

Economic Evaluation of Adding Daratumumab to Carfilzomib and Dexamethasone for Relapsed or Refractory Multiple Myeloma

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Objective: To assess the cost-effectiveness of adding daratumumab to carfilzomib and dexamethasone (KdD) in patients with relapsed or refractory multiple myeloma (RRMM).

Materials and Methods: A Markov model was established to estimate health and economic outcomes of carfilzomib and dexamethasone (Kd) with or without daratumumab for RRMM patients over a lifetime horizon. The patients and intervention of the two arms were modeled according to the CANDOR trial. Costs were collected from the Chinese health system perspective. One-way sensitivity analysis and probabilistic sensitivity analysis were performed to evaluate the robustness of our conclusions.

Results: Compared with the Kd arm, KdD achieved an additional 0.537 quality-adjusted life-years (QALYs) at an incremental cost of \$138,084, resulting in an incremental cost-utility ratios (ICURs) of \$257,319 per QALY. Uncertainty analyses revealed that the model is robust to all the input parameters.

Conclusion: From the Chinese healthcare system perspective, adding daratumumab to the Kd regimen for patients with RRMM appears to lack cost-effectiveness. Exploring alternative avenues such as negotiating for a more favorable price or introducing a financial assistance program dedicated to daratumumab and/or carfilzomib could prove to be an effective strategy in enhancing accessibility of this combination.

Keywords: cost-effectiveness, daratumumab, multiple myeloma, Markov model, China

Introduction

Multiple myeloma (MM) ranks as the second most prevalent hematological malignancy on a global scale.¹ The approval of innovative therapeutics, such as proteasome inhibitors (PIs), immunomodulatory drugs (IMiDs), and monoclonal antibodies, has led to improved survival rates among MM patients.² Nonetheless, a notable portion of patients experience relapse or develop treatment resistance.

Carfilzomib, a second-generation proteasome inhibitor (PI), has garnered approval for treating relapsed/refractory multiple myeloma (RRMM). Carfilzomib-containing regimens are prominently featured in treatment guidelines for patients with previously treated myeloma.³ Daratumumab, a first-in-class IgG1K monoclonal antibody against CD38, was approved by the US Food and Drug Administration (FDA) in 2015. In 2019, daratumumab became the first monoclonal antibody approved for the treatment of multiple myeloma in China. In the CANDOR trial, the addition of daratumumab to carfilzomib and dexamethasone (KdD) showcased a significant extension in progression-free survival (PFS) and a promising trend towards overall survival (OS) benefit when compared to carfilzomib + dexamethasone (Kd) among RRMM patients.^{3,4} The median PFS was 28.4 months (95% confidence interval [CI], 22.7–36.2) in the KdD

group and 15.2 months (95% CI, 11.1–19.9) in the Kd group, with a hazard ratio (HR) of 0.64 (95% CI, 0.49–0.83). The median OS was 50.8 months (95% CI, 44.7 to not estimable [NE]) in the KdD group and 43.6 months (95% CI, 35.3 to NE), with an HR of 0.78 (95% CI, 0.60–1.03). Compared with the kd regimen, the KdD regimen did not significantly increase the occurrence of adverse reactions. The results of the CANDOR study reinforce the notion that KdD represents a standard of care for RRMM.

As of our current knowledge, there is no available publication on the economic evaluation of KdD treatment for patients with RRMM. Nonetheless, studies have evaluated the economic outcomes of daratumumab for patients with RRMM. From a US perspective, our previous research and another study have found that adding daratumumab to either a regimen of Vd (bortezomib and dexamethasone) or Rd (lenalidomide and dexamethasone) did not demonstrate cost-effectiveness.^{5,6} Carlson et al conducted a study indicating that daratumumab-based triplet therapies were cost-effective from the US payer perspective.⁷ A manufacturer-sponsored analysis compared the cost-effectiveness of pomalidomide, carfilzomib, and daratumumab for patients with heavily pretreated RRMM, and showed that pomalidomide was marginally dominant compared to both drugs.⁸ Gong et al concluded that daratumumab was cost-effective relative to pomalidomide for patients with RRMM.⁹ A study conducted in Singapore evaluated the cost-effectiveness of daratumumab in combination with Rd for the treatment of RRMM and concluded that this combination was not cost-effective.¹⁰ However, a recent cost-effectiveness and budget impact analysis of daratumumab for RRMM indicated that, compared to KRd (carfilzomib, lenalidomide, and dexamethasone), adding daratumumab to Rd (DRd) is a cost-effective regimen for RRMM under the Iranian willingness-to-pay threshold.¹¹ There is a scarcity of studies evaluating the cost-effectiveness of daratumumab from a Chinese perspective. While our previous study examined the cost-effectiveness of daratumumab for newly diagnosed MM patients from a Chinese healthcare perspective,¹² it remains unclear whether adding daratumumab to Kd treatment proves cost-effective for RRMM in China. Thus, this study aimed to evaluate the cost-effectiveness of KdD from the Chinese healthcare perspective utilizing the latest data derived from the CANDOR trial.

Materials and Methods

Methodological Design

A Markov model was developed to estimate the long-term health and economic outcomes of KdD and Kd in patients with RRMM. Employing TreeAge pro software (TreeAge Software, Williamstown, MA), a cost-utility analysis was carried out. The simulated outcomes of the model were represented by total costs, quality-adjusted life years (QALYs), and incremental cost-utility ratios (ICURs). To align with the China Guidelines for Pharmacoeconomic Evaluations (2020), all costs and utilities were discounted at a 5% yearly rate.¹³ The average exchange rate in 2022, with 1 US dollar (USD) = 6.73 Chinese Yuan (RMB), was utilized.¹⁴ In accordance with the recommendation of the China Guidelines for Pharmacoeconomic Evaluations, a willingness-to-pay (WTP) threshold of \$38,201/QALY was applied, corresponding to three times the per-capita gross domestic product (GDP) of 2022.¹⁵ The current economic evaluation was conducted in accordance with the Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) statement.¹⁶ The CHEERS 2022 Checklist is provided in [Supplementary Table S8](#).

Model Patients and Intervention

The patients population and treatment intervention were aligned with the final analysis of the CANDOR trial.⁴ In summary, a total of 466 eligible patients from 102 international medical centers were randomly assigned in a 2:1 ratio to receive either a 28-day cycle of KdD or Kd treatment. Patients with RRMM who were eligible had an Eastern Cooperative Oncology Group performance status of 0 to 2, had received 1 to 3 previous lines of therapy, and had achieved a partial or better response to at least one prior therapy. A total of 466 patients were randomly assigned, with 312 and 154 patients enrolled in the KdD and Kd arms, respectively. The baseline characteristics of the patients were generally balanced between the two arms ([Supplementary Table S1](#)). Both treatment arms received carfilzomib intravenously on days 1, 2, 8, 9, 15, and 16 of each cycle. The initial dose for cycle 1 was 20 mg/m² on days 1 and 2, followed by 56 mg/m² in subsequent cycles. Dexamethasone was administered orally or intravenously at a weekly dose of 40mg (or 20mg for patients aged over 75 years). When taken on consecutive days, a split dose of 20mg dexamethasone was

administered daily. In the KdD arm, patients received daratumumab intravenously at a dose of 8 mg/kg on days 1 and 2 of each cycle, followed by administrations every 2 weeks for 4 cycles, and then every 4 weeks thereafter. All patients continued to receive their assigned study therapy until confirmed disease progression, unacceptable toxicity, death, or loss to follow-up.

Model Structure

The analysis model utilized in this study comprised three mutually exclusive health states: stable disease with KdD treatment or Kd treatment (SD State), progressive disease with subsequent treatment (PD State) and death ([Supplementary Figure S1](#)). In a nutshell, all diagnosed RRMM patients initially started in the SD state and received KdD or Kd therapy until disease progression or unacceptable toxicity. Upon entering the PD state, patients could receive subsequent therapy until death. The Markov model employed a cycle length of 28 days, mirroring the therapy cycle of KdD and Kd. Following the recommendation of the China Guidelines for Pharmacoeconomic Evaluations, this study was analyzed from the perspective of Chinese healthcare using a half-cycle correction and a lifetime horizon.

The transition probabilities for each state were derived from final analysis of the CANDOR trial.⁴ Initially, data points from the survive curves (including PFS and OS of the two arms) were extracted using GetData Graph Digitizer software version 2.20. These extracted points, along with the number of patients at risk and total events, were then used to reconstruct the individual patient-level data (IPD) using the standard techniques by Guyot et al.¹⁷ Subsequently, the reconstructed IPD was employed to fit different parametric survival models, such as exponential, Weibull, log-normal, and log-logistic. Based on the Akaike information criterion ([Supplementary Table S2](#)), it was determined that the exponential and log-normal distributions provided the best fit for the OS and PFS curves, respectively.

Based on the fitted survival models, the parameters lambda (λ) of exponential, mu (μ) and sigma (σ) of log-normal were estimated. The estimated parameters were displayed in [Table 1](#). The lognormal parameters were then used to calculate the PFS rates in each cycle based on the following formula:

$$S(t) = 1 - \Phi\left(\frac{\ln(t) - \mu}{\sigma}\right)$$

where the Φ defines the cumulative probability function, the t is survival time. The mortality rates in each cycle were calculated as $\exp(-\lambda t)$. In addition, the background mortality rate for each age group was taken into account in our analysis, based on Chinese life tables ([Supplementary Table S3](#)).¹⁸ The extrapolations of PFS and OS curves beyond the trial's time scope were based on selected survival distributions: exponential for OS and log-normal for PFS. These extrapolated curves, alongside the original curves from the CANDOR trial, are depicted in [Supplementary Figure S2](#).

Health-State Utility Estimates

Baseline utilities of SD State and PD State were 0.810 and 0.715, respectively ([Table 1](#)), based on our previous study and relevant studies.^{5,6,21} In this model evaluation, we considered the utility decrements associated with adverse events (AEs). The disutility and mean duration of each AE were obtained from the published literature,^{5,22,23} which are displayed in the [Supplementary Table S4](#). The AE disutility of 1 cycle for each arm was calculated by multiplying the duration-adjusted utility decrement by the relevant proportion. Consequently, disutility of 0.069 and 0.049 were added to the utility of SD State in KdD and Kd arms, respectively. The QALYs in each health state are estimated by multiplying the time spent in that state by the relevant health state utility.

Cost Estimates

Direct medical costs were collected in accordance with the clinical practice of the CANDOR trial, including drug and administration costs; cost of evaluation and management, laboratory tests, AE management, subsequent treatment and monitoring of post progression.

The unit cost of each drug was derived from the site of the big data service platform for China's health industry.¹⁹ The average body surface area of 1.72 m² and weight of 65 kg were used to estimate the drug costs of each cycle based on the schedule of the treatment intervention in the CANDOR trial. Intravenous administration cost of each infusion was

Table 1 Model Parameters, Ranges, and Distribution for the Sensitivity Analysis

Variable	Base Value (Range)	Distribution
Exponential OS survival model with KdD arm ^a	$\lambda = 0.01307744$	—
Exponential OS survival model with Kd arm ^a	$\lambda = 0.01556741$	—
Log-normal PFS survival model with KdD arm ^a	$\mu = 3.344659$; $\sigma = 1.656417$	-
Log-normal PFS survival model with Kd arm ^a	$\mu = 2.772083$; $\sigma = 1.532737$	-
Drug and administration costs (\$)		
Daratumumab/mg ¹⁹	1.74 (1.392–2.088)	Gamma
Carfilzomib/mg ¹⁹	5.44 (4.352–6.528)	Gamma
Dexamethasone/mg ¹⁹	0.021 (0.0168–0.0252)	Gamma
Intravenous administration, /infusion ²⁰	18.6 (14.88–22.32)	Gamma
Cost of Evaluation and management (\$)/cycle ^b	223 (178.4–267.6)	Gamma
Cost of Laboratory tests (\$)/cycle ^b	168 (134.4–201.6)	Gamma
AEs cost for KdD ^c	845.33 (676.27–1014.40)	Gamma
AEs cost for Kd ^c	768.02 (614.41–921.62)	Gamma
Subsequent treatment cost (\$)/cycle ^d		
KdD/cycle	2862 (2289.6–3434.4)	Gamma
Kd/cycle	2541 (2032.8–3039.2)	Gamma
Monitoring cost for post progression (\$)/cycle ^b	130 (104–156)	Gamma
Risk of subsequent lines treatment in KdD arm ⁴	49% (39.2–58.8%)	Beta
Risk of subsequent lines treatment in Kd arm ⁴	68% (54.4–81.6%)	Beta
Health state utilities ⁵		
Stable disease baseline	0.81 (0.79–0.85)	Beta
Progressive disease	0.715 (0.60–0.79)	Beta
Disutility for KdD, one cycle ^c	0.069 (0.055–0.082)	Beta
Disutility for Kd, one cycle ^c	0.049 (0.039–0.058)	Beta
Discount rate (%) ¹³	5 (0–8)	Fixed in PSA

Notes: ^aEstimated from the CANDOR study. ^bEstimated by local charge and adjusted by a physician. ^cEstimated, from [Supplemental Table S3](#). ^dEstimated, from [Supplemental Table S7](#).

Abbreviations: OS, Overall survival; PFS, Progression-free survival; KdD, carfilzomib, daratumumab and dexamethasone; Kd, carfilzomib and dexamethasone; AE, adverse event; PSA, probabilistic sensitivity analysis.

derived from another cost analysis of China.²⁰ The costs of evaluation and management, laboratory and monitoring for post progression were estimated according to local charges and adjusted by a physician from a Chinese health system perspective.

AEs of grade ≥ 3 that occurred more than 5% or with a between-treatment difference of $>2\%$ were included in the model. The AE management costs were estimated by multiplying the proportion of AEs by the relevant management cost per incident. The percentages and unit costs of the AEs were derived from the trial and the published literature,^{5,20,24,25} and are displayed in [Supplementary Table S4](#). The AE management costs were calculated as 845.33 and 768.02 USD with KdD and Kd, respectively.

According to the CANDOR study, 153 (49%) patients in the KdD arm and 105 (68%) patients in Kd arm received subsequent therapies.⁴ Therefore in the model, the proportion of the KdD arm and Kd arm receiving the subsequent treatment was assumed to be 49% and 68%, separately. Subsequent treatment costs of two arms were estimated by weighted means of different regimens according to the approach of our previous economic analysis.⁵ Based on the CANDOR study,⁴ subsequent therapies were largely similar between treatment arms, except that patients in KdD arm were 4 times less likely to receive an anti-CD38 monoclonal antibody therapy isatuximab or daratumumab (KdD, 7% [23/312]; Kd, 28% [43/154]. Considering isatuximab was not yet on the marketed in China, we assumed 15.03% (23/153) in the KdD arm and 40.95% (43/105) in the Kd arm received daratumumab monotherapy for patients received subsequent therapies. The percentages of the other subsequent regimens were reassigned and normalized to sum to 100%, according to the reported weighted means of the common regimens for patients with RRMM.²⁶ The reassigned percentages of subsequent regimens are shown in [Supplementary Table S5](#). The dosage and course of these subsequent

regimens are from the relevant clinical literature; and the unit cost of each drug was derived from the site of the big data service for China's health industry.¹⁹ Costs associated with different treatment regimens were calculated in [Supplementary Table S6](#). The cost of subsequent treatment for each cycle of the two groups was calculated based on the costs of different treatment regimens and their percentages. Then, the weighted subsequent treatment costs were calculated at 2,862 USD for KdD and 2,541 for Kd ([Supplementary Table S7](#)).

Sensitivity Analyses

A series of sensitivity analyses were conducted to assess the robustness of the model and how the results varied along with the substantial uncertainty of input parameters. In one-way sensitivity analysis, the sensitive factors were identified by varying the input parameters individually. The ranges of them were obtained from the relevant derivation or varied by $\pm 30\%$ of the base values. In probabilistic sensitivity analysis, Monte Carlo simulations of 1,000 iterations were performed by setting patterns of appropriate distribution for each parameter. All input parameters of the model, along with their ranges and distributions, were collected in [Table 1](#).

Results

Base-Case results

In the base-case analysis, the model simulated the patients' life time for KdD and Kd regimens. The results of the base-case analysis are presented in [Table 2](#). For patients with RRMM, adding daratumumab to Kd produced 3.803 QALYs, which was 0.537 more than patients in Kd group. The total cost per patient in KdD and Kd arms was \$300,588 and \$162,474, respectively. The ICUR for KdD arm versus Kd arm was \$257,319 per QALY.

Sensitivity Analyses Results

The results of one-way sensitivity analysis were depicted in a tornado diagram ([Figure 1](#)), in which the input parameters were displayed in descending order of affecting ICUR. The cost of daratumumab had the most effects on the ICUR. Other sensitive parameters included discount rate, cost of carfilzomib, utility of progressed disease, cost of subsequent treatment for kd. All of the input parameters failed to result in an ICUR below the WTP threshold of \$38,201/QALY.

The ICURs for 1,000 iterations in the probabilistic sensitivity analysis are shown in the scatterplot ([Figure 2](#)), which indicated that all of the dots were above the WTP threshold of \$38,201/QALY. The cost-effectiveness acceptability curves, shown in [Supplementary Figure S3](#), reflected the varying probability of cost-effectiveness under different WTP thresholds, and suggested that the sensitivity range of WTP was 150,000 to 400,000 USD/QALY.

Discussion

The addition of daratumumab to a regimen of Kd treatment in RRMM has shown significant prolongation of PFS and a trend towards OS benefit in the CANDOR trial.^{3,4} However, it remains unclear whether this combination is cost-

Table 2 Base-Case Model Results

	Kd	KdD	Difference
Drug cost (\$)	103,257	250,078	146,821
Administration cost (\$)	3,677	7,021	3,344
Adverse events cost (\$)	845	768	-77
Cost of Evaluation and management (\$)	7,348	10,613	3,265
Subsequent treatment cost (\$)	38,965	21,969	-16,996
Other health-related expenses (\$)	8,382	10,109	1,727
Total costs (\$)	162,474	300,558	138,084
Total QALY	3.266	3.803	0.537
ICUR (\$/QALY)	-	-	257,319

Abbreviations: Kd, carfilzomib and dexamethasone; KdD, daratumumab plus carfilzomib and dexamethasone; QALY, quality-adjusted life-year; ICUR, incremental cost-utility ratio.

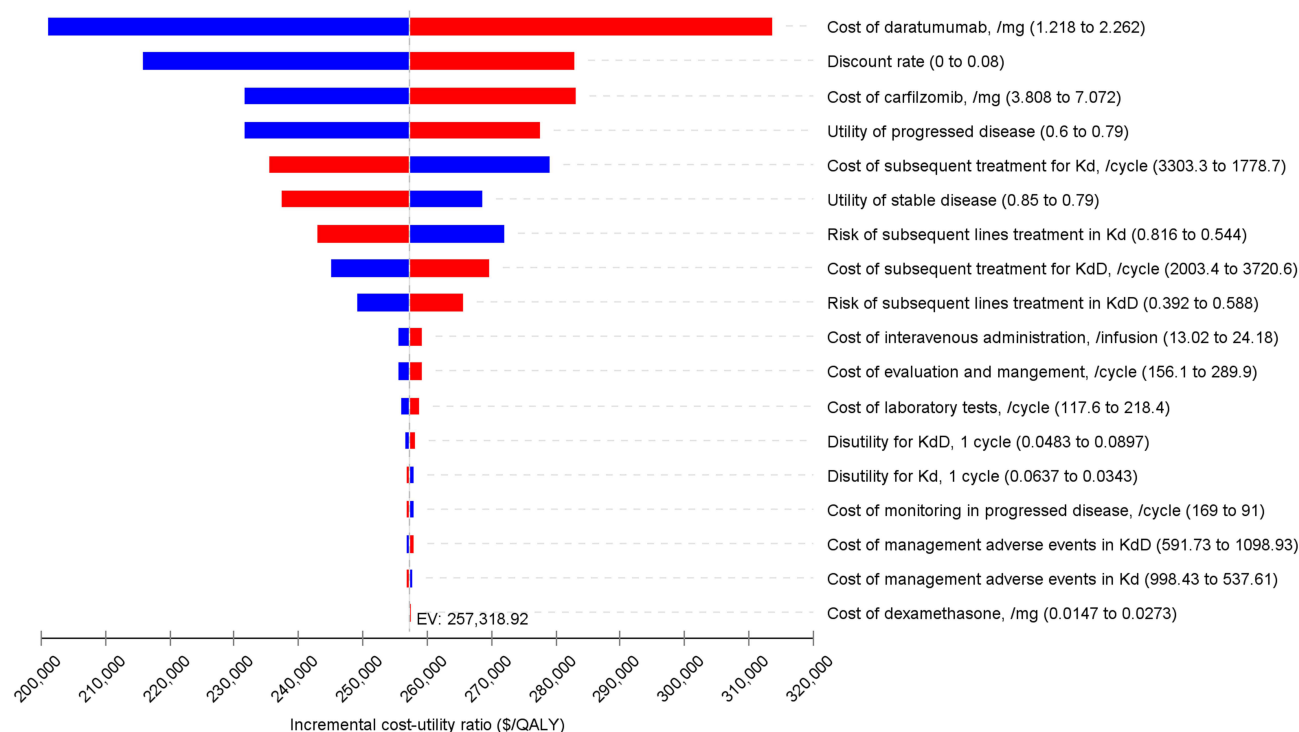


Figure 1 The results of one-way sensitivity analysis. KdD: carfilzomib, daratumumab and dexamethasone; Kd: carfilzomib and dexamethasone.

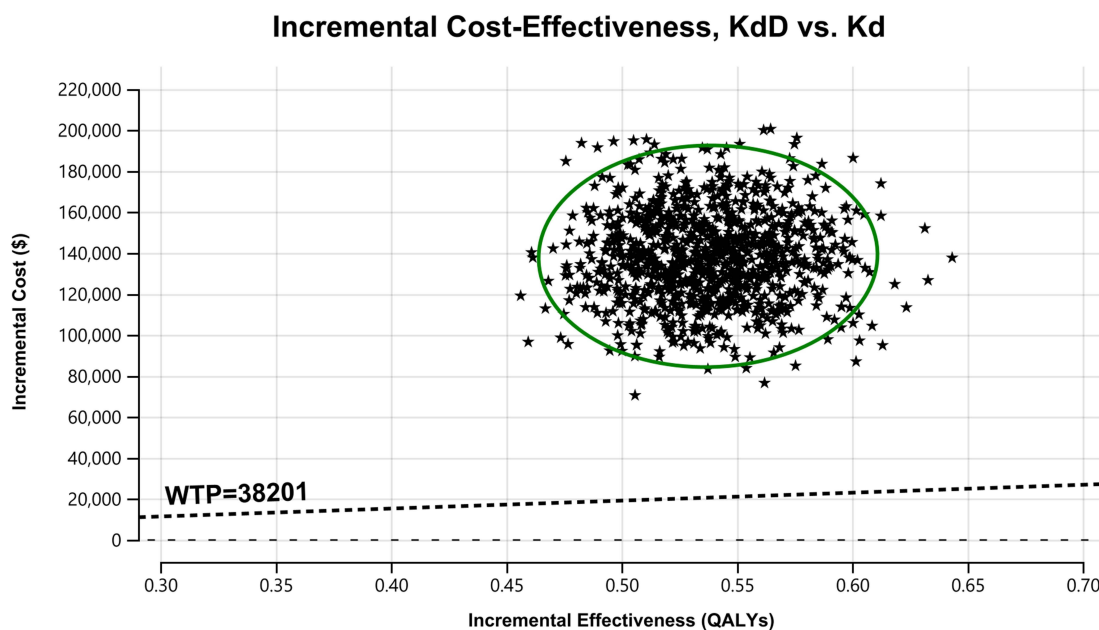


Figure 2 The results of probabilistic sensitivity analysis. KdD: carfilzomib, daratumumab and dexamethasone; Kd: carfilzomib and dexamethasone.

effective in RRMM in China. In this study, we conducted a cost-effectiveness analysis of adding daratumumab to Kd for patients with RRMM from a Chinese healthcare perspective. The efficacy and safety data were derived from the CANDOR trial, while costs were collected from published literature or estimated based on local charges. The base-case results indicated an ICUR of \$257,319 per QALY gained for KdD versus Kd, which exceeded the WTP threshold of \$38,201/QALY.

Our investigation demonstrated robust outcomes across all input parameters, as indicated by the sensitivity analyses. Although factors such as the cost of daratumumab, discount rate, cost of carfilzomib, and utility of progressed disease had a material impact on the ICUR, none of them resulted in an ICUR below the WTP threshold. The probabilistic sensitivity analyses revealed that all dots were above the WTP threshold, indicating a 0% probability of KdD being cost-effective. Only if the WTP threshold exceeds \$150,000/QALY, would there be a chance for the KdD treatment to be considered cost-effective. It is worth noting that mainland China comprises 31 province-level administrative units with significant variations in the per-capita GDP. In 2022, the per-capita GDP ranged from \$6,622 in Gansu province to \$28,278 in Beijing city. However, even when using Beijing's per-capita GDP as the recommended WTP threshold ($3 \times \$28,278 = \$84,834$), it still falls far below \$150,000/QALY.

Although our study suggests that the incorporation of daratumumab into the Kd regimen may lack cost-effectiveness at its current price in China, it is crucial to acknowledge the substantial advantages and tolerability associated with daratumumab. The one-way sensitivity analysis underscored the cost of daratumumab as the most influential determinant affecting the ICUR. The impact of variations in the price of daratumumab on the ICUR is illustrated in [Supplementary Figure S4](#). At a WTP threshold of 38,201 USD/QALY, the likelihood of KdD treatment being cost-effective was 0%, 0%, 0%, and 0.5%, respectively, when daratumumab was priced at 100%, 50%, 20%, and 10% of its current value. At a WTP threshold of 84,834 USD/QALY in Beijing (an example of an affluent region), the probabilities were 0%, 0.2%, 16.3%, and 41.4%, respectively. Clearly, even with a 90% reduction in the price of daratumumab, the probability of KdD being cost-effective in the general regions remained significantly low (0.5%). Conversely, in affluent regions (such as Beijing, Shanghai, and Jiangsu), KdD treatment would be considered cost-effective at price reductions of 20% or more of the current cost of daratumumab. Given the imperative nature of providing optimal treatment for patients, potential measures such as price reduction or the implementation of a financial assistance program specifically for daratumumab could be contemplated to enhance accessibility.

Previous research has explored the cost-effectiveness of daratumumab-based triplet therapies versus doublet regimens in the treatment of relapsed and refractory multiple myeloma (RRMM). A study from the United States, for instance, compared the cost-effectiveness of daratumumab-based triple therapies for patients with RRMM.⁶ The findings indicated that, compared to the Vd regimen, the ICUR for the DVd regimen (daratumumab plus Vd) was \$284,180 per QALY, while for the DRd regimen (daratumumab plus Rd), the ICUR was \$1,369,602 per QALY. Only when the price of daratumumab was reduced to 37% of its current price was the addition of daratumumab to Vd considered cost-effective at a WTP of \$50,000 per QALY. This study concluded that adding daratumumab to either Vd or Rd did not demonstrate cost-effectiveness. Our previous research also evaluated the cost-effectiveness of DVd and Vd, reporting an ICUR of \$213,164 per QALY.⁵ A price variation analysis suggested that daratumumab would be cost-effective at a WTP of \$150,000/QALY when priced at 30% of its current value. Additionally, a study in Singapore assessed the cost-effectiveness of the DRd therapy compared to Rd in RRMM patients.¹⁰ The ICUR for the DRd regimen was \$576,247 per QALY, compared to Rd. Even with a 20% reduction in the cost of daratumumab and a 80% reduction in the cost of lenalidomide, the ICURs remained high at \$470,400 and \$152,860 per QALY gained. The study concluded that the DRd regimen was not a cost-effective use of healthcare resources in Singapore. Based on a network meta-analysis, Carlson et al demonstrated that DVd was cost-effective from a US payer perspective.⁷ The findings indicated that, compared to the Rd regimen, the estimated ICURs for DVd were \$50,704 per QALY for second-line therapy and \$60,359 per QALY for third-line therapy; for DRd, the ICURs were \$187,728 per QALY and \$216,360 per QALY for second and third-line therapy, respectively. To the best of our knowledge, our current study is the first economic evaluation of adding daratumumab to Kd to patients with RRMM from the Chinese healthcare perspective. We believe that our findings provide crucial information for decision makers in China.

Certain assumptions are indeed inherent to the mathematical modeling process. For instance, the use of three mutually exclusive health states in our model was specifically chosen to closely align with the natural progression of RRMM. This approach allows for a more realistic simulation of the disease trajectory, thereby enhancing the model's predictive accuracy. Additionally, other assumptions within the manuscript, such as the simulation of subsequent treatments and extrapolations of PFS and OS curves, were made to more closely reflect clinical reality and improve the model's applicability to real-world scenarios. The digitizing software used in this study was validated by comparing our

extrapolated curves with the original curves from the CANDOR trial, as shown in [Supplementary Figure S2](#). The near-perfect overlap observed in this comparison strongly supports the reliability and accuracy of the software. This validation process ensures that our extrapolated data are consistent with the original trial data, thereby enhancing the credibility of our findings.

Several limitations should be acknowledged in our study. Firstly, the extrapolation of clinical trial results to a broader population is a common challenge in modeling studies. In this study, we relied on exponential and log-normal distributions to extrapolate OS and PF curves beyond the timeframe of the clinical trial. While this approach introduces some degree of uncertainty, it is widely accepted in the field and helps to provide a more comprehensive view of long-term outcomes. Secondly, by focusing on AEs of grade ≥ 3 that occurred in more than 5% of patients or had a between-treatment difference of $>2\%$, our economic evaluation may not fully capture the costs associated with less common AEs or those with lower risk. However, the objective of the economic evaluation was to estimate the ICUR between the two treatment arms, and the impact of AEs with lower risk on the final result would be modest. It is also important to note that patients with grade 1/2 AEs rarely require additional treatment, which mitigates some uncertainty. Additionally, the findings of the one-way sensitivity analyses showed that the ICUR was not sensitive to cost of management AEs. Thirdly, the utility values used in our study were obtained from published literature and may not completely reflect the quality of life experienced by patients in the CANDOR trial. Although the utilities for disease progression and stable disease had a sensitive impact on the results ([Figure 1](#)), even under extreme variations, the ICUR remained above the WTP threshold. To further examine the impact of utility values, we conducted a 2-way sensitivity analysis with a broader variation of $\pm 20\%$ (See [Supplementary Figure S5](#)), which confirmed that KdD did not become cost-effective compared to the Kd arm. The cost data used in this study were derived from a combination of local databases and published literature. While this approach provides a robust foundation for our cost estimates, we recognize the potential for biases inherent in any data source. To address this, we conducted sensitivity analyses that demonstrated the minimal impact of cost variations on the model's outcomes. This suggests that our findings are relatively insensitive to minor fluctuations in cost data, thereby enhancing the reliability of our conclusions. Finally, although our study is limited by its focus on the Chinese healthcare system, it remains a pioneering economic evaluation of the KdD regimen for RRMM patients. This first-of-its-kind analysis not only informs current decision-making in China but also serves as a valuable reference for future studies and for countries with comparable healthcare systems.

Conclusions

Adding daratumumab to a regimen of carfilzomib and dexamethasone for patients with RRMM is unlikely to be cost-effective from the perspective of Chinese healthcare system. Lowering the price or implementing a financial assistance program for daratumumab and/or carfilzomib to lower the cost of the regimen may be more viable options.

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Disclosure

All authors declare no conflicts of interest in this work.

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