

# Population Impact of Performing *BRCA1/2* Testing to Guide Metastatic Castration-Resistant Prostate Cancer Treatment in Spain

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## Objective

To evaluate the population-level clinical impact in Spain measured in total additional life-years (LYs) and quality-adjusted life-years (QALYs) of implementing *BRCA1/2* testing versus no *BRCA1/2* testing to guide first-line treatment decisions with talazoparib plus enzalutamide for patients with mCRPC based on TALAPRO-2 data.



## Context

Talazoparib plus enzalutamide is currently reimbursed by the National Health System in Spain only for mCRPC patients with *BRCA1/2* mutations (germline and/or somatic). According to literature, approximately 10% of mCRPC patients have *BRCA1/2* mutations.

## Background

- Poly ADP-ribose polymerase inhibitors (PARPi) have changed the treatment paradigm for metastatic castration-resistant prostate cancer (mCRPC), and currently, *BRCA1/2* and HRR germline and somatic testing are recommended in clinical guidelines for these patients.
- Talazoparib (TALA), a PARPi, with enzalutamide (ENZ, an androgen-receptor pathway inhibitor [ARPi]) showed statistically significant benefit in overall survival (OS) over ENZ in the TALAPRO-2 (TP-2) trial, including the *BRCA1/2* subgroup<sup>1,2,3</sup>.

## Materials and Methods

A partitioned survival model informed by OS, radiographic progression-free survival (rPFS), and health utilities. Epidemiological data provided frequency of *BRCA1/2* mutation (10%) patients<sup>4</sup> (Figure 1).

Two strategies compared: no testing and universal germline and somatic *BRCA1/2* testing in mCRPC patients in Spain (Table 1).

### Universal *BRCA1/2* testing in mCRPC:

- BRCA1/2* mutated (BRCAm) patients** rPFS and OS were estimated via parametric survival models fitted to TP-2 data for TALA + ENZ.
- Non-BRCAm patients** rPFS and OS were based on hazard ratios (HRs) from TP-2 data for ENZ and indirect treatment comparisons (ITCs) for abiraterone (ABI), and docetaxel (DOC).

### rPFS and OS estimation for non-BRCAm patients

ENZ	ABI	DOC
HRs estimated for non-BRCAm vs BRCAm based on TP-2 data.	HRs ABI vs non-BRCAm ENZ from ITC. <sup>5</sup>	HRs DOC vs non-BRCAm ENZ from ITC. <sup>5</sup>
rPFS HR = 0.48 (95% CI: 0.309, 0.755)	ABI vs ENZ: rPFS HR = 1.42 (95% CI: 1.15, 1.77)	DOC vs ENZ: rPFS HR = 1.04 (95% CI: 0.50, 2.54)
OS HR = 0.60 (95% CI: 0.365, 0.971)	OS HR = 1.21 (95% CI: 0.97, 1.51)	OS HR = 1.90 (95% CI: 1.34, 2.72)

### No testing, unselected patients treated with ENZ, ABI, or DOC:

- The life years (LY) and quality-adjusted life years (QALY) were calculated as the weighted average of the outcomes for BRCAm and non-BRCAm patients.
- BRCAm results were based on TP-2 data for ENZ and ITCs for ABI and DOC.

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

## Results

The analysis estimated 7,543 newly diagnosed mCRPC patients on active treatments in Spain in 2024, of which 754 are estimated to be BRCAm according to literature<sup>4</sup> (Figure 2).

- Over a lifetime, universal *BRCA1/2* testing in mCRPC would provide 0.25 LY and 0.24 QALY gains per mCRPC patient versus no testing (Table 3).
- For patients with mCRPC, universal *BRCA1/2* testing in mCRPC would yield additional 1,909 LYs and 1,793 QALYs over lifetime versus no testing (Table 3, Figure 3).

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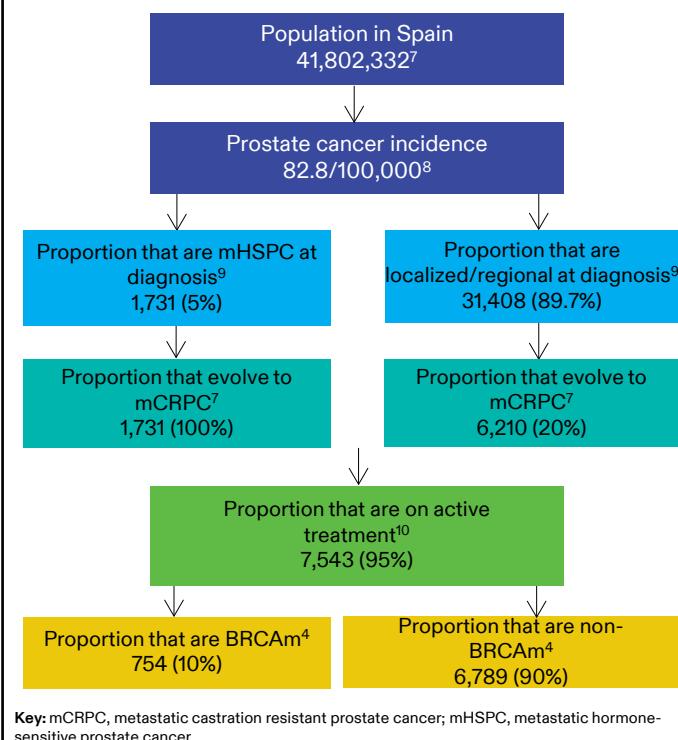
**Table 1. mCRPC testing and treatment analysis**

	No <i>BRCA1/2</i> testing	Universal <i>BRCA1/2</i> testing	
Population	Unselected patients	Non-BRCAm	BRCAm
Treatment	Non-targeted treatments: ENZ (35%), ABI (37%), or DOC (28%) <sup>6</sup>		Targeted treatment: TALA + ENZ

Note: The impact of testing is the difference between two strategies regarding patient-level or population-level LYs and QALYs.

Key: ABI, abiraterone; DOC, docetaxel; ENZ, enzalutamide; LY, life year; mCRPC, metastatic castration resistant prostate cancer; QALY, quality adjusted life year; TALA, talazoparib.

**Figure 1. Spain mCRPC patient cohort**



Key: mCRPC, metastatic castration resistant prostate cancer; mHSPC, metastatic hormone-sensitive prostate cancer.

**Table 3. Summary of model results**

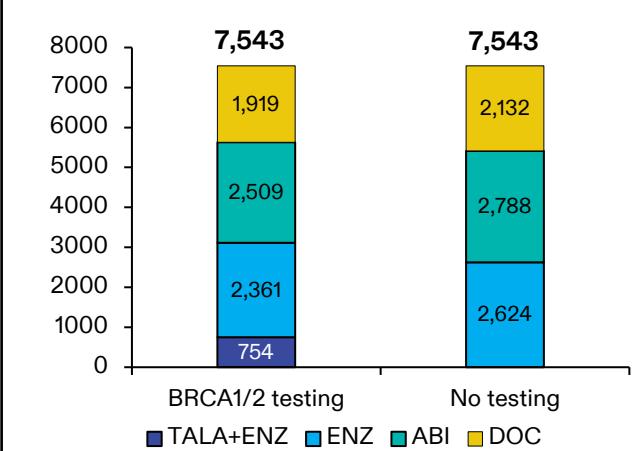
Impact of <i>BRCA1/2</i> testing – patient-level		
Testing strategy	LYs	QALYs
<i>BRCA1/2</i> testing	4.01	2.98
No testing	3.76	2.74
Incremental	0.25	0.24

Impact of <i>BRCA1/2</i> testing – population-level		
Testing strategy	LYs	QALYs
<i>BRCA1/2</i> testing	30,248	22,489
No testing	28,338	20,696
Incremental	1,909	1,793

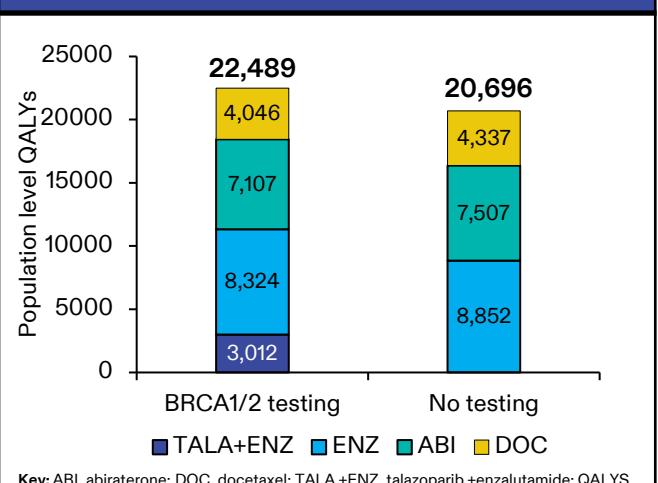
Key: LYs, life years; QALYs, quality adjusted life years.

**Figure 2. Total mCRPC patients treated with each first-line treatment**



Key: ABI, abiraterone; DOC, docetaxel; mCRPC, metastatic castration resistant prostate cancer; TALA+ENZ, talazoparib +enzalutamide.

**Figure 3. Population-level QALYs by treatment**



Key: ABI, abiraterone; DOC, docetaxel; TALA+ENZ, talazoparib +enzalutamide; QALYs, quality-adjusted life-years.

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

Population	LYs/QALYs			
	TALA+ENZ	ENZ	ABI	DOC
BRCAm (10%)	4.92 / 3.99	3.05 / 2.01*	2.18 / 1.44*	1.86 / 1.36*
Non-BRCAm (90%)	N/A	4.75 / 3.53	4.02 / 2.83	2.73 / 2.11
Unselected patients	N/A	4.58 / 3.37	3.83 / 2.69	2.64 / 2.03

Note: \*These values are only used as inputs in the no *BRCA1/2* testing strategy to calculate the weighted average of the outcomes with non-targeted treatments for BRCAm and non-BRCAm patients.

Key: ABI, abiraterone; DOC, docetaxel; ENZ, enzalutamide; LYs, life years; QALYs, quality adjusted life years; TALA, talazoparib.

## Conclusions



- A universal *BRCA1/2* testing approach in prostate cancer yields meaningful clinical gains at the population-level by detecting *BRCA1/2*-deficient patients who would benefit from a targeted PARPi-based treatment with talazoparib in combination with enzalutamide.
- These results support implementing universal germline and somatic testing of *BRCA1/2* alterations for all mCRPC patients in Spain to enable optimal, personalized treatment.