance to third-generation EGFR tyrosine kinase inhibitors, several novel therapeutic strategies have been investigated for patients with EGFR-mutated advanced NSCLC. These include PD-1/VEGF bispecific antibodies such as ivonescimab[10], EGFR–MET bispecific antibody–based combinations involving amivantamab with chemotherapy or lazertinib[43, 44], and Trop-2–targeted ADCs such as datopotamab deruxtecan[16]. However, recent economic evaluations have suggested that these agents do not currently represent cost-effective treatment options in either China or the U.S. Against this background[42, 45-50], the present study provides the first comprehensive pharmacoeconomic assessment comparing sac-TMT with platinum-based chemotherapy in patients with EGFR-mutated NSCLC who have developed resistance to EGFR-TKI therapy. By evaluating both the U.S. payer perspective and the Chinese healthcare system perspective, our analysis highlights a pronounced difference in the economic value of sac-TMT between the two healthcare settings. Specifically, sac-TMT demonstrates borderline cost-effectiveness in China, where the WTP threshold reflects middle-income country economic standards, whereas the therapy does not appear economically favorable in the U.S. under current

pricing conditions. These findings emphasize the importance of region-specific pricing and reimbursement strategies that account for differences in healthcare financing structures, economic capacity, and policy priorities when assessing the value of innovative cancer therapies.

The scenario analyses further support the stability of the primary findings. Although increasing the cost of subsequent treatments led to higher ICER values, this change had little influence on the overall conclusions for the U.S. because the base-case ICER for sac-TMT substantially exceeded the accepted WTP threshold. This observation suggests that the lack of cost-effectiveness observed in the U.S. analysis is unlikely to be altered by reasonable variations in post-progression treatment costs. In addition, subgroup analyses indicated that the economic value of sac-TMT was closely related to improvements in survival outcomes of patients. Patients with T790M-positive tumors showed the most favorable economic results, largely due to the greater OS benefit observed in this subgroup, which may reflect the availability of more effective targeted therapies after disease progression. Nevertheless, these subgroup findings should be interpreted cautiously because of the relatively small number of patients within each subgroup, and the reliance on hazard ratios to estimate subgroup-specific survival outcomes may

introduce additional uncertainty.

The rapid expansion of the global ADC market provides important context for the interpretation of these findings. By 2025, more than 20 ADC products will have collectively generated approximately \$16.51 billion in global revenue, representing an annual growth rate of roughly 27%. China has become an increasingly influential contributor to this field, with substantial progress in ADC target identification, molecular engineering, and clinical development of ADCs. In this context, the potential cost-effectiveness of sac-TMT in China is particularly noteworthy, given the high prevalence of EGFR-mutated NSCLC and the ongoing need to allocate limited healthcare resources efficiently within the national medical insurance system. In contrast, the markedly higher treatment costs observed in the U.S. substantially limit the economic feasibility of sac-TMT. These results highlight the potential need for meaningful price reductions or the adoption of alternative reimbursement strategies, such as value-based pricing, to enhance the affordability and accessibility of this therapy in the US healthcare system.

This study has several limitations. First, the clinical data used in the model were primarily derived from the OptiTROP-Lung04 trial[15], which was largely conducted in Chinese populations. Consequently, differences

in demographic characteristics, treatment patterns, and healthcare costs between Chinese and U.S. patients may affect the generalizability of the findings to the U.S. healthcare context. Second, the diversity of subsequent treatment options following disease progression, including chemotherapy, targeted therapy, and immunotherapy, introduces additional complexity into the model. Because the OptiTROP-Lung04 trial did not provide detailed information on specific second-line therapies, assumptions were required regarding post-progression treatment patterns and best supportive care. Third, health utility data were not directly collected from the clinical trial. The absence of EQ-5D measurements, which represent the standard instrument for utility assessment in economic evaluations, required the use of utility estimates derived from previously published studies. To minimize this limitation, we selected utility values from the EVOKE-01 trial[31], which evaluated a comparable Trop-2–targeted ADC in NSCLC and therefore provides a relevant approximation of HRQoL outcomes in this patient population.

Conclusion

This pharmacoeconomic analysis indicates that sacituzumab tirumotecan may represent a marginally cost-effective treatment alternative to

520 platinum-based chemotherapy for patients with EGFR-mutated advanced
521 NSCLC who have developed resistance to EGFR-TKI therapy within the
522 Chinese healthcare system. In contrast, from the perspective of the U.S.
523 payer, sac-TMT is unlikely to be considered cost-effective under current
524 pricing conditions. Price simulation analyses suggest that the cost of sac-
525 TMT would need to decrease to below \$3,333.75 per treatment cycle to
526 meet the established U.S. willingness-to-pay threshold. These findings
527 provide important evidence to inform policy discussions regarding drug
528 pricing, reimbursement decisions, and resource allocation and may assist
529 policymakers, payers, and pharmaceutical manufacturers in improving
530 access to innovative oncology treatments across different healthcare
531 systems.

532 **Declarations**

534 **Ethics approval and consent to participate**

535 Because our study used publicly available research data and did not involve
536 individual patient information, it was exempt from requiring ethical
537 approval by an institutional review board or patient consent.

538 **Consent for publication**

539 Not applicable.

Availability of data and materials

The datasets generated or analyzed during this study are included in this published article (and supplementary information files), and they are available from the corresponding author upon reasonable request.

Competing interests

The authors declare no competing interests.

Funding

This work is supported by Self-raised Funds Research Project of the Guangxi Zhuang Autonomous Region Health Commission (Z-C20250176) and Discipline Cluster Construction Fund of Nanxishan Hospital of Guangxi Zhuang Autonomous Region.

Author contributions

Conceptualization: Wenwang Lang. Data curation: Wenwang Lang, Qinling Jiang, Qi Ai, Xianling Zhao, Liang Xiao. Formal analysis: Wenwang Lang, Huiqing Jiang. Funding acquisition: Yulong He, Qinling Jiang. Investigation: Wenwang Lang, Liang Xiao. Methodology: Wenwang Lang, Yulong He, Huiqing Jiang, Xianling Zhao. Resources: Wenwang Lang, Yulong He, Qinling Jiang, Xianling Zhao. Software: Wenwang Lang, Yulong He, Qi Ai, Liang Xiao. Supervision: Qinling Jiang. Validation: Qi Ai. Writing – original draft: Wenwang Lang. Writing – review & editing:

Wenwang Lang, Yulong He, Huiqing Jiang, Qi Ai, Xianling Zhao, Liang Xiao. All authors have reviewed and approved the manuscript.

Acknowledgements

Not applicable.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F: **Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries.** *CA Cancer J Clin* 2021, **71**(3):209-249.
2. Thai AA, Solomon BJ, Sequist LV, Gainor JF, Heist RS: **Lung cancer.** *Lancet* 2021, **398**(10299):535-554.
3. Zhang Y, Vaccarella S, Morgan E, Li M, Etcheberry J, Chokunonga E, Manraj SS, Kamate B, Omonisi A, Bray F: **Global variations in lung cancer incidence by histological subtype in 2020: a population-based study.** *Lancet Oncol* 2023, **24**(11):1206-1218.
4. Melosky B, Kambartel K, Häntschel M, Bennetts M, Nickens DJ, Brinkmann J, Kayser A, Moran M, Cappuzzo F: **Worldwide Prevalence of Epidermal Growth Factor Receptor Mutations in Non-Small Cell Lung Cancer: A Meta-Analysis.** *Mol Diagn Ther* 2022, **26**(1):7-18.
5. Zhou F, Guo H, Xia Y, Le X, Tan DSW, Ramalingam SS, Zhou C: **The changing treatment landscape of EGFR-mutant non-small-cell lung cancer.** *Nat Rev Clin Oncol* 2025, **22**(2):95-116.
6. Hendriks LEL, Remon J, Faivre-Finn C, Garassino MC, Heymach JV, Kerr KM, Tan DSW, Veronesi G, Reck M: **Non-small-cell lung cancer.** *Nat Rev Dis Primers* 2024, **10**(1):71.
7. Fu K, Xie F, Wang F, Fu L: **Therapeutic strategies for EGFR-mutated non-small cell lung cancer patients with osimertinib resistance.** *J Hematol Oncol* 2022, **15**(1):173.
8. Wang Y, Zhang L, Zhan J, Wen L, Zhao X, Sun H, Chen X, Zhang Y, Chen G, Zhao Y *et al*: **Comparative efficacy and safety of post-TKI treatments for advanced EGFR-mutant non-small-cell lung cancer: a systematic review and network meta-analysis.** *Lung Cancer* 2026, **212**:108914.
9. Lu S, Wu L, Jian H, Chen Y, Wang Q, Fang J, Wang Z, Hu Y, Sun M, Han L *et al*: **Sintilimab plus bevacizumab biosimilar IBI305 and chemotherapy for patients with EGFR-mutated non-squamous non-small-cell lung cancer who progressed on EGFR tyrosine-kinase inhibitor therapy (ORIENT-31): first interim results from a randomised, double-blind, multicentre, phase 3 trial.** *Lancet Oncol* 2022, **23**(9):1167-1179.
10. Fang W, Zhao Y, Luo Y, Yang R, Huang Y, He Z, Zhao H, Li M, Li K, Song Q *et al*: **Ivonescimab Plus Chemotherapy in Non-Small Cell Lung Cancer With EGFR Variant: A Randomized Clinical Trial.** *Jama* 2024, **332**(7):561-570.

- 596 11. Mok T, Jänne PA, Nishio M, Novello S, Reck M, Steuer C, Wu YL, Fougerey R, Fan PD, Meng J *et al*: **HERTHENA-Lung02: phase III study of patritumab deruxtecan in advanced EGFR-mutated NSCLC after a third-generation EGFR TKI**. *Future Oncol* 2024, **20**(15):969-980.
- 597
- 598
- 599 12. Passaro A, Wang J, Wang Y, Lee SH, Melosky B, Shih JY, Wang J, Azuma K, Juan-Vidal O, Cobo M *et al*: **Amivantamab plus chemotherapy with and without lazertinib in EGFR-mutant advanced NSCLC after disease progression on osimertinib: primary results from the phase III MARIPOSA-2 study**. *Ann Oncol* 2024, **35**(1):77-90.
- 600
- 601
- 602
- 603 13. Shimizu T, Sands J, Yoh K, Spira A, Garon EB, Kitazono S, Johnson ML, Meric-Bernstam F, Tolcher AW, Yamamoto N *et al*: **First-in-Human, Phase I Dose-Escalation and Dose-Expansion Study of Trophoblast Cell-Surface Antigen 2-Directed Antibody-Drug Conjugate Datopotamab Deruxtecan in Non-Small-Cell Lung Cancer: TROPION-PanTumor01**. *J Clin Oncol* 2023, **41**(29):4678-4687.
- 604
- 605
- 606
- 607
- 608 14. Zhao S, Cheng Y, Wang Q, Li X, Liao J, Rodon J, Meng X, Luo Y, Chen Z, Wang W *et al*: **Sacituzumab tirumotecan in advanced non-small-cell lung cancer with or without EGFR mutations: phase 1/2 and phase 2 trials**. *Nat Med* 2025, **31**(6):1976-1986.
- 609
- 610
- 611 15. Fang W, Wu L, Meng X, Yao Y, Zuo W, Yao W, Xie Y, Zhang Y, Cui J, Zhang Y *et al*: **Sacituzumab Tirumotecan in EGFR-TKI-Resistant, EGFR-Mutated Advanced NSCLC**. *N Engl J Med* 2026, **394**(1):13-26.
- 612
- 613
- 614 16. Ahn MJ, Tanaka K, Paz-Ares L, Cornelissen R, Girard N, Pons-Tostivint E, Vicente Baz D, Sugawara S, Cobo M, Pérol M *et al*: **Datopotamab Deruxtecan Versus Docetaxel for Previously Treated Advanced or Metastatic Non-Small Cell Lung Cancer: The Randomized, Open-Label Phase III TROPION-Lung01 Study**. *J Clin Oncol* 2025, **43**(3):260-272.
- 615
- 616
- 617
- 618 17. Paz-Ares LG, Juan-Vidal O, Mountzios GS, Felip E, Reinmuth N, de Marinis F, Girard N, Patel VM, Takahama T, Owen SP *et al*: **Sacituzumab Govitecan Versus Docetaxel for Previously Treated Advanced or Metastatic Non-Small Cell Lung Cancer: The Randomized, Open-Label Phase III EVOKE-01 Study**. *J Clin Oncol* 2024, **42**(24):2860-2872.
- 619
- 620
- 621
- 622 18. Fang W, Li X, Wang Q, Meng X, Zheng W, Sun L, Yao W, Zhuang W, Fan Y, Zhuo M *et al*: **Sacituzumab tirumotecan versus docetaxel for previously treated EGFR-mutated advanced non-small cell lung cancer: multicentre, open label, randomised controlled trial**. *Bmj* 2025, **389**:e085680.
- 623
- 624
- 625
- 626 19. Yin Y, Fan Y, Ouyang Q, Song L, Wang X, Li W, Li M, Yan X, Wang S, Sun T *et al*: **Sacituzumab tirumotecan in previously treated metastatic triple-negative breast cancer: a randomized phase 3 trial**. *Nat Med* 2025, **31**(6):1969-1975.
- 627
- 628
- 629 20. Zhu Y, Jiang S, Shi Y, Wang S, Yuan F, Zhou F, Jiang K, Zhang X, Seneviratne L, Yu G *et al*: **Sacituzumab tirumotecan in participants with advanced or metastatic urothelial carcinoma and disease progression after chemotherapy and immune checkpoint inhibitors**. *Ann Oncol* 2026, **37**(3):378-387.
- 630
- 631
- 632
- 633 21. Husereau D, Drummond M, Augustovski F, de Bekker-Grob E, Briggs AH, Carswell C, Caulley L, Chaiyakunapruk N, Greenberg D, Loder E *et al*: **Consolidated Health Economic Evaluation**
- 634

635 **Reporting Standards 2022 (CHEERS 2022) Statement: Updated Reporting Guidance for Health**
636 **Economic Evaluations.** *Clin Ther* 2022, **44**(2):158-168.

637 22. **Head and Neck Cancers, Version 1.2026, NCCN Clinical Practice Guidelines In Oncology**
638 **[www.nccn.org/patients]**

639 23. Wang J, Qiu T, Ren S: **Updates to the 2024 CSCO advanced non-small cell lung cancer**
640 **guidelines.** *Cancer Biol Med* 2025, **22**(2):77-82.

641 24. [<https://www.yaozh.com/>.]

642 25. Zhu Y, Liu K, Qin Q, Zhu H: **Serplulimab plus chemotherapy as first-line treatment for**
643 **extensive-stage small-cell lung cancer: A cost-effectiveness analysis.** *Front Immunol* 2022,
644 **13**:1044678.

645 26. Liu L, Wang L, Chen L, Ding Y, Zhang Q, Shu Y: **Cost-effectiveness of sintilimab plus**
646 **chemotherapy versus chemotherapy alone as first-line treatment of locally advanced or**
647 **metastatic oesophageal squamous cell carcinoma.** *Front Immunol* 2023, **14**:1092385.

648 27. Cao X, Zhang M, Li N, Zheng B, Liu M, Song X, Cai H: **First-line nivolumab plus chemotherapy**
649 **versus chemotherapy alone for advanced gastric cancer, gastroesophageal junction cancer,**
650 **and esophageal adenocarcinoma: a cost-effectiveness analysis.** *Ther Adv Med Oncol* 2023,
651 **15**:17588359231171038.

652 28. Shu Y, Tang Y, Ding Y, Xu P, Zhang Q: **Cost-effectiveness of sacituzumab tirumotecan versus**
653 **chemotherapy for patients with metastatic triple-negative breast cancer in China.** *Breast*
654 2025, **83**:104550.

655 29. Li X, Lu Y, Lu Y, Zhou M, Xie X, Zhou Y, Qiu J, Dai Z, Chang F: **Cost-effectiveness of rilertinib**
656 **versus osimertinib in second-line treatment in EGFR T790M resistance mutation advanced**
657 **non-small cell lung cancer in China.** *Front Pharmacol* 2025, **16**:1628024.

658 30. Liu S, Jiang N, Dou L, Li S: **Cost-effectiveness analysis of serplulimab plus chemotherapy in the**
659 **first-line treatment for PD-L1-positive esophageal squamous cell carcinoma in China.** *Front*
660 *Immunol* 2023, **14**:1172242.

661 31. Reinmuth N, Couraud S, Paz-Ares L, Garassino MC, Baijal S, Daniel D, Garrido P, Kato T, Percent
662 I, Rittmeyer A *et al*: **Patient-Reported Symptoms and Quality of Life With Sacituzumab**
663 **Govitecan Versus Docetaxel in Metastatic NSCLC: The Phase 3, Randomized EVOKE-01 Trial.**
664 *JTO Clin Res Rep* 2026, **7**(2):100929.

665 32. **Medicare Physician Fee Schedule Look-Up Tool**
666 **[<https://www.cms.gov/medicare/physicianfee-schedule/search>]**

667 33. Shao T, Zhao M, Liang L, Tang W: **Serplulimab Plus Chemotherapy vs Chemotherapy for**
668 **Treatment of US and Chinese Patients with Extensive-Stage Small-Cell Lung Cancer: A Cost-**
669 **Effectiveness Analysis to Inform Drug Pricing.** *BioDrugs* 2023, **37**(3):421-432.

670 34. Wong W, Yim YM, Kim A, Cloutier M, Gauthier-Loiselle M, Gagnon-Sanschagrin P, Guerin A:
671 **Assessment of costs associated with adverse events in patients with cancer.** *PLoS One* 2018,
672 **13**(4):e0196007.

- 673 35. Su D, Wu B, Shi L: **Cost-effectiveness of Atezolizumab Plus Bevacizumab vs Sorafenib as First-**
674 **Line Treatment of Unresectable Hepatocellular Carcinoma.** *JAMA Netw Open* 2021,
675 **4(2):e210037.**
- 676 36. Yue X, Li Y, Wu J, Guo JJ: **Current Development and Practice of Pharmacoeconomic Evaluation**
677 **Guidelines for Universal Health Coverage in China.** *Value Health Reg Issues* 2021, **24:1-5.**
- 678 37. Murray CJ, Evans DB, Acharya A, Baltussen RM: **Development of WHO guidelines on**
679 **generalized cost-effectiveness analysis.** *Health Econ* 2000, **9(3):235-251.**
- 680 38. Neumann PJ, Cohen JT, Weinstein MC: **Updating cost-effectiveness--the curious resilience of**
681 **the \$50,000-per-QALY threshold.** *N Engl J Med* 2014, **371(9):796-797.**
- 682 39. Latimer NR: **Survival analysis for economic evaluations alongside clinical trials--extrapolation**
683 **with patient-level data: inconsistencies, limitations, and a practical guide.** *Med Decis Making*
684 2013, **33(6):743-754.**
- 685 40. Rulli E, Ghilotti F, Biagioli E, Porcu L, Marabese M, D'Incalci M, Bellocco R, Torri V: **Assessment**
686 **of proportional hazard assumption in aggregate data: a systematic review on statistical**
687 **methodology in clinical trials using time-to-event endpoint.** *Br J Cancer* 2018, **119(12):1456-**
688 **1463.**
- 689 41. Chueh CH, Tsai YW, Chen ZR, Shiu MN, Wen YW, Chiang NJ: **Cost-Effectiveness Analysis of a**
690 **New Second-Line Treatment Regimen for Advanced Intrahepatic Cholangiocarcinoma:**
691 **Biomarker-Driven Targeted Therapy of Pemigatinib Versus 5-FU Chemotherapy.**
692 *Pharmacoeconomics* 2023, **41(3):307-319.**
- 693 42. Zeng F, Li S, Deng P: **Cost-effectiveness analysis of datopotamab deruxtecan versus docetaxel**
694 **for previously treated advanced or metastatic non-small cell lung cancer.** *Cost Eff Resour Alloc*
695 2025, **23(1):77.**
- 696 43. Cho BC, Lu S, Felip E, Spira AI, Girard N, Lee JS, Lee SH, Ostapenko Y, Danchaivijitr P, Liu B *et al*:
697 **Amivantamab plus Lazertinib in Previously Untreated EGFR-Mutated Advanced NSCLC.** *N*
698 *Engl J Med* 2024, **391(16):1486-1498.**
- 699 44. Zhou C, Tang KJ, Cho BC, Liu B, Paz-Ares L, Cheng S, Kitazono S, Thiagarajan M, Goldman JW,
700 Sabari JK *et al*: **Amivantamab plus Chemotherapy in NSCLC with EGFR Exon 20 Insertions.** *N*
701 *Engl J Med* 2023, **389(22):2039-2051.**
- 702 45. Long R, Kuang W, Zhou Q: **Ivonescimab plus chemotherapy in advanced or metastatic**
703 **non-squamous non-small cell lung cancer with EGFR variant in China: a cost-effectiveness**
704 **analysis.** *Transl Lung Cancer Res* 2025, **14(5):1622-1634.**
- 705 46. Zhang H, Li Y, Liu Y, Li H, Wang H: **Cost-effectiveness analyses of amivantamab plus lazertinib**
706 **and lazertinib versus osimertinib in non-small cell lung cancer with EGFR mutations.** *Front*
707 *Pharmacol* 2025, **16:1527614.**
- 708 47. Wu Q, Li Q, Qin Y: **A cost-effectiveness analysis of amivantamab plus lazertinib versus**
709 **osimertinib in the treatment of US and Chinese patients with EGFR-mutated advanced non-**
710 **small cell lung cancer.** *Lung Cancer* 2025, **203:108533.**

- 711 48. Cao Y, Yi H, Shi F, Wei X, Han S: **Cost-effectiveness analysis of amivantamab plus chemotherapy**
712 **for non-small cell lung cancer patients with epidermal growth factor receptor exon 20**
713 **insertions in the United States.** *Int J Clin Pharm* 2024, **46**(6):1335-1344.
- 714 49. Yue P, Zhang M, Feng Y, Gao Y, Sun C, Chen P: **Cost-effectiveness analysis of amivantamab plus**
715 **chemotherapy versus chemotherapy alone in NSCLC with EGFR Exon 20 insertions.** *Front*
716 *Oncol* 2024, **14**:1368804.
- 717 50. Song Y: **Cost-effectiveness of datopotamab deruxtecan in previously treated advanced**
718 **nonsquamous NSCLC.** *Medicine (Baltimore)* 2025, **104**(20):e42419.
- 719
720
721