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Summary

Background

Lenalidomide maintenance is standard after autologous stem-cell transplantation (ASCT) in multiple myeloma, but its efficacy in high-risk patients is limited. The intensified triplet of carfilzomib, lenalidomide, and dexamethasone (KRd) has shown improved outcomes in the ATLAS trial, yet its cost-effectiveness from the US payer perspective remains unknown. We aimed to evaluate the cost-effectiveness of KRd versus lenalidomide monotherapy as post-ASCT maintenance in patients with newly diagnosed multiple myeloma.

Methods

We developed a three-state Markov model (progression-free survival, progressive disease, death) with a 28-day cycle and a 10-year horizon, from the US payer perspective. Clinical inputs were derived from the ATLAS trial (NCT02659293). Transition probabilities were estimated by parametric survival fitting (Gamma for KRd PFS, Gompertz for KRd OS; log-normal for lenalidomide PFS and OS). Costs (2025 USD) included drug acquisition, adverse event management, routine monitoring, subsequent therapy, and hospice care. Utilities were sourced from published literature with disutilities applied for grade ≥3 adverse events. One-way, probabilistic, and scenario sensitivity analyses were performed. The willingness-to-pay (WTP) threshold was $150,000 per QALY.

Findings

The KRd group incurred $482,294 and accumulated 1.59 QALYs versus $355,162 and 1.15 QALYs for lenalidomide, yielding an incremental cost-effectiveness ratio (ICER) of $288,936 per QALY—well above the WTP threshold. One-way sensitivity analysis identified PFS utility and carfilzomib cost as key drivers. Probabilistic sensitivity analysis showed low cost-effectiveness probability at $150,000/QALY. Scenario analysis indicated that a ~48% reduction in carfilzomib cost would bring the ICER below the WTP threshold.

Interpretation

From the US payer perspective, KRd maintenance is not cost-effective compared with lenalidomide monotherapy at current prices. Carfilzomib cost is the primary driver of the ICER. Price negotiations or risk-sharing agreements could make KRd economically viable, supporting its clinical benefit with improved affordability.

1.Introduction

Globally, multiple myeloma is the second most frequently occurring haematological malignancy, marked by a relapsing-remitting course and enhanced osteoclastic activity[1].Its aggressive progression and frequent recurrences translate into substantial clinical and economic challenges for the U.S. healthcare system[2].For patients with newly diagnosed multiple myeloma who are eligible for transplantation, induction therapy followed by autologous hematopoietic stem cell transplantation

(ASCT) is currently the standard of care in Western countries, and post-transplant maintenance therapy is the core intervention to prolong progression-free survival and reduce the risk of relapse[3].

Lenalidomide monotherapy is the classic maintenance regimen after autologous stem cell transplantation, and has been proven by multiple randomized controlled trials to effectively delay disease progression. However, its efficacy in patients with high-risk cytogenetics is limited, leaving considerable room for optimization[4].Carfilzomib is an epoxyketone proteasome inhibitor that selectively and irreversibly binds to the constitutive proteasome and immunoproteasome, and has shown therapeutic activity against multiple myeloma5.With the widespread availability of targeted agents and accumulating clinical evidence, the intensified combination regimen of carfilzomib plus lenalidomide plus dexamethasone (KRd) has been increasingly used as post-transplant maintenance therapy. Although multi-drug combination regimens can enhance antitumor efficacy, they also alter the adverse event profile and increase the risk of moderate-to-severe toxicities[5].During long-term maintenance therapy for myeloma, treatment-related adverse events of grade ≥3, such as hematologic toxicity, infections, and peripheral neuropathy, are very common. These events not only reduce patients' quality of life and lower health utility values, but also generate substantial incremental medical expenditures—including outpatient visits, hospitalizations, emergency care, and symptomatic medications[6]，—and represent a significant source of hidden costs in U.S. oncology care. Multiple U.S. pharmacoeconomic studies have confirmed that moderate-to-severe adverse events substantially increase the overall healthcare costs across the full treatment cycle of myeloma patients, and that differences in safety profiles between regimens directly affect the final cost-effectiveness evaluation results[7].

In recent years, with deeper understanding of MM and the development of novel agents, treatment options for lenalidomide-refractory MM have significantly expanded, including, for example, lenalidomide plus bortezomib plus dexamethasone[8]、and isatuximab plus bortezomib plus lenalidomide plus dexamethasone[9].However, pharmacoeconomic studies comparing the combination regimen of carfilzomib plus lenalidomide plus dexamethasone (KRd) with lenalidomide monotherapy remain scarce, making it difficult to fully inform clinical drug selection and reimbursement decisions in the United States. This study was conducted based on the ATLAS clinical trial3（ClinicalTrials.gov:NCT02659293、EudraCT：2015–002380–42）, an international, multicenter, randomized, open-label Phase III study carried out in the United States and Poland. With a median follow-up of 69 months, the trial fully disclosed the efficacy data and grade-specific adverse event profiles of the two regimens, providing authoritative clinical baseline information for the present study.

2.Methods

2.1. Study Design

The population for this model was derived from the ATLAS trial[3].In the ATLAS trial ，patients in the intervention group (carfilzomib–lenalidomide–dexamethasone) received 28-day cycles of treatment: carfilzomib was administered intravenously at 20 mg/m² on days 1 and 2 of cycle 1, at 36 mg/m² on days 1, 2, 8, 9, 15, and 16 of cycles 1–4, and at 36 mg/m² on days 1, 2, 15, and 16 of cycles 5–36; lenalidomide 25 mg orally on days 1–21; and dexamethasone 20 mg orally on days 1, 8, 15, and 22.Patients in the control group (lenalidomide alone) received lenalidomide maintenance monotherapy at a starting dose of 10 mg/d orally once daily for the first 3 cycles, with dose adjustment to the optimal dose (≤15 mg/d) based on tolerability thereafter, in 28-day cycles. Per the ATLAS trial design , patients

in the intervention group who achieved minimal residual disease (MRD) negativity with standard-risk cytogenetics after cycle 6 could switch to lenalidomide monotherapy after cycle 8.Both groups continued treatment until disease progression or unacceptable toxicity. In the cost-effectiveness analysis model, subsequent treatment costs were included in the post-progression cost category, assuming that patients received subsequent anti-myeloma therapy (including CAR-T cell therapy, bispecific antibodies, or anti-BCMA antibody–drug conjugates) after disease progression, with costs calculated based on the median treatment duration and incurred as a one-time cost at progression. The subsequent treatment costs were estimated using the Micromedex RED BOOK and CMS Medicare ASP pricing filesBaseline characteristics of the ATLAS trial population have been previously reported ; the model population reflects the intent-to-treat population of that trial..

2.2.Model structure

Based on the ATLAS trial[3], a three-state Markov model was constructed using TreeAge Pro 2022 to compare the cost-effectiveness of the two regimens for the treatment of multiple myeloma.The Markov model comprised three mutually exclusive health states (Figure 1): progression-free survival, progressive disease, and death. The model cycle length was 28 days, consistent with the dosing regimen. The time horizon was set at 10 years. All patients entered the model in the PFS state, and as cycles progressed, patients could only transition from one state to another or remain in the current state.In each cycle, patients received the corresponding drug treatment, incurring associated costs and health outcomes. All patients entered the model in the progression-free survival state. Within each discrete cycle, patients could either remain in the current state or transition to other health states based on transition probabilities. In each cycle, patients in the progression-free survival state received the corresponding treatment according to their group assignment and accumulated associated costs and health outcomes. The core output indicators of the model included costs, quality-adjusted life-years (QALYs), and incremental cost-effectiveness ratios (ICERs). ICER = cost / QALY.

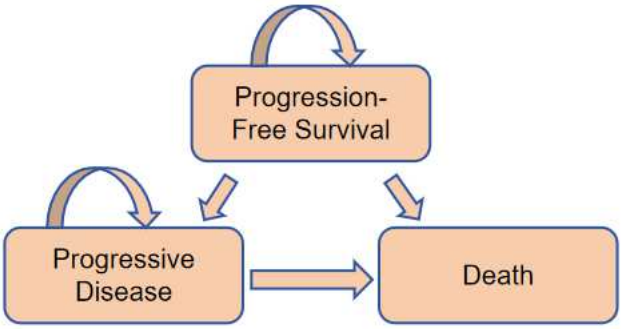


Figure 1. Structure of the Markov model

2.3. Clinical data

We used GetData Graph Digitizer software to extract data from the Kaplan–Meier curves, and performed parameter fitting using R version 4.5.1. Six parametric distributions—Exponential, Weibull, Gamma, Gompertz, Log-logistic, and Lognormal—were applied to fit the survival data for progression-free survival (PFS) and overall survival (OS)[10].Based on the Akaike information criterion (AIC) and Bayesian information criterion (BIC) (Table 1), supplemented by visual inspection of the fitted curves against the original Kaplan–Meier curves, the distribution with the lowest AIC/BIC

values and the best visual agreement was selected as the optimal parametric distribution[11].Analysis results showed that the optimal fitted distribution for PFS in the carfilzomib + lenalidomide + dexamethasone group was the Gamma distribution, and for OS was the Gompertz distribution; while the optimal fitted distributions for both PFS and OS in the lenalidomide monotherapy group were Log-normal distributions. Transition probabilities between health states were calculated based on the parameter formulas corresponding to each optimal distribution model. To account for background mortality in the model (i.e., patients transitioning directly from the “alive” state to the “death” state without disease progression), we used the overall U.S. population mortality rate of 0.0083 for the year 2021, as published in the 2023 National Vital Statistics Reports (NVSR), as the background mortality risk parameter[12].

Table 1. Based on Akaike information criterion (AIC) and Bayesian information criterion (BIC)

Variable	PFS curve				OS curve			
	KPd group		Lenalidomide group		KPd group		Lenalidomide group	
Curve distribution	AIC	BIC	AIC	BIC	AIC	BIC	AIC	BIC
Exponenial	631.5551	634.0324	406.3939	408.9157	367.0117	369.4890	206.5476	209.0694
Gamma	630.0418	634.9964	406.4962	411.5398	363.1128	368.0675	208.5396	213.5832
Gompertz	631.5421	636.4967	408.2210	413.2646	362.2686	367.2232	207.3369	212.3805
Weibull	630.0581	635.0128	406.9252	411.9688	362.6412	367.5959	208.5470	213.5905
Log-logistic	631.1326	636.0872	405.6798	410.7234	363.5165	368.4712	208.0449	213.0885
Log-normal	636.8288	641.7834	404.0112	409.0547	366.3862	371.3409	206.4082	211.4518

2.4. Costs and utilities

This study was conducted from the US payer perspective. Total costs included drug acquisition costs, routine visit costs, hospice care costs, and costs for managing treatment-related grade ≥3 adverse events (AEs), among others (Table 2). US drug prices were obtained from Drugs.com and the National Cancer Institute (NCI) website. All costs were adjusted to 2025 US dollars using the Consumer Price Index (CPI) inflation calculator from the US Bureau of Labor Statistics (BLS) to maintain price consistency.The dose cost calculation based on body surface area was performed using the average body surface area of US adults of 1.73 m^2, as proposed by the Du Bois and Du Bois formula[13]and it was assumed that no drug waste occurred. The model assumed that all adverse events occurred in the first treatment cycle, and that the same patient could experience multiple adverse events. The incidence rates of grade ≥3 adverse events and subsequent treatment patterns were derived from the ATLAS trial[3].In this trial, the most common grade 3–4 adverse events in the carfilzomib + lenalidomide + dexamethasone (KRd) group versus the lenalidomide monotherapy (R) group included neutropenia (48% vs 59%), thrombocytopenia (13% vs 6%), and upper respiratory tract infection (9% vs 3%). Other cost data were sourced from publicly available databases and peer-reviewed literature. Since the ATLAS trial did not report corresponding utility values, utility values for the progression-free survival (PFS) and progressive disease (PD) states were taken from published literature. To avoid potential bias from applying the same utility values to both the KRd and R groups, this study incorporated disutility values for grade ≥3 adverse events with an incidence exceeding 5% in each treatment group[14]，thereby improving the accuracy of health utility values for each group. Costs and utility parameters strictly followed the US guidelines for health economic evaluation and were calibrated using an annual

discount rate of 3%[15].

Table 2. Model parameters and distributions

Variable	Baseline value	Maximum	Minimum	Distribution	Source
Drug cost (USD)					
Carfilzomib week 1	18619.5	22343.4	14895.6	Gamma	[16]
Carfilzomib weeks 2–4	22343.4	26812.08	17874.72	Gamma	[16]
Carfilzomib weeks 5–36	14895.6	17874.72	11916.48	Gamma	[16]
Lenalidomide	10632.09	12758.508	8505.672	Gamma	[16]
Dexamethasone	22.4	26.88	17.92	Gamma	[16]
Adverse event management cost (USD)					
Neutropenia	167.00	201.00	134.00	Gamma	[17]
Thrombocytopenia	167.00	201.00	134.00	Gamma	[17]
Upper respiratory tract infection	369.73	443.68	295.78	Gamma	[18]
Leukopenia	8,593.00	10,311.60	6,874.40	Gamma	[16]
Diarrhea	1,700.00	2,040.00	1,360.00	Gamma	[16]
Subsequent treatment drug cost					
Lenalidomide	10632.09	12758.508	8505.672	Gamma	[19]
Other costs					
Monthly monitoring during PFS	188.91	226.69	151.13	Gamma	[16]
Monthly monitoring after progression	445.03	534.04	356.02	Gamma	[16]
Outpatient follow-up visits	674.08	808.90	539.26	Gamma	[16]
Serum free light chain (sFLC) testing	222.48	266.98	177.98	Gamma	[16]
Hospice care	6280.00	7536.00	5024.00	Gamma	[20]
Utility values					
Utility of PFS	0.65	0.62	0.68	Beta	[21]
Utility of PD	0.59	0.56	0.62	Beta	[21]
Disutility of thrombocytopenia	0.008	0.0088	0.0072	Beta	[18]
Disutility of anemia	0.25	0.275	0.225	Beta	[18]
Disutility of neutropenia	0.145	0.1595	0.1305	Beta	[18]
Disutility of upper respiratory tract infection	0.14	0.154	0.126	Beta	[18]
Disutility of leukopenia	0	0	0	Beta	[16]
Discount rate (%)	3	5	0	Uniform	[21]

2.5.Probabilistic analysis

We performed one-way sensitivity analysis (OWSA) and probabilistic sensitivity analysis (PSA) to evaluate the impact of model parameter uncertainty on the economic evaluation results. In the OWSA, the variation range of each parameter was set based on the 95% confidence interval reported in the literature or ±20% of the baseline value, and each variable was varied one at a time to identify factors with significant influence on the economic outcomes.The range of the discount rate was set as 0–0.03 based on US cost-effectiveness analysis research practice[22],and the results were presented as tornado diagrams. For the PSA, all parameters were assigned as random variables: cost parameters followed a Gamma distribution, utility and probability parameters followed a Beta distribution, and the discount rate followed a Uniform distribution. Based on 10,000 Monte Carlo simulations, cost-effectiveness scatter plots and acceptability curves were generated to test the robustness of the model.According to the commonly used willingness-to-pay threshold in the United States, this study adopted $150,000 per quality-adjusted life-year (QALY) as the benchmark[23].

2.6.Scenario analysis

The pharmacoeconomic evaluation revealed that fluctuations in the acquisition cost of carfilzomib in the carfilzomib + lenalidomide + dexamethasone regimen significantly influenced the model results and the ICER. Therefore, this study conducted scenario analyses to simulate, under conditions where the price remained unchanged while the willingness-to-pay (WTP) threshold was increased to 2-fold ($300,000/QALY), 3-fold ($450,000/QALY), and 4-fold ($600,000/QALY), or under potential price reductions of carfilzomib achievable through National Medical Insurance negotiations or market competition (30%, 40%, 50%, and 60%), the probability of the carfilzomib + lenalidomide + dexamethasone regimen being considered cost-effective compared with lenalidomide monotherapy, and the corresponding changes in the ICER. This indicates that drug pricing is the core determinant driving the cost-effectiveness of the carfilzomib + lenalidomide + dexamethasone regimen.

3. Results

3.1.Base-case analysis results

Based on the Markov model run over a 10-year time horizon, the base-case analysis results for each treatment group were summarized, including total costs and health utility values (QALYs). The carfilzomib + lenalidomide + dexamethasone (KRd) group incurred a total cost of $482,294 and accumulated 1.59 QALYs, while the lenalidomide monotherapy group incurred a total cost of $355,162 and accumulated 1.15 QALYs. The incremental cost between the two groups was $127,132, and the incremental utility was 0.44 QALYs, yielding an incremental cost-effectiveness ratio (ICER) of $288,936.36 per QALY. This value is substantially higher than the commonly used willingness-to-pay (WTP) threshold in the United States ($150,000/QALY). Taken together, from the US payer perspective, the KRd regimen as post-transplant maintenance therapy is not cost-effective compared with lenalidomide monotherapy, as shown in Table 3.

Table 3. Base-case analysis results

Group	Tolal cost（USA）	Incremental cost (USD)	Utility (QALYs)	Incremental utility	ICER(USD/QALY)

				(QALYs)	
KRd group	482,294	127,132	1.59	0.44	288,936.36
Lenalidomide group	355,162	–	1.15	–	–

3.2.Sensitivity analysis

The results of the one-way sensitivity analysis (OWSA) are presented as a tornado diagram (Figure 2). The results showed that the variable with the greatest impact on ICER uncertainty was the utility value for progression-free survival (PFS), followed by the cost of carfilzomib during the 2- to 4-week treatment cycles. The utility value for the progressive disease state, the cost of carfilzomib after 5 weeks of treatment, and the subsequent treatment costs in the lenalidomide group had a moderate impact on the results, while the utility decrements and costs associated with adverse events (such as thrombocytopenia, neutropenia, and upper respiratory tract infection) had relatively little influence on the outcomes.

3.3. Scenario analysis

The results of the probabilistic sensitivity analysis are presented as a scatter plot (Figure 3) and a cost-effectiveness acceptability curve (Figure 4). The results showed that the 95% confidence interval for the ICER ranged from $240,256 to $1,389,689 aaper QALY. At a willingness-to-pay (WTP) threshold of $150,000 per QALY, the vast majority of ICER scatter points lay above the threshold line, indicating a low probability that the carfilzomib + lenalidomide + dexamethasone regimen is cost-effective compared with lenalidomide monotherapy. Furthermore, the cost-effectiveness acceptability curve further showed that the probability of the KRd regimen being cost-effective gradually increased as the WTP threshold rose. From this, we can conclude that when the WTP reaches approximately $290,000 per QALY, the probability of being cost-effective for the KRd group and the lenalidomide group is similar; beyond this point, the advantage probability of the KRd regimen further increases, which provides the basis for the subsequent scenario analyses.

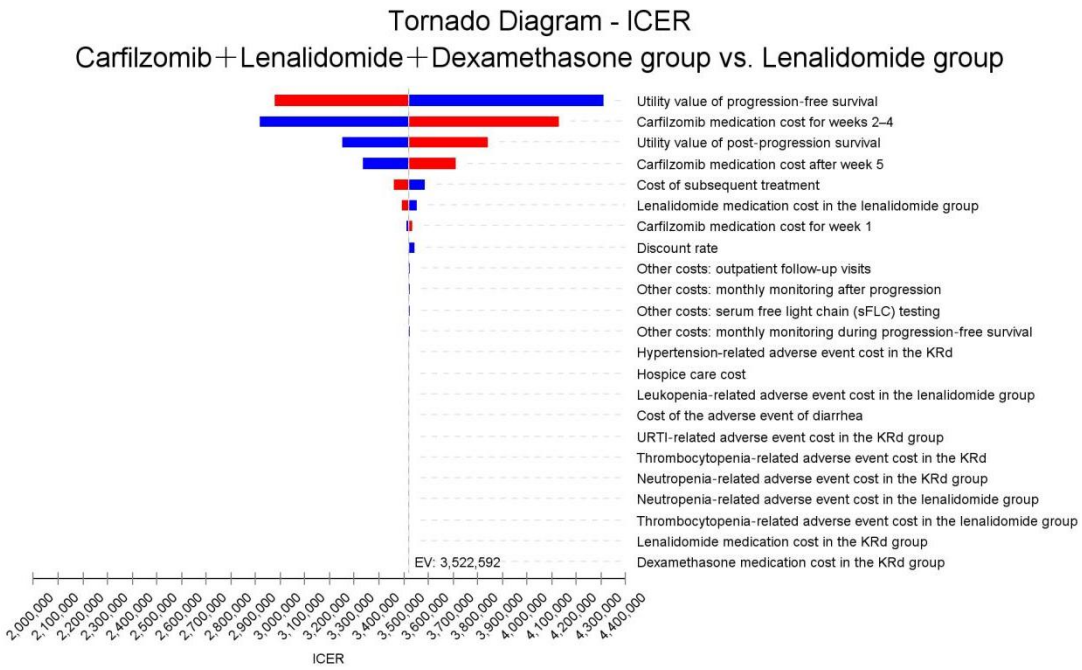


Figure 2. Tornado plot

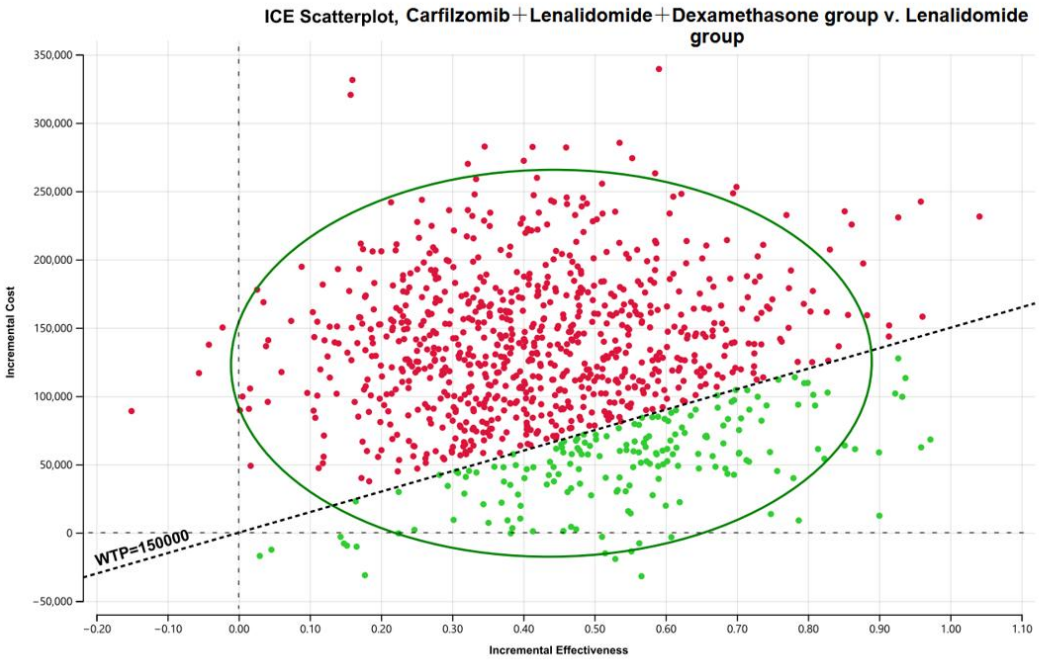


Figure 3. Scatter plot from the probabilistic sensitivity analysis (PSA)

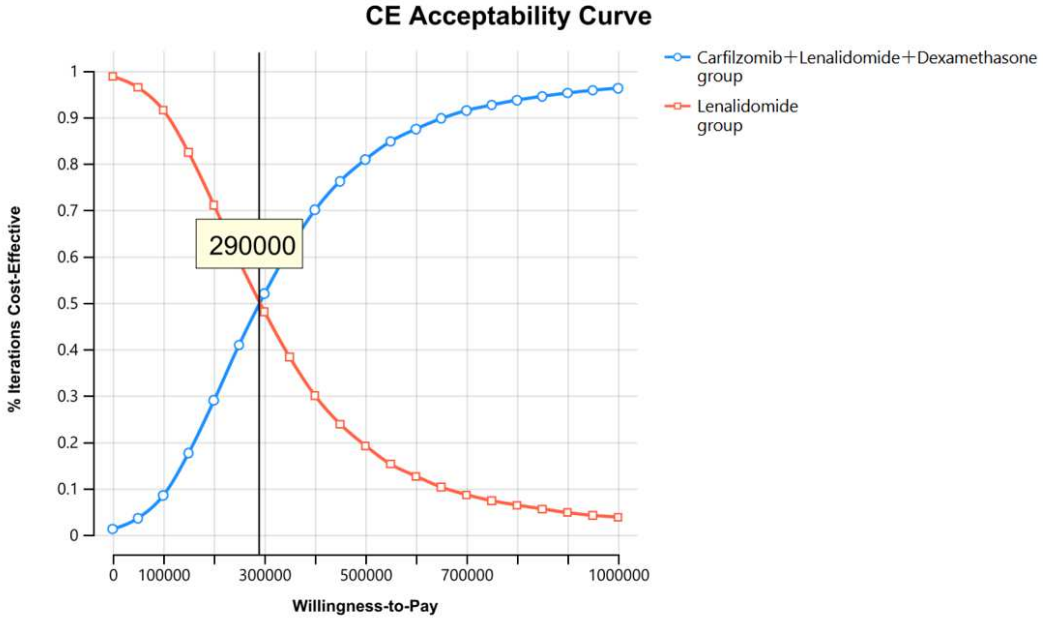


Figure 4. Cost-effectiveness acceptability curve (CEAC)

3.4.Scenario analysis

The results of the scenario analysis are detailed in Table 4. From the US payer perspective, under the scenario of fixed drug prices, as the willingness-to-pay (WTP) threshold increased stepwise from $150,000/QALY to $600,000/QALY, the probability of the carfilzomib + lenalidomide + dexamethasone regimen being cost-effective compared with lenalidomide monotherapy gradually rose from a relatively low level. This indicates that the setting of the WTP threshold has a significant impact on the economic conclusions; the higher the threshold, the greater the likelihood that the intervention strategy will be judged as cost-effective.

Under the scenario with the WTP threshold fixed at $150,000/QALY, when the acquisition cost of carfilzomib in the carfilzomib + lenalidomide + dexamethasone regimen was reduced by 30%, 40%, 50%, and 60%, respectively, the ICER values showed a stepwise decrease, from $202,255/QALY to $115,574/QALY. When the cost of carfilzomib was reduced by approximately 48%, the ICER fell below the WTP threshold of $150,000/QALY, at which point the carfilzomib + lenalidomide + dexamethasone regimen could be considered cost-effective compared with lenalidomide monotherapy. These findings indicate that drug pricing is the core determinant driving the cost-effectiveness of the carfilzomib + lenalidomide + dexamethasone regimen.

Table 4. Scenario analysis results

Scenario	WTP threshold (USD/QALY)	Cost reduction (%)	ICER (USD/QALY)	Cost-effective
Base-case analysis	150,000	0%	288,936	No
Scenario 1	150,000	30%	202,255	No
Scenario 2	150,000	40%	173,362	No

Scenario 3	150,000	50%	144,468	Yes
Scenario 4	150,000	60%	115,574	Yes
Scenario 5	300,000	0%	288,936	Yes
Scenario 6	450,000	0%	288,936	Yes

4.Discussion

From our model, we conclude that the KRd regimen, when used as maintenance after autologous transplantation, is more expensive and lacks cost-effectiveness compared with lenalidomide monotherapy. Total costs and QALYs for the KRd arm were $482,294 and 1.59, versus $355,162 and 1.15 for the control. The differences in cost and utility amounted to $127,132 and 0.44 QALYs, translating to an ICER of $288,936 per QALY. As documented in reference[11], the standard WTP threshold in the United States is $150,000 per QALY, and our ICER greatly surpasses that figure. The one-way sensitivity analysis revealed that the price of carfilzomib was the principal factor inflating total costs, while the incremental survival gain was limited. However, we caution that these findings should not be used to withhold the KRd regimen, because doing so might preclude patients from significant clinical benefit.

When compared with earlier pharmacoeconomic studies on the KRd regimen, our findings are not entirely consistent. One such study, conducted by Jakubowicz et al. within the ASPIRE trial framework, evaluated the KRd versus Rd combination in relapsed/refractory multiple myeloma (1–3 prior lines) from the US payer perspective, and estimated an ICER of $107,520 per QALY for the KRd arm[16].This ICER is substantially lower than that of the present study. The differences primarily arise from the following aspects: first, the study populations differ—Jakubowiak et al. focused on patients with relapsed/refractory disease (1–3 prior lines of therapy), whereas the present study targeted newly diagnosed patients receiving post-transplant maintenance therapy, with fundamental differences in baseline prognosis, treatment duration, and expected survival benefit between the two populations; second, the comparator regimens differ—the control group in Jakubowiak et al was Rd (lenalidomide + dexamethasone), while the control group in the present study was lenalidomide monotherapy[24];Third, treatment duration differs—in the ATLAS trial, the KRd regimen could be administered for up to 36 cycles (approximately 3 years), whereas the treatment duration in the ASPIRE trial was relatively shorter, leading to substantial differences in the cumulative drug costs of the KRd group between the two studies; and fourth, differences in assumptions regarding long-term survival extrapolation may also affect QALY estimations.Goudarzi et al. evaluated the cost-effectiveness of the carfilzomib-containing regimen from the Chinese healthcare system perspective, and similarly showed that differences in cost structures across healthcare systems can significantly influence the ICER[25].In addition, studies have indicated that the carfilzomib + lenalidomide + dexamethasone regimen is among the most expensive treatment options from the US Medicare payer perspective, with total costs for lenalidomide-containing regimens ranging from approximately $126,000 to $256,000[26].These differences highlight that, when interpreting cost-effectiveness study results, careful consideration must be given to differences in study populations, lines of therapy, choice of comparator regimens, treatment duration, and variations in healthcare resource cost structures across countries.The findings of this study have multiple implications for clinical practice, healthcare reimbursement decisions, and drug pricing. Although the carfilzomib + lenalidomide + dexamethasone regimen does not demonstrate cost-effectiveness compared with lenalidomide monotherapy at current pricing levels, the superior clinical efficacy

confirmed by the ATLAS trial—a median progression-free survival of 72.8 months and a 4-year progression-free survival rate of 67.5%—provides important therapeutic benefits for post-transplant patients.Based on the results of the ATLAS and FORTE trials[27], the 2025 NCCN Multiple Myeloma Guidelines have upgraded carfilzomib + lenalidomide (KR) from "useful in certain circumstances" to "other recommended regimens" as a post-transplant maintenance therapy option. This suggests that in individualized treatment decisions, beyond cost-effectiveness, factors such as clinical efficacy, patient tolerability, quality of life improvement, and MRD status should also be considered as important components of a comprehensive evaluation.

The scenario analyses point to a clear conclusion: the cost of carfilzomib is the key driver of the overall cost-effectiveness of the KRd regimen. Simulations indicate that a price reduction of approximately 48% would bring the ICER below the commonly cited willingness-to-pay threshold of $150,000 per QALY, providing a quantitative basis for payers and manufacturers to explore outcomes-based risk-sharing arrangements or price-volume agreements in access negotiations. In the U.S. context, growing governmental attention and regulatory actions aimed at lowering prescription drug prices further underscore the real-world relevance of our findings—at current pricing, the ICER for KRd far exceeds most acceptable thresholds, and routine reimbursement of this regimen as maintenance therapy would impose a substantial financial burden on the healthcare budget. From a hospital operations perspective, promoting outpatient administration of carfilzomib also represents a viable strategy for improving economic efficiency.

Several key strengths characterise our study. The clinical inputs were drawn from the ATLAS trial – a multicentre, randomised phase III investigation – guaranteeing robust data quality (as reported in the ATLAS trial). We built a Markov model to project 10-year health and economic outcomes, covering a wide spectrum of costs (including those for subsequent therapies, routine monitoring, and end-of-life care). The dependability of our conclusions was tested using three types of sensitivity analyses (one-way, probabilistic, and scenario).

Nevertheless, some caveats must be recognised. To begin with, the controlled nature of trial settings may not fully mirror real-world practice, potentially skewing cost estimates. Secondly, the ATLAS protocol permitted MRD-guided de-escalation to lenalidomide alone in roughly 40% of the KRd cohort (according to the ATLAS trial); while this reduces drug expenditure over time, it adds a layer of complexity to model extrapolation. Thirdly, we employed the publicly listed price for carfilzomib, which may overrepresent the actual reimbursement amount (based on drug pricing databases). Fourthly, we had to rely on mathematical extrapolation to estimate survival beyond the trial follow-up, introducing further uncertainty. Fifthly, we omitted productivity losses and other indirect costs, which could mean that the full socioeconomic benefit of KRd is underestimated.

Despite these shortcomings, our work emphasises the decisive role of drug price in shaping the economic attractiveness of KRd, and offers valuable evidence for healthcare payers when making coverage decisions.

5.Conclusion

Our findings indicate that, from the U.S. payer perspective, the carfilzomib–lenalidomide–dexamethasone regimen is not cost-effective compared with lenalidomide monotherapy as maintenance therapy after autologous stem cell transplantation at current pricing levels. The cost of carfilzomib is

the primary driver of the ICER; a price reduction of approximately 48% would be required for the KRd regimen to reach the commonly accepted willingness-to-pay threshold.

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Conflicts of interest: None declared.

Uncategorized References

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