# Cost-effectiveness of Niraparib with Abiraterone Acetate and Prednisone for treatment of Metastatic Castration-Resistant Prostate Cancer (mCRPC).

Emeka E.Duru, BPharm[1], T. Joseph Mattingly II, PharmD, MBA, PhD[1], Daniel C. Malone, PhD, FAMCP[1]

[1]University of Utah, College of Pharmacy, Salt Lake City, Utah, USA

EE29

## Background

- Metastatic castration resistant prostate cancer (mCRPC) is an advanced form of prostate cancer that have developed resistance to systemic therapies, such as androgen deprivation therapy and chemotherapy[1].
- Niraparib, a Poly-ADP ribose polymerase (PARP) Inhibitor have been approved in combination with abiraterone acetate and prednisolone (AAP) for the treatment of mCPRC patients with deleterious or suspected HRR gene mutation in August 2023 by the Food and Drug Administration (FDA)[2].
- In the MAGNITUDE trial, niraparib plus AAP prolonged radiographic progression-free survival, rPFS (median rPFS 19.5 versus 10.9 months, HR=0.55, CI= 0.39-.78) compared to placebo plus AAP in the *BRCA 1/2* subgroup; and in the total HRR + cohort (HR = 0.76, CI 0.60-0.97)[3].
- Despite these promising results, there is no economic evaluation data on this new therapy, making it difficult for clinicians to determine the optimal treatment choice for their patients.

## Objective

- To evaluate the cost-effectiveness of niraparib plus AAP versus standard of care, AAP alone for mCRPC patients with BRCA1/2 mutations from a US healthcare system perspective.

## Methods

- **Target Population**: Patients with metastatic castration-resistant prostate cancer (mCRPC) with BRCA1/2 gene mutation.
- **Intervention:** Niraparib combined with Abiraterone Acetate and Prednisone (Akeega)®.
- **Comparator**: Abiraterone Acetate + Prednisone (SOC).
- **Analytical model:** Partitioned survival model (PSM) with a 28-day cycles length and life-time time horizon.
- **Perspective**: US healthcare sector.
- **Discount rate**: 3% for both costs and utilities.
- A partitioned survival model (PSM) was constructed in TreeAge Pro to conduct a cost-effectiveness analysis using data from the MAGNITUDE second interim analysis (IA2).
- The PSM had three mutually exclusive health states: Progression-free disease state (PFD), progressed disease (PD), and death.
- Transition probabilities derived from overall survival and progression-free survival data from the interim secondary analysis (IA2) of the MAGNITUDE trial Kaplan-Meier curves.7
- Web plot digitizer (version 4.5; https://OS curves. automeris.io/WebPlotDigitizer) was used to gather the survival data points from the PFS and OS curves.
- Parametric modeling was used to extrapolate data beyond the time endpoint in the clinical trials using standard statistical analyses described by Hoyle et al[4].
- Parametric survival regressions were fitted using the flexsurv package in R (version 4.3.1, R Foundation for Statistical Computing).
- Survival data points were then used to fit the following parametric survival functions: Weibull, log-normal, log-logistic, exponential, Gompertz. The model selection was based on goodness of fit, Akaike information criterion value (AIC).
- Weibull and Loglogistic functions were the most reasonable functions with the lowest AIC value in each case.
- Drug acquisition costs for the selected treatment strategy were sourced from the Department of Veterans Affairs' latest Federal Supply Schedule contract to reflect the actual drug costs to federal agencies after discounts and rebates; while treatment specific costs including outpatient, monitoring and lab testing (CT scan and bone imaging), follow-up, best-supportive care, disease progression, end-of-life care and all adverse events costs were derived from published literature.
- Utility values for progression-free disease (PFD), progressed disease (PD) and disutility for AE were also based on previously published studies.

**Table 1: Model input parameters**

| Parameter | Base case | Range | Distribution |
|---|---|---|---|
| **Survival model for Niraparib + AAP** | | | |
| **Model for PFS** | Shape: 1.45, Scale: 15.92 | | Loglogistic |
| **Model for OS** | Shape: 1.53, Scale: 38.86 | | Weibull |
| **Survival model for AAP** | | | |
| **Model for PFS** | Shape: 1.47, Scale: 10.28 | | Loglogistic |
| **Model for OS** | Shape: 1.54, Scale: 36.44 | | Weibull |
| **Utility Values** | | | |
| **PFD** | 0.76 | 0.65 – 0.87 | Beta |
| **PD** | 0.37 | 0.33 – 0.41 | Beta |
| **Disutility grade ≥3 AE** | - 0.58 | 0.05 | Beta |
| **Drug cost (per cycle)** | | | |
| **Niraparib® 200mg** | 15,899 | 12,750 – 19,000 | Gamma |
| **Abiraterone® 1000mg** | 9,519 | 7,650 – 11,430 | Gamma |
| **Prednisone 10mg** | 16.33 | 13 - 20 | Gamma |
| **Administration costs** | | | |
| **Outpatient costs** | 1,811 | 1,449 – 2,173 | Gamma |
| **Imaging and tests** | 1,138 | 911 – 1,366 | Gamma |
| **Disease progression** | 2,342 | 390 - 2516 | Gamma |
| **Follow-up costs** | 601 | 486 - 729 | Gamma |
| **Supportive care** | 5,963 | 4,770 – 7,155 | Gamma |
| **End-of-life care** | 16,468 | 13,174 – 19,761 | Gamma |
| **Adverse Events costs (per event)** | | | |
| **Grade >3 AE** | 96,946 | 77,550 – 116,340 | Gamma |

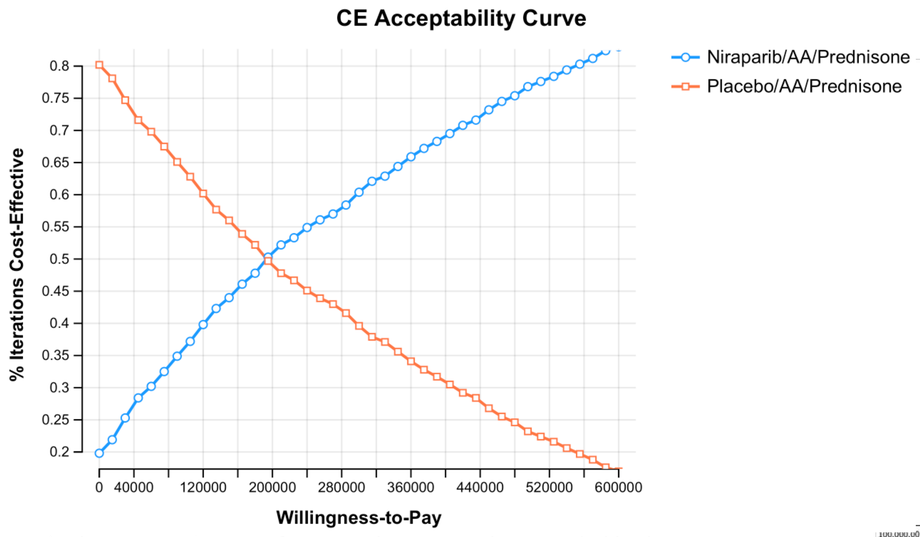
## Results

- At a WTP threshold of $150,000 and $200,000 per QALY, the probability of niraparib being cost-effective was 43% and 51%, respectively (Figure 1).
- Total discounted QALY's over the modeled time horizon were higher for niraparib + AAP than Pbo + AAP (1.65 vs. 1.42 QALY's) (Table 2).
- Total discounted costs were also higher for nira + AAP ($289,705) than Pbo + AAP ($219,511). (Table 2)

**Table 2: Summary of costs and outcomes in Base-case analysis**

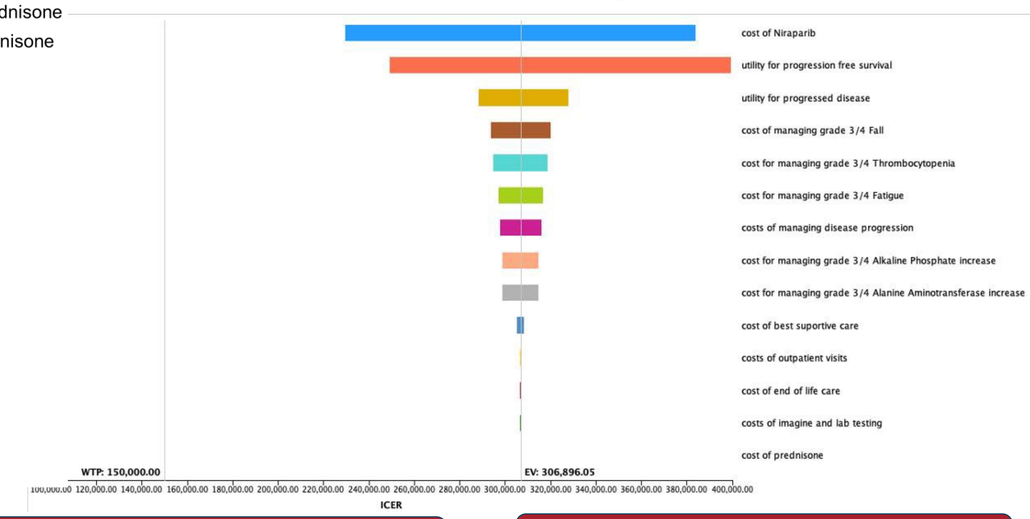
| | Nira + AAP | Pbo + AAP |
|---|---|---|
| **Total Costs** | | |
| **Progression Free State** | $255,329 | $174,406 |
| **Post-Progression** | $34,375 | $45,104 |
| **Total Costs** | $289,705 | $219,511 |
| **Incremental Costs** | - | $70,193 |
| **Total Quality-Adjusted Life Years (QALY's)** | | |
| **Progression Free State** | 1.37 | 1.01 |
| **Post-Progression** | 0.28 | 0.41 |
| **Total** | 1.65 | 1.42 |
| **Incremental QALY'S** | - | 0.23 |
| **ICER, $ per QALY** | 306,890 | |
| **Net Monterey Benefits (NMB)** | | |
| **Progression Free State** | -49,557 | -23,246 |
| **Post-Progression** | 7,458 | 17,036 |
| **Total** | -42,098 | -6,213 |

**Figure 1: Cost-effectiveness acceptability curve**




- The ICER was $306,890 for niraparib + AAP vs. pbo + AAP. (Table 2)
- The one-way sensitivity analysis revealed that the most sensitive inputs were the cost of niraparib, the utility of progression-free state and progressed disease, and the cost of managing grade ¾ fall. (Figure 2)
- This CEA is based on an interim analysis of the MAGNITUDE trial. It provides valuable early insights, especially for time-sensitive decision-making in clinical settings; health economists and decision-makers must consider these results preliminary.

**Figure 2: Sensitivity analysis (Tornado diagram)**




## Conclusion

- Niraparib combination therapy with AAP is unlikely to be a cost-effective therapy for patients with advanced or metastatic castration-resistant prostate cancer in the U.S.

## References

COLLEGE OF PHARMACY UNIVERSITY OF UTAH
L. S. SKAGGS PHARMACY INSTITUTE

Emeka Elvis Duru, BPharm
elvis.duru@utah.edu

*Presented at ISPOR 2024, Atlanta, May 5th – 8th, 2024*