CO48

Population Impact of Performing HRR Testing for Guiding Metastatic Castration-Resistant Prostate Cancer (mCRPC) Treatment in the US

Authors: Annika Bjerke[1], Berra Patterson[1], Michael Zielinkski[2], Neo Su[2], Allison Thompson[2], Yang Meng[1]

[1]Lumanity, Bethesda, Maryland, USA; [2]Pfizer, Inc., New York, New York, USA

INTRODUCTION

- Talazoparib (an oral poly ADP-ribose polymerase [PARP] inhibitor, PARPi) in combination with enzalutamide (an androgen receptor pathway inhibitor) was approved by the FDA in June 2023 as first-line treatment for homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC) population based on superior efficacy over enzalutamide in the TALAPRO-2 trial (NCT03395197)[1,2,3]
  - Radiographic progression-free survival (rPFS): hazard ratio (HR) = 0.45 (95% confidence interval [CI], 0.33-0.61; P < 0.0001)
  - Overall Survival (OS): HR = 0.69 (95% CI, 0.46 to 1.03; P = 0.07)
- Currently, HRR testing rates are low (around 18.2% globally and 38.2% in the US)[4], which limits the use of more effective targeted treatments (e.g. talazoparib + enzalutamide) for HRR-deficient patients. Additionally, although HRR test is commercially available, none are currently FDA-approved[5]

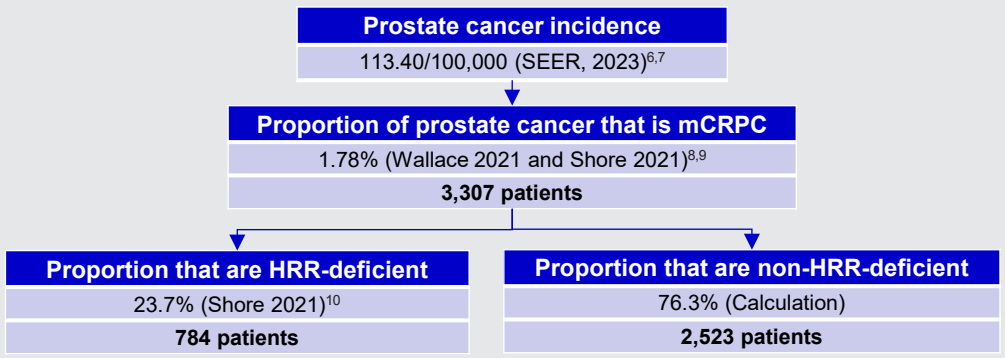
OBJECTIVES

To assess the US population-level clinical impact (total additional life years [LYs] and quality adjusted life years [QALYs]) of performing HRR testing, versus no HRR testing, to guide first-line treatment for patients with mCRPC

METHODS

Epidemiological data estimated the total incident mCRPC patients and the number of HRR-deficient and non-HRR-deficient patients in the US in 2024 (Figure 1)

Figure 1. US mCRPC cohort



Note: The proportion of HRR-deficient in mCRPC estimated in the US (23.7%) is similar to the proportion in TALAPRO-2 (21.0%)

A model was developed for talazoparib + enzalutamide in first line mCRPC for the all-comers and HRR-deficient patient populations using a partitioned survival modeling approach based on rPFS and OS

- Parametric survival models were fitted to patient-level data from TALAPRO-2
- HRs for other treatments were estimated from indirect treatment comparisons (ITC)
- Health state utilities were derived from EQ-5D-5L data in TALAPRO-2

The model was used to assess two testing strategies: no HRR testing and universal HRR testing (Table 1)

Table 1. Testing and treatment strategies

	No HRR Testing	Universal HRR Testing	
Population	All (all-comers)	Non-HRR-deficient	HRR-deficient
Treatments	Non-targeted treatments: enzalutamide, abiraterone, or docetaxel (based on market share)		PARPi-based treatment (represented by talazoparib + enzalutamide)
The impact of testing is the difference between two strategies in terms of patient or population LYs and QALYs			

Universal Testing, HRR-deficient

- LY and QALY results for talazoparib + enzalutamide were directly obtained from the model

Universal testing, non-HRR deficient treated with enzalutamide

- Market shares, enzalutamide 35%, abiraterone, 45%, docetaxel, 20%, were based on literature[11]
- rPFS and OS were estimated for non-HRR-deficient patients treated with enzalutamide versus HRR-deficient patients treated with enzalutamide using patient-level data from TALAPRO-2
  - rPFS HR = 0.66 (95% CI, 0.47-0.91)
  - OS HR = 0.73 (95% CI, 0.52-1.04)

Universal testing, non-HRR-deficient treated with abiraterone or docetaxel

- rPFS and OS HRs (based on network meta-analysis) for these treatments vs. enzalutamide were applied to rPFS and OS for non-HRR-deficient patients to estimate rPFS, OS and the resulting LYs and QALYs
- Abiraterone vs enzalutamide: rPFS HR = 1.64; OS HR = 1.21
  - Docetaxel vs enzalutamide: rPFS HR = 1.07; OS HR = 0.90
- HRs were from all-comers in the NMA as non-HRR-deficient-specific HRs were unavailable

No testing, all-comers

- LYs and QALYs for all-comers were weighted averages of outcomes of HRR-deficient (23.7%) and non-HRR-deficient treatments (76.3%)
- Non-HRR-deficient LYs and QALYs: previously described
- HRR-deficient treated with enzalutamide or abiraterone LYs and QALYs: based on the model
- HRR-deficient treated with docetaxel LYs and QALYs: derived similarly to non-HRR-deficient, the rPFS and OS for docetaxel vs enzalutamide (HR = 1.07 and 0.9, respectively) were applied

Table 2. Summary outcomes of LYs and QALYs by population, testing strategy, and treatment

Testing Strategy	Population	LYs/QALYs			
		Talazoparib + enzalutamide	Enzalutamide (35%)	Abiraterone (45%)	Docetaxel (20%)
Universal HRR Testing	HRR-deficient	3.56 / 2.59	N/A	N/A	N/A
	Non-HRR-deficient	N/A	3.49 / 2.45	3.10 / 2.07	3.73 / 2.56
No HRR Testing	All-comers	N/A	2.87 / 1.94	2.32 / 1.64	3.07 / 2.03

RESULTS

The universal testing strategy provides 0.21 LY and 0.18 QALY gains per mCRPC patient over lifetime (Table 3).

For the 2024 US population cohort, the total lifetime clinical benefits are 700 additional LYs and 599 additional QALYs (Table 3)

Table 3. Summary of model results

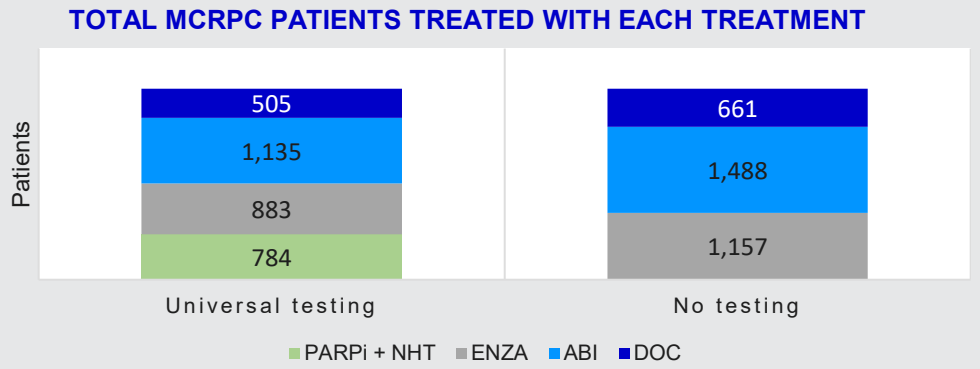
Impact of HRR testing – patient level results

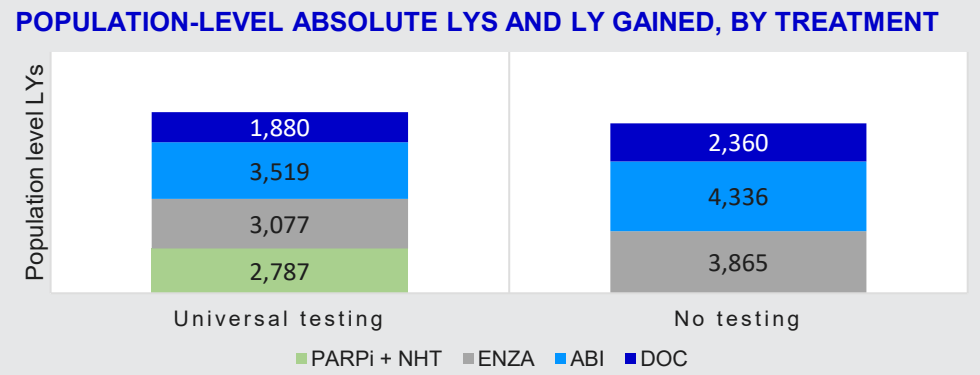
Testing Strategy	LYs	QALYs
Universal Testing	3.41	2.37
No testing	3.19	2.19
Incremental	**0.21**	**0.18**

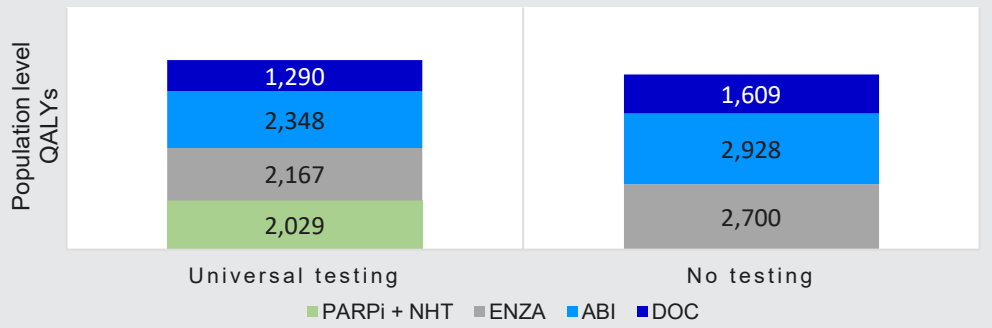
Impact of HRR testing – population level results

Testing Strategy	LYs	QALYs
Universal Testing	11,262	7,835
No testing	10,562	7,236
Incremental	**700**	**599**

Figure 2. Population level model results by testing strategy and treatments received







Key: TALA + ENZA, talazoparib in combination with enzalutamide; ABI abiraterone; DOC, docetaxel.

CONCLUSIONS

- The universal HRR testing strategy results in substantial population-level clinical benefit by identifying HRR-deficient patients who would benefit from targeted PARPi-based treatments including talazoparib with enzalutamide
- HRR testing should be performed for mCRPC patients to improve population-level health benefits in the US

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