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# Cost-Effectiveness of Abiraterone, Apalutamide, Enzalutamide, and Docetaxel Doublets for Metastatic Hormone-Sensitive Prostate Cancer: A Real-World Evidence Analysis

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## Background

- Prostate cancer is the most common non-skin cancer and second leading cause of cancer deaths in US adult men; 8% present with metastatic disease[1,2]
- Metastatic hormone-sensitive prostate cancer (mHSPC) is an advanced form of prostate cancer associated with an estimated 5-year survival below 40%[2]
- In clinical practice, first-line mHSPC treatment comprises androgen deprivation therapy (ADT) plus docetaxel, or an androgen receptor pathway inhibitor (ARPI), with triplet regimens reserved for eligible patients[3]
- Existing cost-effectiveness analyses rely on trial-based survival data, limiting generalizability to real-world patients and country-specific value assessments

## Objective

- To estimate the cost-effectiveness of four first-line mHSPC doublet regimens in the United States using real-world survival data

## Methods

### Model structure

- Three-state partitioned survival model
  - Progression-free
  - Post-progression
  - Death
- Monthly cycle
- Lifetime horizon
- US healthcare sector perspective
- 3% discount rate

### Population

- Claims-derived cohort of 9,141 mHSPC patients (mean age: 69.4 years) who initiated ADT treatment within 4 months of diagnosis, and received index treatment with abiraterone (n = 3,968), apalutamide (n = 1,096), enzalutamide (n=1,902) or docetaxel (n=2,175) within 4 months of ADT initiation

### Treatment strategies

- Abiraterone 250mg tablet (generic) + ADT
- Apalutamide 60mg tablet + ADT
- Enzalutamide 40mg capsule + ADT
- Docetaxel 75 mg/m$^2$ + ADT

ADT included medical castration (leuprolide, goserelin, triptorelin, relugolix and degarelix) and one-time bilateral orchiectomy

### Survival inputs

- Overlap propensity score weighted parametric distributions were derived for OS and PFS from the real-world cohort[4]
- Best fitting survival distribution was selected based on AIC, visual inspection and clinical plausibility
  - **OS**: Weibull (abiraterone, apalutamide, enzalutamide); exponential (docetaxel)
  - **PFS**: Log-logistic (all four treatments)

### Costs

- Drug costs obtained from sources reflecting national average prices
- Administration costs derived from the CMS Physician Fee Schedule
- Health state costs sourced from published literature
- Inflated to 2025 USD

### Utilities & Outcomes

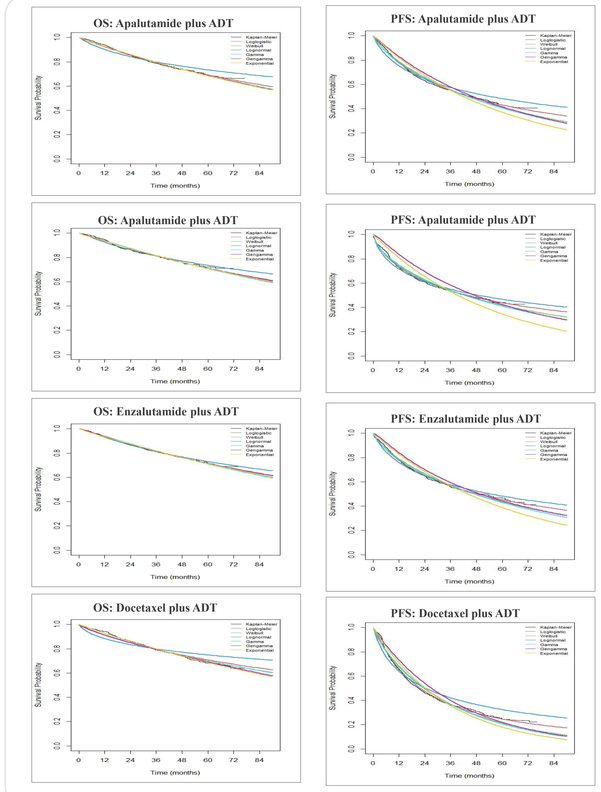
- Utilities for mHSPC and mCRPC derived from published literature
- Outcomes included LYs, QALY, evLYs, and ICER in cost/QALY and cost/evLYG

### Sensitivity/Scenario Analyses

- One-way sensitivity and probabilistic sensitivity analysis were performed
- **Scenario 1**: Tab 500mg abiraterone formulation pricing
- **Scenario 2**: Brand-name abiraterone pricing
- **Scenario 3**: 5-year time horizon

## Results

***Figure 1.*** **Weighted OS and PFS parametric distributions**




**ADT**: androgen deprivation therapy; **OS**: overall survival, **PFS**: progression-free survival

***Table 1.*** **Select model parameters**

| Parameters | Base case | Lower bound | Upper bound | Distribution | Reference/Comment |
|---|---|---|---|---|---|
| **Drug cost ($)** | | | | | |
| Abiraterone | 129.06 | 103.25 | 154.87 | Gamma | NADAC (generic)[5] |
| Apalutamide | 11,156.61 | 8,925.29 | 13,397.93 | Gamma | 29% discount to WAC[6] |
| Enzalutamide | 10,900.59 | 8,720.47 | 13,080.71 | Gamma | 29% discount to WAC[6] |
| Docetaxel | 100.16 | 80.13 | 120.19 | Gamma | CMS ASP[7] |
| **Medical ADT cost ($)[a]** | | | | | |
| Leuprolide | 176.447 | 141.16 | 211.74 | Gamma | CMS ASP[7] |
| Goserelin | 733.67 | 586.93 | 880.40 | Gamma | CMS ASP[7] |
| Triptorelin | 474.84 | 379.87 | 569.81 | Gamma | CMS ASP[7] |
| Degarelix | 355.84 | 284.672 | 427.00 | Gamma | CMS ASP[7] |
| Relugolix | 1,933.65 | 1546.92 | 2320.38 | Gamma | 30% discount to WAC |
| **Surgical ADT cost ($)[ab]** | | | | | |
| Bilateral orchiectomy | 14,755.94 | 9,481 | 20,031 | Gamma | Paul et al[8] |
| **Drug administration cost ($)[a]** | | | | | |
| Docetaxel | 119.36 | 95.49 | 143.23 | Gamma | CMS Physician Fee Schedule[9] |
| Leuprolide, goserelin, triptorelin, degarelix | 34.93 | 27.94 | 41.92 | Gamma | CMS Physician Fee Schedule[9] |
| **Health state cost ($)** | | | | | |
| mHSPC | 4,095.21 | 3032.40 | 5158.02 | Gamma | Wang et al[10] |
| mCRPC (docetaxel and apalutamide) | 13,808.10 | 12,315.32 | 15,300.88 | Gamma | Wang et al[10] |
| mCRPC (enzalutamide) | 15,976.66 | 14,249.43 | 17,703.89 | Gamma | Wang et al[10] |
| mCRPC (abiraterone) | 19,339.87 | 17,249.22 | 21,430.52 | Gamma | Wang et al[10] |
| **Health state utility** | | | | | |
| mHSPC (docetaxel) | 0.067 | 0.0602 | 0.0735 | Beta | Morgans et al[11] |
| mHSPC (abiraterone, apalutamide, enzalutamide) | 0.072 | 0.0632 | 0.0815 | Beta | Feyerbend et al[12] |
| mCRPC | 0.061 | 0.0539 | 0.0677 | Beta | Lloyd et al[13] |

ADT: androgen deprivation therapy, AHRQ: Agency for healthcare research and quality healthcare cost and utilization project, ALT: alanine aminotransferase, CMS: Centers for Medicare and Medicare services, mHSPC: metastatic hormone-sensitive prostate cancer, mCRPC: metastatic castration-resistant prostate cancer, WAC: wholesale acquisition cost
[a]monthly costs before incorporating utilization rates
[b]applied as a one-time cost

## Results (continued)

***Table 2.*** **Base-case cost-effectiveness results**

| Treatment strategy | Cost ($) | LYs | QALYs | evLYs | ICER (cost/QALY) | ICER (cost/evLYG) | Comparator |
|---|---|---|---|---|---|---|---|
| **Abiraterone** | 716,701 | 7.50 | 5.37 | 5.37 | Reference | Reference | |
| **Docetaxel** | 747,672 | 7.47 | 4.95 | 4.95 | Dominated | Dominated | Abiraterone |
| **Enzalutamide** | 1,239,303 | 7.72 | 5.80 | 5.83 | 1,214,802 | 1,158,762 | Abiraterone |
| **Apalutamide** | 1,248,750 | 7.67 | 5.75 | 5.77 | Dominated | Dominated | Enzalutamide |

evLYG: equal value of life years gained, ICER: incremental cost-effectiveness ratio, LYs: life years, QALYs: quality-adjusted life years

- Docetaxel was dominated by abiraterone; fewer QALYs (4.95) at higher cost ($747,672)
- Apalutamide was dominated by enzalutamide; fewer QALYs (5.75) at higher cost ($1,248,750)
- Enzalutamide generated the most QALYs (5.83), with an ICER of $1,214,802/QALY vs abiraterone

***Table 2.*** **Scenario analyses**

| Treatment strategy | Cost ($) | LYs | QALY | evLYs | ICER (cost/QALY) | ICER (cost/evLYG) | Comparator |
|---|---|---|---|---|---|---|---|
| **500mg abiraterone tablet ($843/month)** | | | | | | | |
| **Docetaxel** | 747,672 | 7.47 | 4.95 | 4.95 | Reference | Reference | |
| **Abiraterone** | 755,550 | 7.50 | 5.37 | 5.37 | 18,663 | 18,578 | Docetaxel |
| **Enzalutamide** | 1,239,303 | 7.72 | 5.80 | 5.83 | 1,124,495 | 1,1072,847 | Abiraterone |
| **Apalutamide** | 1,248,750 | 7.67 | 5.75 | 5.77 | Dominated | Dominated | Enzalutamide |
| **Branded-name abiraterone ($8,992.57/month)** | | | | | | | |
| **Docetaxel** | 747,672 | 7.49 | 4.95 | 4.95 | Reference | Reference | |
| **Abiraterone** | 1,199,016 | 7.50 | 5.37 | 5.37 | 1,092,211 | 1,071,061 | Docetaxel |
| **Enzalutamide** | 1,239,303 | 7.70 | 5.80 | 5.82 | 93,690 | 89,527 | Abiraterone |
| **Apalutamide** | 1,248,750 | 7.72 | 5.75 | 5.77 | Dominated | Dominated | Enzalutamide |
| **5-year time horizon** | | | | | | | |
| **Abiraterone** | 380,979 | 4.15 | 3.21 | 3.21 | Reference | Reference | |
| **Docetaxel** | 402,191 | 4.16 | 2.96 | 2.96 | Dominated | Dominated | Abiraterone |
| **Enzalutamide** | 730,786 | 4.24 | 3.41 | 3.41 | 1,779,205 | 1,713,760 | Abiraterone |
| **Apalutamide** | 737,437 | 4.23 | 3.38 | 3.38 | Dominated | Dominated | Enzalutamide |

evLYG: equal value of life years gained, ICER: incremental cost-effectiveness ratio, LYs: life years, QALYs: quality-adjusted life years

### Generic 500mg abiraterone ($843/month)

- Docetaxel became least costly treatment
- Abiraterone was cost-effective at $18,663/QALY vs docetaxel

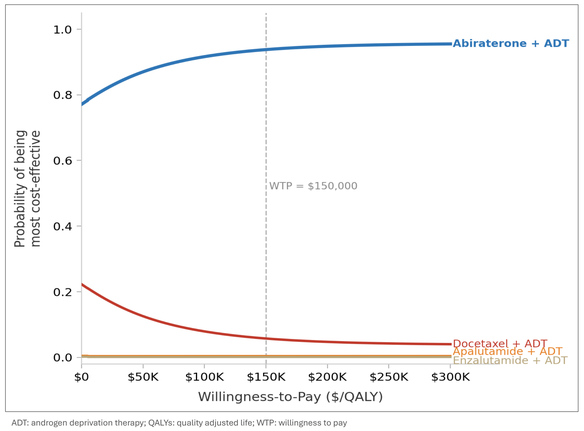
### Brand-name abiraterone ($8,993/month)

- Docetaxel became the most cost-effective strategy
- Enzalutamide cost-effective at $93,690/QALY vs abiraterone

### 5-year time horizon

- Pattern consistent with base-case cost-effectiveness results

***Figure 2.*** **Cost Effectiveness Acceptability Curve**

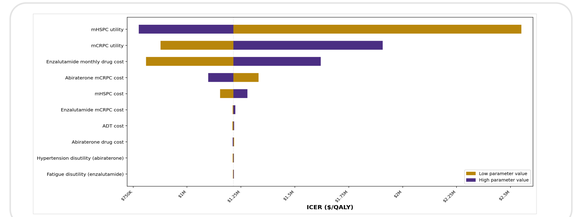



ADT: androgen deprivation therapy; QALYs: quality adjusted life; WTP: willingness to pay

- Abiraterone had the highest probability of being the most-effective treatment at all observed WTP thresholds, reaching approximately 95% at $150,000/QALY

## Results (continued)

***Figure 3.*** **Tornado plot: Enzalutamide ADT vs. Abiraterone + ADT**




## Key takeaways

- **Abiraterone was the most cost-effective first-line mHSPC strategy, driven by generic pricing**
- **Docetaxel was dominated by abiraterone**
- **Apalutamide was dominated by enzalutamide**
- **Enzalutamide was not cost-effective relative to abiraterone**
- **Cost-effectiveness of abiraterone was attenuated under 500mg tablet formulation pricing and reversed under brand-name pricing, with docetaxel emerging as the most cost-effective strategy in the latter scenario**
- **Results were robust over a 5-year time horizon**
- **Findings were most sensitive to drug acquisition costs, health state costs and health state utilities**

## Limitations

- **Model structure**: Partitioned survival model assumes OS/PFS independence; may not fully capture endpoint dependencies or long-term extrapolation uncertainty
- **Treatment assumptions**: Uninterrupted treatment until progression assumed; no dose modifications or early discontinuation modeled
- **Residual confounding**: Propensity score weighting adjusts for observed confounders but cannot eliminate all observational bias
- **Static pricing**: Drug costs modeled to be constant over time; generic enzalutamide/apalutamide entry anticipated near term and could substantially shift hierarchy

## Conclusion

- Using real-world survival data, abiraterone is the most cost-effective first-line treatment for mHSPC, driven primarily by generic drug availability, and offering superior value compared to other doublet regimens

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