

# Cost-effectiveness of datopotamab deruxtecan in previously treated advanced nonsquamous NSCLC

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## Abstract

**Background:** To evaluate the cost-effectiveness of datopotamab deruxtecan (Dato-DXd) in patients with previously treated advanced nonsquamous non-small-cell lung cancer from the perspective of a payer in the United States.

**Methods:** A partitioned survival model with 3 states was employed to simulate patients receiving Dato-DXd or docetaxel (Dato-DXd or docetaxel group). The data on cost and health preferences were collected from the literature.

**Results:** The Dato-DXd group generated an additional 0.11 quality-adjusted life years (QALYs) compared with the docetaxel group but at an additional cost of \$119,575. This leads to incremental cost-effectiveness ratios of \$1,054,809 per QALY. The results of the univariate sensitivity analysis indicated that the cost of Dato-DXd, the utility of progression-free survival, and progressive disease had the greatest impacts on the outcomes. The probability sensitivity analysis showed that Dato-DXd had a 0% chance of being considered cost-effective. When the cost of Dato-DXd decreased to 0.116 times the current price, the incremental cost-effectiveness ratio would decrease to a level below the willingness-to-pay threshold of \$150,000/QALY.

**Conclusion:** In our model, from the perspective of a U.S. payer, Dato-DXd was not considered cost-effective for previously treated advanced nonsquamous non-small-cell lung cancer at a willingness-to-pay threshold of \$150,000/QALY. This underscores the importance of assessing the cost-effectiveness of new treatments in the context of limited healthcare resources. Given the escalating costs of cancer care and the increasing demand for efficacious therapies, it is imperative that policymakers take into account not only the immediate costs of treatments but also their wider, long-term repercussions on patient outcomes and the sustainability of the healthcare system.

**Abbreviations:** AE = adverse event, Dato-DXd = datopotamab deruxtecan, HRQoL = health-related quality of life, ICER = incremental cost-effectiveness ratio, NSCLC = non-small-cell lung cancer, OS = overall survival, PD = progressive disease, PFS = progression-free survival, QALY = quality-adjusted life year, WTP = willingness-to-pay.

**Keywords:** cost-effectiveness, datopotamab deruxtecan, NSCLC, partitioned survival model, quality-adjusted life years

## 1. Introduction

According to data provided by the American Cancer Society, it is estimated that in 2024, there will be approximately 234,580 new cases and 125,070 deaths from lung cancer in the U.S. alone.<sup>[1]</sup> Non-small-cell lung cancer (NSCLC) is the leading cause of death among all malignancies in Western countries. Given its prevalence, it is not surprising that NSCLC, constituting 85% of lung cancer cases, generally carries a poor prognosis.<sup>[2]</sup> Histologically, most cases of NSCLC are nonsquamous (adenocarcinomas or large-cell carcinomas). The prognosis for patients with advanced nonsquamous NSCLC remains very poor. In fact, the 5-year survival rates in the United States for patients diagnosed with adenocarcinoma or large-cell carcinoma of the lung or bronchus are

7.5% and 4.4%, respectively.<sup>[3]</sup> The prognosis is not optimistic for advanced NSCLC that has progressed after previous treatment.<sup>[4]</sup>

Antibody–drug conjugate has demonstrated great potential to treat patients with advanced cancers.<sup>[5]</sup> Datopotamab deruxtecan (Dato-DXd) is an antibody–drug conjugate that comprises a recombinant humanized anti-TROP2 IgG1 monoclonal antibody conjugated to a topoisomerase I inhibitor, DXd, via a tetrapeptide linker.<sup>[6]</sup> In the advanced/metastatic solid tumors from the phase I TROPION-PanTumor01 study, patients received Dato-DXd at a dose of 6 mg/kg, resulting in encouraging and sustained antitumor activity. Specifically, among patients with NSCLC, the objective response rates reached 26.0%, with a median progression-free survival (PFS) of 6.9 months for this

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

This study is based on publicly available datasets and does not involve personal information of specific patients, therefore ethics approval and consent to participate were not required.

Supplemental Digital Content is available for this article.

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cohort.<sup>[7]</sup> In addition, data presented at the European Lung Cancer Congress, held from March 20 to 23, 2024, further support the efficacy of Dato-DXd. These data indicate that the nonsquamous NSCLC subgroup in the Dato-DXd TROPION-Lung01 study showed impressive results, providing additional evidence for its use in both driver gene-negative and driver gene-positive nonsquamous NSCLC populations.<sup>[8]</sup> As of the data cutoff date of March 29, 2023, it was observed that the Dato-DXd group significantly extended PFS by almost 2 months compared with the docetaxel group, achieving a median PFS of 5.5 versus 3.6 months, with a hazard ratio of 0.63 and a 95% confidence interval of 0.51 to 0.79. The interim overall survival (OS) results supported a survival benefit for the Dato-DXd group compared with the docetaxel group, with an OS hazard ratio of 0.79 and a 95% confidence interval of 0.60 to 1.02, resulting in a median OS of 13.4 months for the Dato-DXd group and 11.4 months for the docetaxel group.<sup>[8]</sup>

On the basis of these compelling results, Dato-DXd therapy appears to be a viable and beneficial option for patients with previously treated advanced nonsquamous NSCLC. As an innovative medication, Dato-DXd presents a promising treatment strategy, holding the potential to significantly improve outcomes for this challenging patient population.

Although Dato-DXd demonstrates promising therapeutic efficacy, its comparatively high price and the lack of preceding pharmacoeconomic analyses render it vital to promptly evaluate its cost-effectiveness. Undertaking research in this field is essential to aiding policymakers in formulating well-informed decisions regarding the judicious allocation of limited healthcare resources. Our objective is to present a comprehensive and rigorous exploration of Dato-DXd's pharmacoeconomic significance from the perspective of US healthcare payers.

## 2. Materials and methods

### 2.1. Model construction

To assess the financial and medical implications of Dato-DXd, the TreeAge Pro 2022 software was used to create a partitioned survival model encompassing 3 distinct health states: PFS, progressive disease (PD), and death, as outlined in Figure S1, Supplemental Digital Content, <https://links.lww.com/MD/O866>. The PFS state served as the initial state, while death represented the ultimate state. Patients in the PFS state, following their initial treatment, could potentially transition to either PD or death. In contrast, those in the PD state and undergoing subsequent treatments might progress toward death. Remaining in the same condition was also a possibility after each cycle. When the disease progressed, patients were unable to go back to their prior condition.

### 2.2. Model parameter

In this model, each cycle was designed to last 3 weeks. This model employs half-cycle correction and applies a 3% annual discount rate for both cost and lifespan projections.<sup>[9]</sup> The model's timeframe, ranging from 63 to 77 years of age, was selected to match both the median age of TROPION-Lung01 trial participants and the average US lifespan at birth.<sup>[10]</sup>

### 2.3. Participants in the model structure

The primary clinical information originated from the TROPION-Lung01 trial.<sup>[8]</sup> Participants were randomly divided into 2 separate cohorts, maintaining a balanced 1:1 ratio: the Dato-DXd cohort (6 mg/kg administered every 3 weeks) and the docetaxel cohort (75 mg/m<sup>2</sup> administered every 3 weeks for 4 cycles). Subsequent therapy after PD receives the best supportive care. All patients were provided with end-of-life care once they

reached the terminal stage preceding their death. Drug dosages were calculated based on the average body surface area of 1.82 m<sup>2</sup> and weight of 70 kg for Americans.<sup>[11]</sup>

### 2.4. Costs estimates

We incorporated an analysis of health resource utilization and direct medical costs (Table 1). The drug prices were obtained from the Centers for Medicare & Medicaid Services and Drugs.com.<sup>[8,13]</sup> The costs associated with managing adverse events (AEs), medication administration, end-of-life palliative care, best supportive care, and disease management (encompassing costs related to hospitalization, computed tomography scans, and laboratory tests) were obtained from previously published databases.<sup>[11,12,14–17]</sup> On the basis of the TROPION-PanTumor01 trial, the costs related to computed tomography scans were incurred initially at the outset, followed by recurring expenses at 6-week intervals for the initial 36-week period, and subsequently at 12-week intervals thereafter.<sup>[7]</sup> The cost of administration was recorded in every treatment cycle, and the cost of laboratory testing was also recorded in every treatment cycle, with both being conducted at a consistent frequency during the follow-up period. To accommodate inflationary changes and align the figures with the projected values of US dollars in 2024, we employed both the American consumer price index and the Tom inflation calculator for accurate cost adjustment computations.<sup>[18]</sup>

### 2.5. Survival data reconstruction

To extract the survival data from the PFS and OS curves of the TROPION-Lung01 trial, we employed the GetData Graph Digitizer software (Figure S2, Supplemental Digital Content, <https://links.lww.com/MD/O866>). Use the calibration tools within the software to align the X-axis and Y-axis with the corresponding scales of the Kaplan–Meier curve for PFS or OS. Then, record each data point along the PFS or OS curve.

### 2.6. Progression transition estimates

We use the reconstructed patient-level data and R software to model the reconstructed survival data as several parametric distributions, including Weibull distribution, exponential distribution, gamma distribution, Gompertz distribution, generalized gamma distribution, log-logistic distribution, and log-normal distribution, and use the algorithm developed by Hoyle et al.<sup>[19]</sup> to generate the simulated patient data. We calculated the Akaike information criterion and Bayesian information criterion for each parametric model using R software to facilitate a comparison of their goodness of fit and to select the most suitable model for further analysis (Table S1, Supplemental Digital Content, <https://links.lww.com/MD/O867>). Microsoft Excel software was used to calculate time-dependent transition probabilities for both patient groups, incorporating data from the TROPION-Lung01 trial. The background death rates for each age cohort were evaluated using life tables specific to Americans (Table S2, Supplemental Digital Content, <https://links.lww.com/MD/O867>).<sup>[10]</sup>

### 2.7. Health-state utilities

We assign the health-related quality of life (HRQoL) values of 0.673, 0.473, and 0 to PFS, PD, and death, respectively, based on data from previously published literature on patients with NSCLC.<sup>[11]</sup> This HRQoL, as reported by patients, offers a comprehensive assessment of their overall health status, well-being, and daily activities. These HRQoL values represent individuals with advanced NSCLC, being compromised primarily because of both the underlying disease and the consequences of treatment.

**Table 1**  
**Model parameters and distributions.**

Variable	Baseline value (references)	Range		Distribution
		Minimum	Maximum	
Gamma PFS survival model with Dato-DXd group	Shape = 1.436,349 Rate = 0.193,959	–	–	–
Log-logistic PFS survival model with docetaxel group	Shape = 1.75,525 Scale = 3.44,230	–	–	–
Weibull OS survival model with Dato-DXd group	Shape = 1.3,733,388 Scale = 0.0,191,359	–	–	–
Gamma OS survival model with docetaxelgroup	Shape = 1.635,716 Rate = 0.114,562	–	–	–
Grade ≥ 3 AEs incidence in Dato-DXd group				
Stomatitis	0.07 <sup>[8]</sup>	0.056	0.084	Beta
Grade ≥ 3 AEs incidence in docetaxel group				
Neutropenia	0.22 <sup>[8]</sup>	0.176	0.264	Beta
AEs cost (US \$)				
Stomatitis	18 383.08 <sup>[12]</sup>	14 706.46	22 059.70	Gamma
Neutropenia	15 195.45 <sup>[11]</sup>	12 156.36	18 234.54	Gamma
AEs disutility				
Stomatitis	−0.14 <sup>[12]</sup>	−0.112	−0.168	Beta
Neutropenia	−0.35 <sup>[11]</sup>	−0.28	−0.42	Beta
Utility				
Progression-free survival	0.673 <sup>[11]</sup>	0.5384	0.8076	Beta
Progressed disease	0.473 <sup>[11]</sup>	0.3784	0.5676	Beta
Drug cost (US \$)				
Dato-DXd/100 mg	2854.57 <sup>[13]</sup>	2283.656	3425.484	Gamma
Docetaxel/1 mg	0.8717 <sup>[13]</sup>	0.6968	1.0452	Gamma
The cost of tumor imaging per cycle (US \$)	661.99 <sup>[14]</sup>	529.59	794.39	Gamma
The cost of laboratory testing per cycle (US \$)	364.77 <sup>[15]</sup>	291.82	437.72	Gamma
The cost of administration per cycle (US \$)	169.27 <sup>[11]</sup>	135.42	203.12	Gamma
The cost of physician visit per cycle (US \$)	165.01 <sup>[16]</sup>	132.01	198.01	Gamma
The cost of best supportive care per cycle (US \$)	481.57 <sup>[17]</sup>	385.26	577.88	Gamma
The one-time cost of end-of-life care during the terminal stage (US \$)	10,923.49 <sup>[17]</sup>	8738.79	13,108.19	Gamma
Discount rate (%)	3 <sup>[11]</sup>	0	5	Fixed in PSA
Body surface area (m <sup>2</sup> )	1.82 <sup>[11]</sup>	1.456	2.184	Normal
Body weight (kg)	70 <sup>[11]</sup>	56	84	Normal

AE = adverse effect, Dato-DXd = datopotamab deruxtecan, OS = overall survival, PFS = progression-free survival, PSA = probabilistic sensitivity analyses.

HRQoL can be quantified as a health state utility value, which ranges from 0 (indicating death) to 1 (representing full health). Health state utility values account for factors such as the line of treatment, AEs, response status, and prognostic indicators. Following conventional research practices, the initial cycle of the models incorporates the reduction in QALYs due to AEs, with a focus on severe AEs (grade 3 or higher) related to treatment that occur at a frequency of at least 5%. This is because minor AEs generally do not necessitate medical intervention or lead to substantial treatment costs.<sup>[9,20–22]</sup>

## 2.8. Observe and measure indicators

Our analytical approach centered primarily on quality-adjusted life years (QALYs), overall costs, and incremental cost-effectiveness ratios (ICERs). A predefined willingness-to-pay (WTP) threshold of \$150,000/QALY was applied to evaluate the financial implications of the study.<sup>[23]</sup>

## 2.9. Univariate and probabilistic sensitivity analyses

The impact of key parameters on the ICER was evaluated through a univariate sensitivity analysis. The tornado diagram was used to visualize the range of values within ±20% of the baseline for each parameter and its corresponding effect on the ICER. To further exemplify the probabilistic sensitivity analysis, we conducted 1000 Monte Carlo simulations. These simulations involved simultaneously and randomly varying predefined parameters in accordance with designated

distribution patterns; notably, costs followed gamma distributions, while proportions and utilities followed beta distributions (Table 1).

## 2.10. Scenario analysis

We also conduct scenario analyses that take into consideration potential real-world variations in drug pricing, where the price of Dato-DXd ranges between 0.1 times and 1.0 times its base price (\$1198.92–\$11,989.19 per cycle), thus enhancing the relevance of our findings to healthcare decision-makers.

## 3. Results

### 3.1. Model validation

Our simulated median PFS and median OS values closely corresponded with those documented in the TROPION-Lung01 trial. Specifically, our estimations generated a median PFS of 5.5 months for the Dato-DXd group and 3.6 months for the docetaxel group, matching the findings of the TROPION-Lung01 trial with high accuracy. In terms of median OS analysis, our projections indicated an OS of 13.3 months for the Dato-DXd group and 11.4 months for the docetaxel group, which closely aligned with the TROPION-Lung01 trial data reporting OS values of 13.4 and 11.4 months for the Dato-DXd and docetaxel groups, respectively (Table S3, Supplemental Digital Content, <https://links.lww.com/MD/O867>).

### 3.2. Base case results

In the framework of our model, the total accumulated costs amounted to \$160,205 for the Dato-DXd group and \$40,630 for the docetaxel group. The Dato-DXd group achieved 0.73 QALYs, whereas the docetaxel group achieved 0.62 QALYs. As a result, Dato-DXd demonstrated an increase of 0.11 QALYs at an additional expenditure of \$119,575 compared with the docetaxel group. This resulted in an ICER of \$1,054,809/QALY, thus exceeding the predetermined WTP threshold of \$150,000/QALY (Table 2).

### 3.3. Sensitivity analysis

The tornado diagram shows that the cost of Dato-DXd and the utility of PFS and PD had the greatest influence on the results, while other variables had a minimal effect (Fig. 1). The fact that there is no overlap between the resulting ICER and the WTP values when all parameters fluctuate within their designated ranges demonstrates the robustness of our model.

**Table 2**

Base-case results of the model.

Group	Costs (U.S. \$)	ΔCosts (US \$)	QALYs	ΔQALYs	ICER (US \$)/QALY
Docetaxel	40,630	—	0.62	—	—
Dato-DXd	160,205	119,575	0.73	0.11	1,054,809

Dato-DXd = datopotamab deruxtecán, ICER = incremental cost-effectiveness ratio, QALYs = quality-adjusted life-years.

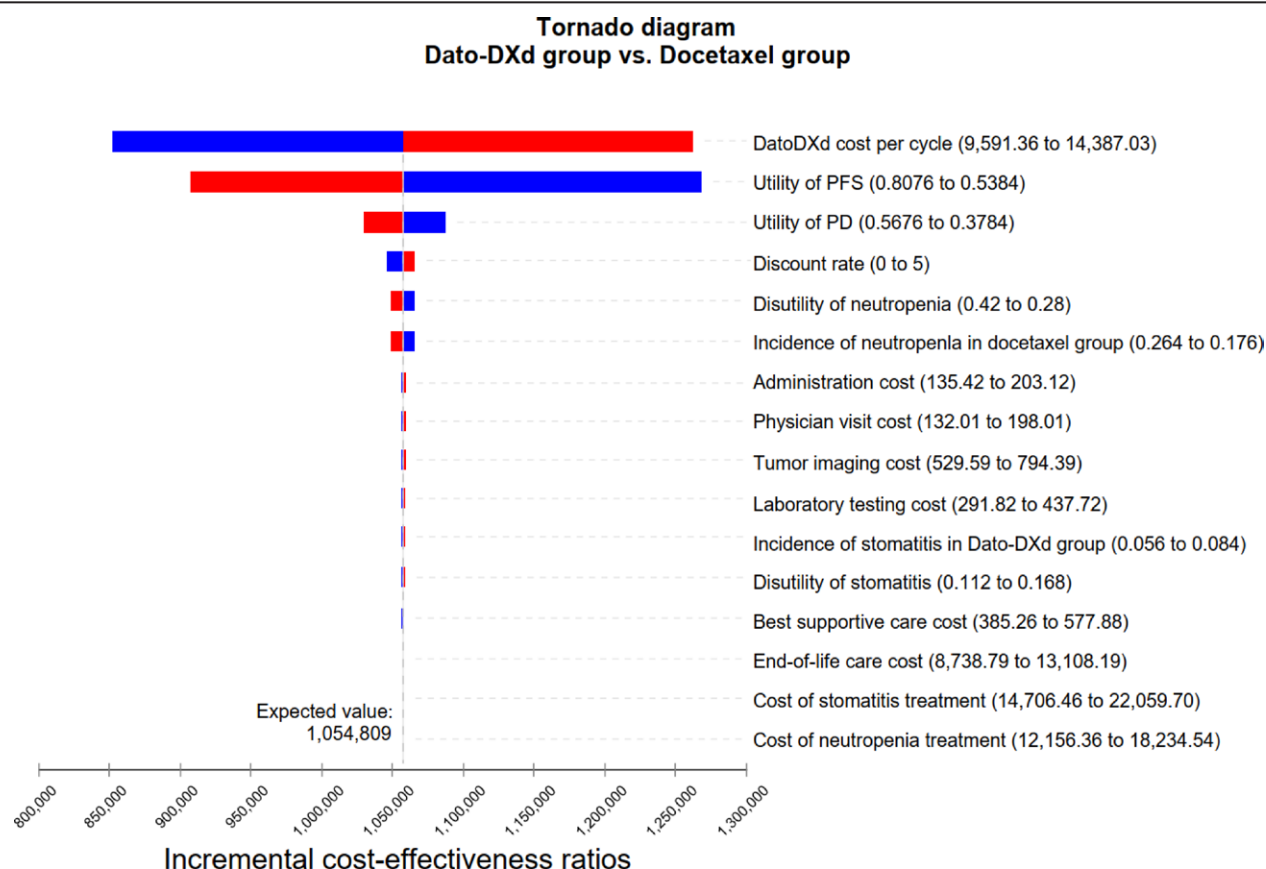
We conducted a Monte Carlo simulation with a sample size of 1000, which indicates that all scattered points are located in the first quadrant of the coordinate axis and positioned above the WTP line. This suggests that the Dato-DXd regimen has the potential to achieve more QALYs, although at an increased cost (Fig. 2). Furthermore, the sensitivity analysis of probability indicates that Dato-DXd would not be considered cost-effective for patients with a predetermined WTP threshold. Only when the WTP threshold exceeds \$1,048,000, Dato-DXd has better cost-effectiveness than docetaxel (Fig. 3).

### 3.4. Scenario analysis

In the scenario analysis, we permitted the price of Dato-DXd to vary within the range of 0.1 times to 1.0 times the current price, keeping other parameters unchanged. Upon the cost of Dato-DXd dropping to 0.116 times (\$1389.97 per cycle) the current price, the ICER would fall below the WTP threshold of \$150,000/QALY, as illustrated in Figure 4.

## 4. Discussion

Our baseline analysis, derived from the model, indicates that while the Dato-DXd achieves superior health outcomes (yielding 0.73 QALYs in comparison to 0.62 QALYs), it is not deemed economically viable due to its high ICER of \$1,054,809 per QALY. Furthermore, our probabilistic sensitivity analyses confirm that Dato-DXd does not emerge as a cost-effective treatment option, as its costs surpass the



**Figure 1.** Tornado diagram for univariate sensitivity analyses. The tornado diagram demonstrated the parameters from one-way sensitivity analysis that have the most significant influence on ICER. The analysis compared Dato-DXd group with the docetaxel group. The bars on the plot represent the potential effect of each parameter on the ICER, with the width of the bar indicating the range of the parameter. The red part of the bar represents high input values of the variables, while the blue part represents low values. Dato-DXd = datopotamab deruxtecán, ICER = incremental cost-effectiveness ratio, PD = progressive disease, PFS = progression-free survival.



WTP threshold of \$150,000/QALY when compared with chemotherapy.

The favorable results observed in the TROPION-Lung01 trial emphasize the remarkable efficacy of Dato-DXd as a prospective revolutionary treatment for individuals diagnosed with advanced nonsquamous NSCLC. However, the significant economic implications associated with this innovative therapeutic approach raise concerns regarding its accessibility and cost-efficiency for a broader patient population.

The sensitivity analysis in this model is most significantly influenced by the substantial cost of Dato-DXd. Despite fluctuations in the price of Dato-DXd within a certain range (\$2283.66–3425.48 per 100mg), the ICER consistently surpasses \$150,000/QALY, highlighting its lack of economic viability. If Dato-DXd's cost dropped to 0.116 times the current price, then the ICER would be below the \$150,000/QALY WTP threshold. Consequently, a feasible approach to improving the cost-effectiveness of treatment would be to reduce the cost of Dato-DXd.

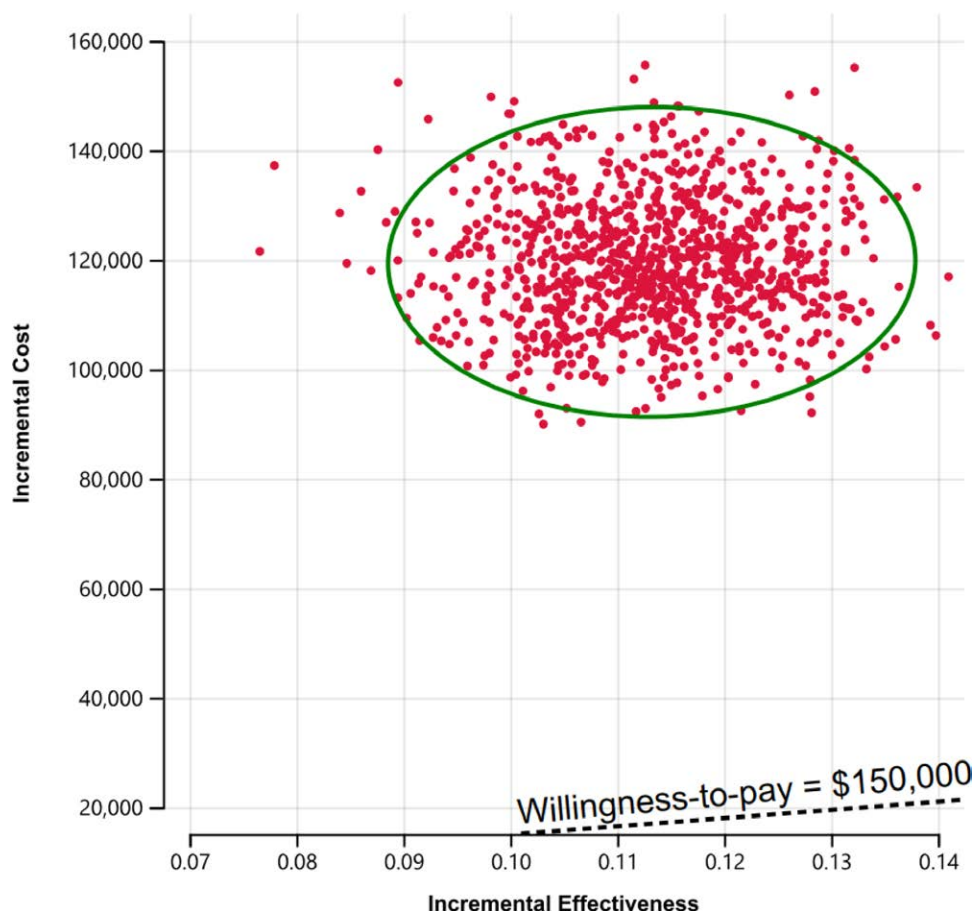
The sensitivity analysis conducted within this model is predominantly impacted by the utility values linked to PFS and PD statuses, which were sourced from previously published research based on data from previously published literature on patients with NSCLC. Because it is not available to acquire the value of health utility for nonsquamous NSCLC, we conducted the sensitivity analysis. Even after accounting for a substantial range of utility values, the ICER persistently exceeds \$150,000/

QALY. This further emphasizes the resilience and reliability of the model's findings.

In the United States, the healthcare insurance system faces challenges in covering the costs of new medications, particularly high-priced innovative drugs. While the Food and Drug Administration approves a significant number of new drugs each year, many patients are unable to afford these treatments due to their high costs. Health insurance plans and private insurers often determine coverage based on cost-benefit analyses of these medications. In some cases, even when high-priced drugs like Dato-DXd can significantly improve a patient's quality of life or life expectancy, there are often difficulties in securing insurance coverage due to their high ICER. Therefore, balancing costs and benefits is a crucial consideration within the healthcare insurance system.

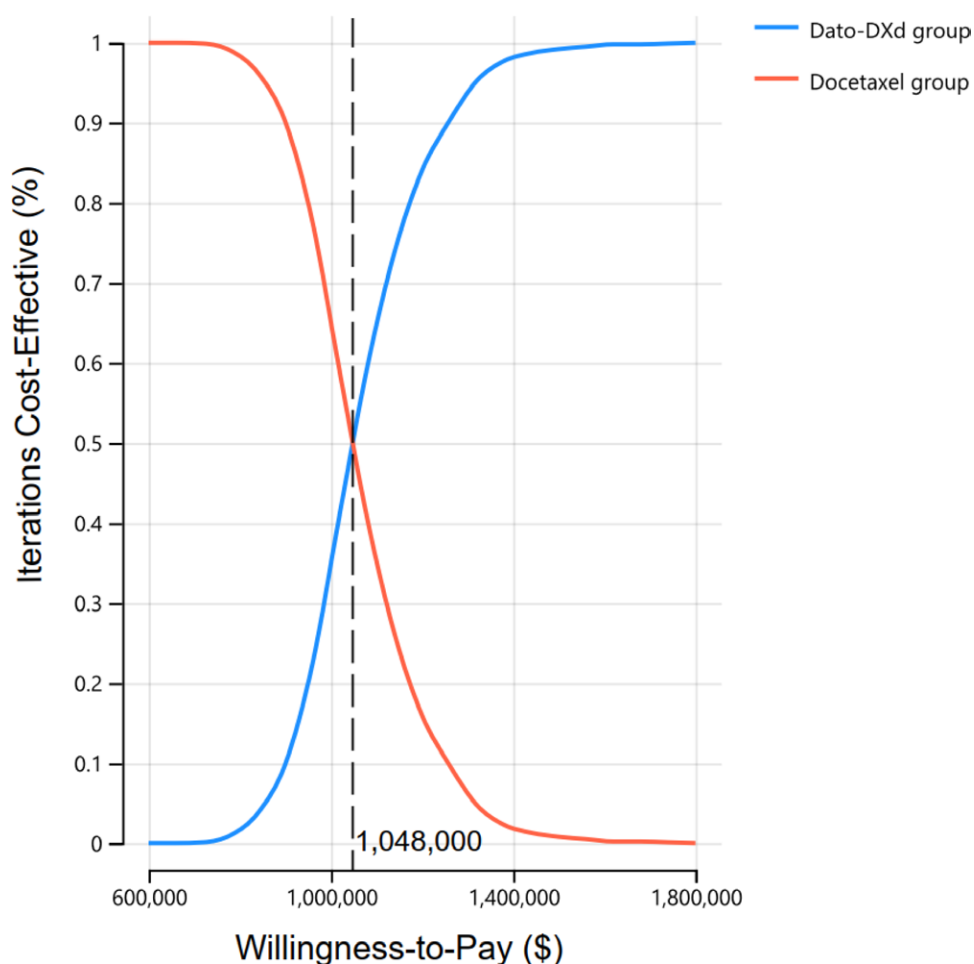
Under the US health insurance system, the high cost of drugs, particularly innovative ones like Dato-DXd, can impose a significant financial burden on patients with cancer, often forcing them to postpone or abandon crucial treatment plans.<sup>[24,25]</sup> This economic toxicity not only affects individuals' health but also has a broader social impact.<sup>[26,27]</sup> One of the root causes of this issue lies in the high pricing of drugs, which is partly attributed to the significant costs involved in research and development, the associated risks, and the potential market exclusivity granted by innovative and unique pharmacological mechanisms.

### Incremental cost-effectiveness scatter plot Dato-DXd group vs. Docetaxel group



**Figure 2.** Incremental cost-effectiveness scatter plot diagram for Dato-DXd. The Monte Carlo simulation with 1000 samples indicates that all points are located in the first quadrant and above the willingness-to-pay line, suggesting the potential of the Dato-DXd regimen to achieve more QALYs, albeit at an increased cost. Dato-DXd = datopotamab deruxtecan, QALY = quality-adjusted life year.

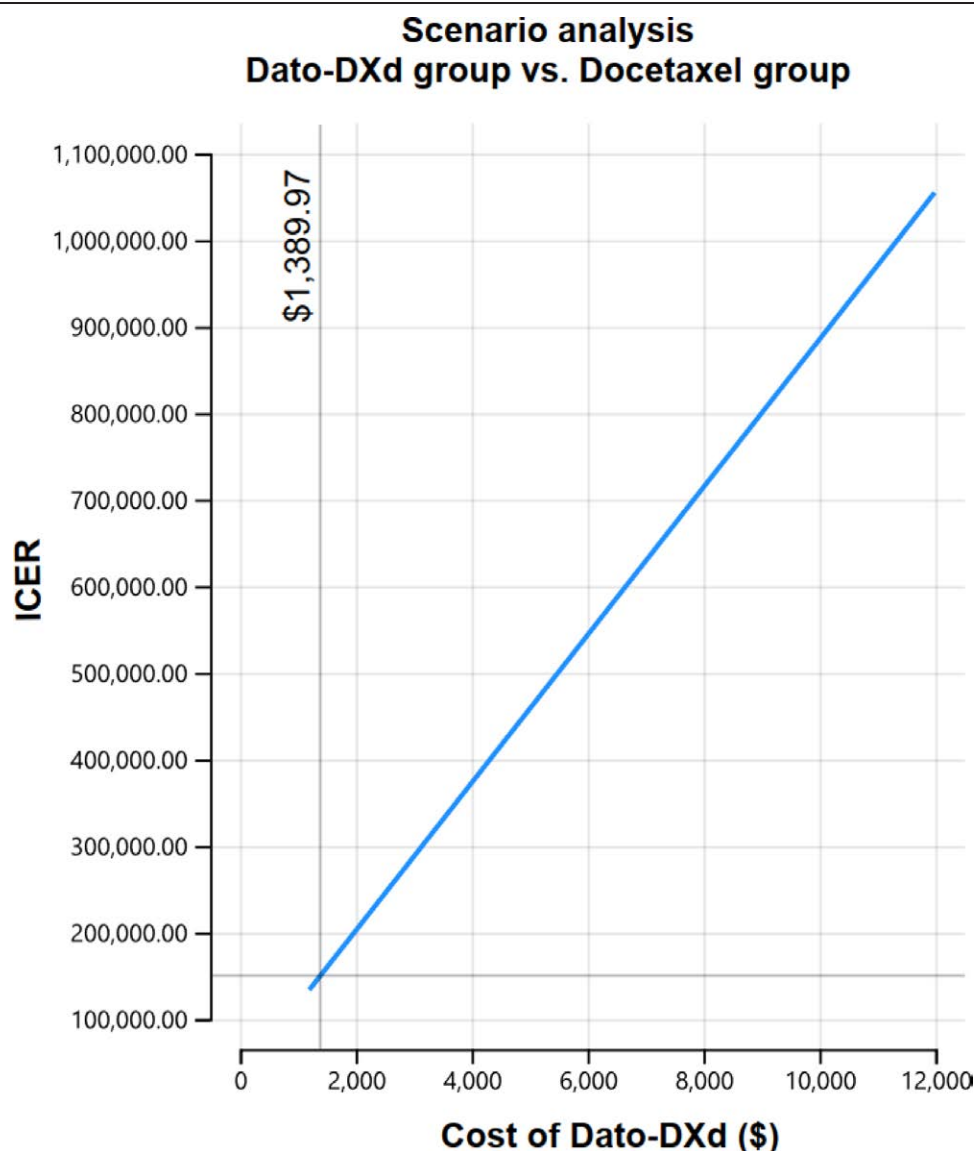
## Cost-effectiveness acceptability curve



**Figure 3.** The cost-effectiveness acceptability curves for probabilistic sensitivity analyses. When the willingness-to-pay surpasses \$1,048,000, Dato-DXd group is considered cost-effective compared with the docetaxel group. Dato-DXd = datopotamab deruxtecan, ICER = incremental cost-effectiveness ratio.

The United States, while valuing drug innovation to maintain its global leadership, also recognizes the need to address the challenge of aligning drug prices with their efficacy and value. To this end, several measures are being explored, including modifying the Food and Drug Administration's drug approval process to incorporate cost-effectiveness analysis, strengthening drug price negotiations, implementing stricter pricing regulations, and promoting the development of generic drugs. Furthermore, it is essential to establish a mechanism for cost-sharing among the government, enterprises, patients, and society. In addition, enterprises should be encouraged to actively shoulder their social responsibilities by making charitable donations, offering preferential pricing, and exploring other means to ease the financial strain on patients. Through future real-world studies, we may observe whether it is possible to optimize the drug delivery strategy, such as by adjusting the dose and frequency of administration, to reduce the total cost of medication while ensuring that patients receive similar therapeutic effects. Moreover, improving the cost-effectiveness of Dato-DXd goes beyond mere price reductions; it involves identifying subpopulations that may derive the most significant benefit in subsequent studies. These efforts aim to strike a balance between fostering innovation and ensuring affordability, ultimately reducing the financial burden on patients and guaranteeing access to innovative treatments for all who need them.

It is important to acknowledge that this study has specific limitations. One limitation arises from our decision to narrow the focus exclusively to AEs with an incidence rate of at least 5% and those of severity grade 3 or above. Indeed, while this approach enables a more precise analysis, it also carries the risk of underestimating the ICER. Importantly, the incorporation of less severe and infrequent AEs into our assessment has minimal impact on both the overall treatment costs and the consideration of AEs. As a result, the validity of our findings remains unaffected. Another limitation is that the research findings were derived from a randomized clinical trial, rather than a prospective real-world study. The stability of the model increases with the maturity of the available data. In the real world, patients who often have chronic conditions and comorbidities, the interplay between cancer and these other conditions can also affect cost-effectiveness in cancer treatment. Moreover, the financial impact can affect patients' ability to adhere to treatment plans, and ultimately their health outcomes. Future research is warranted to determine whether our model- and trial-based results can be replicated with extended follow-up in real-world conditions. Despite the aforementioned limitations, our study offers invaluable initial understanding regarding the cost-effectiveness of Dato-DXd in treating NSCLC, taking into account the viewpoint of healthcare payers in the United States.



**Figure 4.** Results of scenario analysis for different costs of Dato-DXd. Upon the cost of Dato-DXd dropping to 0.116 times (\$1389.97 per cycle) the current price, the ICER would fall below the WTP threshold of \$150,000/QALY. Dato-DXd = datopotamab deruxtecán, ICER = incremental cost-effectiveness ratio, QALY = quality-adjusted life year, WTP = willingness-to-pay.

## 5. Conclusion

In conclusion, from the viewpoint of US healthcare payers, Dato-DXd is unlikely to be cost-effective for platinum-resistant NSCLC. A feasible approach to enhancing the cost-effectiveness of treatment lies in reducing the cost of Dato-DXd.

## Author contributions

**Conceptualization:** Ying Song.  
**Data curation:** Ying Song.  
**Formal analysis:** Ying Song.  
**Investigation:** Ying Song.  
**Methodology:** Ying Song.  
**Resources:** Ying Song.  
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**Validation:** Ying Song.  
**Visualization:** Ying Song.  
**Writing – original draft:** Ying Song.  
**Writing – review & editing:** Ying Song.

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