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Cost-Effectiveness of Systemic Treatments for Metastatic Castration-Sensitive Prostate Cancer: An Economic Evaluation Based on Network Meta-Analysis

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Supplemental Materials

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Abstract

Objectives: To assess the cost-effectiveness of systemic treatments for metastatic castration-sensitive prostate cancer from the US healthcare sector perspective with a lifetime horizon.

Methods: We built a partitioned survival model based on a network meta-analysis of 7 clinical trials with 7287 patients aged 36 to 94 years between 2004 and 2018 to predict patient health trajectories by treatment. We tested parameter uncertainties with probabilistic sensitivity analyses. We estimated drug acquisition costs using the Federal Supply Schedule and adopted generic drug prices when available. We measured cost-effectiveness by an incremental cost-effectiveness ratio (ICER).

Results: The mean costs were approximately $392 000 with androgen deprivation therapy (ADT) alone and approximately $415 000, $464 000, $597 000, and $959 000 with docetaxel, abiraterone acetate, enzalutamide, and apalutamide, added to ADT, respectively. The mean quality-adjusted life-years (QALYs) were 3.38 with ADT alone and 3.92, 4.76, 3.92, and 5.01 with docetaxel, abiraterone acetate, enzalutamide, and apalutamide, added to ADT, respectively. As add-on therapy to ADT, docetaxel had an ICER of $42 069 per QALY over ADT alone; abiraterone acetate had an ICER of $58 814 per QALY over docetaxel; apalutamide had an ICER of $1979 676 per QALY over abiraterone acetate; enzalutamide was dominated. At a willingness to pay below $50 000 per QALY, docetaxel plus ADT is likely the most cost-effective treatment; at any willingness to pay between $50 000 and $200 000 per QALY, abiraterone acetate plus ADT is likely the most cost-effective treatment.

Conclusions: These findings underscore the value of abiraterone acetate plus ADT given its relative cost-effectiveness to other systemic treatments for metastatic castration-sensitive prostate cancer.

Keywords

chemotherapy; clinical trial; cost-effectiveness; drug therapy; economic evaluation; hormonal therapy; network meta-analysis; partitioned survival model; prostate cancer

Introduction

Prostate cancer is the most common malignancy and the second leading cause of cancer death among men in the United States.[1] It puts a tremendous burden on the health system, with 248 530 new cases and 34130 deaths expected in 2021 alone.[1] Most prostate cancer deaths were due to metastases.[2] Long-term androgen deprivation therapy (ADT) had been the standard of care for metastatic prostate cancer since the first report of its hormonal dependence in the 1940s.[3] Nevertheless, metastatic prostate cancers that initially responded to ADT, known as metastatic castration-sensitive prostate cancers (mCSPCs), developed resistance to ADT and progressed to metastatic castration-resistant prostate cancer (mCRPC) in 2 to 3 years.[4,5] When treated with ADT alone, patients with mCSPC had a median survival of 3 to 4 years.[4,5]

Since 2015, pharmaceutical innovation has resulted in the introduction of several new treatments that have changed the disease outlook. Docetaxel, abiraterone acetate, enzalutamide, and apalutamide, used as concomitant treatments with ADT, have shown in randomized clinical trials to delay disease progression and (or) improve overall survival (OS).[4–9] Thus, these treatments have been approved by the US Food and Drug Administration and European Medicines Agency and recommended by the National Comprehensive Cancer Network and the European Society for Medical Oncology for mCSPC treatment.[10,11]

Nevertheless, with distinct pharmacologic mechanisms, these treatments are associated with different safety and efficacy profiles. Meanwhile, costs vary widely across treatments, ranging from hundreds of US dollars (USDs) to hundreds of thousands of USDs per standard treatment course. The cost calculus has also changed because some treatment (docetaxel and abiraterone acetate) has become generically available in the United States, whereas others (enzalutamide and apalutamide) remain under patent protection.[12] In Europe, a similar price disparity is expected in 2022 when abiraterone acetate's regulatory exclusivity expires.[13] Moreover, although previous work examined the cost-effectiveness of certain treatments for mCSPC,[14,15] to the best of our knowledge, none compared the cost-effectiveness of the current market basket of treatments.

Thus, we examined the cost-effectiveness of systemic treatments for mCSPC from a US healthcare sector perspective over a lifetime horizon. We reasoned that such information, which weighs treatment efficacy, safety, and costs, may better inform clinical practice and reimbursement policy.

Methods

Target Population and Treatment Strategies

Our target population was patients with mCSPC receiving treatments at cancer centers in the United States. In particular, these patients have pathologically confirmed prostate adenocarcinoma with radiologic evidence of metastatic disease sensitive to ADT. We assessed 5 treatment strategies: (1) docetaxel 75 mg/m^2 intravenous injection every 3 weeks for 6 cycles plus long-term ADT, (2) abiraterone acetate 1000 mg and prednisone

5 mg oral administration daily till radiographic progression plus long-term ADT, (3) enzalutamide 160 mg oral administration daily till radiographic progression plus long-term ADT, (4) apalutamide 240 mg oral administration daily till radiographic progression plus long-term ADT, and (5) long-term ADT alone. ADT can be goserelin 3.6 mg subcutaneous implantation every month, histrelin acetate 50 mg subcutaneous implantation every 12 months, leuprolide 7.5 mg subcutaneous injection every month, triptorelin 3.75 mg intramuscular injection every month, or degarelix 80 mg subcutaneous injection every month.[10] The study assumed that patients were equally likely to receive any of these ADTs, given that they were eligible backbone ADTs in included trials and have similar safety and efficacy in lowering serum testosterone to a castrate level.[16,17]

Decision Analytic Model and Treatment Efficacy

We used a partitioned survival model to characterize disease progression and treatment efficacy in a cohort of 7500 simulated patients with mCSPC as they experienced 3 different health states: mCSPC, mCRPC, and death. The partitioned survival model is the most commonly used decision analytic approach for appraisals of interventions for advanced or metastatic cancers,[18] in part because it aligns well with the endpoints of clinical trials.[18] The proportion of patients in each health state after each model cycle of 1 month was determined from the radiographic progression-free survival (rPFS) and OS curves. The height at a point in time under the rPFS curve indicates the proportion of patients remaining in mCSPC state at that time; the height at a point in time above OS curve indicates the proportion of patients deceased at that time; the height at a point in time between the rPFS and OS curve indicates the proportion of patients in mCRPC state at that time (Fig. 1).

We derived rPFS and OS curves for each treatment based on a recently published systematic review and network meta-analysis by our team.[12] In brief, we systematically searched bibliographic databases, trial registries, and regulatory documents for mCSPC trials and used Bayesian parametric survival network meta-analysis to synthesize data from 7 eligible trials. We estimated the time-varying hazard ratios of rPFS and OS between chemohormonal therapy (docetaxel/abiraterone acetate/enzalutamide/apalutamide) plus ADT and ADT alone. We then derived the expected survival curves for chemohormonal therapy plus ADT by applying the hazard ratios to the reference survival curves for ADT alone, which were obtained by synthesizing survival curves of ADT alone arms across trials.

The reference OS curve of ADT alone was calibrated with long-term survival data from a cancer registry to improve survival extrapolation beyond the trial period and ensure external validity. In particular, we assembled a cohort of prostate cancer patients from the Surveillance, Epidemiology, and End Results (SEER) program SEER*Stat Database[19] with selection criteria resembling the trial population—patients with histologically confirmed prostate adenocarcinoma, aged 35 years and older, and who had metastasis at diagnosis. Note that patients with mCSPC identified from SEER database were based on stage at the initial diagnosis due to data availability, whereas approximately 85% of trial patients had metastasis at diagnosis. Considering the temporal trend in treatment pattern, we required that patients were diagnosed after 2004, the earliest trial enrollment. To ensure that SEER data reflect survival with ADT alone, we used a cutoff of August 2015, when the first report

was published showing the benefit of chemohormonal therapy plus ADT for mCSPC.[5] We allowed trial and SEER survival curves to have different scale and shape parameters to let the SEER data inform long-term survival while accounting for the heterogeneity between trial and SEER populations (prevalent vs incident mCSPC) and settings (closely monitored vs real-world). Further details are provided in Appendix Method 1 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.10.016. The simulated cohort was modeled for 30 years, after which point the mortality rate reached 100%, that is, a lifetime horizon as recommended.[20]

The face validity (model structure and assumption, data sources, and results) of the model was evaluated by medical oncologists in the authors. Coding accuracy was checked by a structured "walk-through" wherein the author responsible for coding explained the code to the senior author involved in the analysis. The model results were compared with previous publications for cross-validation.

Costs

We derived the costs of implementing each treatment from the formal US healthcare sector perspective,[20] which included direct healthcare costs to third-party payers and patients out-of-pocket, from the treatment itself and follow-up care. We evaluated costs in 2020 USDs, including treatment costs, health state costs, and costs incurred by treatment-related adverse events (AEs). The costs estimated for previous years were inflated to 2020 USDs based on the medical care component of the consumer price index.[21]

Treatment-specific costs

We included acquisition and administration costs as treatment-specific costs. We sourced drug acquisition costs from the Department of Veterans Affairs' latest Federal Supply Schedule contract to reflect the actual drug costs to federal agencies after discounts and rebates.[22] We used generic drug prices when generics were available. We sourced administration costs of docetaxel and ADT from Medicare Physician Fee Schedule by the Current Procedural Terminology codes.[23] Individual treatment-specific costs, which were included as monthly costs and applied to the corresponding treatment durations, are listed in Table 1.[22–25] The treatment durations for abiraterone acetate, enzalutamide, and apalutamide in mCSPC setting were estimated to be 75% of the time patients spent in the mCSPC state, based on available clinical trial data.[8] An average body surface area of 1.9 m^2 for adult men were used to calculate drug dosage. Vial wastage for an average patient was considered; vial sharing was not allowed.

Health state costs

Health state costs included costs incurred within the healthcare system net of treatment-specific costs. We derived health state costs by aggregating healthcare costs associated with clinical encounters for a cohort of patients with mCSPC and mCRPC. The cohort was identified using the International Classification of Diseases, Tenth Revision, codes in the IBM MarketScan Commercial Claims and Encounters and Medicare Supplemental database.[26] This database collects health insurance claims for working adults and retirees with employer-sponsored health insurance from 2007 to 2019. For patients with mCSPC,

we defined their time in mCSPC state by subsequently identifying their first diagnosis of mCRPC (Appendix Method 2 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.10.016).

We then identified and deducted treatment-specific costs from mCSPC state costs, using the National Drug Code, Healthcare Common Procedure Coding System, and Current Procedural Terminology codes of the treatment strategies compared. We estimated the mCRPC state costs for patients receiving abiraterone acetate/enzalutamide as mCSPC treatment separately to reflect the clinical practice that patients who progressed from mCSPC to mCRPC while on abiraterone acetate or enzalutamide did not repeat the same treatment.[10] Individual health state costs, which were included as monthly costs and applied to time in the respective health states, are listed in Table 1.[22–25]

AE costs

We obtained AE costs from the Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project[27] using the International Classification of Diseases, Tenth Revision, codes of individual AEs. We used hospital costs, which were weighted national estimates from the Healthcare Cost and Utilization Project Nationwide Inpatient Sample. Appendix Table 1 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.10.016 listed individual AE costs, which were included as incident costs and applied upon treatment initiation.

Outcomes and Utilities

We evaluated health outcomes in life-years (LYs) and quality-adjusted LYs (QALYs). QALY is a preference-based health outcome measure, calculated by multiplying the length of life, LYs, by the health-related quality of life measured by a utility score on a scale of 0 to 1, in which 0 represents death and 1 represents perfect health. Utility scores differed by health state and were reduced by treatment-related AEs—disutility. We calculated LYs and QALYs for individual patients in the simulated cohort to estimate the expected LYs and QALYs (95% confidence intervals) for an average patient.

Health state utilities were sourced from literature: 5-level EQ-5D utility scores for mCSPC and mCRPC.[24,25] Individual health state utilities are available in Table 1.[22–25] AE disutilities were also obtained from literature, including disutility scores derived from 5-level EQ-5D, 3-level EQ-5D, time trade-off, and standard gamble. Individual AE disutilities are available in Appendix Table 2 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.10.016. Health state utilities were included as monthly utilities and applied to time in the respective health states. AE disutilities were included as monthly disutilities and applied to the first 6 months, because studies suggest that the impact of AEs (eg, fatigue) on health-related quality of life resolves after 6 months.[28,29]

AE Probabilities

The probabilities of AEs were informed by drug labels approved by the Food and Drug Administration, which include comprehensive AE information from clinical trials and observational data. We included AEs rated as grade 3 to 4 in severity per Common

Terminology Criteria for Adverse Events[30] and occurred in 0.5% of the patient population, considering their medical significance (eg, hospitalization indicated) and cost and utility implications. The AEs, along with their probabilities for each treatment, are provided in the Appendix Table 3 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.10.016.

Analysis and Discount Rate

The expected costs and QALYs for each treatment were derived by assigning the corresponding costs and utility scores to the time patients residing in each health state. AE-related costs and disutilities were applied to those experiencing them. Cost-effectiveness was measured by the incremental cost-effectiveness ratio (ICER)—the additional costs incurred per QALY gained. A range of willingness-to-pay (WTP) thresholds, from $0 to $200 000 per QALY gained, were used to investigate the likelihood that alternative treatments were most cost-effective. Both costs and health outcomes were discounted at an annual rate of 3% to reflect present values, as recommended.[20]

Sensitivity Analysis

We performed sensitivity analyses to address the uncertainties in parameter values and decision making. We incorporated uncertainties in parameter values of disease progression, treatment effect, cost, and utility in the probabilistic sensitivity analysis. We ran a model simulation with 7500 iterations; each iteration represents a set of random samples from the Markov Chains of Bayesian parametric survival network meta-analysis (which reflect the distribution of the shape and scale of survival curves for the underlying population from which the included trial population were sampled) and the distributions of cost and utility (Table 1 and the Appendix Tables 1 and 2 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.10.016). The choice to use 7500 iterations was motivated by the number iterations for Bayesian parametric survival network meta-analysis and an established rule that the Monte Carlo standard error is < 5% of the posterior SD.[31] We also performed a deterministic sensitivity analysis to test the sensitivity of results to changes in key parameter values such as hazard ratios, drug acquisition costs, health state costs, and utilities. Given that the hazard ratios for rPFS and OS were time varying, the changes in hazard ratios were applied to all time points. We presented decision uncertainties using the cost-effectiveness acceptability curve, which depicts each treatment's probability of being the most cost-effective one over a range of WTP thresholds. We used WINBUG version 1.4.3[32] for survival modeling and R version 4.0.3[33] for economic modeling.

Results

The expected short-term OS under ADT alone reflects the average of observed survivals across trials included in the network meta-analysis[12] (Appendix Fig. 1 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.10.016). The expected long-term OS under each treatment strategy is provided in Appendix Figure 2 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.10.016.

Health Outcomes, Costs, and Cost-Effectiveness

Chemohormonal therapy plus ADT resulted in increased LYs, QALYs, and costs compared with ADT alone, driven primarily by gains in time spent in mCSPC state and higher treatment-specific costs (Appendix Tables 4 and 5 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.10.016). We reported discounted cost-effectiveness results in Table 2 in which costs and health outcomes were discounted at an annual rate of 3% to reflect present value. The mean QALYs (95% confidence interval) were 3.38 with ADT alone, 3.92 with docetaxel plus ADT, 3.92 with enzalutamide plus ADT, 4.76 with abiraterone acetate plus ADT, and 5.01 with apalutamide plus ADT. The mean costs were $391976 with ADT alone, $414 693 with docetaxel plus ADT, $464 097 with abiraterone acetate plus ADT, $596 620 with enzalutamide plus ADT, and $959 016 ($673 017-$1311560) with apalutamide plus ADT.

Compared with ADT alone, docetaxel plus ADT resulted in an ICER of $42 069 per QALY gain. Compared with docetaxel plus ADT, abiraterone acetate plus ADT resulted in an ICER of $58 814 per QALY gain. Compared with abiraterone acetate plus ADT, apalutamide plus ADT resulted in an ICER of $1979 676 per QALY gain. Enzalutamide plus ADT was dominated by docetaxel plus ADT, given that it resulted in higher costs for the same QALYs (Fig. 2). We reported undiscounted results in Appendix Table 6 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.10.016. The relative value of treatments was consistent when costs and health outcomes were not discounted.

Sensitivity Analysis

Results from probabilistic sensitivity analysis showed that at a WTP threshold below $50 000 per QALY, docetaxel plus ADT had the highest probability of being the most cost-effective treatment, and at any WTP threshold between $50 000 and $200 000 per QALY, abiraterone acetate plus ADT had the highest probability of being the most cost-effective treatment. The likelihood of a treatment being the most cost-effective across all treatments against a range of WTP thresholds was plotted in Figure 3. The distributions of cost and QALY for each treatment accounting for uncertainties in treatment effect, costs, and utilities are plotted in Figure 2.

Results from deterministic sensitivity analyses suggested that parameters with the greatest impact on ICERs (chemohormonal therapy plus ADT vs ADT alone) were hazard ratios, health state costs, and drug acquisition costs (Appendix Fig. 3 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.10.016). In particular, for docetaxel plus ADT, hazard ratios of rPFS and OS were the most influential parameter on ICER. For abiraterone acetate, mCSPC state costs were the most influential parameter on ICER. For apalutamide and enzalutamide, drug acquisition costs were the most influential parameter on ICER.

Discussion

We assessed the cost-effectiveness of systemic treatments for mCSPC from a US healthcare sector perspective over a lifetime horizon, accounting for their efficacy, safety, and costs. Chemohormonal therapy plus ADT resulted in increased QALYs and costs compared with

ADT alone. Compared with docetaxel plus ADT, abiraterone acetate plus ADT resulted in higher QALYs, 4.76 versus 3.92, with slightly higher costs, $464 097 versus $414 693, corresponding to an ICER of $58 814 per QALY gain. In contrast, enzalutamide or apalutamide plus ADT was not cost-effective. Enzalutamide plus ADT incurred higher costs for the same QALYs compared with docetaxel plus ADT. Apalutamide plus ADT incurred much higher costs than abiraterone acetate plus ADT for slightly higher QALYs, corresponding to an ICER of $1979 676 per QALY gain. At a WTP threshold below $50 000 per QALY, docetaxel plus ADT was likely the most cost-effective treatment, whereas at any WTP threshold between $50 000 and $200 000 per QALY, abiraterone acetate plus ADT was likely the most cost-effective treatment. The $50 000 per QALY gain threshold has been used as a benchmark for the value of care in the United States for 2 decades,[34] and a range of different WTP thresholds were examined in this work to allow decision making based on available resources and possible alternative uses of those resources.

To the best of our knowledge, this is the first cost-effectiveness analysis involving all major systemic treatments for mCSPC. Our findings may help to inform both clinical practice and reimbursement policy for this relatively common and costly condition. By assessing the relative value of different treatments, our study can help decision makers prioritize high-value treatments, promote efficient use of limited resources, and ensure better patient outcomes. For example, drug coverage with different levels of copayment can be applied to mCSPC treatments based on their relative value—value-based formulary.[35] That is, drugs with higher value (lower ICER) are placed on lower tiers and subject to lower copayments, whereas drugs with lower value (higher ICER) are placed on higher copayment tiers to disincentivize use. Research has shown that aligning drug copayment tiers with value reduces medication expenditures without negatively affecting medication utilization, health service utilization, or nonmedication expenditures.[35,36] Furthermore, payers and manufacturers can negotiate drug prices based on the relative value of available mCSPC treatments—value-based drug pricing.[37] As a preamble of a large-scale value-based drug pricing reform, the Centers for Medicare and Medicaid Services issued a new rule in December 2020, supporting value-based purchasing arrangements with pharmaceutical manufacturers in Medicaid.[37] Cancer drugs that are not cost-effective might be prioritized for formulary and price negotiations.

Previous cost-effectiveness analyses only assessed the addition of abiraterone acetate or docetaxel to ADT for mCSPC. Similar to our finding, a 2019 study using a US healthcare sector perspective found that docetaxel plus ADT provides high value for money with an ICER for $34723 per QALY compared with ADT alone.[14] Nevertheless, this previous analysis used brand-name drug cost for abiraterone acetate, which are no longer relevant given its generic availability and price. A 2018 study assessed the cost-effectiveness of docetaxel plus ADT for mCSPC from the UK National Health Service perspective and reported LY and QALY gains similar to our estimation, although costs are not comparable between the 2 health systems.[38]

As with any economic evaluation, our analysis has limitations, many of which are governed by the data we had available and the assumptions of our model. First, some of the clinical trials we used to estimate OS benefits, such as the available trials for enzalutamide plus

ADT, had limited follow-up. An update of the current analysis is necessary when new evidence becomes available from ongoing clinical trials. Second, subgroup analyses, such as cost-effectiveness stratified by baseline prostate-specific antigen level, were not feasible because subgroups were not consistently defined across trials, and for the disease volume (high vs low), which was defined consistently across trials, subgroup results were not available for all treatments for OS. Third, despite the extensive use of partitioned survival model by health technology assessment agencies such as the National Institute for Health and Care Excellence in the UK, it is worth noting that this approach assumes that the OS and rPFS functions modeled are independent. Nevertheless, dependencies exist between OS and rPFS, given that progression is considered prognostic for death. For the within-trial period, these dependencies were reflected in trial data and closely modeled. Nevertheless, beyond trial duration, the dependencies may not be well extrapolated based simply on trends observed within trials. To improve OS extrapolation, we included real-world longer-term data from the SEER program to inform long-term survival modeling.

Conclusions

These findings underscore the value of abiraterone acetate plus ADT given its relative cost-effectiveness to other systemic treatments for mCSPC.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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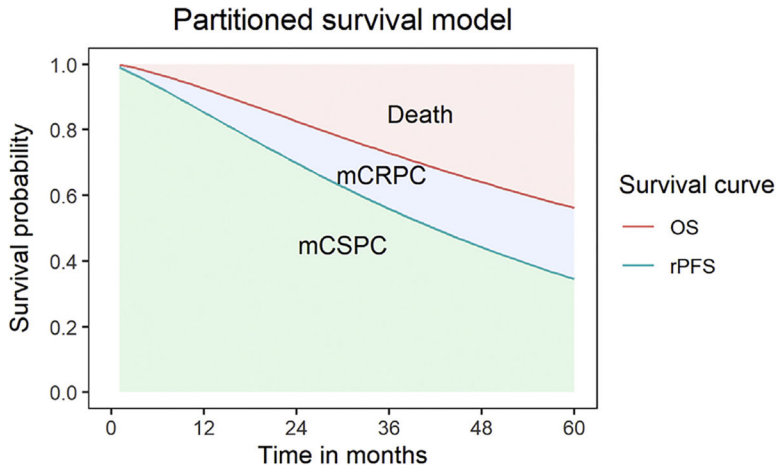

Figure 1.

Partitioned survival model. The area under the rPFS curve indicates the proportion of patients remaining in mCSPC state over time; the area above OS curve indicates the proportion of patients deceased over time; the area between the rPFS and OS curve indicates the proportion of patients in mCRPC state over time.

mCRPC indicates metastatic castration-resistant prostate cancer; mCSPC, metastatic castration-sensitive prostate cancer; OS, overall survival; rPFS, radiographic progression-free survival.

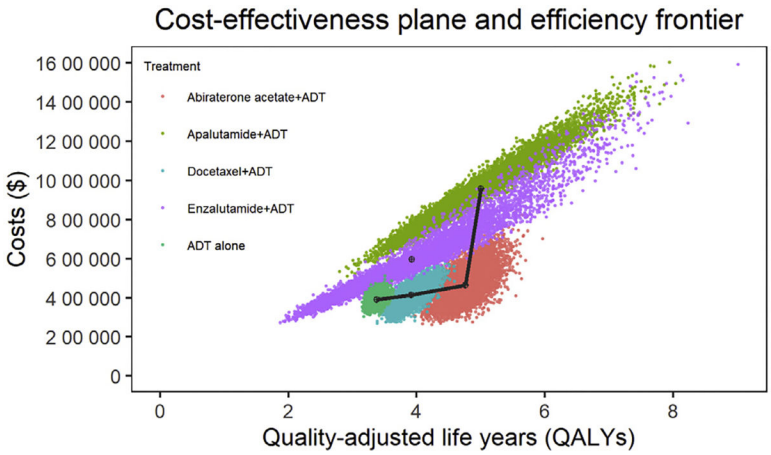

Figure 2.

Cost-effectiveness plane and efficiency frontier. The cost-effectiveness plane plots the costs against the QALYs for each treatment. The scattered points represent 7500 model iterations in the probabilistic sensitivity analysis, where values of parameter inputs (including treatment effect, cost, and utility) were drawn from their respective distributions. The circles represent the mean costs and QALYs of individual treatments. The line connecting successive circles is called the *"*cost-effectiveness frontier.*"* The gradient of a line segment represents the ICER comparing 2 treatment alternatives. The steeper the gradient, the higher the ICER. Treatments on the right end of a line segment are cost-effective at a willingness-to-pay threshold lower than the ICER represented by that line segment. Treatments not on the frontier are not cost-effective at any willingness-to-pay thresholds. Because for the same QALYs, they resulted in higher costs than other treatments.

ADT indicates androgen deprivation therapy; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year.

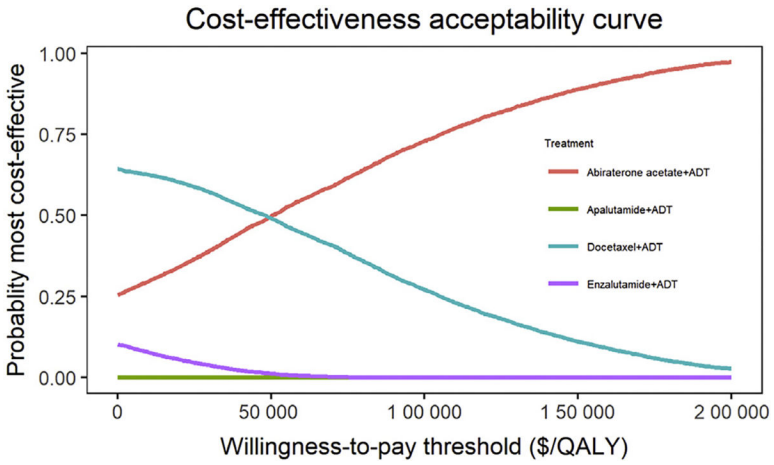

Figure 3.

Cost-effectiveness acceptability curve. The cost-effectiveness acceptability curve plots the probability of a treatment being the most cost-effective across all treatments against a range of willingness-to-pay thresholds. The probabilities were derived from 7500 model iterations in the probabilistic sensitivity analysis where values of parameter inputs (including treatment effect, cost, and utility) were drawn from their respective distributions.

ADT indicates androgen deprivation therapy; QALY, quality-adjusted life-year.

Table 1.

Costs and utility parameter input.

Unit	Unit description	Unit mean cost/utility	SE	Distribution	Source	Note
Treatment-specific cost—drug acquisition cost, 2020 $						
Docetaxel	160 mg/8 mL	55.99	NA	NA	22	NA
Abiraterone	250 mg TAB*120	405.78			22	
Prednisone	5 mg TAB*100	13.22			22	
Apalutamide	60 mg TAB*120	10 830.17			22	
Enzalutamide	40 mg CAP*120	7403.32			22	
Goserelin	3.5 mg INJ, implant	305.51			22	
Histrelin	50 mg implant	4269.76			22	
Leuprolide	7.5 mg/KIT, INJ, SUSP, SA	91.61			22	
Triptorelin	3.75 mg/VIL, INJ, SUSP, SA	653.86			22	
Degarelix	80 mg/VIL, INJ	241.21			22	
Treatment-specific cost—drug administration cost, 2020 $						
Docetaxel	Chemo IV infusion 1 hr	142.55	NA	NA	23	CPT: 96413
Goserelin, leuprolide, triptorelin, degarelix	Chemo hormonal antineoplastic SQ/IM	32.12			23	CPT: 96402
Histrelin	Remove/insert drug implant	149.77			23	CPT: 11 983
Health state cost, 2020 $						
mCSPC	Yearly cost	43 760.08	5794.29	Gamma	MarketScan Claims and Medicare Supplement data analysis	Net of treatment-specific cost
mCRPC (docetaxel, apalutamide, enzalutamide)	Yearly cost	147 548.80	8138.46			Patients who progressed from mCSPC to mCRPC while on abiraterone acetate or enzalutamide did not repeat the same treatment
mCRPC (abiraterone)	Yearly cost	206 659.31	11 398.86			
mCRPC (enzalutamide)	Yearly cost	170 721.23	9416.60			
Health state utility						
mCSPC	Yearly utility	0.8	0.008	Truncated normal	24	Tool: EQ-5D-5L
mCRPC	Yearly utility	0.716	0.013		25	

CAP indicates capsule; CPT, Current Procedural Terminology; EQ-5D-5L, EQ-5D-5 level; INJ, injection; IV, intravenous; mCSPC, metastatic castration-sensitive prostate cancer; mCRPC, metastatic castration-resistant prostate cancer; NA, not applicable; SE, standard error; SQ/IM, subcutaneous/intramuscular; SUSP, suspended; SA, sustained action; TAB, tablet; VIL, vial.

Table 2.

Cost-effectiveness results (discounted).

Treatment	Mean life-years* (95% CI)	Mean QALYs* (95% CI)	Mean costs,* $ (95% CI)	ICER, $/QALY
ADT alone	4.42 (4.25–4.59)	3.38 (3.24– 3.52)	391 976 (343172–442 455)	NA
Enzalutamide plus ADT	4.96 (3.04–8.19)	3.92 (2.41–6.34)	596 620 (351 169–1 090 043)	Dominated†
Docetaxel plus ADT	5.11 (4.68–5.58)	3.92 (3.60–4.27)	414693 (327 800–505 878)	42 069 (vs ADT alone)
Abiraterone acetate plus ADT	6.06 (5.43–6.78)	4.76 (4.29–5.29)	464097 (326 833–646 606)	58 814 (vs docetaxel plus ADT)
Apalutamide plus ADT	6.53 (4.65–8.88)	5.01 (3.64–6.70)	959 016 (673 017–1 311 560)	1 979 676 (vs abiraterone acetate plus ADT)

ADT indicates androgen deprivation therapy; CI, confidence interval, ICER, incremental cost-effectiveness ratio, NA, not applicable; QALY, quality-adjusted life-year.

*Life-years, QALYs, and costs were discounted at an annual rate of 3% to reflect present value. Costs were in 2020 US dollars.

†Enzalutamide plus ADT was dominated by docetaxel plus ADT, given that it resulted in higher costs for the same QALYs.