Cost-Effectiveness Analysis of Olaparib and Niraparib with Abiraterone versus Abiraterone for BRCA-mutated mCRPC in Taiwan

HTA54

Pei-Lien Lin[1], Ming-Neng Shiu[1], Shih-Tsung Huang[1]
[1]Department of Pharmacy, National Yang Ming Chiao Tung University, Taipei, Taiwan.

Contact
Pei-Lien Lin M.S
Email: dalinlinda66@gmail.com

Introduction

- In 2022, prostate cancer(PC) was the fourth most common cancer in Taiwan and ranked as the sixth-leading cause of cancer-related mortality.[1]
- 1st-line treatment for locally advanced and distant PC are Androgen deprivation therapy (ADT) and its combined therapy. About 95% of patients initially respond to ADT and is called metastatic castration-sensitive PC(mCSPC). However, nearly all mCSPC will progress to metastatic castration-resistant PC(mCRPC).[2]
- Approximately 20–30% of mCRPC patients carry germline BRCA1/2 gene mutations, which demonstrates poorer prognosis.[3][4]
- **Olaparib(OLA)** and **Niraparib(NIRA) with Abiraterone/Prednisolone(AAP)** were proved to prolong radiographic progression free survival(rPFS) in BRCA-mutated mCRPC patients.
  - ✓ PROpel trial[5] (1st line OLA+AAP vs AAP): HR of OS= 0.26 [95% CI, 0.14-0.56]; HR of rPFS= 0.23 [95% CI, 0.12-0.43]
  - ✓ MAGNITUDE trial[6] (1st line NIRA+AAP vs AAP): HR of OS= 0.96 [95% CI, 0.57-1.63]; HR of rPFS= 0.53 [95% CI, 0.36-0.79]
- Based on reimbursement and market price, OLA and NIRA incur an **add-on annual cost** of around **NTD 1,700,000** and **NTD 865,000** compared with AAP.
- When a drug demonstrates superior efficacy yet comes at a higher cost, cost-effectiveness analysis is required to determine whether the treatment offers sufficient value for reimbursement.
- No related cost-effectiveness analysis studies have been published.

Objective

To assess the **cost-effectiveness** of olaparib/abiraterone/prednisolone, niraparib/abiraterone/prednisolone and abiraterone/prednisolone for **BRCA-mutated metastatic castration-resistant prostate cancer** from **Taiwan public payer** prospective.

Methods

- Population: mCRPC patients with BRCA mutation • Perspective: Public Payer
- Comparator arm: AAP • Treatment arm: OLA+AAP, NIRA+AAP
- Model: Treatment and control arms were constructed by different model types to better align with the reimbursement situation in Taiwan. A **30-year partitioned survival model for the treatment arm** and a **combined partitioned survival/state transition model for the control arm** were used. Models then divided memberships into **three and four states**, respectively.【**Figure 2**】
- Efficacy inputs: From **network meta-analysis** of clinical trials, which were **PROpel and MAGNITUDE trial**. Survival inputs of **PROfound trial** (second-line OLA vs abiraterone/enzalutamide) were then incorporated in the control arm through **state transition model**.【**Figure 1**】
  - ✓ KM plot was digitized using WebPlotDigitizer® and pseudo IPD were generated using the digitize function in the R® IPDfromKM package
  - ✓ Standard parametric (exponential, lognormal, Weibull, loglogistic, Gompertz and Gamma) and fractional polynomial models were fit to the clinical data.
  - ✓ For extrapolating survival beyond the trial, data was adjusted **by Taiwan general population mortality**. Fitness was assessed through looic and visualization.
- Cost inputs:
  - ✓ Drug acquisition cost: From Taiwan reimbursement and market price.
  - ✓ Health state cost: Collected from the Year. 2018~2022 of **National Health Insurance Research Database(NHIRD)**, Taiwan.【**Table 1, 2**】

Figure 1. Efficacy inputs

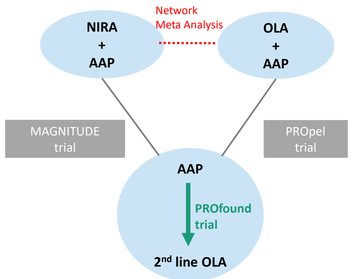


Table 1. Health state Cost and utility inputs

	Cost (NTD) From NHIRD	Utility (QALY)	Utility Source
rPF state (95% CI)	12,915 (11,357~14,472)	0.80 (SE= 0.021)	Rathkopf DE et al. Patient-reported outcomes in MAGNITUDE trial. Eur Urol. 2024.
PD state (95% CI)	57,000 (51,221~62,780)	0.63 (SE= 0.0643)	Castro E et al. Health state utility values in mCRPC: A systematic review and meta-analysis. Oncologist. 2024.
PD1 (95% CI)	31,844 (28,897~34,790)	0.70 (SE= 0.0714)	
PD2 (95% CI)	52,619.6 (39,643~65,595)	0.63 (SE= 0.0643)	
Palliative (95% CI)	93,592.64 (82,280~104,903)	0.5 (SE= 0.0549)	
Death	0	0	

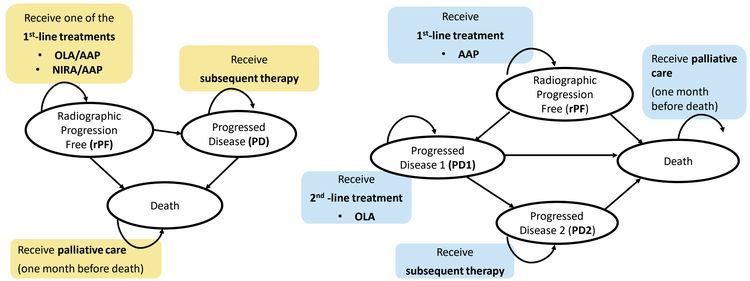
Methods (cont.)

- Utility inputs: From previous literature.【**Table 1**】
- A **30-year time horizon** and **1-month cycle length** were used, and a 3% discount rate was applied to costs and QALYs.
- Willingness-to-pay threshold: 3 times the per capita GDP, which is **3,032,670 NTD/QALY**

Table 2. Medication Cost

(Per cycle)	OLA + AAP	NIRA + AAP	AAP	2nd-line OLA
Medication Cost (NTD)	NTD 189,720	NTD 118,800	NTD 46,680	NTD 143,040

Figure 2. Model Construction



Results

- The modelled survival curves are shown in **Figure 3** and **Figure 4**.

Figure 3. OS, rPFS extrapolation and Kaplan-Meier curves of first-line treatments

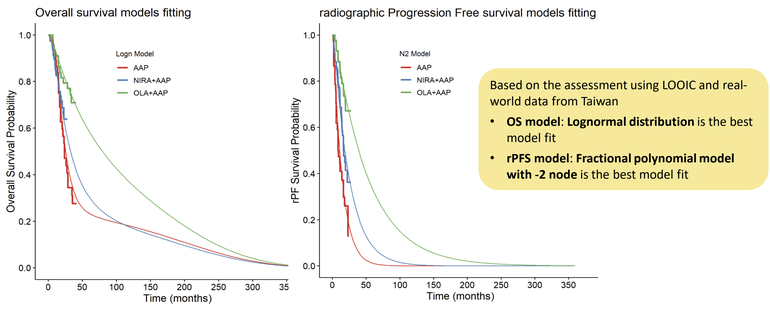
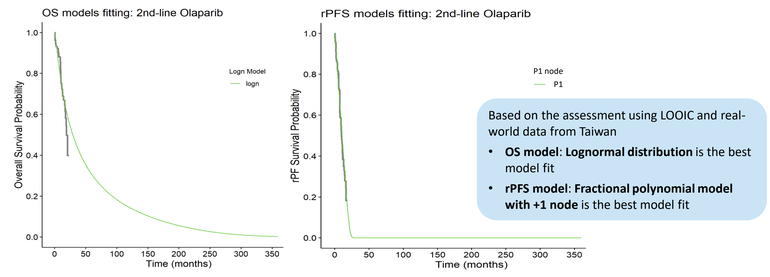


Figure 4. OS, rPFS extrapolation and Kaplan-Meier curves of 2nd-line OLA



- Based on data from the network meta-analysis of PROpel and MAGNITUDE trial, and also survival inputs from PROFOUND trial, the cost-effectiveness of three strategies are presented in **Table 3**.

Table 3. Cost-effectiveness of OLA+AAP, NIRA+AAP and 1st-line AAP with 2nd-OLA

Base Case	1st-line OLA+AAP vs 1st-line AAP	1st-line NIRA+AAP vs 1st-line AAP	1st-line OLA+AAP vs 1st-line NIRA+AAP
Inc Cost (NTD)	7,650,647	523,944	7,126,703
Inc QALYs	1.97	-0.06	2.67
ICER	4,384,160	Dominated	3,510,691

Results (cont.)

- Compare OLA+AAP vs AAP, top parameters that have the greatest impact on the result is the drug cost of olaparib.【**Figure 5A**】
- Compare OLA+AAP vs NIRA+AAP, top parameters that have the greatest impact on the result is also the drug cost of olaparib. And might will reverse the result.【**Figure 5B**】

Figure 5A. OLA+AAP vs AAP

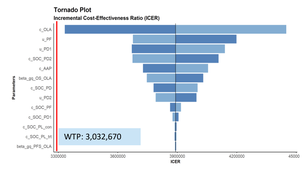
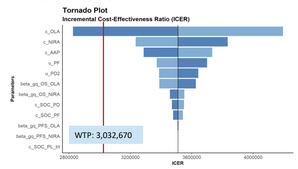


Figure 5B. OLA+AAP vs NIRA+AAP



- After 5,000 Monte Carlo simulations, when WTP threshold is below **3,790,000** NTD/QALY, 1st-line AAP with 2nd-line OLA is likely the most cost-effective treatment. At WTP threshold above, 1st-line OLA+AAP is likely the most cost-effective treatment.【**Figure 6**】

Figure 6A. CE acceptability curve

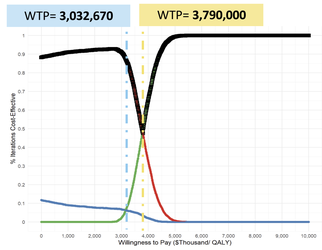
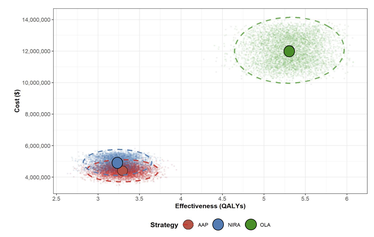


Figure 6B. CE plane scatterplot



- Scenario analysis-1: Despite model construction of three-state partitioned survival model, 1st line AAP remains the most cost-effective option.【**Table 4A**】
- Scenario analysis-2: If the price of OLA is reduced by 40%, OLA + AAP would become cost-effective compared to AAP alone.【**Table 4B**】

Table 4A. Scenario analysis: Cost-effectiveness of OLA+AAP, NIRA+AAP vs. 1st-line AAP

Scenario-1	1st-line OLA+AAP vs 1st-line AAP	1st-line NIRA+AAP vs 1st-line AAP	1st-line OLA+AAP vs 1st-line NIRA+AAP
Inc Cost (NTD)	11,759,907	1,925,204	7,126,703
Inc QALYs	2.36	0.85	2.03
ICER	3,830,647	6,016,263	3,494,050

Table 4B. Scenario analysis: Price Reduction of OLA (OLA+AAP vs AAP)

Price Reduction of OLA	10%	10%	30%	40%
ICER	3,613,605	3,333,695	3,053,785	2,773,875

Discussion

- The **strengths** of the analysis include incorporates official survival rate data of Taiwan in survival model selection process and real-world NHIRD cost data for localization purpose. And the condition of 2nd line OLA was considered.
- Key **limitations** of this study include the necessity of extrapolating short-term trial outcomes to a lifetime horizon, introducing uncertainty in the results. Additionally, the NHIRD lacks specific information to distinguish disease progression, requiring the use of a proxy operational definition as a substitute.
- Despite these limitations, sensitivity analyses suggest that results were robust to uncertainty in most model parameters.

Conclusion

Findings suggest that AAP is likely to be a cost-effective first-line treatment option for BRCA-mutated mCRPC from Taiwan public payer perspective.

References: 1. 2022 Taiwan Cancer Registry Report (2023). Health Promotion Administration. 2. Freedland SJ, Ke X, Lafeuille MH, et al. Identification of patients with metastatic castration-sensitive or metastatic castration-resistant prostate cancer using administrative health claims and laboratory data. Curr Med Res Opin. 2021;37(4):609-622. 3. Verry C, Vincendeau S, Massetti M, et al. Pattern of clinical progression until metastatic castration-resistant prostate cancer: An epidemiological study from the European Prostate Cancer Registry. Target Oncol. 2022;17(4):441-451. 4. Lozano R, Castro E, Aragón IM, et al. Genetic aberrations in DNA repair pathways: a cornerstone of precision oncology in prostate cancer. Br J Cancer. 2021;124(3):552–563. 5. Saad F, Clarke NW, Oya M, et al. Olaparib plus abiraterone versus placebo plus abiraterone in metastatic castration-resistant prostate cancer (PROpel): final overall survival results of a phase 3 trial. Lancet Oncol. 2023;24(10):1094-1108. 6. Chi KN, Sandhu S, Smith MR, Attard G, Saad M, Olmos D, Castro E, Roubaud G, Pereira de Santana Gomes AJ, Small EJ, Rathkopf DE, Gurney H, Jung W, Mason GE, Dibaj S, Wu D, Diorio B, Uttishak K, Del Corral A, Francis P, Kim W, Efstathiou E. Niraparib plus abiraterone acetate with prednisone in patients with metastatic castration-resistant prostate cancer and homologous recombination repair gene alterations: second interim analysis of the randomized phase III MAGNITUDE trial. Ann Oncol. 2023 Sep;34(9):772-782.