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REVIEW ARTICLE

Ovarian cancer in Portugal: a real-world evidence review

Cancro do ovário em Portugal: uma revisão da evidência do mundo real

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Abstract

The primary objective of this study was to address the gap in national data on the ovarian cancer (OC) patient pathway in Portugal. We aggregated and synthesized real-world evidence (RWE) studies conducted by AstraZeneca Portugal between 2016 and 2025 on OC, including fallopian tube and primary peritoneal carcinoma, to provide an overview of the patient journey. Moreover, we performed a literature search to include additional studies, using the keywords "ovarian cancer" AND "real world" OR "RWE" OR "real world evidence" AND "patient journey" AND "Portugal," but no relevant citations were identified in PubMed. This review includes five studies presented at various national and international meetings. The PADOC and the IPOP OC studies evaluated the prevalence of *BRCA* pathogenic variants in somatic and germline related to OC; the MAP-OCSur study focused on characterization of OC surgery in Portugal; the Portuguese subanalysis of the RESPONSE trial described the standard of care in patients with OC in Portugal; and the OLA effectiveness evaluated the use of olaparib in platinum-sensitive relapsed OC. The mentioned RWE studies play a crucial role in characterizing the OC patient pathway in Portugal, by enhancing the understanding of both the disease and patient profile, as well as identifying existing evidence gaps. This review illustrates the current state of OC care in Portugal, raising awareness of challenges and highlighting opportunities to improve access and patient outcomes.

Keywords: *Real-world evidence. Ovarian cancer. Fallopian tube carcinoma. Primary peritoneal carcinoma. Standard of care. Patient journey. Portugal.*

Resumo

O objetivo primário deste estudo foi adereçar a lacuna de dados nacionais sobre a jornada das doentes com cancro do ovário (CO) em Portugal. Agregámos e sintetizámos estudos de geração de evidência (RWE) conduzidos pela AstraZeneca Portugal entre 2016 e 2025 em CO, incluindo carcinoma das trompas de Falópio e carcinoma peritoneal primário, para fornecer uma visão global do percurso das doentes. Além disso, realizámos uma pesquisa bibliográfica para incluir estudos adicionais, utilizando as palavras-chave "ovarian cancer" E "real world" OU "RWE" OU "real world evidence" E "patient journey" E "Portugal", mas não foram identificadas citações relevantes no PubMed. Esta revisão inclui cinco estudos apresentados em vários encontros nacionais e internacionais. Os estudos PADOC e IPOP OC avaliaram a prevalência de variantes patogénicas *BRCA*, somáticas e germinativas, relacionadas com CO; o estudo MAP-OCSur centrou-se na caracterização da cirurgia em CO em Portugal; a subanálise portuguesa do ensaio RESPONSE descreveu o padrão de tratamento em

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Date of reception: 02-10-2025
Date of acceptance: 12-02-2026
DOI: 10.24875/RPO.25000022

Available online: 29-06-2026
Rev. Port. Oncol. 2026;9(1):13-23
www.rponcologia.com

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doentes com CO em Portugal; e o estudo OLA effectiveness avaliou a utilização de olaparib no CO recorrente sensível à platina. Os estudos de RWE referidos desempenham um papel crucial na caracterização da jornada das doentes com CO em Portugal, ao aprofundar o conhecimento da doença e do perfil das doentes, bem como ao identificar lacunas de evidência existentes. Esta revisão ilustra o estado atual dos cuidados de saúde em CO em Portugal, sensibilizando para os desafios e destacando oportunidades para melhorar o acesso e os resultados em saúde das doentes.

Palavras-chave: *Evidência do mundo real. Cancro do ovário. Carcinoma das trompas de Falópio. Carcinoma peritoneal primário. Padrão de tratamento. Jornada do doente. Portugal.*

Key issues

- Real-world evidence (RWE) refers to the analysis and interpretation of data from real-world practice.
- RWE may help clinicians and health policymakers identify gaps in ovarian cancer (OC) patient pathways and define strategies to overcome the difficulties.
- RWE on *BRCA* mutations in Portuguese OC patients aligns with the published data.
- RWE on surgery in OC patients in Portugal shows a low number of complete and optimal cytoreduction, suggesting a need for improvement.
- Portuguese RWE on the use of olaparib in platinum-sensitive relapsed OC supports efficacy data of randomized clinical trials (RCTs) despite a higher-than-expected need for dose reductions, suggesting a need for clinician training in safety management of PARP inhibitors.

Introduction

The importance of an optimized patient journey

Ovarian cancer (OC) is the most lethal type of gynecologic cancer and one of the principal causes of death from cancer in women worldwide.[1] In 2022, almost 325,000 women were diagnosed with OC, and around 207,000 died.[2] Of those, 682 new cases were diagnosed in Portugal, with 472 deaths attributed to OC.[3]

Genetic predisposition is one of the main risk factors for developing OC cases, with around 10% of OC cases associated with germline mutations. The genes most commonly mutated are *BRCA1* and *BRCA2,* involved in the DNA repair pathway, which confer a 40% and 18% lifetime risk of OC, respectively. Mutations in other genes that also increase OC risk include *BRIP1*, *PALB2*, *ATM*, *RAD51C, RAD51D, CHEK2*, *MLH1*, *MSH2,* and *TP53.* The guidelines recommend genetic testing, since it can guide diagnosis and medical management of high-risk populations.[4-6]

The non-specific signs and symptoms of this malignancy and the absence of a validated screening method make early detection of OC difficult. Consequently, around 60% of OC is detected in an advanced stage (III or IV), when it has often already spread to other locations besides the ovary.[1,7] Radical surgery and chemotherapy are the mainstream treatments; however, around 70% of patients relapse within the first 3 years.[8] Despite the advances in treatments, the prognosis of OC remains poor, with a 5-year survival rate after diagnosis of 26% for stage III OC and 14% for stage IV disease.[9]

Portugal has one of the lowest incidence rates of OC among European countries, with 12 cases/100,000 inhabitants,[3] a statistic that may partially reflect underdiagnosis and could be potentially related to non-recognition of symptoms. According to one study, 84.2% of Portuguese women do not recognize the symptoms of OC, which could contribute to delayed diagnosis.[10] As a result, most OC cases are diagnosed in advanced stages, and 22% of patients proceed directly to best supportive care without receiving any therapeutic intervention.[10] This lack of awareness and absence of standardized emergency protocols prolongs the patient journey from symptom onset to referral. Identifying OC related symptoms remains an evidence gap, and ongoing research in Portugal is crucial to raise awareness among patients and healthcare professionals.

Understanding the trends in patient care and outcomes in real-world clinical practice has unquestionable value, allowing the identification of gaps that may be addressed,[11] but also the points of action that can contribute to improving patient and disease management.

The primary objective of this review was to assemble some real-world evidence (RWE) published on patients with OC in Portugal, including fallopian tube and primary peritoneal carcinoma, presented in various national and international meetings to evaluate the “state of the art” in OC in Portugal regarding testing of *BRCA*

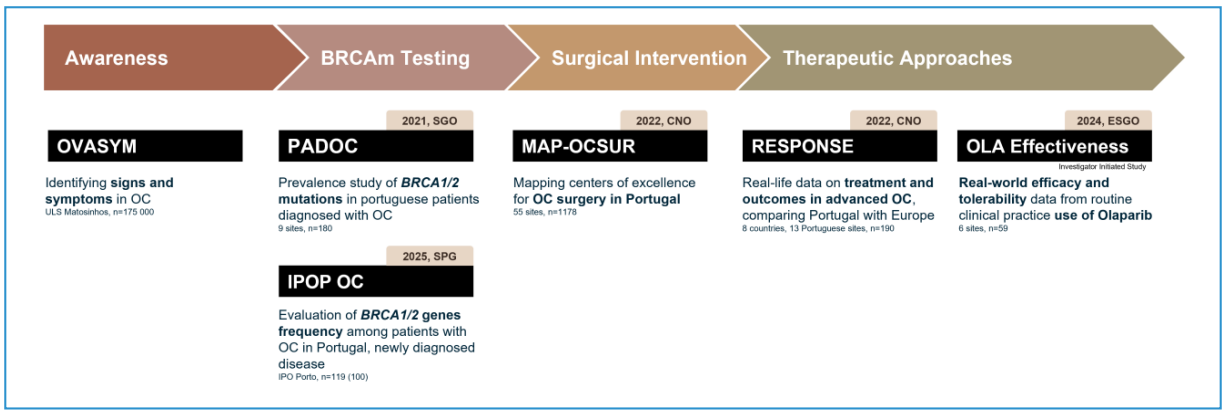

Figure 1. Real-world evidence regarding ovarian cancer in Portugal conducted by AstraZeneca Portugal between 2016 and 2025. CNO: National Congress of Oncology (Congresso Nacional de Oncologia); ESGO: European Society of Gynaecological Oncology; OC: ovarian cancer; SGO: Society of Gynecologic Oncology; SPG: Portuguese Society of Gynecology (Sociedade Portuguesa de Ginecologia), 2025.

mutations (*BRCAm*), surgery, and first and second line of therapy (Fig. 1).

BRCA1/2 mutation testing

Epithelial OC is associated with defective homologous recombination DNA repair in around half of the diagnosed cases, which include germline and/or somatic *BRCA1/2* mutations.[12] These mutations are associated with a family history of cancer and are a risk factor for developing OC.[12] In addition to *BRCA1/2*, other genes related to hereditary OC should also be considered in germline genetic testing, as they may provide valuable information for genetic counseling, even though targeted therapies are not currently available for all these gene mutations.[12] Maintenance therapy with a poly (adenosine diphosphate-ribose) polymerase inhibitor (PARPi) after platinum-based chemotherapy in patients with recurrent platinum-sensitive high-grade OC is a new standard of care option. The benefits of PARPi have been demonstrated in OC with homologous recombination deficiency (HRD), particularly in patients with a *BRCAm.*[12]

Considering the importance of *BRCA* status for genetic counseling and maintenance therapy with PARPi in advanced stages, all patients with high-grade OC should be tested for *BRCA1/2* mutations at diagnosis. Therefore, national and international guidelines recommend testing for both germline and somatic *BRCAm.*[12,13]

A significant percentage of patients are unaware of *BRCA*-related cancers in their family, and, before the PADOC and the IPOP OC studies, data on the prevalence of *BRCAm* in Portugal were scarce.[14] Given the value of *BRCAm* testing, these two studies were conducted in Portugal to determine the presence of *BRCAm* in patients with OC and further understand the prevalence of these mutations in the Portuguese OC population.

PADOC - Nationwide prevalence study of BRCA1/2 germline and somatic variants in patients diagnosed with non-mucinous OC in Portugal

The PADOC study[14] is an interventional, ambispective, multicenter study that included women aged 18 years or older diagnosed with non-mucinous epithelial OC, fallopian tube, or primary peritoneal carcinoma between January 01, 2014, and December 31, 2016. The study aimed to determine the prevalence of *BRCA1/2* variants (somatic and germline) in patients diagnosed with non-mucinous OC in several Portuguese hospitals nationwide to define the best strategy for screening germline/somatic variants in these genes in a routine diagnostic setting.

The study included 165 patients from 9 national reference centers for diagnosis and treatment of OC, with a median age at diagnosis of 58 years. Most patients (n = 124; 75.2%) were diagnosed with advanced disease, 93 had stage III (56.4%), and 31 had stage IV (18.8%). Formalin-fixed paraffin-embedded tumor tissue and a peripheral blood sample were available for 153; for the remaining 12 patients, only blood samples were available. Among the 153 tumors analyzed, 127 (83.0%) had pure serous histology, including 117 (76.5%) high-grade serous OC (HGSOC) and 9 (5.9%) low-grade serous OC. Non-serous histology was

observed in 26 tumors (17.0%), comprising 12 (7.8%) clear-cell carcinomas, 4 (2.6%) endometrioid carcinomas, and 10 (6.5%) other histologic subtypes.

Of the 153 samples screened for germline/somatic *BRCA1/2* variants, 32 (20.9%) patients harbored deleterious variants: 17 patients (54.5%) with a *BRCA*1 variant and 15 patients (45.5%) with a *BRCA2* variant. A total of 24 (15.7%) patients had germline variants (12 in the *BRCA1* gene and 12 in the *BRCA2* gene), and 8 (5.2%) presented mutations that were found to be somatic (5 in *BRCA1* and 3 in *BRCA2*). In addition, one *BRCA1* germline variant was detected in one of the 12 patients for whom only the blood sample was available. The most frequent germline deleterious variants were the *BRCA1* c.5266dup and the *BRCA2* c.3114dup, each representing 12% (3/25) of the germline pathogenic variants found in this series. The germline founder variant *BRCA2* c.156_157insAlu was only detected in one of the patients, representing 8.3% (1/12) of the *BRCA2* germline pathogenic variants found in this series. The two germline rearrangements, *BRCA2* c.156_157insAlu and *BRCA1* c. (80 + 1_81-1)_(134 + 1_135-1) del, identified in the respective blood samples, were not detected by the NGS tumor assay pipeline. Variants of unknown significance (VUS) were identified in seven (4.6%) of the 153 patients in which variant screening of the *BRCA1/2* genes was performed. Within this group, four (2.6%) patients had a germline VUS, and three (2%) patients had a somatic VUS.

A higher prevalence of pathogenic variants was observed among patients with HGSOC, namely 21 of 117 (17.9%) carried germline variants, and 29 of 117 (24.8%) carried either germline or somatic variants (16 in *BRCA1* and 13 in *BRCA2*). Among the 26 tumors with other histologies, three harbored a deleterious germline *BRCAm*: one occurred in a clear-cell carcinoma (1 of 12; 8.3%) and two in tumors classified as other histologies (2 of 10; 20%).

There was a statistically significant difference in age at diagnosis between the patients with somatic mutations (mean age of 68.1 years) and those with germline mutations (mean age of 54.6 years) ($p < 0.001$).

Regarding the family history of *BRCA*-related cancers for the total study population, 76.4% (n = 126) of the participants had no personal history of breast cancer. In the series of 153 patients, 32 reported having a family history of *BRCA*-related cancers, most of them in 1st relatives (n = 22; 68.8%). Within the germline and the somatic *BRCA1/2* mutated groups, 12 out of 24 (50%) and 2 out of 8 (25.0%) patients, respectively, reported having a family history of *BRCA*-related disease. However, the difference was not statistically significant.

In conclusion, the PADOC study showed a prevalence of 20.9% of *BRCA1/2* mutations in patients with OC in Portugal, with germline mutations accounting for 15.7% and somatic mutations for 5.2%. These results are consistent with the literature prevalence of *BRCAm* and highlight the importance of performing broad genetic testing, even without a family history of *BRCA*-related cancers, leading to the identification of more patients with a higher likelihood of benefiting from PARPi targeted therapy.[15]

IPOP OC - Evaluation of BRCA1/2 gene frequency among newly diagnosed patients with OC in Portugal: a single-center, retrospective cohort, database real-world study

A retrospective cohort, observational study was conducted on new patients diagnosed with non-mucinous epithelial OC, including carcinosarcomas, at a single comprehensive cancer center (IPO-Porto, Portugal), where *BRCA1/2* testing at diagnosis began to be implemented in clinical practice in 2017.[16]

This study included female patients aged 18 years or more with confirmed newly diagnosed non-mucinous epithelial OC who underwent surgery or biopsy at IPO-Porto between January 01, 2017, and December 31, 2019. Patients were required to have up to 5 years of data available until December 2022. This project aimed to evaluate the frequency of *BRCA1/2* mutations, either somatic or germline, in patients newly diagnosed with non-mucinous epithelial OC at a single comprehensive cancer center.

After a database search, 228 patients were identified, of which 119 were included in the study. The other 109 patients were excluded due to oncology disease-specific treatments before admission or outside IPO-Porto (n = 37), no medical appointments at IPO-Porto (n = 64), enrolled in a clinical trial (n = 2), and lost to follow-up (n = 6).

Genetic testing was performed in 100 patients, with 19 patients excluded, mainly due to a lack of conditions for systemic treatment (n = 7) and overall survival (OS) < 3 months (n = 9). *BRCA1/2* mutations were identified in 15 patients (15.0%), characterized as germline *BRCA1* (n = 4), somatic *BRCA1* (n = 5), germline *BRCA2* (n = 3), and somatic *BRCA2* (n = 3). Table 1 summarizes the patients' demographic and clinical characteristics overall and in *BRCA*-mutated patients.

There were no differences in the frequency of *BRCA1/2* mutations considering primary debulking

Table 1. Baseline demographic and clinical characteristics of the IPOP OC study population

Characteristics	*BRCAm*		Overall
	Negative	Positive	
	(n = 85)	(n = 15)	(n = 100)
Age at diagnosis			
Mean (SD)	62.0 (11.4)	59.2 (8.12)	61.6 (11.0)
Median (min, max)	63.0 (32.0, 81.0)	59.0 (46.0, 72.0)	62.0 (32.0, 81.0)
BMI at diagnosis			
Mean (SD)	26.7 (5.07)	27.6 (6.39)	26.8 (5.27)
Median (min, max)	26.3 (16.8, 40.1)	27.6 (18.3, 43.9)	26.3 (16.8, 43.9)
Missing	1 (1.2)	-	1 (1.0)
ECOG at diagnosis (%)			
0	46 (54.1)	9 (60.0)	55 (55.0)
1	22 (25.9)	4 (26.7)	26 (26.0)
2	14 (16.5)	1 (6.7)	15 (15.0)
3	3 (3.5)	1 (6.7)	4 (4.0)
Family history (breast or ovary/uterus) (%)			
No	53 (62.4)	9 (60.0)	62 (62.0)
Yes	27 (31.8)	6 (40.0)	33 (33.0)
Missing	5 (5.9)	-	5 (5.0)
Patient history (other cancer diseases) (%)			
No	72 (84.7)	12 (80.0)	84 (84.0)
Yes	13 (15.3)	3 (20.0)	16 (16.0)
Histology (%)			
Endometrioid	14 (16.5)	-	14 (14.0)
Other	14 (16.5)	1 (6.7)	15 (15.0)
Serous	57 (67.1)	14 (93.3)	71 (71.0)
Grade (%)			
Well-differentiated	11 (12.9)	-	11 (11.0)
Moderately differentiated	2 (2.4)	-	2 (2.0)
Poorly differentiated	58 (68.2)	12 (80.0)	70 (70.0)
Grade cannot be assessed	14 (16.5)	3 (20.0)	17 (17.0)
Tumor location (%)			
Ovary	61 (71.8)	8 (53.3)	69 (69.0)
Fallopian tube	23 (27.1)	7 (46.7)	30 (30.0)
Fallopian tube/ ovary/peritoneum	1 (1.2)	-	1 (1.0)
FIGO staging (%)			
I-II	24 (28.2)	3 (20.0)	27 (27.0)
III	41 (48.2)	6 (40.0)	47 (47.0)
IV	20 (23.5)	6 (40.0)	26 (26.0)

SD: standard deviation; BMI: body mass index; ECOG: Eastern Cooperative Oncology Group; FIGO: International Federation of Gynecology and Obstetrics.

surgery (PDS) (n = 6) or interval debulking surgery (IDS) (n = 6), and 20.0% of patients with *BRCA1/2* mutations were treated only with palliative chemotherapy.

The results of this study indicate a 15.0% prevalence of *BRCA1/2* mutations in patients with OC, with germline mutations accounting for 7.0% and somatic mutations for 8.0%. This prevalence is lower than reported in previous publications, such as the PADOC study.

Given that this is a single cancer-center study, and some patients were excluded because they received treatment prior to admission or outside IPO-Porto, there could be some bias in the patient selection that would justify the different prevalence of *BRCAm*. The lower prevalence of germline mutations observed in this study, compared to other publications, may be attributed to the close monitoring of familial risk and implemented genetic counseling appointments at IPO Porto, which facilitate prophylactic surgeries and monitor *BRCAm* carriers. Overall, this finding highlights the relevance of prevention strategies for OC.[17,18]

Surgical intervention

Despite the advances in treatments, OC still has a poor prognosis. Multiple studies have shown that optimal primary cytoreduction surgery (without residual disease) improves patient survival.[19-21] Surgery reduces tumor burden but also allows for the pathological diagnosis of the OC subtype and the establishment of appropriate systemic treatment based on tumor and patient characteristics.[22]

The surgical management of advanced OC is complex and is a major component of the multidisciplinary management of the disease. Assuring the quality of the surgery has a high impact on the survival of patients with advanced OC.

The European Society of Gynaecologic Oncology (ESGO) developed a list of quality indicators for advanced OC surgery to audit and improve clinical practice, including, among other criteria, a benchmark of at least 24 cytoreductive surgeries per center per year as a quality indicator.[23,24] Portugal is one of the few European countries without ESGO-certified centers, which may indicate a higher number of suboptimal surgeries performed. The need to evaluate the status of OC surgery in Portuguese centers led to the MAP-OCSur study, designed to map national surgery centers and characterize surgical quality and patient outcomes.[25]

MAP-OCSur – MAPping OC Surgery centers in Portugal

MAP-OCSur[25] is a retrospective study based on hospital records from the Unified Health System (SUS, *Sistema Único de Saúde*). Registries of hospital production from 55 hospitals were included according to the following criteria: International Classification of Diseases, Tenth Revision (ICD-10) OC diagnosis code in 2017 or 2018; OC surgical procedure in 2018; or surgical ICD-10 codes (excisions and resections of ovaries, uterus, fallopian tubes, and lymph nodes or excisions of the peritoneum). Additional surgical procedures were analyzed to characterize the surgeries (omentum, colon, small intestine, peritoneum, and other intra-abdominal organs). Hospitals were classified into six categories: oncological Centers, University Hospitals, regional Hospitals, medium Hospitals, small Hospitals, and very small Hospitals.

There were 1778 patients identified with an ICD-10 code of OC, fallopian tube, or peritoneum cancer diagnosis. Of these, 57% (n = 672) were 70 years or older at diagnosis. In 2018, 514 patients underwent surgical/biopsy procedures (70 biopsy only; 448 surgery and biopsy), and 59% (n = 303) of them underwent additional surgery procedures: 42% (n = 215) omentum, 25% (n = 128) colorectum, 24% (n = 121) peritoneum, 6% (n = 30) small intestine, and 6% (n = 33) other organs.

Around 50% of the patients had surgical treatment at Oncological Centers or University Hospitals. On average, Oncological Centers performed 37 surgical procedures, University Hospitals carried out 20 surgeries, and the other hospital categories performed 20 surgical procedures (Table 2).

Although ICD-10 is complex and missing data may introduce bias, this study represents the first attempt to map OC surgery in Portugal.

OC is an uncommon tumor usually diagnosed in the advanced stage. Surgical treatment is complex, time-consuming, and potentially associated with a high rate of complications; therefore, patients must be referred to specially dedicated hospitals. This study revealed that only the Oncological Centers performed more than 24 surgical procedures, one of the criteria of the ESGO certification. A national study must be carried out to define the number of centers needed for the surgical treatment of patients with advanced OC in Portugal.

Therapeutic approaches

The standard of care for OC consists of PDS followed by carboplatin plus paclitaxel, or neoadjuvant chemotherapy followed by IDS or palliative treatment when extensive surgery or complete tumor resection is not feasible. The maintenance therapies available for platinum-sensitive OC include bevacizumab and PARPi, such as niraparib, rucaparib, and olaparib.[26] These targeted therapies have become essential in OC treatment, demonstrating a significant improvement in patients' outcomes.[26]

Based on the phase III SOLO-2 trial[27] results, olaparib, a PARPi, was initially approved as maintenance therapy for platinum-sensitive relapsed OC in patients with BRCAm. Later, the substantial impact of olaparib on survival outcomes observed in the phase III SOLO-1 trial[13] led to extending the approval to frontline maintenance in *BRCAm* patients. Olaparib received European Medicines Agency (EMA) approval in December 2014. In Portugal, reimbursement began in September 2019 for platinum-sensitive relapsed OC maintenance in *BRCAm* patients and in January 2022 for first-line treatment in *BRCAm* patients. This delay impacted national implementation and contributed to an initial learning curve in managing treatment-related toxicities. The phase III PAOLA-1 trial led to the EMA approval of olaparib combined with bevacizumab as first-line maintenance for HRD-positive advanced OC in November 2020. However, this combination is not currently available for clinical use in Portugal, limiting patient access to this therapeutic option.

Two real-world studies were conducted in Portugal to characterize the treatment of advanced OC. One evaluated the standard of care and identified patients eligible for PARPi, whereas the other assessed the effectiveness and tolerability of olaparib in platinum-sensitive relapsed OC. The findings from these studies may help identify opportunities to improve clinical practice and optimize access to targeted therapies.

RESPONSE – Real-life data on treatment and outcomes in advanced OC: an observational, multinational cohort study

The main purpose of RESPONSE[28] was to describe the standard of care of patients with newly diagnosed advanced (stage III or IV) high-grade serous or endometrioid OC in eight countries (Austria, Belgium, Denmark, Finland, the Netherlands, Norway, Portugal, and Israel). Other objectives included determining the percentage of patients undergoing PDS with complete or optimal resection, characterizing the effects of *BRCA* status, estimating how many patients would be candidates for first-line PARPi maintenance treatment, and

Table 2. Number of ovarian cancer patients and surgical procedures in the different hospitals included in MAP-OCSur study

Hospital category	n hospitals	n hospitals with surgical procedures	n total surgeries	n procedures/hospital
IPO – oncology hospital	3	3	111	37
Central university hospitals	6	6	119	20
Regional hospitals	10	10	114	11
Medium hospitals	17	14	84	6
Small hospitals	12	8	20	3
Very small hospitals	5	0	0	0

evaluating the use of bevacizumab on patients' outcomes.

Each country retrospectively identified patients until a target of 120 was reached, with all patients followed for at least 20 months. 1119 women with high-grade serous or endometrioid OC between 2002 and 2018 were included. Most of the patients (97.5%) had high-grade serous carcinoma, and 66.9% of all patients had stage III disease. *BRCA* testing was available in 66% of the patients (739 of 1119), showing that 11.7% had a germline *BRCAm*, and 5.8% had a somatic *BRCAm*. Around a fourth of patients (26.6%) received bevacizumab simultaneously with first-line chemotherapy and as maintenance.

Regarding surgery, 41% of the patients underwent PDS, and 39.3% had IDS. Of those who had PDS, 55.5% had complete resection (no visual residual disease > 1 cm after surgery), and 15.1% had optimal resection (residual disease of ≤ 1 cm). Of the patients who underwent IDS, 63.9% had complete resection, and 20.9% had optimal resection.

The response to treatment, defined as the proportion of patients with a normal CA-125 level or > 90% decrease from the baseline CA-125 level, was achieved by 66.2% of patients, while, according to physician assessment, 78.9% had a response to treatment (53.2% had a complete response [CR] and 25.7% had a partial response [PR]). These results suggest that 78.9% of the patients would have been eligible for PARPi maintenance.

The disease status of the patients was followed up for at least 20 months. Six months after the completion of chemotherapy, 71.9% of the patients were disease-free, 26.2% had progressive disease, and 1.9% had died. After at least 20 months of follow-up, 32.9%, 46.4%, and 20.9% were disease-free, had progressive disease, or had died, respectively.

Bevacizumab significantly improved the OS of patients (hazard ratio [HR] 0.62; 95% confidence interval [CI] 0.42-0.91; p = 0.01), but not the progression-free survival (PFS). The presence of a *BRCAm* had a significant positive effect on PFS (HR 0.60; 95% CI 0.41-0.84; p < 0.01), whereas the effect on OS was uncertain.

Even though the results may not apply to other regions, this study offers valuable insight into the treatment landscape of OC in Europe.

RESPONSE – Portuguese cohort

In November 2022, a poster summarizing the Portuguese results compared to the global RESPONSE results was presented at the 19th *Congresso Nacional de Oncologia.*[10] Portugal included patients from 13 centers in Portugal, exceeding the target of 120 patients with a total of 190 participants. The majority of these patients were diagnosed between 2015 and 2018 (n = 140).

Similar to the overall RESPONSE population, approximately 68% of the Portuguese patients had stage III disease. The proportion of patients with a germline *BRCAm* was higher in Portugal than in the global cohort (20.0% vs. 11.7%) and exceeded rates reported in the PADOC and IPOP OC studies.

The median time from diagnosis to surgery was higher in the Portuguese population, with 2.5 months from diagnosis to PDS and 5 months from diagnosis to IDS, compared to 0.5 months and 3.5 months in the overall RESPONSE population, respectively.

In Portugal, 26% of patients had no surgery, 50% underwent PDS, and 22% received palliative chemotherapy (vs. 19%, 41%, and 10% globally). A complete

Table 3. Comparing clinical data from the global RESPONSE study versus data from the Portuguese cohort

Parameter	RESPONSE (n = 1119) (%)	Portugal (n = 190) (%)
High-grade serous tumor	97.5	96.8
Stage III	66.9	68.4
ECOG 0-1	69.6	72.6
Family history of ovarian/breast cancer	~5%/~22	~5%/~22
*gBRCA*1/2m	11.7	20
Surgery	80.1% (surgery); 19.9% (no surgery)	73.7 (surgery); 26.3 (no surgery)
PDS and IDS	40.8 (PDS); 39.3 (IDS)	50.7 (PDS); 49.3 (IDS)
Use of chemotherapy in 1st line	1L: ~38; Neo: ~50; palliative: ~10	1L: ~30; Neo: ~48; palliative: ~22
CA-125	60.60	~60

1L: first line; ECOG: Eastern Cooperative Oncology Group; gBRCA1/2m: BRCA1/2 germline mutation; IDS: interval debulking surgery; Neo: neoadjuvant; PDS: primary debulking surgery.

cytoreduction was achieved in 37% of patients who had PDS (vs. 55% globally), and 59% of the patients who underwent IDS (vs. 64%), whereas 11% of PDS (vs. 15%) and 14% of the IDS (vs. 21%) had residual disease of ≤ 1 cm. Table 3 identifies the clinical data from the Portuguese cohort versus the global study.

The histology, percentage of stage III disease, PDS, and CA-125 expression were comparable between the Portuguese patients and the overall RESPONSE population. However, the median time from diagnosis to surgery was longer in Portugal compared with the global cohort, both PDS and IDS. Furthermore, complete and optimal cytoreduction rates were lower in Portugal than in RESPONSE.

These findings indicate opportunities to reduce time to surgery and improve surgical outcomes in Portugal.

OLA effectiveness beyond trials: olaparib's real-world data in platinum-sensitive relapsed OC – a multicenter experience from Portugal

The study OLA effectiveness aimed to assess the effectiveness and tolerability of olaparib in real-world settings across multiple centers in Portugal, exploring the extent to which phase III trial outcomes are replicated in clinical practice.[29] The effectiveness and tolerability of olaparib were evaluated regardless of *BRCA* status, adding valuable RWE for local authorities and potentially informing future treatment guidelines.

This retrospective study included patients with platinum-sensitive relapsed OC, fallopian tube cancer, or primary peritoneal cancer who were treated with olaparib as maintenance therapy, irrespective of *BRCAm* status. Clinical data were collected at diagnosis and recurrence, before and after initiating olaparib treatment. The primary objectives were to evaluate olaparib's effectiveness by calculating median PFS and OS from the start of olaparib treatment to radiologically confirmed disease progression and death/last contact, respectively, and to evaluate tolerability (CTCAE v5.0).[30] Secondary objectives included assessing olaparib effectiveness according to *BRCAm* status and patient response to subsequent lines of chemotherapy after olaparib treatment. Patients were recruited from six Portuguese hospitals, with 59 patients meeting the inclusion criteria.

Table 4 shows the baseline characteristics and prior treatment patterns of patients included in the OLA effectiveness study. Of the 59 patients, 17 (29%) were aged ≥ 65 years, 33 (56%) had an Eastern Cooperative Oncology Group (ECOG) 0, and 24 (41%) had an ECOG 1. In total, 45 patients (76%) had *BRCAm*, subdivided as follows: 24 patients with *BRCA1*, 19 with *BRCA2*, and 2 with mutations in both *BRCA1* and *BRCA2*. Among those with *BRCAm*, 31 were germline, whereas 14 were somatic. The remaining 14 patients (24%) were *BRCA* wild-type (*BRCAwt*). At the time of diagnosis, 97% had HGSOC, predominantly with stage III (70%) and stage IV (22%).

Regarding prior treatments, 54% of patients received two prior lines of platinum-based chemotherapy, whereas 46% received more than two. The response to the most recent line of platinum chemotherapy included 21 patients (36%) achieving a CR and 38 patients (64%)

Table 4. Patient characteristics and prior therapies (n = 59) in the OLA effectiveness study

Patient characteristics	n (%)
Age	
< 65 years	42 (71)
≥ 65 years	17 (29)
ECOG at baseline	
0	33 (56)
1	24 (41)
2	2 (3)
Surgery in first line treatment	
Surgery performed - yes	56 (95)
Upfront surgery	32 (54)
Interval surgery	24 (41)
R0	34 (61)
High-grade serous ovarian cancer	
Yes	57 (97)
No	2 (3)
FIGO stage at diagnosis	
I	2 (3)
II	3 (5)
III	41 (70)
IV	13 (22)
Time to recurrence after penultimate platinum-based regimen (platinum sensitivity)	
6-12 months	22 (37)
> 12 months	37 (63)
Surgery for the current relapse	
Yes	15 (25)
No	44 (75)
Number of prior platinum-based therapies	
2	32 (54)
> 2	27 (46)
Response to the most recent platinum-based therapy	
CR	21 (36)
PR	38 (64)
Prior bevacizumab	
Yes	20 (34)
No	39 (66)
BRCA mutation status	
BRCAm	45 (76)
BRCA1/BRCA2/BRCA1+2	24/19/2
Germline/Somatic	31/14
BRCAwt	14 (24)

ECOG: Eastern Cooperative Oncology Group; FIGO: International Federation of Gynecology and Obstetrics; PR: partial response; CR: complete response; *BRCAwt:* BRCA wild-type; *BRCAm: BRCA* mutated.

achieving a PR. Concerning platinum sensitivity, 63% of patients had a platinum-free interval of more than 12 months, whereas 37% had a platinum-free interval of 6-12 months. Surgery was performed in 95% of patients during their first-line treatment, with upfront surgery conducted in 54% of the patients and interval surgery in 41%, achieving R0 resection in 61% of the cases.

The median duration of olaparib treatment was 8 months (range, 2-65). Treatment was discontinued in 45 patients (75%), mainly due to disease progression (42 patients), whereas 14 patients (24%) remained on the therapy at study end. Notably, 4 patients (7%) received olaparib for 5 years or longer. Median PFS was 12 months (95% CI 8.4-15.6), with better outcomes in patients with *BRCAm* than in those with *BRCAwt* (13 vs. 4 months; log-rank p = 0.007). Median OS was 28 months (95% CI, 21.2-34.7), longer in *BRCAm* than *BRCAwt* patients (30 vs. 22 months), though the difference was not statistically significant (log-rank p = 0.266).

Upon disease progression, 39 of the 42 patients who experienced progression received a subsequent line of chemotherapy, with a median of 2 lines per patient (range, 1-4 lines). Of these, 62% received platinum-based chemotherapy, and 15% also received bevacizumab. The median PFS of subsequent chemotherapy was 5 months (95% CI 3.8-6.2), with similar values regardless of whether patients received platinum-based or non-platinum-based regimens (5 vs. 4 months, respectively; log-rank p = 0.426).

Treatment-related toxicities of any grade occurred in 41 patients (69%), leading to dose reductions in 27 patients (46%) and permanent treatment discontinuation in 3 patients (5%) due to severe adverse events, including anemia, acute myeloid leukemia, and acute renal failure. Grade ≥ 3 toxicities were reported in 13 patients (22%). Adverse events included anemia in 42% of patients (grade ≥ 3 anemia in 12%), nausea in 19%, asthenia in 12% (with 2% grade ≥ 3), thrombocytopenia in 3% (all grade ≥ 3), and neutropenia in 3% (all grade ≥ 3). Additional adverse events were vomiting in 5%, leucopenia in 2%, lymphopenia in 2% (grade 3), rash in 2%, and single cases of acute renal failure and acute myeloid leukemia.

This is the first multicenter study in Portugal to demonstrate the effectiveness and safety of olaparib in a real-world platinum-sensitive relapsed OC population. The findings indicate that olaparib is effective as a maintenance therapy in *BRCAm* platinum-sensitive relapsed OC patients and can also benefit selected

BRCAwt patients. Despite a higher-than-expected rate of dose reductions (46%), the low rate of permanent discontinuations reflects a manageable safety profile with appropriate monitoring, supporting olaparib's feasibility in clinical practice. The significant benefits observed in *BRCA*m patients align with phase III trial data, although it highlights challenges in toxicity management in real-world settings.

These results emphasize the need for continued research, clinician training in toxicity management, and faster and more comprehensive access to innovative therapies. This study provides valuable RWE by documenting treatment patterns, clinical responses, and associated challenges that can inform local treatment guidelines and healthcare policy. Olaparib's RWE reaffirms its role as an effective maintenance therapy option in platinum-sensitive relapsed OC patients.

Conclusion

RWE studies offer vital insights into healthcare by providing comprehensive data on patients and disease characterization, and helping healthcare professionals to understand the journey from diagnosis to treatment. Furthermore, assessing diagnosis methods and treatment effectiveness in real-world settings could offer practical outcomes that complement clinical trial data. Overall, RWE studies play a crucial role in enhancing personalized patient care, optimizing treatment strategies, improving healthcare systems, and can contribute to health policy changes.

The RWE gathered and presented in this manuscript emphasizes several insights and gaps from the Portuguese OC patient journey that need to be addressed. One important finding is that the prevalence of *BRCA* pathogenic variants in OC in Portugal aligns with what is described in the literature; however, there appears to be a disparity in germline mutations, highlighting the need for genetic testing in all patients. The MAP-OCSur study revealed that in Portugal, only the Oncological Centers meet one of the quality indicators of the ESGO certification. Furthermore, the RESPONSE trial results point out the importance of shortening the time from diagnosis to surgery and improving OC surgery outcomes in Portugal, given its great importance in the prognosis of the disease. These key highlights may trigger a broader discussion on the establishment of specialized reference centers for OC surgery in Portugal, which is crucial for enhancing surgical care and patient outcomes. Regarding targeted therapies, which can improve long-term disease control, the OLA effectiveness study shows olaparib's similar clinical results, but higher dose-reduction rates than reported in clinical trials, suggesting a need for better management of the PARPi toxicity that enables clinical benefit without compromising the quality of life.

Although these results do not represent all the Portuguese OC patients, nor all the hospitals that treat OC, the studies presented in this review offer a comprehensive evaluation of the disease in Portugal. Additional studies could be implemented to improve knowledge that encompasses all the pathways of OC patients, including disease symptoms, time to diagnosis and treatment, and palliative care characterization. When interpreting these results, the retrospective design of the studies should be considered, which can be associated with certain biases, such as patient identification issues and missing data.

Nevertheless, RWE represents an important tool in the generation of evidence, allowing for a comprehensive assessment of therapeutic effectiveness in real-world clinical practice and characterizing the patient journey and clinical outcomes. This review summarizes five studies that characterize the standard of care for OC on diagnosis and treatment, identify gaps and unmet needs, and, ideally, provide valuable insights into patient pathways, with the aim of improving care and prognosis for this disease in Portugal.

Funding

The funding for this article was provided by AstraZeneca Portugal.

Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

References

1. Gaona-Luviano P, Medina-Gaona LA, Magaña-Pérez K. Epidemiology of ovarian cancer. Chin Clin Oncol. 2020;9:47.
2. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74:229-63.
3. Ferlay J, Ervik M, Lam F, Laversanne M, Colombet M, Mery L, et al. Global Cancer Observatory: Cancer Today (Version 1.1). Lyon, France: International Agency for Research on Cancer; 2024. Available from: https://gco.iarc.who.int/today [Last accessed on 2025 Feb 12].
4. Maioru OV, Radoi VE, Coman MC, Hotinceanu IA, Dan A, Eftenoiu AE, et al. Developments in genetics: better management of ovarian cancer patients. Int J Mol Sci. 2023;24:15987.
5. Samuel D, Diaz-Barbe A, Pinto A, Schlumbrecht M, George S. Hereditary ovarian carcinoma: cancer pathogenesis looking beyond BRCA1 and BRCA2. Cells. 2022;11:539.
6. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology (NCCN guidelines®). In: Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer. Ver. 1. United States: National Comprehensive Cancer Network; 2025.
7. Torre LA, Trabert B, DeSantis CE, Miller KD, Samimi G, Runowicz CD, et al. Ovarian cancer statistics, 2018. CA Cancer J Clin. 2018;68:284-96.
8. Ledermann JA, Raja FA, Fotopoulou C, Gonzalez-Martin A, Colombo N, Sessa C, et al. Newly diagnosed and relapsed epithelial ovarian carcinoma: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013;24 Suppl 6:vi24-32.
9. Gaitskell K, Hermon C, Barnes I, Pirie K, Floud S, Green J, et al. Ovarian cancer survival by stage, histotype, and pre-diagnostic lifestyle factors, in the prospective UK million women study. Cancer Epidemiol. 2022;76:102074.
10. Batarda ML, Abreu M, Malheiro M, Portela C, Camacho C, Marques C, et al. Quão diferente é Portugal de outros países europeus no tratamento de doentes com cancro do ovário: Subanálise do estudo RESPONSE. In: Poster Apresentado no 19º Congresso Nacional de Oncologia: 16-18 de Novembro 2022. Porto: Portugal.
11. Eisenhauer EA. Real-world evidence in the treatment of ovarian cancer. Ann Oncol. 2017;28 Suppl 8:viii61-5.
12. González-Martín A, Harter P, Leary A, Larusso D, Miller RE, Pothuri B, et al. Newly diagnosed and relapsed epithelial ovarian cancer: ESMO clinical practice guideline for diagnosis, treatment and follow-up. Ann Oncol. 2023;34:833-48.
13. Moore K, Colombo N, Scambia G, Kim BG, Oaknin A, Friedlander M, et al. Maintenance olaparib in patients with newly diagnosed advanced Ovarian cancer. N Engl J Med. 2018;379:2495-505.
14. Cardoso C, Vaz F, Nabais H, Frutuoso C, Couto MR, Broco S, et al. Prevalence study of BRCA1/2 mutations in Portuguese patients diagnosed with non-mucinous ovarian cancer, fallopian tube invasive neoplasia or peritoneal primary cancer (PADOC). Gynecol Oncol. 2021;162:S244-5.
15. Norquist BM, Harrell MI, Brady MF, Walsh T, Lee MK, Gulsuner S, et al. Inherited mutations in women with Ovarian carcinoma. JAMA Oncol. 2016;2:482-90.
16. Lopes AR, Pereira D, Teixeira M, Peixoto A, Bento MJ, Leite-Silva P, et al. POA01 - frequência de mutações BRCA1/2 em doentes com cancro do ovário: estudo retrospetivo da vida real. In: Poster Apresentado na 205ª Reunião da Secção Portuguesa de Ginecologia Oncológica; 17-18 De Janeiro. Porto: Portugal; 2025.
17. Peixoto A, Pinto P, Guerra J, Pinheiro M, Santos C, Pinto C, et al. Tumor testing for somatic and germline $BRCA_1$/$BRCA_2$ variants in Ovarian cancer patients in the context of strong founder effects. Front Oncol. 2020;10:1318.
18. Birgisdóttir A, Myklebust TÅ, Bjørnslett M, Rognlien VW, Paulsen T, Dørum A. BRCA mutation testing and association with oncologic outcome and incidence of ovarian cancer in Norway. Int J Gynecol Cancer. 2025;35:100029.
19. Cardillo N, Devor E, Calma C, Pedra Nobre S, Gabrilovich S, Bender DP, et al. Investigating the effect of optimal cytoreduction in the context of platinum sensitivity in high-grade serous ovarian cancer. Acta Obstet Gynecol Scand. 2022;101:1085-92.
20. Jiang R, Feng Y, Chen Y, Cheng X, Shi T, Gao W, et al. Surgery versus no surgery in platinum-sensitive relapsed ovarian cancer: final overall survival analysis of the SOC-1 randomized phase 3 trial. Nat Med. 2024;30:2181-8.
21. Harter P, Sehouli J, Vergote I, Ferron G, Reuss A, Meier W, et al. Randomized trial of cytoreductive surgery for relapsed ovarian cancer. N Engl J Med. 2021;385:2123-31. Erratum in: N Engl J Med. 2022;386:704.
22. Lheureux S, Braunstein M, Oza AM. Epithelial ovarian cancer: evolution of management in the era of precision medicine. CA Cancer J Clin. 2019;69:280-304.
23. ESGO Center Accreditations. Available from: https://www.esgo.org/ovarian-cancer-surgery-accreditation.
24. Fotopoulou C, Concin N, Planchamp F, Morice P, Vergote I, Du Bois A, et al. Quality indicators for advanced ovarian cancer surgery from the European Society of Gynaecologic Oncology (ESGO): 2020 update. Int J Gynecol Cancer. 2020;30:436-40.
25. Frutuoso C, Completo J, Bernardo F. MAP-OCSUR Mapeamento dos centros que realizam cirurgia do cancro do ovário em Portugal. In: Poster Apresentado no 19º Congresso Nacional de Oncologia: 16-18 De Novembro. Porto: Portugal; 2022.
26. Colombo N, Sessa C, Du Bois A, Ledermann J, McCluggage WG, McNeish I, et al. ESMO-ESGO consensus conference recommendations on ovarian cancer: pathology and molecular biology, early and advanced stages, borderline tumours and recurrent disease†. Ann Oncol. 2019;30:672-705.
27. Pujade-Lauraine E, Ledermann JA, Selle F, Gebski V, Penson RT, Oza AM, et al. Olaparib tablets as maintenance therapy in patients with platinum-sensitive, relapsed ovarian cancer and a BRCA1/2 mutation (SOLO2/ENGOT-Ov21): a double-blind, randomised, placebo-controlled, phase 3 trial. Lancet Oncol. 2017;18:1274-84.
28. Marth C, Abreu MH, Andersen KK, Aro KM, De Lurdes Batarda M, Boll D, et al. Real-life data on treatment and outcomes in advanced ovarian cancer: an observational, multinational cohort study (RESPONSE trial). Cancer. 2022;128:3080-9.
29. Da Silva FF, Lopes AR, Silva BM, Guedes H, De Almeida SB, Simões P, et al. 1096 beyond trials: olaparib's real-world data in platinum-sensitive relapsed ovarian cancer - multicenter experience from Portugal. Int J Gynecol Cancer. 2024;34 Suppl 1:A399.
30. Department of Health and Human Sevices. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. United States: Department of Health and Human Sevices; 2017.