Cost-Effectiveness of Olaparib vs. Rucaparib for Patients With Metastatic Castration-Resistant Prostate Cancer – The Canadian Perspective

Ivan Yanev[1,2], Armen G. Aprikian[3], Brendan L Raizenne[4] and Alice Dragomir[3,5]

1. Centre for Outcomes Research and Evaluation, Research Institute of McGill University Health Centre, Montreal, QC H4A 3J1, Canada; 2. Experimental Surgery, McGill University, Montreal, QC H3A 0G4, Canada. 3. Division of Urology, Department of Surgery, McGill University, Montreal, QC H3A 0G4, Canada.4. Division of Urology, Centre Hospitalier de l'Université de Montréal, 900 St. Denis, Montréal, QC, H2X 0A9, Canada. 5. Faculty of Pharmacy, University of Montreal, 2940 Chem. de Polytechnique, Montréal, QC H3T 1J4, Canada.

PT44

Introduction

- Metastatic castration-resistant prostate cancer (mCRPC) is the terminal stage of prostate cancer (PCa) and is responsible for most PCa related deaths.
- Through phase III clinical trials, olaparib (ola) and rucaparib (ruca), (poly(adenosine diphosphate–ribose) polymerase inhibitors (PARPI) have demonstrated outcome improvements in mCRPC patients with alterations of BRCA1/2 who having progressed on second-generation androgen-receptor pathway inhibitor. While improving outcomes, ora and ruca contribute to the ever-growing economic burden of PCa. Cost-effectiveness analyses are needed to estimate their economic impact.

Objectives

- **Primary objective**: to evaluate the cost-effectiveness of ola and ruca versus physician's choice (docetaxel or ARPI) for mCRPC patients with BRCA1/2 mutations from a Canadian healthcare system perspective.
- **Secondary objective**: to propose a price that would satisfy local cost-effectiveness thresholds.

Methods

- **Model:** Partitioned survival analysis built in TreeAge Pro© (Figure 1)
- **Population:** mCRPC male patients with BRCA1/2 mutation who have progressed on ARPI
- **Survival inputs:** Extracted Kaplan-Meier survival curves from published clinical trials (PROFound and TRITON3)
- **PARPI treatments:** Ola and ruca
- **Comparators:** Doce (chemotherapy) & ARPI (mix of abiraterone [33.6%] and enzalutamide [66.4%])
- **Time horizon:** Patient lifetime (max 5 years)
- **Perspective:** Canadian healthcare system
- **Annual discount rate:** 1.5%
- **After progression:** Doce or cabazitaxel if doce was the initial treatment
- **Adverse events (AE):** Costs and disutility values were applied according to AE rates reported in clinical trials

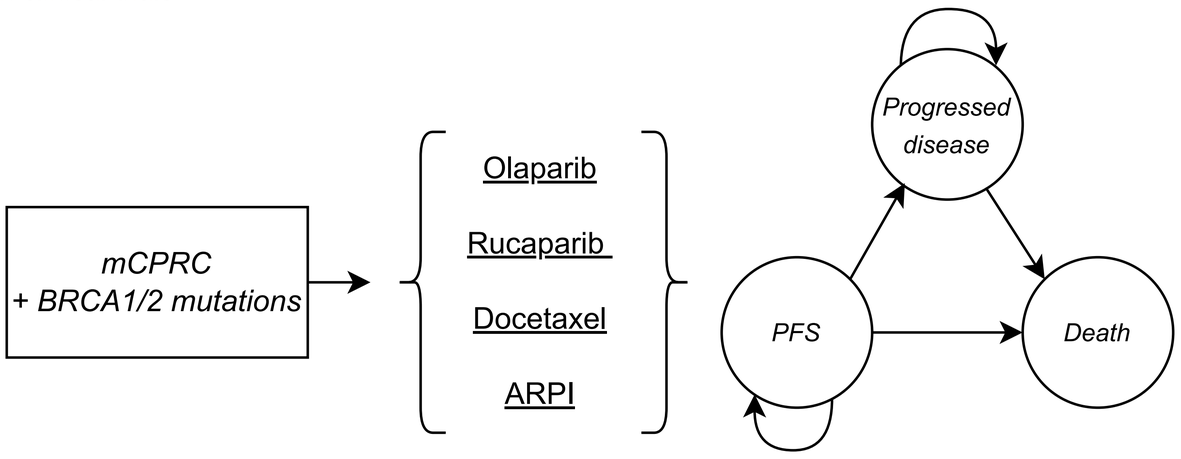

Figure 1. Partitioned Survival Model Structure

(mCRPC, metastatic castration-resistant prostate cancer; BRCA 1/2, breast cancer gene 1 or 2; ARPI, androgen receptor pathway inhibitors (abiraterone acetate with prednisone or enzalutamide); PFS, progression-free survival.)

Table 1. Population Characteristics (ARPI, androgen receptor pathway inhibitors; ECOG PS, Eastern Cooperative Oncology Group Performance Status)

Trial	PROFound		TRITON 3	
	Olaparib	ARPI	Rucaparib	ARPI + Doce
Age	68	67	70	71
Race (% white)			74%	76%
Gleason score 8+ (%)	67%	67%	64%	71%
Bone metastasis	35%	28%	87%	84%
Viceral metastasis	28%	39%	27%	34%
ECOG PS				
0	52%	41%	49%	50%
1	41%	55%	51%	50%
2	7%	4%		
Previous taxane use				
Docetaxel	46%	39%	23%	21%
Cabazitaxel	1%	0%		
Docetaxel + Cabazitaxel	18%	24%		
Previous NHT use				
Abiraterone	38%	35%	56%	59%
Enzalutamide	42%	48%	44%	45%
Abiraterone + Enzalutamide	20%	17%	0	0

- Medication and non-pharmaceutical costs were extracted from the Quebec Health Insurance Board medication list.
- Ruca is not commercially available in Canada. It was hypothesized that it will be priced on par with olaparib.
- Cost for adverse events were extracted from the Ontario Case Costing Initiative.
- Doce regiment was considered to be given for 6 cycles.

Table 2. Survival and Utility Inputs

Parameter name	Shape/ Mean log	Scale/rate/sdlog/sd	Distribution	Source
PFS curves				
Rucaparib	1.713	11.45	Log Logistic	Fizazi et al. 2023
Olaparib	0.086	0.0135	Gompertz	de Bono et al. 2020
ARPI	1.6579	0.8423	Log Normal	Fizazi et al. 2023
Docetaxel	1.9729	0.7646	Log Normal	Fizazi et al. 2023
OS curves				
Rucaparib	2.216	0.0805	Gamma	Fizazi et al. 2023
Olaparib	1.610	24.93	Weibull	de Bono et al. 2020
ARPI	1.766	25.974	Weibull	Fizazi et al. 2023
Docetaxel	1.766	25.974	Weibull	Fizazi et al. 2023
Utilities				
PFS	0.60	0.0615	Beta	Robson et al. 2017
PD	0.36	0.022	Beta	Robson et al. 2017

Results

- Ruca provides better survival benefit in terms of quality-adjusted life years (QALY) than ola, but at a higher cost (ICER $292,147/QALY).
- When compared to doce, ola and ruca provided additional 0.07 and 0.25 QALY, with additional costs of $78,246 and $129,547, resulting in ICERs of $1,078,005/QALY and $522,504/QALY, respectively.
- While ARPI was dominated by doce, it still remains a relevant option as some patients are unfit for chemotherapy.
- When compared to ARPI, ola and ruca demonstrated clinical benefit and ICERs of $612,655/QALY and $418,218/QALY respectively.

Table 3. Cost-Effectiveness Results

Strategy	Cost ($)	Incr Cost ($)	Eff (QALY)	Incr Eff (QALY)	ICER ($/QALY)
Docetaxel	$ 57,321		0.87		
ARPI	$ 66,048	$ 8,727	0.82	-0.04	Dominated
Olaparib	$ 135,667	$ 78,346	0.94	0.07	$ 1,078,005
Rucaparib	$ 186,868	$ 129,547	1.11	0.25	$ 522,504

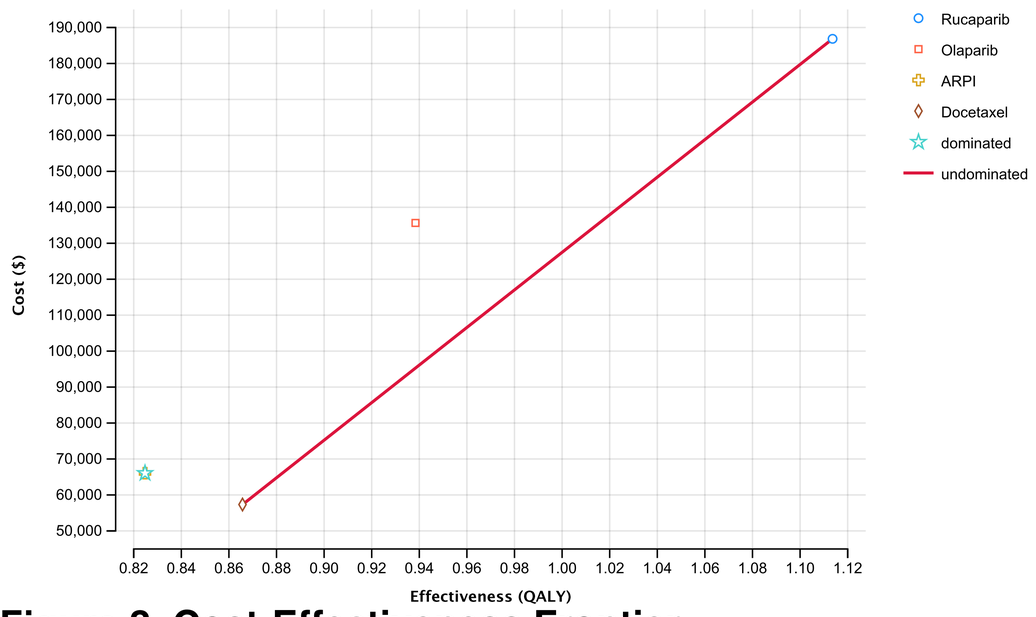

Figure 2. Cost-Effectiveness Frontier

Price threshold analysis:

- 150,000$/QALY threshold: reduction of 80% and 70% for olaparib's and rucaparib's prices, respectively.
- 100,000$/QALY threshold: reduction of 84% and 80% for olaparib's and rucaparib's prices, respectively.

Limitations

- TRITON3's population could potentially be more advanced (higher % of patients with bone metastasis)
- Controls in the two trials are not equivalent as the PROFOUND trial did not include docetaxel as an option for the standard of care.
- The choice of parametric model to extrapolate survival beyond reported time could incorporate an important bias.
- TRITON3 does not report PFS for the BRCA subgroup stratified by treatment, so an approximation was made using the ITT population.
- Drug acquisition price is the most important source of uncertainty.

Conclusions

While providing survival benefit to mCRPC patients presenting alterations of BRCA1/2 genes, the cost of ola and ruca requires major reductions to be considered cost-effective in the Canadian healthcare perspective. As the PARPI landscape is rapidly evolving with the arrival novel treatments aiming to target specific patient populations, further cost-effectiveness analyses are needed to optimize resource allocation.

Acknowledgements

100 DAYS ACROSS CANADA – CYCLING FOR PROSTATE CANCER RESEARCH
Prostate Cancer Canada
MOVEMBER® FOUNDATION
RQRM – RÉSEAU QUÉBÉCOIS DE RECHERCHE SUR LES MÉDICAMENTS

McGill

Contact

E-mail: Yanev.Ivan@mail.McGilll.ca

LinkedIn: ← Scan this