Cost-Effectiveness of Abiraterone, Enzalutamide, and Apalutamide in Metastatic Castration-Sensitive Prostate Cancer (mCSPC): A Partitioned-Survival Model

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Background and Objectives

- Prostate cancer is the second leading cause of death and second most common cancer among American men[1]
- Incidence of metastatic prostate cancer (mPCa) in the US increased by 5.3% and 6.5% in men aged 45 – 74 and >75 from 2010 to 2018[2]
- mCSPC has largely been treated with androgen deprivation therapy (ADT) alone or ADT plus docetaxel through the past few decades[3]
- Emergence of antiandrogen therapies like abiraterone acetate, apalutamide, and enzalutamide in the last decade has transformed the treatment landscape[4]
- As of November 2018, there are low-priced, generic versions of abiraterone acetate while apalutamide and enzalutamide are still under market exclusivity
- **Objective:** To compare the cost-effectiveness of abiraterone, enzalutamide, and apalutamide in addition to ADT in treating mCSPC from US payer perspective

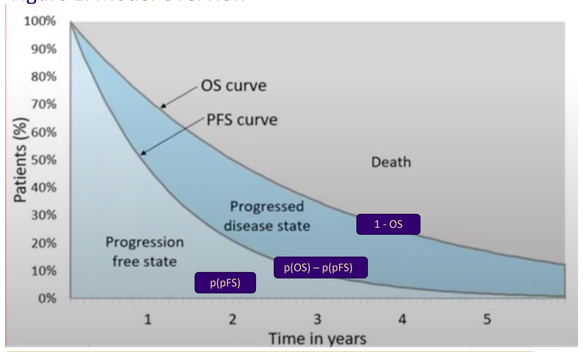
Methods

- Partitioned-Survival model of 70 year-old male cohort transitioning through three discrete health states: pre-progression, progressed, and death
- Patients treated with treatment strategies of interest during pre-progression and accrued equal QALYs and costs inn progressed state
- Primary outputs of model were costs in $USD 2022, life-years (LYs), and quality-adjusted life-years (QALYs) used to calculated incremental cost-effectiveness ratios (ICERs)
- Outcomes collected over lifetime horizon, until cohort age 100, over 28-day cycles and discounted at 3% per year and were evaluated using a willingness-to-pay (WTP) threshold of US$150,000
- Utility values for pre-progression states and adverse event probabilities were EQ-5D values mapped from FACT-P scores from respective phase 3 trials[5]
- Survival and progression risk was estimated by extrapolating overall (OS) and progression-free survival (pFS) curves from phase 3 trials using Automeris web plot digitizer and curve fitting method detailed in Hoyle and Henley, 2011[6]
- Drug costs were obtained from Redbook and National Drug Acquisition Cost (NADAC) data
- All other parameters were obtained from literature
- One-way (OWSA) and probabilistic sensitivity analyses (PSA) conducted to evaluate uncertainty of model

Table 1: Treatment Strategies and Curve Fits

	Abiraterone	Enzalutamide	Apalutamide
Dosage	Abiraterone acetate 1000mg + prednisone 5mg daily + ADT	Enzalutamide 160mg daily + ADT	Apalutamide 240mg daily + ADT
Trial	LATITUDE	ARCHES	TITAN
pFS	loglogistic	lognormal	loglogistic
OS	loglogistic	loglogistic	lognormal

Figure 1: Model Overview[7]



*proportion of cohort in each state is calculated at every cycle with the above equations

Results

Table 2: Base-Case Costs, Lys, and QALYs

	Costs	Life-Years	QALYs
AA + ADT	$536,109	5.88	4.47
ENZ + ADT	$1,455,624	7.84	5.76
APA + ADT	$1,399,218	7.23	5.35

Abiraterone acetate = AA, Enzalutamide = ENZ, Apalutamide = APA

Table 3: Base-Case Incremental Results

	Costs	QALYs	ICER
APA vs AA	$863,109	0.88	$984,970/QALY
ENZ vs APA	$56,406	0.41	$138,545/QALY

- ENZ + ADT resulted in the most life-years and QALYs gained
- At a WTP threshold of $150,000, APA was not cost-effective compared to AA, but ENZ was cost-effective when compared to APA

Figure 2: State Probability Trace

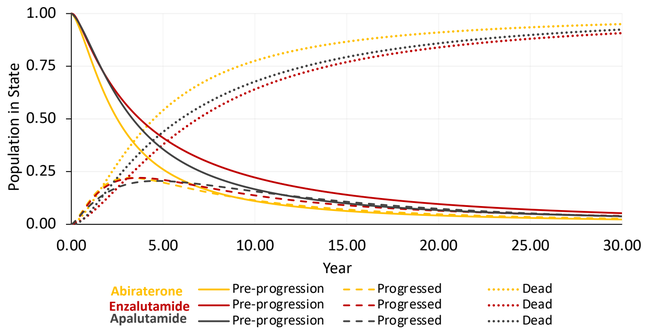


Figure 3: OWSA Costs

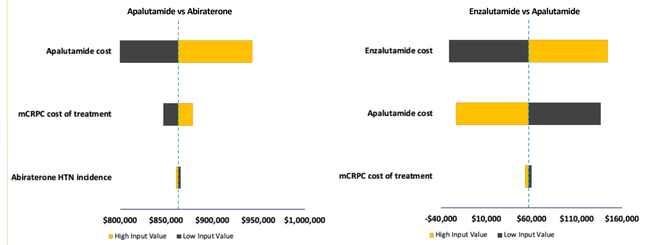
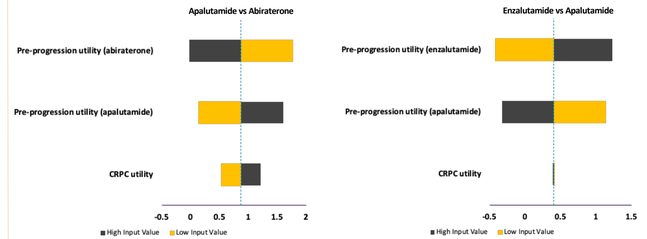
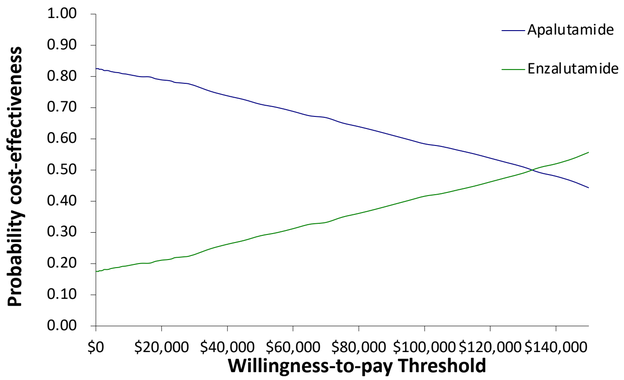


Figure 4: OWSA QALYs



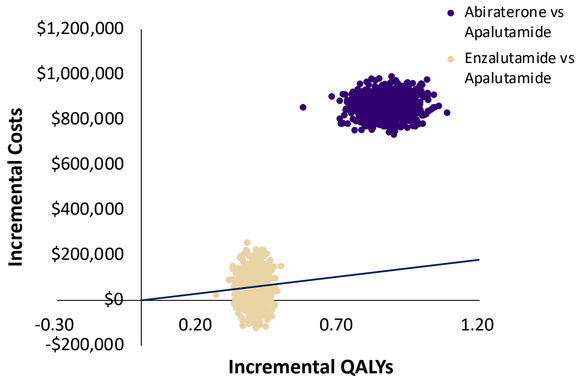
- Abiraterone dominated apalutamide when using the high-input value of pre-progression utility for abiraterone
- Apalutamide dominated enzalutamide when using the high-input and low-input values of pre-progression utility for apalutamide and enzalutamide, respectively
- Enzalutamide dominated apalutamide when using the high-input and low-input values of cost for apalutamide and enzalutamide, respectively

Figure 5: Cost-Effectiveness Acceptability Curve



Abiraterone was cost-effective compared to apalutamide 100% of the time at all WTP thresholds from $0 to $150,000

Figure 6: Cost-Effectiveness Plane



Conclusions

- Abiraterone acetate plus ADT is the preferred treatment strategy for mCSPC at a WTP threshold of $150,000
- Enzalutamide was was cost-effective compared to apalutamide at base-case, but results were heavily influenced by pre-progression utility and cost estimates
- In a probabilistic sensitivity analysis, enzalutamide was cost-effective compared to apalutamide roughly 56% of the time

Limitations

- Patient population in trials used to estimate progression and mortality differed with regards to inclusion of low and high risk patients as well prior docetaxel use
- Survival curves extrapolated with plot digitizers and R code may not be equally well-fit for all strategies
- mCRPC health state costs may be inflated relative to pre-progression costs due to inclusion of additional medical services that were left out in the pre-progression state

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