EE418

Estimating Costs Avoided by Preventing Recurrences with a BRCA Testing Strategy in High-Risk HER2-negative Adjuvant Breast Cancer Patients in Spain

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Background

- Breast cancer management has become increasingly individualized with the identification of key biomarkers such as HER2, BRCA mutations, and hormone receptors (HR), all critical in guiding therapeutic decisions and prognostic assessment.
- Patients with gBRCAm often present with more aggressive disease biology and distinct clinicopathological features, which substantially increase their risk for developing both breast and ovarian cancer[1].

Objectives

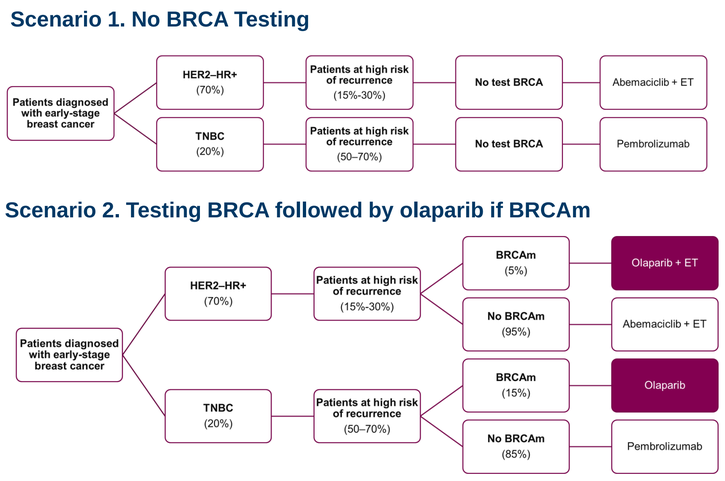
This study present two main objectives:

1) to estimate the clinical benefit, in terms of avoided cancer recurrences, of performing BRCA mutation (BRCAm) testing at the time of adjuvant therapy selection in high-risk HER2-negative breast cancer patients in Spain, followed by olaparib treatment for gBRCAm patients, versus a scenario without BRCA testing
2) To quantify the direct and indirect costs associated with these avoided recurrences and their impact to the Spanish National Health System.

Methods

- A health-economic model was developed based on the annual incidence of breast cancer in Spain (37,682)[2], a cohort in which ≈90% of the new cases are detected in early stage[3].
- According to histological subtype classification of breast cancer, approximately 70% of cases are hormone receptor–positive (HR+)[4], while up to 20% are classified as triple-negative breast cancer (TNBC)[4].
- The prevalence of BRCA mutations varies significantly according to breast cancer subtype, with approximately 5% of patients with HR+[5] tumors and about 15% of those with TNBC[6].
- The model utilizes a decision tree to compare two scenarios for patients considered at high risk of recurrence: a scenario without BRCA testing, where high-risk HER2-negative, HR+ patients receive abemaciclib + endocrine therapy (ET) and TNBC patients receive pembrolizumab as adjuvant therapies (Scenario 1); and a second one including BRCA testing, in which identified patients with gBRCAm receive adjuvant olaparib +/- ET and patients with non-BRCAm received abemaciclib + ET or pembrolizumab (Scenario 2) as represented in Figure 1.

Figure 1. Testing strategies and associated treatments



- The model structure and the underlying assumptions were validated by a panel of four medical oncology experts representing different regions of Spain.
- The difference in the number of recurrences between these strategies was calculated using the proportion of patients without disease progression (endpoints EFS and iDFS) after 4 years retrieved from the clinical trials OlympiA[7], MonarchE[8] and KEYNOTE-522[9].
- Given that, in the abemaciclib and pembrolizumab clinical trials, populations were not pre-stratified by BRCA mutation status, an efficacy adjustment for the BRCAm population was conducted for these therapies. This adjustment was based on the progression-free survival hazard ratios extracted from observational studies in metastatic populations[10,11], as well as the efficacy outcomes observed in the pivotal trials (MonarchE and KEYNOTE-522, respectively).
- Efficacy assumptions reflected in Table 1 were validated by the expert panel.

Table 1. Proportion of Patients Free (iDFS/EFS) from Recurrence at Year 4

Treatment and patient profile	HER2- HR+		TNBC	
	ITT	BRCAm	ITT	BRCAm
Olaparib +/- ET	Not applicable	82.9%	Not applicable	83.1%
Abemaciclib + ET	86.0%	76.9%	Not applicable	
Pembrolizumab	Not applicable		82.5%	75.2%

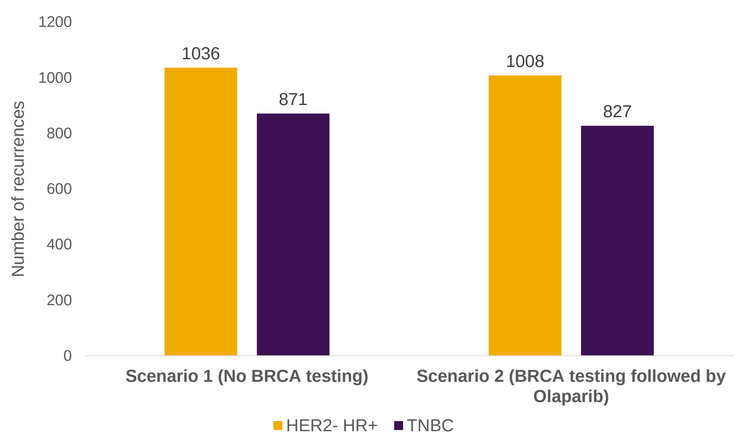
- Once the difference in the number of recurrences between both strategies was calculated, the associated cost of those recurrences in terms of direct and indirect costs for the Spanish National Health System (NHS) and society was estimated.
- Regarding the economic parameters: all the analysis were conducted using list prices of the drugs; and direct and indirect costs were extracted from literature and adjusted for inflation to € 2025 values.

Results

Recurrences avoided by BRCA testing

Implementing BRCA testing followed by treating patients with gBRCAm with olaparib **prevented a total of 72 recurrences** (28 corresponding to HR+ HER2- and 44 corresponding to TNBC) compared to a scenario of not performing BRCA testing.

Figure 2. Number of recurrences at year 4 by molecular subtype



Those recurrences were classified as locally advanced or metastatic based on the distribution presented in Table 2.

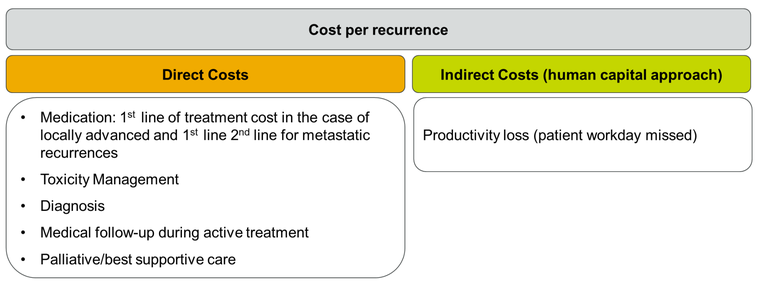
Table 2. Distribution of avoided recurrences at year 4 by type and molecular subtype

	Type of recurrence	Distribution	Number of avoided recurrences
HER2- HR+[12]	Locally advanced	18%	5
	Metastatic	82%	23
TNBC[13]	Locally advanced	25%	11
	Metastatic	75%	33

Economic impact of the avoided recurrences

The economic impact of avoided recurrences for the healthcare system was estimated by including both direct healthcare costs and indirect costs resulting from patients' loss of work productivity (Figure 3). The cost inputs used in this analysis were derived from two published economic studies[14,15] and adjusted for inflation to reflect values in euros (€, 2025).

Figure 3. Breakdown of cost items included in the calculation of total cost per recurrence



The **estimated cost per recurrence varied, from €15,561 to €243,434**, depending on the clinical type of recurrence and the molecular subtype (Table 3)

Table 3. Total cost per recurrence by type and molecular subtype and avoided costs from BRCA testing

	Type of recurrence	Total cost per recurrence	Nº of avoided recurrences	Avoided costs
HER2-HR+	Locally advanced	€79,067	5	€395,336
	Metastatic	€243,434	23	€5,598,972
TNBC	Locally advanced	€15,561	11	€171,175
	Metastatic	€77,698	33	€2,564,024

- The implementation of BRCA testing followed by the subsequent treatment of patients with gBRCAm with olaparib **resulted in savings of more than €12.3M for the system**.
- Savings were attributable to both the reduced direct and indirect costs associated with avoided recurrences (€8.7M) and lower treatment costs in the adjuvant phase in the scenario with olaparib (€3.6M), as reflected in Table 4.

Table 4. Savings for the Spanish System of implementing BRCA testing followed by olaparib if BRCAm

Adjuvant treatment cost	Avoided Recurrences	Total savings for Spanish National Health System
€3,629,459	€8,729,507	**€12,358,96**

Limitations

- Lack of solid evidence of abemaciclib and pembrolizumab in patients with gBRCAm.
- Possible overestimation of drug costs as pharmacological costs were calculated using list prices, which may exceed actual expenditures.
- Management in post-recurrence reflects an average of the currently available options, which could vary with new therapies and evolving patterns of use for currently available therapies.

Conclusions

- Implementing BRCA testing and treating patients with gBRCAm with olaparib prevented a total of 72 recurrences compared to a scenario of not performing BRCA testing.
- These avoided recurrences translate to an estimated total cost saving of €12.3M million for the Spanish National Health System.

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