Cost-Effectiveness Analysis of Abiraterone and Sipuleucel-T in Asymptomatic Metastatic Castration-Resistant Prostate Cancer

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Abstract

Of patients diagnosed with prostate cancer, 0% to 20% experience disease progression to metastatic castration-resistant prostate cancer (mCRPC). Recently, 4 novel therapies have been introduced for the treatment of mCRPC; of these, abiraterone and sipuleucel-T have been studied in the asymptomatic, pre-docetaxel population. Both have shown clinical benefits compared with placebo. This study evaluated the cost-effectiveness of abiraterone acetate and sipuleucel-T compared with prednisone in asymptomatic, pre-docetaxel mCRPC from a US societal perspective. A Markov model was constructed to simulate stable disease, progressed disease, and death. Survival and event rates were derived from published clinical trial data. Costs were derived from the literature and government reimbursement schedules. Outcomes were measured as average cost-effectiveness ratios (ACERs), incremental cost-effectiveness ratios (ICERs), and net monetary benefits (NMBs). One-way and probabilistic sensitivity analyses were conducted to test the robustness of the model. The base-case ACER was \$114K/quality-adjusted life-years (QALY) for abiraterone, \$85K/QALY for sipuleucel-T, and \$31K/QALY for prednisone. The base-case ICER was \$389K/QALY for abiraterone and \$547K/QALY for sipuleucel-T. Prednisone dominates both abiraterone and sipuleucel-T in terms of NMB at willingness-to-pay (WTP) thresholds of \$400K or less. One-way sensitivity analyses revealed that the model was most sensitive to overall survival and utility inputs. Probabilistic sensitivity analyses showed abiraterone to be cost-effective 50% or more of the time at a WTP of greater than \$400K, whereas sipuleucel-T was cost-effective 50% or more of the time at a WTP of greater than \$270K. Neither abiraterone nor sipuleucel-T was found to be cost-effective compared with prednisone in the treatment of asymptomatic, pre-docetaxel mCRPC. (*J Natl Compr Canc Netw* 2014;12:1417-1425)

Prostate cancer is the most commonly diagnosed cancer among men in the United States, and the second leading cause of cancer-related deaths.^{1,2} Of those diagnosed, 10% to 20% will experience progression to metastatic disease, with treatment options previously limited to docetaxel or mitoxantrone chemotherapy, or long-term prednisone therapy; however, these therapies are limited by the severity of side effects and limited benefits regarding survival.³

Since 2010, 5 agents have been approved by the FDA for the treatment of docetaxel-refractory metastatic castration-resistant prostate cancer (mCRPC): abiraterone, radium-223, cabazitaxel, enzalutamide, and sipuleucel-T. Although all have shown efficacy in the symptomatic, post-docetaxel mCRPC population, abiraterone, enzalutamide, and sipuleucel-T have also shown efficacy in the asymptomatic, pre-docetaxel population.^{4,5} This is reflected in the most recent version of the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Prostate Cancer, which includes these therapies for asymptomatic mCRPC.⁶

Abiraterone, administered orally in combination with prednisone, is an inhibitor of androgen synthesis.^{7,8} Despite having low testosterone levels, patients with mCRPC remain highly responsive to abiraterone, indicating that the cancer continues to have androgenic activity. The survival benefit seen in symptomatic patients with post-docetaxel mCRPC in the COU-AA-301 clinical trial led to FDA approval in 2011.⁹

Sipuleucel-T is a novel immunotherapy designed to elicit an immune response triggered by the prostatic acid phosphatase (PAP) antigen.¹⁰ Antigen-presenting cells are removed and cultured in a central manufacturing facility in media containing PAP, then reinfused into the patient to elicit an immune response.⁵ Each treatment course requires a total of 3 infusions at 2-week intervals. Sipuleucel-T's efficacy was demonstrated in the IMPACT trial, leading to FDA approval in 2010.⁵

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Previous cost-effectiveness studies related to mCRPC have focused on the post-docetaxel population. One analysis found abiraterone to be cost-effective with an incremental cost-effectiveness ratio (ICER) of \$91K/quality-adjusted life-years (QALY) compared with mitoxantrone.¹¹ The United Kingdom's National Institute for Health and Care Excellence (NICE) recommended abiraterone for use in the post-docetaxel population, with a base-case ICER of £46,800/QALY^{9,12}; NICE's appraisal of sipuleucel-T is pending.¹³ To date however, no analyses have evaluated these therapies in the asymptomatic, pre-docetaxel mCRPC population. Thus, the purpose of this analysis was to evaluate the cost-effectiveness of abiraterone and sipuleucel-T relative to prednisone in asymptomatic, pre-docetaxel mCRPC from a US societal perspective.

Methods

Model

A lifetime Markov cohort model was constructed from the US societal perspective to simulate the base-case scenario of a 70-year-old man diagnosed with asymptomatic mCRPC with no prior chemotherapy (Figure 1). The model structure was identical for all 3 treatment arms (abiraterone, prednisone, and sipuleucel-T), with treatment-specific model inputs. Markov health states included were stable disease, progressed disease, and death. Stable disease was defined as lack of cancer progression, and progressed disease was determined based on radiographic progression defined in the clinical trials.

The model cycle length was 1 month. Because the diagnosis of mCRPC is associated with a short life expectancy, the time horizon for this analysis

was lifetime to capture the full impact of drug treatment on overall survival benefit and lifetime costs. The model was run until 99% of patients were in the death state for each treatment arm.

Patient distribution in the abiraterone and prednisone arms was assumed to be equal to the COU-AA-302 clinical trial for abiraterone, whereas the distribution for sipuleucel-T was assumed to be equal to the IMPACT trial for sipuleucel-T. Prednisone was chosen as the treatment comparator rather than the placebo used in the IMPACT trial because of expert criticism that the placebo infusion in the sipuleucel-T trial was harmful to the control group.¹⁴

Asymptomatic mCRPC was defined in the clinical trials based on the Brief Pain Inventory–Short Form questionnaire scores and ECOG functional status. The former assesses pain severity and interference with activities of daily living on a scale of 0 to 10, with 0 to 1 being asymptomatic and 2 to 3 being mildly symptomatic.¹⁵ The ECOG classification system grades functional capacity in patients with cancer on a scale of 0 to 5, with 0 being full activity and 5 representing death. For asymptomatic mCRPC, ECOG functional capacity was rated as 0 (asymptomatic) or 1 (mildly symptomatic).¹⁶ The base-case scenario was chosen to be representative of the clinical trials.

Probabilities

Transition probabilities (Table 1) were derived for each health state from the overall survival and progression-free survival data published in clinical trials using the declining exponential approximation of life expectancy (DEALE) method.¹⁷ Baseline age-adjusted mortality was incorporated to include death from other causes in the calculation of the transition probabilities.¹⁸ The calculated probabilities were then used to determine the percentage of patients in each health state per month. Using the probabilities, overall survival gained was determined for each treatment arm.

Adverse event probabilities were derived from the clinical trials. Only adverse events significantly different from prednisone or unique because of the mechanism of action were included in the model (Table 2). All adverse events included were those rated grade 3 or 4, except for cerebrovascular events, which were included regardless of severity grading. Bone pain was also included, based on the trial-reported median time to opiate use for cancer-related pain.

Figure 1 Markov model.

Table 1 Probabilities

	Stable	Progressed	Death
Abiraterone			
Stable	.940	.041	.019
Progressed	.000	.966	.034
Death	.000	.000	1.000
Prednisone			
Stable	.895	.080	.025
Progressed	.000	.964	.036
Death	.000	.000	1.000
Sipuleucel-T			
Stable	.803	.171	.027
Progressed	.000	.969	.031
Death	.000	.000	1.000

Costs

Costs were in 2013 US dollars (USD) and derived from the literature, the Veterans Affairs Federal Supply Schedule (VA FSS),¹⁹ and the Centers for Medicare & Medicaid Services (CMS)²⁰ reimbursement schedules for laboratory monitoring and procedures, using Current Procedural Terminology (CPT) and Healthcare Common Procedure Coding System (HCPCS) codes. Costs included drug costs, laboratory monitoring, physician office visits, procedural imaging, caregiver costs, adverse events, and all-cause hospitalizations (Table 3).

Drug costs were based on VA FSS prices, which are publicly available and approximate the lowest available drug price, thus closely modeling societal opportunity costs. Costs for laboratory tests, office visits, and imaging were based on CMS reimbursement schedules using CPT and HCPCS codes. Caregiver hours spent on cancer care were derived from the literature, with associated costs calculated using the Bureau of Labor Statistics compensation rate for medical care service workers.^{21,22} Adverse event costs consisted of drug costs plus hospitalizations used to treat the event, based on diagnosis-related group (DRG) codes and the literature.^{23–27} All-cause hospitalization costs were based on the literature.²⁸

Table 2 Adverse Events Included

	Abiraterone	Prednisone	Sipuleucel-T
Cardiac events	5.7%	3.3%	–
Atrial fibrillation	1.3%	0.9%	–
Hypertension	3.9%	2.9%	–
AST/ALT increase	8.3%	1.7%	–
Anemia	–	–	1.5%
Cerebrovascular events	–	–	2.4%

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase.

All costs were adjusted to 2013 USD using the Medical Consumer Price Index.²⁹ An annual discount rate of 3% was applied to all costs.³⁰

Quality of Life

Quality of life (QOL) is incorporated into an economic model using utility weights, with 1 representing perfect health and 0 indicating death. The utility weight is multiplied by life years gained for a given treatment to calculate QALYs. To maintain the US societal perspective, utility values included in the model were based on societal, nonpatient responses to QOL questionnaires related to mCRPC. For stable disease, a utility value of 0.76 was used for all 3 treatment arms, and for progressed disease, a value of 0.65 was used for abiraterone and sipuleucel-T.^{31,32} For prednisone, a utility of 0.58 for progressed disease was used to account for the faster functional decline in this group compared with those treated with abiraterone.^{4,33}

Disutility because of adverse events was also applied to each treatment arm, using the marginal disutility calculated for specific adverse events for patients diagnosed with prostate cancer (ICD-9 185.xx) in the Medical Expenditure Panel Survey.³⁴ The proportion of patients experiencing the adverse event in clinical trials was multiplied by the associated marginal disutility to calculate an overall disutility for that adverse event. The sum of these disutilities was then added to the baseline utility value to calculate an overall treatment-specific utility value that was used in the model. The total disutility was –0.008, –0.004, and –0.008 for abiraterone, prednisone, and sipuleucel-T, respectively.

Analyses

Outcome measures included QALYs and total costs. Average cost-effectiveness ratios (ACERs) were calculated as total costs per total QALYs for each treatment group:

$$ACER = \frac{\text{Total Costs}}{\text{Total QALYs}}$$

Treatment arms were compared in terms of cost per QALY gained using ICERs. The ICER is the ratio of the difference in costs to the difference in effectiveness between 2 alternatives³¹:

$$ICER = \frac{\text{Costs}_{\text{Treatment A}} - \text{Costs}_{\text{Treatment B}}}{\text{QALYs}_{\text{Treatment A}} - \text{QALYs}_{\text{Treatment B}}}$$

Table 3 Costs		
Parameter	Cost (USD)	Reference
Drug Treatment	Per Month	
Abiraterone	4869	VA FSS
Prednisone	0	
Sipuleucel-T	30,221 (per infusion)	
Administration	Per Test	
CT abdomen/pelvis (no contrast)	507	CMS CPT schedule ¹⁹
Bone scanning (whole body)	258	
Electrocardiogram	18	
Outpatient office visit	92	
1-hour chemotherapy infusion	173	
Laboratory Tests	Per Test	
Basic metabolic panel	12	CMS CPT schedule ¹⁹
Hepatic function panel	11	
Lipid panel	14	
CBC	9	
Serum prostate-specific antigen	25	
Prothrombin time	5	
Lactate dehydrogenase level	8	
Adverse events		
Hospitalization Costs	Per Hospitalization	
Atrial fibrillation	5142	CMS acute inpatient PPS ²²
Cardiac disorders ^a	7657	
Cerebrovascular event	9606	
Monthly Care Costs	Per Month	
Atrial fibrillation	1587	Mercaldi et al ²³
Cardiac disorders ^a	1421	Pignone et al, ²⁴ Liao et al, ²⁵ Burton et al ²⁶
Cerebrovascular event	2967	Mercaldi et al ²³
Inpatient Use	Per Month	
All-cause hospitalizations	1800	Mehra et al ²⁷
Emergency department visits	60	

^aIncludes arrhythmias, myocardial infarction, heart failure, transient ischemic attack.

Abbreviations: CMS, Centers for Medicare and Medicaid Services; CPT, Current Procedural Terminology; PPS, Prospective Payment System; VA FSS, Veterans Affairs Federal Supply Schedule.

Through measuring the ICER in terms of cost per QALY gained, different interventions can be compared across a standard metric, and a treatment is deemed cost-effective if its ICER is less than \$150K/QALY, or approximately 3 times the gross domestic product per capita for the United States.³⁵ For this analysis, ICERs for abiraterone and sipuleucel-T were calculated relative to prednisone-only treatment. An annual discount rate of 3% was applied to all costs and all QALYs.

One-way sensitivity analyses were conducted to test the effect of individual parameters on the results of the model. Survival, costs, and utility values were varied individually according to reported CIs or ranges published in the literature, or by ±20% if no such ranges were reported. ACERs and ICERs were recalculated accordingly.

A probabilistic sensitivity analysis was conducted to test the effect of varying multiple parameters simultaneously on the outcomes of the model. Values for each uncertain parameter were randomly drawn from a prespecified probability distribution via Monte Carlo

simulation (n=10,000 trials). Probability distributions were specified based on reported confidence intervals or other uncertainty measures (eg, standard deviations). Cost-effectiveness acceptability curves were generated for abiraterone and sipuleucel-T to show the probability of each intervention being cost-effective at different willingness-to-pay (WTP) thresholds.

A net monetary benefit (NMB) analysis was conducted to assess the cost-effectiveness of each therapy at varying WTP thresholds.³⁶ NMB is calculated as:

$$NMB = (QALYs \times WTP) - Cost$$

The NMB is plotted against varying WTP thresholds, with each treatment intervention represented by a different line whose slope indicates effectiveness, or QALYs; a steeper slope indicates more QALYs (and thus more effectiveness). The treatment with the highest NMB at a given WTP is considered to be the most cost-effective at that WTP threshold. The incremental NMB can be easily calculated as the vertical distance

between 2 lines. An intervention is “dominated” if its NMB is always lower than another intervention. It is “extended dominated” if the combination of the other interventions always yields a higher NMB.³⁷

Results

Base Case

Abiraterone was associated with the highest number of QALYs gained and the highest cumulative lifetime cost, whereas prednisone was associated with the lowest number of QALYs gained, and the lowest cumulative lifetime cost (Table 4). The total number of QALYs was 1.87 for abiraterone, 1.44 for prednisone, and 1.60 for sipuleucel-T. Cumulative costs for abiraterone, prednisone, and sipuleucel-T were \$214,584, \$44,583, and \$135,994 respectively. This yielded ACERs of \$114,454, \$31,011, and \$84,748, respectively. Compared with prednisone, the ICER was \$388,846 for abiraterone and \$547,298 for sipuleucel-T.

Sensitivity Analyses

Tornado diagrams displaying the sensitivity of the calculated ACERs and ICERs are shown in Figure 2. The model was most sensitive to median overall survival for each drug, drug cost, and the utility value chosen to represent QOL for each health state. Except for median overall survival and utility inputs, model outcomes tended to be more robust for abiraterone than sipuleucel-T. Sipuleucel-T results were also very sensitive to progression-free survival, drug costs, and discount rate.

In the multivariate probabilistic sensitivity analysis, neither abiraterone nor sipuleucel-T was cost-effective at a standard WTP threshold of \$150K/QALY (Figures 3A, B). Only at a WTP of approximately \$400K/QALY did abiraterone become

cost-effective 50% of the time, with this probability increasing as WTP increased. Sipuleucel-T, on the other hand, became cost-effective 50% of the time at a WTP of approximately \$270K/QALY, and increasingly cost-effective as WTP increased.

The NMB was calculated for abiraterone and sipuleucel-T, because some of the ICERs became negative in the one-way sensitivity analysis for sipuleucel-T. As long as WTP was less than or equal to \$400K prednisone dominated both abiraterone and sipuleucel-T. At WTP thresholds greater than \$400K abiraterone dominates both prednisone and sipuleucel-T with higher NMB. Interestingly, at WTP thresholds less than or equal to \$150K/QALY, sipuleucel-T had a higher NMB than abiraterone (although prednisone still dominates both treatments at lower WTP thresholds).

Discussion

This cost-effectiveness analysis evaluated abiraterone and sipuleucel-T against prednisone for the treatment of asymptomatic, pre-docetaxel mCRPC from a US societal perspective. In the base-case analysis, the costs per QALY gained relative to prednisone were \$388,846 for abiraterone and \$547,298 for sipuleucel-T. Even with sensitivity analyses adjusting various model parameters, neither drug reached a cost-effectiveness threshold of \$150K/QALY or less, unless the drug costs of abiraterone and sipuleucel-T were significantly reduced by 65% and 75%, respectively. Based on the results of the probabilistic sensitivity analysis and NMB analysis, neither agent is cost-effective unless the maximum WTP is set at least 2 to 3 times higher than the accepted value.

The model was most sensitive to overall survival associated with each treatment, and the utility values assigned to the health states in the model. This may be because of selection bias in clinical trials due to the enrollment of patients with higher functional status, which may have affected efficacy. In addition, patients with mCRPC may live as long as 13 months after diagnosis despite no treatment, although there is wide variation in survival.³⁸ However, because outcomes are measured in costs per QALY, any changes in survival are likely to have a significant impact on the ICER. Similarly, changes in utility values significantly affect QALYs gained, which translates into wide variation in the ICER calculated.

Table 4 Base-Case Results

	Abiraterone	Prednisone	Sipuleucel-T
Total life years gained	2.70	2.28	2.44
Total QALYs gained	1.87	1.44	1.60
Total lifetime costs (\$USD)	214,584	44,583	135,994
ACER (\$USD/QALY)	114,454	31,011	84,748
ICER* (\$USD/QALY)	388,846	–	547,298

*Compared with prednisone.

Abbreviations: ACER, average cost-effectiveness ratio; QALY, quality-adjusted life-year.

Figure 2 (A) Abiraterone ACER. (B) Sipuleucel-T ACER. (C) Abiraterone ICER. (D) Sipuleucel-T ICER. Abbreviations: ACER, average cost-effectiveness ratio; AE, adverse event; CE, cost-effectiveness; Chemo, chemotherapy; ICER, incremental cost-effectiveness ratio; Labs, laboratory tests; OS, overall survival; PD, programmed disease; PFS, progression-free survival; SD, stable disease; QALY, quality-adjusted life-year. ^aICER for median OS extends to \$4.9 million, not shown. ^bSipuleucel-T is dominated in these situations.

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Figure 3 (A) Abiraterone cost-effectiveness acceptability curve. (B) Sipuleucel-T cost-effectiveness acceptability curve.

Abbreviation: ICER, incremental cost-effectiveness ratio.

In addition, patient populations for the abiraterone and sipuleucel-T studies were not completely identical. In the abiraterone trial, patients were excluded if they had received any prior chemotherapy; in the sipuleucel-T trial, patients were excluded if they had received more than 1 chemotherapy treatment, or received chemotherapy within the 3 months before study enrollment. Among those receiving sipuleucel-T in clinical trials, 18.2% had received 1 prior chemotherapy treatment. Thus, a concern exists that patients in the sipuleucel-T group had more advanced cancer than those in the abiraterone group, leading to an overestimation of the ICERs calculated for sipuleucel-T. However, the inclusion and exclusion criteria were very similar for each drug with regard to ECOG status, and pain, prostate-specific antigen levels, and bone metastases were similar in each group at baseline. Furthermore, sensitivity analyses evaluating survival and severity of disease revealed that even with higher overall survival or less severe disease, sipuleucel-T remains cost-ineffective.

A concern exists that the model does not account for patients switching to other treatments if they experience progression on a single treatment. However, the clinical trials did not provide detailed information regarding which treatments patients were switched to and the associated survival outcomes. It would be unreasonable to extrapolate outcomes from past studies evaluating these alternate treatments to the patient populations studied in COU-AA-302 and IMPACT given that prior treatment with abiraterone or sipuleucel-T may confound any clear survival benefits of the second treatment. Thus, switching was not included in this analysis.

A major limitation of this model is that skeletal-related events (SREs) and associated costs/hospital-

izations were not explicitly included, because these outcomes were not reported in either of the clinical trials used to generate model parameters, although whether this was simply because no SREs occurred during each study period is unclear. Also, patients were allowed to remain on bisphosphonates in each study provided they had been receiving treatment before study initiation.^{4,5} This may also have led to the lack of SREs being reported in either clinical trial. Because SREs may significantly impact morbidity in mCRPC, sensitivity analyses on survival duration and QOL were conducted to test the effects of differential morbidity. Furthermore, all-cause hospitalization costs in patients with mCRPC were included in the model, which presumably would have included hospitalizations for SREs.²⁸

Previous economic assessments found abiraterone to be cost-effective, both from the US societal and the UK payer perspective.^{11,13} However, there are key differences between this analysis and those performed previously. Both the analysis by Zhong et al¹¹ and NICE's assessment of abiraterone focused on the post-docetaxel mCRPC population with an ECOG functional status of 0 to 2, indicating greater disease severity. In a more severe population, the clinical benefits of abiraterone compared with prednisone are likely to be greater; this population is also likely to incur fewer lifetime costs because of a shorter life expectancy. These factors would yield lower ICERs than those found in this analysis. The NICE assessment was also performed from a UK payer perspective, thus the results are not applicable to US society.

The analysis by Zhong et al¹¹ had several limitations, including using a decision tree analysis to

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Figure 4 Net monetary benefits.

model prostate cancer, average wholesale prices minus an arbitrary 17% for drug costs, and utility inputs that were not reflective of societal preferences, thus inaccurately reflecting a US societal perspective. The authors only used a time horizon of 18 months for the entire model, despite survival data available beyond that timeframe. Given these concerns, the study conclusions should be interpreted carefully, and may not be applicable to US society.

To date, no economic evaluation of sipuleucel-T has been completed, and based on this analysis, sipuleucel-T may represent a cost-effective option if the WTP threshold is greater than \$270K. However, its survival benefits were potentially overestimated in clinical trials, given that median overall survival was only 25.8 versus 21.7 months with placebo, and progression-free survival was 3.7 compared with 3.6 months with placebo. Furthermore, a critique of the IMPACT study found significant differences in overall survival depending on age group, suggesting that age dependence on overall survival was stronger than the treatment effect itself.¹⁴ Given these criticisms, the ICER for sipuleucel-T would potentially change if real-world survival data were available for input into the model; sensitivity analyses on survival rates were conducted to address these concerns. A recent subgroup analysis showed median overall survival up to 41.3 months in the least-severe patient quartile (prostate-specific antigen, <22.1), and based on this survival, sipuleucel-T becomes cost-effective with an ICER of \$120K.³⁹

Interpretation of the ICERs calculated for abiraterone and sipuleucel-T raises the question of an “acceptable” ICER in the United States, particularly in oncology. In an effort to limit political concerns related to the “rationing” of health care, the US’s Pa-

tient-Centered Outcomes Research Institute “...shall not develop or employ a dollars-per-quality adjusted life year...as a threshold to establish what type of health care is cost effective or recommended.”⁴⁰ A 2006 survey of US oncologists suggested that the appropriate threshold should be \$300K, or approximately \$378K in 2013 USD.⁴¹ Using this threshold, the base-case ICER for abiraterone is nearly cost-effective at \$389K/QALY, whereas sipuleucel-T remains cost-ineffective.

Conclusions

Although past analyses have focused on the post-docetaxel mCRPC population, a shift in clinical practice to treat pre-docetaxel patients with the newer drugs will likely occur because of a more favorable side-effect profile and ease of administration. As more data become available, future analyses should evaluate the use of the new drugs in the asymptomatic, pre-docetaxel mCRPC population.

This analysis is the first to assess the cost-effectiveness of newer therapies in asymptomatic pre-docetaxel mCRPC. Overall, neither abiraterone nor sipuleucel-T was found to be cost-effective from a US societal perspective in the base case or in sensitivity analyses at an accepted WTP threshold of \$150K/QALY.

References

1. American Cancer Society. Leading New Cancer Cases and Deaths - 2013 Estimates. Available at: <http://www.cancer.org/research/cancerfactstatistics/cancerfactsfigures2013/index>. Accessed July 1, 2013.
2. National Cancer Institute. Surveillance Epidemiology and End Results (SEER) Stat Fact Sheets: Prostate. Available at: <http://seer.cancer.gov/statfacts/html/prost.html>. Accessed July 1, 2013.
3. Kirby M, Hirst C, Crawford ED. Characterising the castration-resistant prostate cancer population: a systematic review. *Int J Clin Pract* 2011;65:1180–1192.
4. Ryan CJ, Smith MR, de Bono JS, et al. Abiraterone in metastatic prostate cancer without previous chemotherapy. *N Engl J Med* 2013;368:138–148.
5. Kantoff PW, Higano CS, Shore ND, et al. Sipuleucel-T immunotherapy for castration-resistant prostate cancer. *N Engl J Med* 2010;363:411–422.
6. Mohler JL, Kantoff PW, Armstrong AJ, et al. NCCN Clinical Practice Guidelines in Oncology: Prostate Cancer. Version 2.2014. Available at: NCCN.org. Accessed April 1, 2014.
7. Zytiga [package insert]. Horsham, PA: Centocor Ortho Biotech; 2011.
8. Attard G, de Bono JS. Translating scientific advancement into clinical benefit for castration-resistant prostate cancer patients. *Clin Cancer Res* 2011;17:3867–3875.
9. de Bono JS, Logothetis CJ, Molina A, et al. Abiraterone and increased survival in metastatic prostate cancer. *N Engl J Med* 2011;364:1995–2005.
10. Provenge [package insert]. Seattle, WA: Dendreon Corporation; June 2011.

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11. Zhong L, Pon V, Srinivas S, et al. Therapeutic options in docetaxel-refractory metastatic castration-resistant prostate cancer: a cost-effectiveness analysis. *PLoS One* 2013;8:e64275.
12. National Institute for Health and Clinical Excellence. Abiraterone for Castration-Resistant Metastatic Prostate Cancer Previously Treated With a Docetaxel-Containing Regimen. NICE Technology Appraisal Guidance, 2012. Available at: guidance.nice.org.uk/ta259. Accessed July 1, 2013.
13. National Institute for Health and Care Excellence. Prostate Cancer (Metastatic, Hormone Relapsed) - Sipuleucel-T (1st Line) [ID573]. NICE Technology Appraisal Guidance. Available at: <http://guidance.nice.org.uk/TA/WaveR/156#keydocs>. Accessed August 1, 2013.
14. Huber ML, Haynes L, Parker C, Iversen P. Interdisciplinary critique of sipuleucel-T as immunotherapy in castration-resistant prostate cancer. *J Natl Cancer Inst* 2012;104:273–279.
15. Cleeland CS. Brief Pain Inventory User Guide. Available at: http://www.mdanderson.org/education-and-research/departments-programs-and-labs/departments-and-divisions/symptom-research/symptom-assessment-tools/BPI_UserGuide.pdf. Accessed July 1, 2013.
16. Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. *Am J Clin Oncol* 1982;5:649–655.
17. Beck JR, Kassirer JP, Pauker SG. A convenient approximation of life expectancy (the “DEALE”). I. Validation of the method. *Am J Med* 1982;73:889–897.
18. Social Security Administration. Period Life Table, 2010. Available at: <http://www.ssa.gov/OACT/STATS/table4c6.html#ss>. Accessed August 1, 2013.
19. US Department of Veterans Affairs. Veterans Affairs Federal Supply Schedule. Contract Catalog. Available at: http://www.va.gov/nac/index.cfm?action=search&template=Search_Pharmaceutical_Catalog. Accessed September 13, 2014.
20. Centers for Medicare and Medicaid Services (CMS). Current Procedural Terminology, Fourth Edition. Available at: <http://www.cms.gov/apps/physician-fee-schedule/>. Accessed June 1, 2013.
21. Hayman JA, Langa KM, Kabeto MU, et al. Estimating the cost of informal caregiving for elderly patients with cancer. *J Clin Oncol* 2001;19:3219–3225.
22. United States Department of Labor. National Compensation Survey: Employer Cost for Employee Compensation. Bureau of Labor Statistics Web site. Available at: <http://www.bls.gov/ncs/data.htm>. Accessed June 1, 2013.
23. Centers for Medicare and Medicaid Services (CMS). Medicare Fee For Service Payment – Acute Inpatient PPS. Available at: <http://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/Acute-Inpatient-Files-for-Download-Items/FY2013-FinalRule-CorrectionNotice-Files.html?DLPage=1&DLSort=1&DLSortDir=descending>. Accessed July 1, 2013.
24. Mercaldi CJ, Siu K, Sander SD, et al. Long-term costs of ischemic stroke and major bleeding events among Medicare patients with nonvalvular atrial fibrillation. *Cardiol Res Pract* 2012;2012:645469.
25. Pignone M, Earnshaw S, Pletcher MJ, et al. Aspirin for the primary prevention of cardiovascular disease in women: a cost-utility analysis. *Arch Intern Med* 2007;167:290–295.
26. Liao L, Anstrom KJ, Gottdiener JS, et al. Long-term costs and resource use in elderly participants with congestive heart failure in the Cardiovascular Health Study. *Am Heart J* 2007;153:245–252.
27. Burton TM, Lacey M, Liu F, et al. One-year follow-up healthcare costs of patients hospitalized for transient ischemic attack or ischemic stroke and discharged with aspirin plus extended-release dipyridamole or clopidogrel. *J Med Econ* 2012;15:1217–1225.
28. Mehra M, Wu Y, Dhawan R. Healthcare resource use in advanced prostate cancer patients treated with docetaxel. *J Med Econ* 2012;15:836–843.
29. United States Department of Labor. Consumer Price Index – All Urban Consumers: Medical Care. Bureau of Labor Statistics. Available at: http://data.bls.gov/timeseries/CUUR0000SAM?output_view=pct_12mths. Accessed July 1, 2013.
30. Gold MR, Siegel JE, Russell LB. Cost-effectiveness in health and medicine. New York, NY: Oxford University Press; 1996.
31. Bremner KE, Chong CA, Tomlinson G, et al. A review and meta-analysis of prostate cancer utilities. *Med Decis Making* 2007;27:288–298.
32. Volk RJ, Cantor SB, Cass AR, et al. Preferences of husbands and wives for outcomes of prostate cancer screening and treatment. *J Gen Intern Med* 2004;19:339–348.
33. Bennett CL, Chapman G, Elstein AS, et al. A comparison of perspectives on prostate cancer: analysis of utility assessments of patients and physicians. *Eur Urol* 1997;32(Suppl 3):86–88.
34. Yeung K, Gong CL. Cost-utility analysis of enzalutamide versus abiraterone for the treatment of docetaxel refractory metastatic castrate resistant prostate cancer. Presented at the 18th Annual International Meeting of the International Society for Pharmacoeconomics and Outcomes Research; May 18–22, 2013; New Orleans, Louisiana. Poster PCN86.
35. World Health Organization. Cost-Effectiveness Thresholds. CHOosing Interventions that are Cost-Effective (WHO-CHOICE). Available at: http://www.who.int/choice/costs/CER_thresholds/en/. Accessed August 1, 2013.
36. Stinnett AA, Mullahy J. Net health benefits: a new framework for the analysis of uncertainty in cost-effectiveness analyses. *Med Decis Making* 1998;18:S68–80.
37. O'Day K, Globe D. Using net benefits to report cost-effectiveness results. Presented at the ISPOR Annual European Congress; November 5–8, 2011. Available at: http://www.ispor.org/congresses/Spain1111/presentations/W30_Globe-Oday.pdf. Accessed August 1, 2013.
38. Hwang SS, Chang VT, Alejandro Y, Mulaparthy S, et al. Study of hormone refractory prostate cancer: hospital care and palliative care resource use at a VA medical center. *Cancer Invest* 2004;22:849–857.
39. Schellhammer PF, Chodak G, Whitmore JB, et al. Lower baseline prostate-specific antigen is associated with a greater overall survival benefit from sipuleucel-T in the Immunotherapy for Prostate Adenocarcinoma Treatment (IMPACT) trial. *Urology* 2013;81:1297–1302.
40. Affordable Care Act. Patient-Centered Outcomes Research Institute. Patient Protection and Affordable Care Act, 42 U.S.C. § 1182(e). 2010.
41. Nadler E, Eckert B, Neumann PJ. Do oncologists believe new cancer drugs offer good value? *Oncologist* 2006;11:90–95.