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Original Article

Cost-effectiveness analysis of treatments for metastatic castration resistant prostate cancer

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Abstract *Objective:* Treatment options for metastatic castration resistant prostate cancer (mCRPC) have expanded rapidly in recent years. Given the significant economic burden, we sought perform a cost-effectiveness analysis (CEA) of the contemporary treatment paradigm for mCRPC.
Methods: We devised a treatment protocol consisting of sipuleucel-T, enzalutamide, abiraterone, docetaxel, radium-223, and cabazitaxel. We estimated number and length of treatments for each therapy using dosing schedules or progression free survival data from published clinical trials. We estimated treatment cost using billing data and Medicare reimbursement values and performed a CEA. Our analysis assumed US$100,000 per life year saved (LYS) as the threshold societal willingness to pay.
Results: Incremental cost-effectiveness ratios (ICER) for strategies incorporating sipuleucel-T that were not eliminated by extended dominance exceeded the societal threshold willingness-to-pay of US$100,000 per LYS, the lowest of which was sipuleucel-T + enzalutamide + abiraterone + docetaxel at US$207,714 per LYS. Enzalutamide + abiraterone + docetaxel exhibited the most favorable ICER among strategies without sipuleucel-T at US$165,460 per LYS.
Conclusion: Based on the available survival data and current costs of treatment, all treatment strategies greatly exceed a commonly assumed societal willingness-to-pay threshold of

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US$100,000 per LYS. Improvements in this regard can only come with a reduction in pricing, better tailoring of treatment or significant enhancements in survival with clinical use of treatment combinations or sequences.

1. Introduction

Prostate cancer is the most common cancer in males in the United States and the second leading cause of cancer death among men, with 180,890 estimated new cases in 2016 and 26,120 deaths [1]. Of men diagnosed with prostate cancer, between 10% and 20% will develop metastatic castration resistant prostate cancer (mCRPC) within 5 years of diagnosis after receiving hormone ablation therapy for metastatic disease at diagnosis or disease recurrence [2]. The first chemotherapeutic agent to show a significant survival benefit for mCRPC, docetaxel, was approved in 2004 and remained the only established treatment with a survival benefit until 2010 [3]. Over the few 2 years, four new therapeutic agents have been introduced that demonstrated survival advantages in this disease setting: sipuleucel-T, cabazitaxel, abiraterone, enzalutamide, and radium-223 [4–8]. Each agent has been shown to have a median survival benefit between 2 and 4 months compared with control [2,9]. In addition to treatments intended to increase overall survival, mCRPC patients typically receive androgen deprivation therapy beyond disease progression, given that mCRPC remains driven by androgen receptor signaling and historical data suggesting better outcomes with continued androgen deprivation. These patients also receive bisphosphonates or denosumab, a human monoclonal RANK-L antibody, to reduce skeletal-related events as a result of bone metastases [10,11].

While these medications have changed treatment patterns for patients with mCRPC, increased focus on healthcare expenditures in the United States has brought the associated cost for new pharmacologic interventions for mCRPC under scrutiny [12,13]. In 2006, US$9.9 billion was spent on prostate cancer care in the US alone [14]. It is estimated that the amount spent in 2010 was US$11.85 billion and is expected to increase to US$15.41 billion by the year 2020 [15]. Given the high cost of treating prostate cancer and the limited cost data in the setting of newly-introduced treatments for mCRPC, we sought to calculate the estimated cost of the new treatment paradigm for mCRPC and perform a cost-effectiveness analysis (CEA) using published survival data.

2. Methods

2.1. Cost and survival estimates for the analysis

Using the 2013 American Urological Association (AUA) Guidelines for mCRPC and a previously published paradigm for the treatment of mCRPC we chose a treatment scheme for a model patient with mCRPC [16,17]. We defined mCRPC as disease progression, a rising prostate specific antigen (PSA) while on androgen ablation, in the setting of metastatic disease. The paradigm consisted of sipuleucel-T, enzalutamide, abiraterone, docetaxel, radium-223, and finally cabazitaxel. Prednisone 10 mg daily is administered during abiraterone, cabazitaxel, and docetaxel treatments and was included in our cost estimation. We excluded the use of tertiary hormone interventions in the mCRPC patient such as bicalutamide, flutamide, and ketoconazole given the lack of consensus on use and impact on survival. It was assumed that the patient would also be receiving denosumab monthly and leuprolide every 3 months for the entire length of survival.

We estimated length of treatment for each therapy using standard dosing schedules or survival data from randomized controlled trials (RCTs) if a standard dosing regimen was not defined. Cost data were obtained from the pharmaceutical provider for our institution, Besse Medical© (Amerisource Bergen Specialty Group, Frisco, TX, USA). CPT® codes for therapy administration on an outpatient basis were chosen based on common practice within our institution, and Medicare reimbursement values (MRV) were obtained through our institutional billing department. Data on survival benefit for each treatment were obtained from published RCTs. Our cost estimation does not include the price of pain medication, radiation therapy for bone metastases, or other palliative therapies such as mitoxantrone.

Overall cost for each treatment was established by multiplying the estimated treatment length or number of cycles by the unit cost obtained from Besse Medical©, the pharmaceutical supplier for our institution. If the medication was administered in office, an additional 6% was added to the total for office administration. For medications coded for injection or chemotherapy infusion, MRVs for the corresponding CPT® codes (96372 and 96365, respectively) were multiplied by the estimated number of treatments and added to the pharmaceutical cost. For medications prescribed orally, the monthly cost of the medication was multiplied by the estimated number of months of treatment received in the clinical trial. Survival benefits were assumed to be additive. We used the median placebo treatment survival time published in a sipuleucel-T phase III RCT (21.7 months) to which we added the median survival benefits of sipuleucel-T (4.1 months), docetaxel (2.4 months), cabazitaxel (2.4 months), abiraterone (3.9 months), radium-223 (3.6 months), and enzalutamide (3.7 months) to estimate the overall survival and length of time patients would receive denosumab and leuprolide treatments (41.8 months) [3–8,18].

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