Cost Effectiveness Analysis of ^{68}Ga-PSMA-11 PET/CT Imaging Followed by ^{177}Lu-PSMA-617 versus Standard of Care in Metastatic Castrate Resistant Prostate Cancer

Barman P[1], Gupta A[1], Papadopoulos G[2], Aristides M[2], Rathi H[1]
[1]Skyward Analytics, Gurugram, India, [2]Lucid Health Consulting, Sydney, Australia

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INTRODUCTION

- **Metastatic castration-resistant prostate cancer (mCRPC)** poses a significant clinical challenge with poor prognosis, affecting over **90,000** Australian men and accounting for over **3,000** cancer-related deaths annually in Australia[1]
- **^{68}Ga-PSMA-11** is a radiotracer for early detection of prostate-specific membrane antigen (PSMA)-expressing cells, while **^{177}Lu-PSMA-617** is a radioligand therapy that selectively targets these cells
- This study aims to assess the cost-effectiveness of **^{68}Ga-PSMA-11 PET/CT** imaging followed by **^{177}Lu-PSMA-617** therapy compared to cabazitaxel or best supportive care (BSC), in mCRPC patients from an Australian healthcare perspective

METHOD

A cost-utility model was developed in Microsoft Excel, using a hybrid model approach which included a decision tree and Partitioned Survival Model (PSM) component from an Australian healthcare system perspective

Model Structure

- Decision Tree Component: This initial component identifies patients eligible for ^{177}Lu-PSMA-617therapy based on ^{68}Ga-PSMA-11 PET/CT imaging **(Figure 1)**
- Partitioned Survival Model (PSM): Following the decision tree, a three-state PSM was employed, modeling patient progression through Progression-Free Survival (PFS), Progressive Disease (PD), and Death **(Figure 2)**

Figure 1. Decision Tree Model Structure

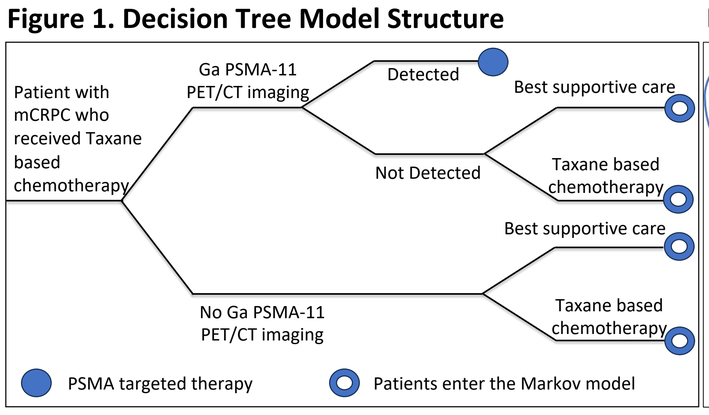
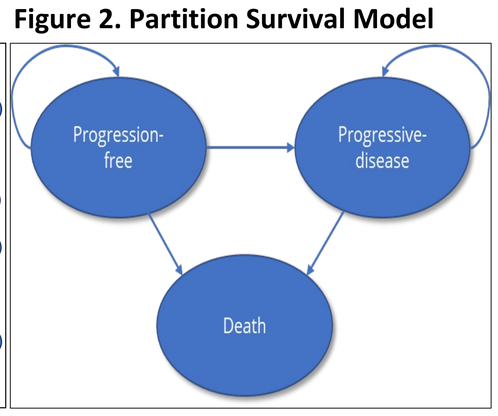


Figure 2. Partition Survival Model



Abbreviations: CT, Computed Tomography; mCRPC, Metastatic castrate resistant prostate cancer; PET, Positron Emission Tomography; PSMA, Prostate-Specific Membrane Antigen.

- **Time horizon**: 10 years
- **Cycle length**: 1 week
- **Discount rate**: Costs and outcomes were discounted at 5%[2]
- **Model outcomes**: Costs, Quality-adjusted life years (QALYs), and ICER
- **Source of efficacy data**: PFS and OS data were sourced from the VISION[3] and TheraP[4] trials for cabazitaxel and BSC comparators, respectively. For the estimation of OS and PFS, Kaplan–Meier (K–M) estimates were used for the initial period of the analysis, applying a 10% 'patients at risk' cut-off to account for uncertainty at the tail of the K–M curve. This was followed by extrapolation using parameterized survival curves
- Costs, utilities, and adverse events were sourced from national reimbursement schedules, prior MSAC submission, and published literature

Table 1 provides a summary of costs and utility inputs used in the model

Table 1. Key Costs and Utility Inputs

Input Parameter	Base Case Value	Source/Assumption
Patient Flow (Decision Tree)		
PSMA Positivity Rate (eligibility for ^{177}Lu-PSMA-617 after imaging)	90%	TheraP trial (Hofman et al., 2021)[4]
Costs (Australian Healthcare System Perspective)		
^{68}Ga-PSMA-11 PET/CT Imaging	AU$1,400 (per scan)	MBS code: 61563/61564[5] TBC (61505 MBS code)
^{177}Lu-PSMA-617 Therapy	AU$6,000 (per 6-week cycle)	MSAC 1686 Submission PSD[6]
^{177}Lu-PSMA-617 Therapy Admin Cost	AU$2,000 (per 6-week cycle)	MSAC 1686 Submission PSD[6]
Cabazitaxel Acquisition Cost	AU$299.21 (per 3-week cycle)	PBS[7]
Cabazitaxel Administration Cost	AU$118.30 (per cycle)	MBS code: 13950[5]
AE Management Costs (e.g., Fatigue, Anemia, Pain)	Varies by AE type (e.g., AU$4,470.84 for Fatigue)	NHCDC[8], AR-DRG 11.0, 2020-21[9]
Disease Management (Monitoring) Costs	Varies by service (e.g., Outpatient visit: AU$46.15)	MBS Handbook[5]; NICE Submission (TA712) for frequency[10]
Terminal Care Cost	AU$2,028 (per week)	Langton et al., 2016[11] (inflated to 2023 AUD using Australian CPI)
Utilities (HRQoL)		
PFS	0.74	MSAC 1686 Submission PSD[6]
PD	0.59	MSAC 1686 Submission PSD[6]
AE Disutilities (e.g., Fatigue: -0.13)	Varies by AE type	Lloyd et al., 2006[12]; Nafees et al., 2008[13]

Abbreviations: AE, Adverse Event; AU$, Australian Dollars; CPI, Consumer Price Index; ERG, Economic Review Group; HRQoL, Health related quality of life; MBS, Medicare Benefits Schedule; MSAC, Medical Services Advisory Committee; NHCDC, National Hospital Cost Data Collection Report; NICE, National Institute for Health and Care Excellence; PBS, Pharmaceutical Benefits Scheme; PD, Progressive Disease; PFS, Progression-Free Survival; PSD, Public Summary Document.

FUNDING This study did not receive any funding, and the authors declare no conflicts of interest

RESULTS

Base Case Cost-Effectiveness

The base case analysis, conducted from an Australian healthcare system perspective over a 10-year time horizon with a 5% annual discount rate for both costs and outcomes, demonstrates that ^{177}Lu-PSMA-617 therapy is more effective but also more costly compared to the standard of care options **(Table 2)**

- ^{177}Lu-PSMA-617 vs. Cabazitaxel: ^{177}Lu-PSMA-617 yielded an incremental 0.143 QALYs at an incremental cost of AU$29,023, resulting in an ICER of AU$203,014/QALY gained
- ^{177}Lu-PSMA-617 vs. BSC: ^{177}Lu-PSMA-617 yielded an incremental 0.342 QALYs at an incremental cost of AU$37,687, resulting in an ICER of AU$110,050/QALY gained
- ^{177}Lu-PSMA-617 vs. Weighted comparator: ^{177}Lu-PSMA-617 yielded an incremental 0.193 QALYs at an incremental cost of AU$31,189, resulting in an ICER of AU$161,741/QALY gained

Table 2. Summary of Base Case Cost-Effectiveness Results

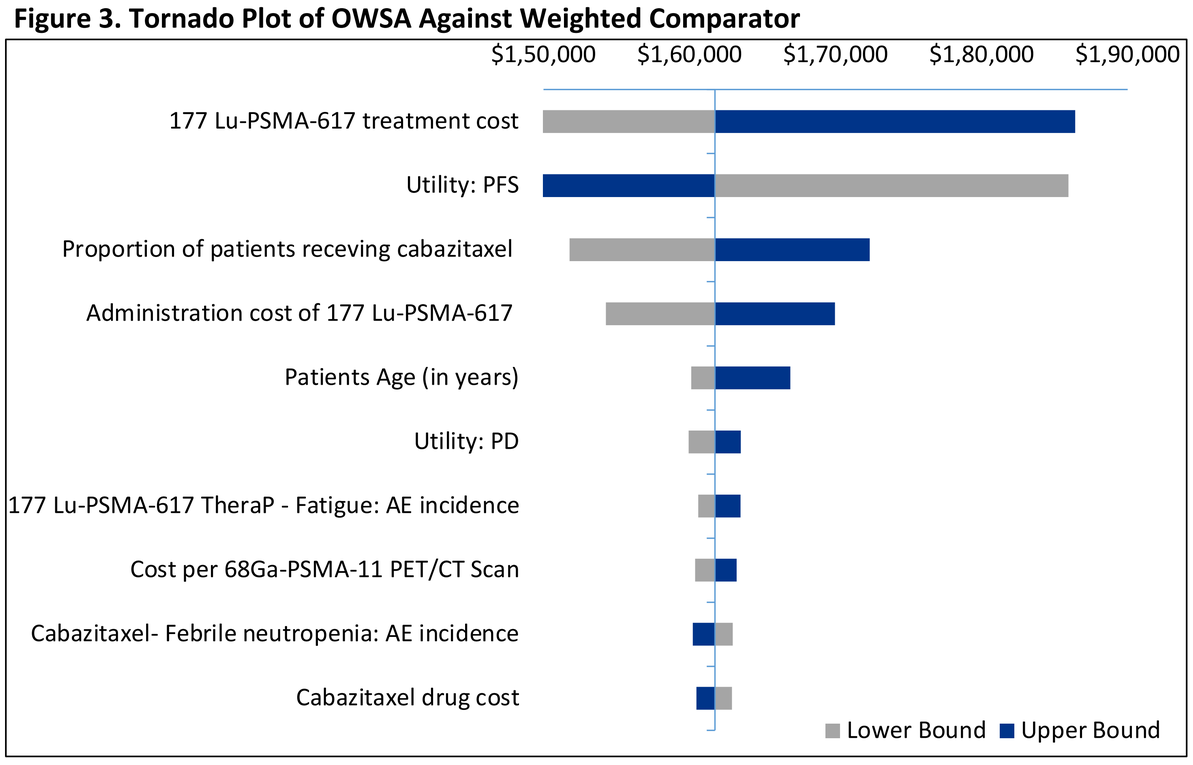
Parameter	^{177}Lu-PSMA-617	Comparator	Incremental	ICER
Vs. Cabazitaxel (TheraP Trial Population)				
Total Cost	AU$40,385	AU$11,362	AU$29,023	
LYs	1.906	1.707	0.199	AU$145,783
QALYs	1.220	1.077	0.143	AU$203,014
Vs. BSC (VISION Trial Population)				
Total Cost	AU$43,871	AU$6,184	AU$37,687	
LYs	1.724	1.292	0.432	AU$87,329
QALYs	1.165	0.822	0.342	AU$110,050
Vs. Weighted Comparator (75% Cabazitaxel, 25% BSC)				
Total Cost	AU$41,257	AU$10,067	AU$31,189	
LYs	1.861	1.603	0.257	AU$121,263
QALYs	1.206	1.013	0.193	AU$161,741

Abbreviations: AU$, Australian dollar; BSC, Best supportive care, ICER, Incremental cost-effectiveness ratio; LYs, Life years; QALYs, Quality-Adjusted Life-Years.

One-Way Sensitivity Analysis (OWSA)

OWSA was conducted to identify key drivers of uncertainty by systematically varying individual model input parameters relative to a weighted comparator (**Figure 3**). The ICER was most sensitive to variations in the cost of ^{177}Lu-PSMA-617 treatment, followed by the PFS utility value and the proportion of patients receiving cabazitaxel

Figure 3. Tornado Plot of OWSA Against Weighted Comparator



Abbreviations: AE; Adverse events; CT: Computed tomography; PD: Progressive disease; PET, Positron Emission Tomography; PFS: Progression free survival; PSMA, Prostate-Specific Membrane Antigen.

Overall, the model was robust with respect to multiple parameters tested under plausible sensitivity analyses with small or moderate changes to the ICER from the base case

CONCLUSIONS

- Improved Clinical Outcomes: ^{68}Ga-PSMA-11 PET/CT imaging followed by ^{177}Lu-PSMA-617 therapy demonstrates improved progression-free and overall survival for patients with mCRPC compared to standard of care, with a manageable safety profile[14]
- Cost-Effectiveness & Value: While associated with higher costs, the therapy offers significant QALY gains. ICER needs to be considered within the context of Australia's willingness-to-pay thresholds and the evolving pricing landscape of radioligand therapy[15]

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