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Cost-Effectiveness of a Genomic Profiling Test for HRD Determination in Ovarian Cancer Into the Current Clinical Practice for Platinum-Sensitive Patients With Advanced Ovarian Cancer in Greece

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Background & Objective

Platinum-sensitive advanced ovarian cancer patients represent a distinct subgroup within the broader ovarian cancer population. These individuals have previously responded well to platinum-based chemotherapy, typically experiencing a period of disease remission following treatment. However, their cancer ultimately recurs, necessitating subsequent lines of therapy. Homologous recombination deficiency (HRD) status plays a pivotal role in the management of these patients. HRD refers to a state in which the DNA repair mechanisms within cancer cells are impaired, leading to increased vulnerability to DNA damage. Research has demonstrated that HRD status is a critical determinant of therapeutic response in ovarian cancer [1]. Patients with HRD-positive tumors tend to exhibit enhanced sensitivity to certain treatment approaches, including poly (ADP-ribose) polymerase (PARP) inhibitors, which have emerged as a promising therapeutic option for this group. Genomic Profiling Test for HRD Determination provide a comprehensive assessment of HRD status by analyzing various genomic alterations and molecular markers. Identifying HRD-positive patients through these tests enables tailored treatment decisions, allowing clinicians to select therapies that are more likely to be effective. Given the evolving landscape of precision medicine in oncology, the accurate determination of HRD status through next-generation sequencing-based tests has become integral to improving outcomes for platinum-sensitive advanced ovarian cancer patients, offering them the potential for more personalized and effective therapeutic interventions. The primary objective of this study was to conduct a comprehensive assessment of the cost-effectiveness of two comparative strategies, while also delving into the financial implications, encompassing both annual considerations and a three-year funding projection. This investigation focuses on the integration of Genomic Profiling Test for HRD Determination into the current clinical management approach for patients with platinum-sensitive advanced ovarian cancer associated with HRD-positive status.

Methods

A comprehensive cost-effectiveness analysis was conducted to evaluate the integration of genomic profiling into the clinical practice for platinum-sensitive patients with advanced ovarian cancer associated with HRD-positive status in Greece, compared to the current standard of care alone. A decision-analytic model was developed to compare the costs, clinical outcomes, and cost-effectiveness of the two strategies. The analysis comprises the comparison between the incorporation of the Genomic Profiling Test for HRD Determination into the current clinical management of advanced ovarian cancer in platinum-sensitive patients with the current standard clinical approach alone. The analysis encompasses the evaluation of the following medications which are part of maintenance therapy: bevacizumab, olaparib, olaparib plus bevacizumab, and niraparib. Potential eligible candidates for undergoing the examination were female patients with advanced-stage ovarian cancer (Stage III, IV) of high grade who had responded to initial treatment.

The analysis considered the time horizon of each maintenance regimen, presenting progression-free survival outcomes within this period, while excluding intervals in which patients experienced relapse. The clinical inputs for this model derived from the literature and various randomized-controlled trials [1-3], encompassing progression-free survival and overall survival data. Data on pharmaceutical, administration, monitoring and other related costs obtained from Greek sources and databases [4-5]. All assessments were conducted using Microsoft Excel 2017.

The primary outcome was measured in terms of cost per quality-adjusted life year without progression-free survival (QALY-PFS). Additionally, a scenario analysis was performed to estimate the cost per quality-adjusted life year (QALY), providing further insights into the economic implications of the intervention. Discounting was applied to both costs and outcomes using a discount rate of 3% per annum.

Table 1: Main Features of Economic Evaluation

Population	Patients with advanced-stage ovarian cancer (Stage III, IV) of high grade who had responded to initial treatment
Intervention	Genomic Profiling Test for HRD Determination
Comparators	Current standard clinical practice alone
Perspective of the analysis	Third-party payer: only third-party payer benefits and costs are included
Economic evaluation	Cost-effectiveness analysis
Time horizon	Time horizon of each maintenance regimen (Progression Free Survival)
Cost inputs	Testing cost, Pharmaceutical cost (related to maintenance therapy) Administration cost, Monitoring cost Hospitalization cost, Adverse event and recurrence cost
Clinical inputs	Progression-free survival (PFS), Health utility
Outputs	Total Costs Incremental cost ICER (cost per QALY-PFS) ICER (cost per QALY)
Discount rate	3% for costs and outcomes

Results

The cost-effectiveness analysis revealed that the integration of Genomic Profiling Test for HRD Determination status into the clinical practice for platinum-sensitive patients with advanced ovarian cancer in Greece has notable implications. While this approach incurred an additional cost of €28,417, it yielded a significant gain of 0.608 in QALY-PFS. This resulted in an incremental cost-effectiveness ratio (ICER) of €46,736 per QALY-PFS, indicating the additional cost required for each quality-adjusted progression-free survival year gained (Table 1).

Moreover, the scenario analysis considered the cost per QALY, providing an overarching view of the economic impact. The integration of genomic profiling was found cost-effective, with the estimated cost per QALY being €28,138. This signifies that the intervention, while incurring higher costs, offers substantial value concerning improvements in patient outcomes.

The Probabilistic Sensitivity Analysis (PSA) conducted in this study revealed robust and promising results, indicating that the intervention consistently maintained cost-effectiveness. In the majority of the simulation runs, as visualized in Figure 1, the intervention exhibited a favorable cost-effectiveness profile, reaffirming its economic viability over a broad range of scenarios.

In addition, we conducted a Cost-Effectiveness Acceptability Curve (CEAC) analysis for threshold values ranging up to 100,000 EUR to assess the probabilities of cost-effectiveness at various levels. For a commonly used threshold of 30,000 EUR, the intervention exhibited a probability of being cost-effective at 67.3%.

Figure 1. Incremental cost-effectiveness plane

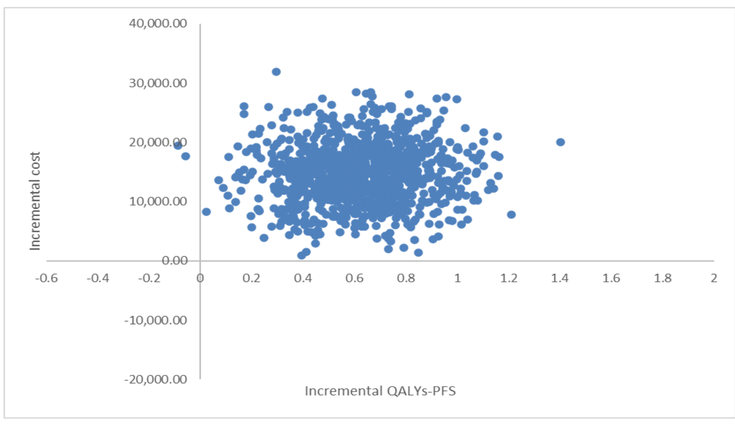

Figure 2. Cost-Effectiveness Acceptability Curve

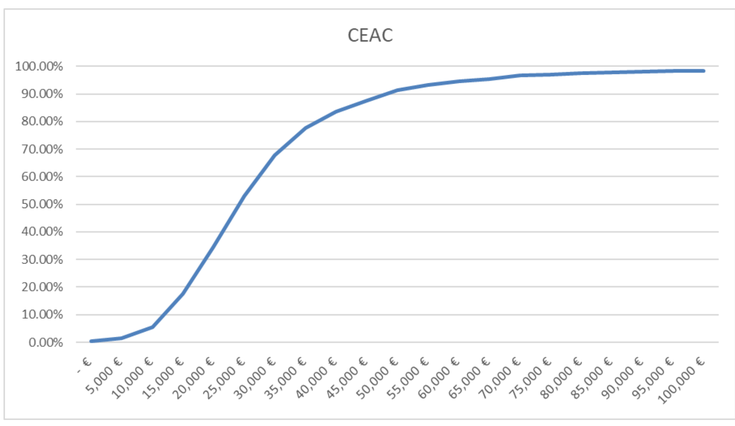

Table 2. Summary results of the cost effectiveness analysis

	Total cost	Incremental Cost	Total QA-PFS	Incremental Total QA-PFS	ICER
Standard clinical approach	**44,504 €**		**1.055**		
Genomic Profiling Test for HRD Determination	**72,921 €**	**28,417 €**	**1.663**	**0.608**	**46,736 € per QALY-PFS**

Conclusions

The present analysis reveals that the revised allocation of available medications, guided by the clinical utility of Genomic Profiling Test for HRD Determination, represents a financially responsible option for the Greek National Health System and the country's largest insurance organization, EOPYY. With documented evidence of the clinical benefits in identifying patients whose cancer is HRD-associated and who can benefit from specialized therapies, coupled with the cost-effectiveness demonstrated in this study, the Genomic Profiling Test for HRD Determination not only enhances clinical practice, but also contributes to optimizing resource allocation. The cost-effectiveness established in this analysis primarily pertains to direct medical expenses directly accountable to the payer. It's important to note that when considering the broader societal costs, which encompass indirect expenses, such as productivity losses, associated with more frequent disease relapses, the financial burden could potentially increase. However, despite these complexities, rigorous sensitivity analysis has shown that Genomic Profiling Test for HRD Determination remains cost-effective for the National Health System and, especially, for the third-party payer, across a spectrum of scenarios that involve fluctuations in pharmaceutical costs and test utilization expenses.

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