Physician-reported patient involvement and treatment decisions in first-line ovarian cancer in the USA and Europe

Kathleen N Moore ,[1] Mansoor R Mirza,[2,3] Charlie Gourley,[4] Sandro Pignata,[5,6] Domenica Lorusso,[7,8] Bradley J Monk ,[9,10] Jalid Sehouli ,[11,12] Jeanne M Schilder,[13] Nathalie D'Esquermes,[14] Antonio González-Martín [15,16]

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/ijgc-2024-005405).

For numbered affiliations see end of article.

Correspondence to
Dr Kathleen N Moore, Stephenson Cancer Center, Gynecologic Cancers Clinic, Oklahoma City, OK 73104, USA; kathleen-moore@ouhsc.edu

For 'Presented at statement' see end of article.

Received 16 February 2024
Accepted 21 May 2024

To cite: Moore KN, Mirza MR, Gourley C, *et al. Int J Gynecol Cancer* Published Online First: [please include Day Month Year]. doi:10.1136/ijgc-2024-005405

ABSTRACT

Objectives Real-world data evaluating how approvals of novel treatment regimens for ovarian cancer have impacted the treatment paradigm, including first-line maintenance, are lacking. This analysis aimed to describe treatment patterns for advanced epithelial ovarian cancer in Europe and the USA in the first-line maintenance setting. Patient characteristics, biomarker testing rates, and drivers of treatment choice were also evaluated.

Methods A retrospective chart review study of electronic medical records in Europe and the USA was conducted for patients diagnosed with epithelial ovarian cancer (June 1, 2017–May 31, 2020), in line with Healthcare Market Research guidelines. Eligible physicians extracted data from electronic medical records by completing standardized patient record forms, including questions on patient involvement in treatment decisions. Patients with advanced (stage III/IV) disease were stratified by country and diagnosis date to provide information on treatment patterns.

Results Patient record forms for 7072 patients with epithelial ovarian cancer were completed by 416 physicians; 5386 patients had stage III/IV ovarian cancer. Over time, the percentage of patients who were tested for *BRCA* mutations or homologous recombination deficiency increased. Patient preference was documented as a reason for treatment selection in approximately one-sixth of cases in the first-line adjuvant and first-line maintenance settings. The use of first-line maintenance poly(ADP-ribose) polymerase inhibitor monotherapy increased over time, while the use of vascular endothelial growth factor inhibitor monotherapy decreased.

Conclusions This real-world study showed that treatment patterns for advanced epithelial ovarian cancer varied by country. Rates of physician-reported patient involvement in treatment decisions in the first-line adjuvant and maintenance treatment settings for ovarian cancer were low, highlighting an unmet need for initiatives to improve patient involvement in shared decision-making regarding maintenance therapy selection.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Since 2018, the first-line maintenance treatment landscape for ovarian cancer has continued to evolve following the FDA and EMA approvals of poly(ADP-ribose) polymerase (PARP) inhibitors as monotherapy or in combination with bevacizumab.

WHAT THIS STUDY ADDS

⇒ Between June 2017 and May 2020, physicians in the USA and Europe reported low rates of patient involvement in first-line treatment decisions for ovarian cancer. Only 56.0% of eligible patients with newly diagnosed advanced ovarian cancer received first-line maintenance therapy during the study. While the proportion of patients receiving PARP inhibitor monotherapy increased over time, the majority (69.8%) of patients who received first-line maintenance therapy received anti-angiogenic agent monotherapy. Approximately 14% of patients with stage III/IV high-grade serous and high-grade endometrioid carcinomas did not undergo genetic testing for *BRCA* and approximately 82% did not undergo testing for homologous recombination deficiency.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The results of this study provide real-world evidence regarding the rationale behind treatment choice, as well as biomarker testing rates and rates of physician-reported patient involvement in treatment decisions in patients with advanced ovarian cancer in the first-line maintenance setting, highlighting unmet needs in the clinical setting.

INTRODUCTION

Ovarian cancer is one of the most common gynecologic cancers.[1] In 2020, approximately 314 000 new cases were diagnosed globally and more than 207 000 ovarian cancer-related deaths occurred.[1] About 70% are high-grade serous adenocarcinomas, and approximately 15% are high-grade endometrioid carcinomas.[2 3] The prevalence of *BRCA* mutations differs by ovarian cancer sub-type and is highest among high-grade serous carcinomas.[3] Because of the non-specific nature of symptoms and the lack of effective screening, ovarian cancer is diagnosed at an advanced stage in approximately 75% of cases.[4 5]

Historically, treatment options for patients with newly diagnosed advanced epithelial ovarian cancer

were limited, and the standard of care consisted of cytoreductive surgery followed by adjuvant platinum and taxane-based combination chemotherapy.[5 6] More recently, in patients ineligible to receive primary cytoreductive surgery, platinum-based neoadjuvant chemotherapy followed by interval cytoreductive surgery and adjuvant chemotherapy was shown to be non-inferior to primary cytoreductive surgery followed by adjuvant chemotherapy.[7 8]

Although response rates to first-line therapy approach 80%,[6] recurrence develops in approximately 70% of patients.[9] Until recently, rechallenge with a platinum-based regimen was the most commonly used treatment approach for platinum-sensitive recurrent epithelial ovarian cancer.[9] Addition of the vascular endothelial growth factor (VEGF) inhibitor bevacizumab to platinum-based chemotherapy was approved for the first-line treatment of advanced epithelial ovarian cancer by the European Medicines Agency (EMA) in 2011[10] and by the US Food and Drug Administration (FDA) in 2018.[11 12] Since 2018, the first-line maintenance treatment landscape for ovarian cancer has continued to evolve with the FDA and EMA approvals of poly(ADP-ribose) polymerase (PARP) inhibitors as monotherapy or in combination with bevacizumab.[13]

Current treatment guidelines recommend biomarker testing in all patients with high-grade ovarian cancer, as *BRCA* mutation and homologous recombination deficiency status can be used to identify patients who derive greater benefit from PARP inhibitor treatment.[14 15] However, although widespread *BRCA*1/2 testing has been commercially available since 2013,[16] the results of one population-based study indicated that only approximately 31% of patients diagnosed with ovarian cancer between 2013 and 2014 underwent genetic testing, suggesting that initial adoption of biomarker testing was low.[17]

There is an increasing interest in evaluating the impact of these approvals on the ovarian cancer treatment paradigm, using real-world data to generate hypotheses for prospective trials and to identify gaps for improved clinical management. Currently, evidence from real-world settings examining the drivers of treatment choice in ovarian cancer is lacking. The primary objective of this analysis was to describe treatment patterns for patients diagnosed with advanced ovarian cancer in Europe and the USA, with a focus on first-line maintenance. Secondary objectives included describing patient characteristics, biomarker testing rates, and drivers of treatment choice, including patient involvement in treatment decisions.

METHODS

Patients and Study Design

A retrospective chart review study of electronic medical records of patients diagnosed with ovarian cancer in Italy, France, Germany, Spain, the UK, and the USA was performed. Eligible patients were diagnosed with epithelial ovarian, fallopian tube, or primary peritoneal cancer (collectively referred to as epithelial ovarian cancer), regardless of the stage of disease, during the pre-defined study period (between June 1, 2017 and May 31, 2020) and were aged ≥18 years at the time of diagnosis. Patients known to have opted out of participation in any research study were excluded in compliance with General Data Protection Regulation. Patients were stratified by country and date of diagnosis to provide information on treatment patterns at different time points into one of three pre-defined cohorts: cohort 1 included patients who were diagnosed between June 1, 2017 and May 31, 2018; cohort 2 included patients who were diagnosed between June 1, 2018 and May 31, 2019; and cohort 3 included patients who were diagnosed between June 1, 2019 and May 31, 2020 (see Online Supplemental Figure 1).

The study adhered to the legal and ethical guidelines of Healthcare Market Research, as per the guidelines of the European Pharmaceutical Market Research Association,[18] British Healthcare Business Intelligence Association,[19] and Pharmaceutical Business Intelligence and Research Group.[20]

Data Collection and Analysis

Patient data were collected via a survey completed by treating physicians (oncologists, gynecologic oncologists, and gynecologists, where applicable; Online Supplemental File 1). Physicians from between 40 and 70 centers in the UK, France, Germany, Spain, and Italy and between 50 and 100 centers in the USA were invited randomly to participate by Genactis (a global strategic market research consultancy) and partners and went through a screening process (telephone or online) consisting of 13 questions to confirm their practice settings and experience. Quota was determined by setting and region (Online Supplemental Table 1), and target sample size was predetermined to reach a CI of 4.4 to 5.0.

Eligible physicians were actively practicing full time as oncologists/gynecologic oncologists, were <62 years of age, and were the primary decision makers for pharmacological treatment for their patients. In addition, eligible physicians had a minimum of 3 years of experience, were treating a minimum of 10 patients with ovarian cancer per year (at least 5 of whom were newly diagnosed with ovarian cancer), and retrieved the electronic medical records for 10–20 patients from their practice. In the USA, physicians employed by the government were unable to be compensated and those licensed to prescribe medication in Minnesota and Vermont were ineligible to participate. To avoid selection bias, physicians selected consecutive cases.

All data were collected directly from physicians using online surveys generated by Genactis (see Online Supplemental File 1). The physicians completed standardized patient record forms using data from the electronic medical record for each patient. The patient record forms contained multiple-choice questions covering patient demographics and clinical characteristics; treatment patterns in the first-line treatment setting, including first-line maintenance; and the level of patient involvement in their treatment plan (see Online Supplemental Table 2). Responses to the multiple-choice questions were collated and summarized descriptively and were not weighted or adjusted. Analyses were conducted in the overall patient population and in the sub-group of patients with stage III/IV ovarian cancer. All analyses were descriptive so significance testing was not conducted.

RESULTS

Patient Demographics

Overall, 7072 patients from 416 physicians (Table 1) based in various practice settings (Online Supplemental Figure 2) were included; of those, 23.8% (1686/7072) had stage I/II ovarian cancer and 76.2% (5386/7072) had stage III/IV ovarian cancer. In the overall study population, 97.5% (6896/7072) of patients

Table 1 Number of participating physicians and patients by country

	USA	Germany	France	Italy	Spain	UK	Total
Participating physicians, n	89	72	71	69	63	52	416
Patients, n	1200	1207	1200	1200	1200	1065	7072

received primary treatment, 62.4% (4303/6896) of whom underwent debulking surgery (primary debulking: 3114/4303; interval debulking: 1189/4303) and 75.8% (5224/6896) of whom received first-line adjuvant therapy. Rates of optimal cytoreduction were low for all countries (see Online Supplemental Table 3). A total of 238 patients were excluded because the reporting physician was not the physician who initiated adjuvant therapy, resulting in 70.5% (4986/7072) of patients who received first-line adjuvant therapy and 47.1% (3331/7072) who went on to receive first-line maintenance therapy. Nearly all patients with stage III/IV disease (97.5% [5251/5386]) received primary treatment; 74.1% (3992/5386) received first-line adjuvant therapy and 56.0% (3016/5386) received first-line maintenance therapy.

The mean age of patients in the overall study population at the time of diagnosis was 61.9 years. Mean age was highest in France (65.4 years) and lowest in the USA (60 years), while mean weight was highest in the USA (72.7 kg) and lowest in Italy (65.1 kg; see Online Supplemental Table 3). The mean (SD) age of patients with stage III/IV ovarian cancer was 63 (10.3) years, and the majority had an Eastern Cooperative Oncology Group performance status (ECOG PS) of 0 or 1 (83.8% [4511/5386]). Most patients with stage III/IV ovarian cancer had high-grade serous carcinomas (60.3% [3249/5386]; Table 2).

Of patients with stage III/IV high-grade serous and high-grade endometrioid carcinomas, 58% (2100/3621) had *BRCA* wild-type disease, 27.9% (1012/3621) tested positive for germline or somatic

Table 2 Demographic information for patients with stage III/IV ovarian cancer

Parameter, n (%)	All patients with stage III/IV ovarian cancer (N=5386)
Histology	
High-grade serous carcinoma	3249 (60.3)
High-grade endometrioid carcinoma	372 (6.9)
Other*	1765 (32.8)
BRCA	
BRCA mutation	1427 (26.5)
BRCA wild-type	3000 (55.7)
Not tested	959 (17.8)
Homologous recombination deficiency	
Homologous recombination deficient	217 (4.0)
Homologous recombination proficient	926 (17.2)
Not tested	4243 (78.8)
Homologous recombination repair	
Homologous recombination repair mutation	146 (2.7)
Homologous recombination repair wild-type	1479 (27.5)
Not tested	3761 (69.8)
Tumor cytoreductive surgery	
Optimal tumor cytoreduction	1236 (23.0)
Suboptimal, no surgery, or unknown	4150 (77.0)
Response to initial treatment	
Complete response or partial response to initial treatment in patients receiving first-line maintenance	1803 (33.5)
Stable disease or progressive disease to initial treatment in patients receiving first-line maintenance	201 (3.7)
Unknown response to initial treatment in patients receiving first-line maintenance	1012 (18.8)
Did not receive first-line maintenance	2370 (44.0)

*Other histologies include clear cell carcinoma, low-grade serous carcinoma, low-grade endometrioid carcinoma, mucinous carcinoma, seromucinous carcinoma, and malignant Brenner tumor.

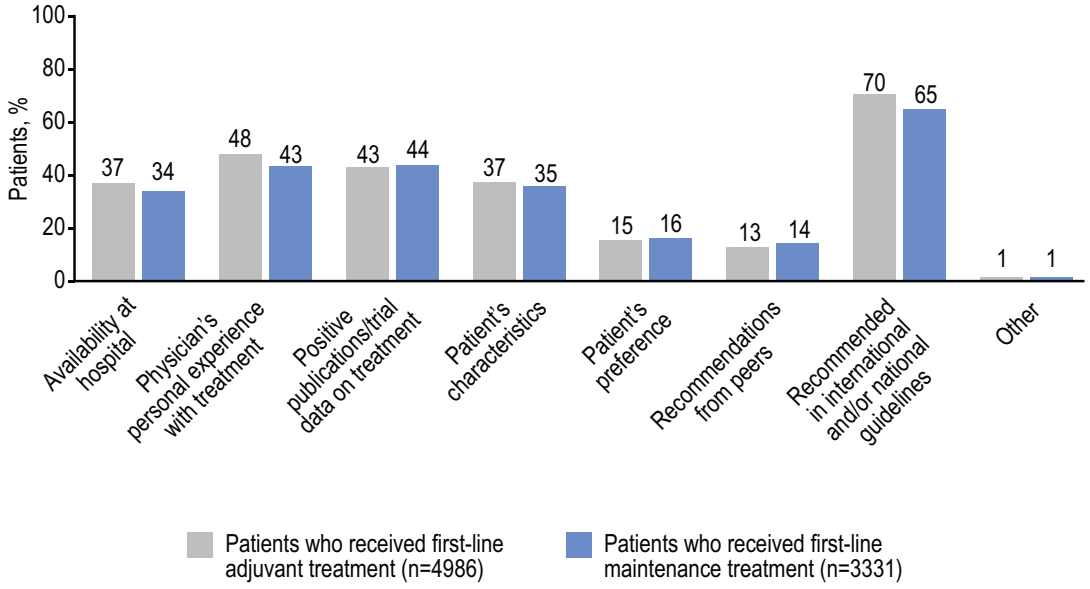

Figure 1 Reasons for treatment choice in the first-line adjuvant and first-line maintenance settings across all countries. Physicians could select more than one option in response to the question "Why did you select this (first-line adjuvant/first-line maintenance) treatment for this specific patient?"

*BRCA*1 or *BRCA*2 mutations, and 14.1% (509/3621) did not undergo *BRCA* testing. Biomarker testing for homologous recombination deficiency status was not performed for 82.4% (2985/3621) of patients with stage III/IV high-grade serous and high-grade endometrioid carcinomas. Of the 5386 patients with stage III/IV disease, 37.2% (2004/5386) received first-line maintenance treatment and had a known response to their initial treatment regimen, 18.8% (1012/5386) received first-line maintenance treatment and had an unknown response to their initial treatment regimen, and 44.0% (2370/5386) did not receive first-line maintenance treatment. Of the 2004 patients who received first-line maintenance treatment and had a known response to their initial treatment regimen, 90.0% (1803/2004) had a complete response or partial response, whereas 10.0% (201/2004) had stable disease (91/201) or progressive disease (110/201; Table 2).

Role of Patient Preference in Treatment Selection

In the patient record forms, physicians were able to select more than one response to the question "Why did you select this (first-line adjuvant/first-line maintenance) treatment for this specific patient?" Across all countries, the most commonly reported factor governing treatment selection in the first-line adjuvant and first-line maintenance settings was recommendation in international and/or national guidelines (Figure 1).

Patient preference was documented in the electronic medical record as a reason for choosing the specific treatment in 15% (754/4986) of cases in the first-line adjuvant setting and 16% (521/3331) of cases in the first-line maintenance setting (Figure 1). Among the 754 patients receiving first-line adjuvant treatment for whom patient treatment preference was documented, 48% received chemotherapy, 47% received chemotherapy in combination with a VEGF inhibitor, and 5% received other treatment. Among the 521 patients receiving first-line maintenance treatment for whom patient treatment preference was documented, 53% received VEGF inhibitor monotherapy, 33% received PARP inhibitor monotherapy, 7% received a VEGF inhibitor in combination with a PARP inhibitor, 5% received chemotherapy, and 2% received another first-line maintenance treatment.

First-Line Maintenance Treatment versus Active Surveillance

Of the 5386 patients with stage III/IV ovarian cancer who were included in this analysis, 93.7% (5047) completed primary treatment, followed by first-line maintenance (3016) or active surveillance (2031). The proportion of patients receiving first-line maintenance increased between cohort 1 (53.0% [879/1660]), cohort 2 (60.5% [1051/1737]), and cohort 3 (65.8% [1086/1650]), whereas the proportion monitored by active surveillance decreased (cohort 1, 47.0% [781/1660]; cohort 2, 39.5% [686/1737]; cohort 3, 34.2% [564/1650]; Figure 2). This trend was evident across all countries except Germany, where the use of first-line maintenance decreased between cohort 1 (70.9% [178/251]), cohort 2 (64.7% [209/323]), and cohort 3 (64.4% [212/329]; Figure 2).

The use of first-line maintenance was highest in France (71.5% [710/993]) and lowest in the UK (47.8% [339/709]). Italy had the largest increase in first-line maintenance use (cohort 1, 43.9% [132/301]; cohort 2, 55.9% [162/290]; cohort 3, 68.0% [189/278]) followed by the UK (cohort 1, 35.2% [82/233]; cohort 2, 49.4% [121/245]; cohort 3, 58.9% [136/231]; Figure 2).

First-Line Maintenance Treatment Regimen

A total of 3016 patients with stage III/IV ovarian cancer received first-line maintenance treatment; 69.8% (2106) received anti-angiogenic agent monotherapy, 23.4% (705) received PARP inhibitor monotherapy, 3.5% (106) received a PARP inhibitor in combination with an anti-angiogenic agent, 2.0% (59) received chemotherapy, and 1.3% (40) received other agents. Numerically, the use of PARP inhibitor monotherapy for first-line maintenance was highest in the USA (40.0% [174/435]) and lowest in France (12.0% [85/710]; Figure 3A). Conversely, the highest rates of anti-angiogenic monotherapy were observed in France (84.8%

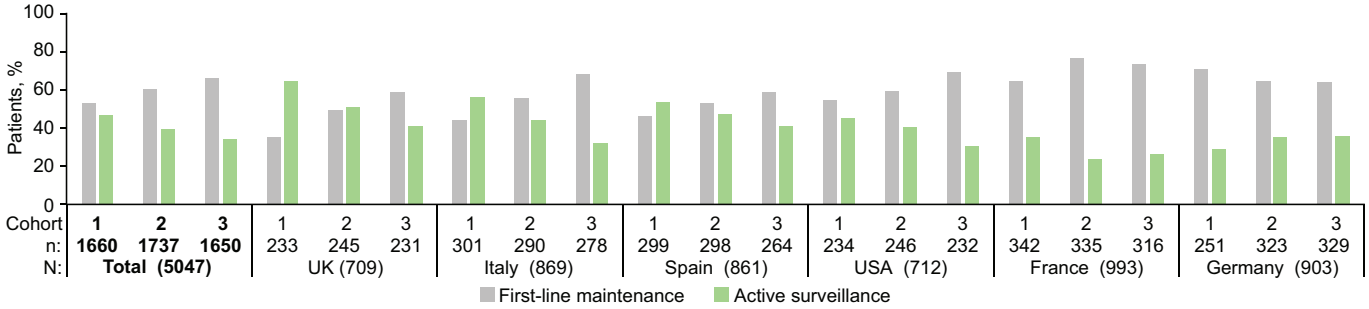

Figure 2 First-line maintenance treatment versus active surveillance in patients with stage III/IV ovarian cancer, overall and by country. First-line maintenance includes, but is not exclusive to, anti-angiogenic monotherapy, PARP inhibitor monotherapy, anti-angiogenic agent plus PARP inhibitor combination therapy, and chemotherapy. Cohort 1: diagnosed June 1, 2017 to May 31, 2018; cohort 2: diagnosed June 1, 2018 to May 31, 2019; cohort 3: diagnosed June 1, 2019 to May 31, 2020. PARP, poly(ADP-ribose) polymerase.

[602/710]), whereas the lowest rates were observed in the USA (42.8% [186/435]; Figure 3A).

Across all countries, the number of patients receiving PARP inhibitors increased between cohort 1 and cohort 3, while the use of anti-angiogenic agents decreased (Figure 3A). The USA was the only country in which more patients received PARP inhibitor monotherapy than anti-angiogenic agent monotherapy in cohort 3 (Figure 3A).

First-Line Maintenance Treatment Regimen by *BRCA* Status

A total of 26.5% (1427/5386) of patients with stage III/IV ovarian cancer tested positive for a germline or somatic *BRCA*1 or *BRCA*2 mutation, whereas 55.7% (3000/5386) were *BRCA* wild-type, and 17.8% (959/5386) were not tested for *BRCA* mutation status (Table 2). Of patients who were tested for *BRCA* and received first-line maintenance, a lower percentage of patients with *BRCA* mutation (39.2% [384/979]; Figure 3B) received anti-angiogenic monotherapy than patients with *BRCA* wild-type (84.2% [1470/1745]; Figure 3C). The use of anti-angiogenic monotherapy decreased between cohort 1 and cohort 3 in both patients with *BRCA* mutation (Figure 3B) and patients with *BRCA* wild-type (Figure 3C). Conversely, more patients with *BRCA* mutation (50.5% [494/979]; Figure 3B) received PARP inhibitor monotherapy than patients with *BRCA* wild-type (11% [197/1745]; Figure 3C). The adoption of PARP inhibitor monotherapy increased between cohort 1 and cohort 3 in both patients with *BRCA* mutation (Figure 3B) and patients with *BRCA* wild-type (Figure 3C).

DISCUSSION

Summary of Main Results

In this retrospective chart review study, treatment patterns for advanced epithelial ovarian cancer varied by country. While the

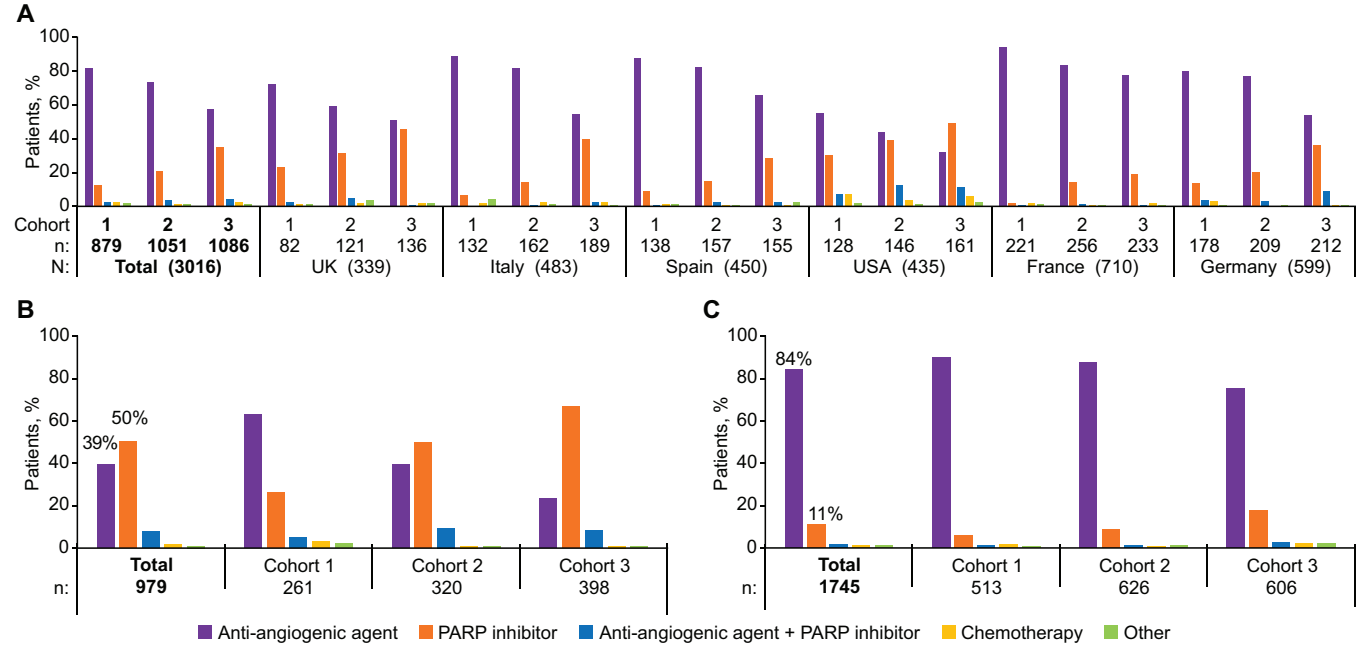

Figure 3 First-line maintenance treatment regimen in patients with stage III/IV ovarian cancer (A) overall and by country; (B) with *BRCA* mutation, overall and by cohort; (C) with *BRCA* wild-type, overall and by cohort. Cohort 1: diagnosed June 1, 2017 to May 31, 2018; cohort 2: diagnosed June 1, 2018 to May 31, 2019; cohort 3: diagnosed June 1, 2019 to May 31, 2020. PARP, poly(ADP-ribose) polymerase.

proportion of patients receiving first-line maintenance increased over time in nearly all countries, rates of physician-reported patient involvement in treatment decisions in the first-line treatment of ovarian cancer and biomarker testing rates for homologous recombination deficiency were low.

Results in the Context of Published Literature

Physician–patient communication has been cited as a critical component of satisfaction with care in patients with ovarian cancer.[21] However, despite increasing recognition that participation in treatment decision-making may be beneficial, many patients with ovarian cancer report that insufficient consultation time often limits their ability to discuss goals, priorities, and quality-of-life concerns with their physicians.[21 22] In this retrospective review of patients' medical charts, rates of physician-reported patient involvement in treatment decisions in first-line treatment of ovarian cancer in the USA and Europe between 2017 and 2020 were low. Patient involvement in treatment decisions was, however, consistent between the first-line adjuvant (15%) and first-line maintenance (16%) settings. The low observed rates of patient involvement in treatment decisions may have reflected the limited number of available treatment options during the time the study was conducted.[21]

In addition, approximately 56% of eligible patients with advanced ovarian cancer received first-line maintenance treatment during the period evaluated in this study. Of eligible patients who received first-line maintenance therapy, the majority (70%) received anti-angiogenic agent monotherapy. This observation was consistent with the treatment landscape at the time the study was conducted, as the VEGF inhibitor bevacizumab was approved for use in advanced ovarian cancer by the EMA in 2011, based on the results of the GOG-0218 and ICON7 trials.[13 23–25]

Over the course of the study, treatment patterns varied considerably by country. Across all countries, increased use of PARP inhibitor monotherapy was observed over time, with a decrease in the use of anti-angiogenic monotherapy as first-line maintenance. For patients in cohort 3 (June 1, 2019 to May 31, 2020), the PARP inhibitors olaparib and niraparib had gained FDA and EMA approvals for the first-line maintenance treatment of advanced ovarian cancer.[13] Variations in the adoption of PARP inhibitor monotherapy may have been the result of differences in the regulatory agency approval timelines for the treatment of ovarian cancer by the FDA and EMA (ie, olaparib was approved by the FDA in 2018 but was not approved by the EMA until 2019, whereas bevacizumab was approved by the EMA in 2011 but was not approved in the USA until 2018), as well as differences in reimbursement patterns by country.[10 11 13 26]

Between cohort 1 and cohort 3, the use of PARP inhibitor monotherapy also increased in patients with *BRCA* mutations in parallel with the evolution of advanced ovarian cancer treatment patterns and the completion of several landmark trials that contributed to PARP inhibitor approvals. The SOLO1 study, published in 2018, was the first randomized phase III trial to examine the effects of olaparib first-line maintenance therapy in patients with newly diagnosed *BRCA1/2*-mutated advanced ovarian cancer, demonstrating that olaparib significantly improved progression-free survival in such patients.[27] The randomized phase III PAOLA-1 study, the results of which were reported in 2019, showed that first-line maintenance therapy with olaparib in combination with bevacizumab provided significant progression-free survival benefit over bevacizumab in combination with placebo, particularly in patients with homologous recombination-deficient tumors (regardless of *BRCA* mutational status).[28] In addition, the randomized phase III PRIMA study, published in 2019, showed that niraparib treatment significantly extended progression-free survival versus placebo in patients with newly diagnosed advanced ovarian cancer, regardless of homologous recombination deficiency status.[29] The low rates of PARP inhibitor and VEGF inhibitor combination therapy observed in the present chart review study reflect the fact that the PAOLA-1 regimen had not yet been widely adopted and approved when this study was conducted and may also have been influenced by the significant progression-free survival benefit that was demonstrated for PARP inhibitor monotherapy in the SOLO1 study. In addition, the use of bevacizumab is restricted to patients with high-risk disease or residual disease in certain countries. These factors, combined with variations in reimbursement patterns by country, likely impacted treatment access and selection.[26]

The results of the SOLO1, PRIMA, and PAOLA-1 studies highlight the importance of biomarker testing and using biomarker status to guide advanced ovarian cancer treatment decisions.[13 23] However, in the present chart review study, approximately 14% of patients with stage III/IV high-grade serous and high-grade endometrioid carcinomas did not undergo genetic testing for *BRCA,* and approximately 82% did not undergo testing for homologous recombination deficiency, highlighting an unmet need to increase testing.

Strengths and Weaknesses

The results of the present analysis reflect an older data set with evolution in practice and may help inform clinicians and payers regarding the uptake of first-line maintenance therapy for ovarian cancer in the USA and Europe. While the large data set in this study (representing approximately 7200 patients from five European countries and the USA) allowed for the characterization of ovarian cancer treatment trends, the descriptive nature of the analysis limited the ability to directly compare patient preferences, treatment patterns, and biomarker testing rates between countries. Furthermore, while key demographic data regarding age, weight, performance status, disease stage, and ovarian cancer histology were collected, additional variables that may have impacted treatment selection, including race/ethnicity and socioeconomic status, were not analyzed in this study.

Real-world evidence studies, such as the present study, allow for the evaluation of clinical practice patterns; however, there are several limitations to real-world data collection.[30] Electronic medical records allow for real-time clinical treatment and outcomes data collection; however, the potential for coding, recording, and interpretive errors exists. In addition, the findings depend on the accuracy of the recorded information or the recall of individuals and the availability of diagnostic tools (eg, homologous recombination deficiency testing) and drugs, which may lead to bias. Clinical data (such as health outcomes and health status) may be limited or missing and often cannot be retrieved retroactively. Additionally, key information regarding therapy selection based on specific demographic factors, including comorbidities, physician and/or patient preference, and level of patient involvement in treatment decision-making, may not be documented in electronic medical records, which may have led to underestimation of the factors that impact treatment choice in the present study. Finally, nuances, such

as overlap between physician recommendations and patient preferences, may not have been accurately reflected in the electronic medical records. Therefore, patient-reported outcome measures should be routinely incorporated in the clinical setting to assess patient quality of life and facilitate discussion of endpoints that are relevant to patients, such as progression-free survival, progression-free survival-2, and time to subsequent therapy.[22]

Implications for Practice and Future Research

The results of this study provide real-world evidence regarding the rationale behind treatment choice, treatment patterns by country, and rates of biomarker testing in patients with advanced ovarian cancer in the first-line maintenance setting, highlighting unmet needs in the clinical setting. Dissemination of these data may help to contextualize and increase awareness regarding how the advanced ovarian cancer treatment paradigm has progressed with the approval of targeted therapies in the era of maintenance therapy.

CONCLUSIONS

In the USA and Europe between 2017 and 2020, rates of physician-reported patient involvement in first-line treatment decisions for ovarian cancer were low. Over time, the percentage of patients who were tested for *BRCA* mutations or homologous recombination deficiency and the use of first-line maintenance PARP inhibitor monotherapy increased, while the use of VEGF inhibitor monotherapy decreased.

Author affiliations
[1]Stephenson Cancer Center, University of Oklahoma, Oklahoma City, Oklahoma, USA
[2]Nordic Society of Gynaecological Oncology Clinical Trial Unit, Copenhagen, Denmark
[3]Department of Oncology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark
[4]Cancer Research UK Scotland Centre, Institute of Genetics and Cancer, University of Edinburgh, Edinburgh, UK
[5]Multicentre Italian Trials in Ovarian Cancer and Gynecologic Malignancies (MITO), Naples, Italy
[6]Department of Urology and Gynecology, Istituto Nazionale Tumori IRCCS Fondazione G Pascale, Naples, Italy
[7]Multicentre Italian Trials in Ovarian Cancer and Gynecologic Malignancies (MITO), Milan, Italy
[8]Humanitas San Pio X, Milan, Humanitas University, Pieve Emanuele, Milan, Italy
[9]The GOG Foundation, Inc, Philadelphia, Pennsylvania, USA
[10]Florida Cancer Specialists and Research Institute, West Palm Beach, Florida, USA
[11]Department of Gynecology with Center for Oncological Surgery, Campus Virchow Klinikum, Charité-Universitätsmedizin Berlin, Berlin, Germany
[12]North-Eastern German Society of Gynecological Oncology (NOGGO), Berlin, Germany
[13]GSK, Indianapolis, Indiana, USA
[14]Genactis, Mougins, France
[15]Grupo Español de Investigación en Cancer ginecológicO (GEICO), Madrid, Spain
[16]Medical Oncology Department, Translational Oncology Group, CIMA, Universidad de Navarra, Cancer Center Clínica Universidad de Navarra, Madrid, Spain

Presented at
Portions of these data were previously presented at the Society of Gynecologic Oncology (SGO) Annual Meeting on Women's Cancer, March 18–21, 2022, Phoenix, AZ, USA; and at the International Gynecologic Cancer Society (IGCS) Annual Global Meeting, September 29–October 1, 2022, New York, NY, USA.

Acknowledgements Trademarks are owned by or licensed to the GSK group of companies. GSK and the authors thank all the study contributors, as well as Talal Ali (formerly of GSK), Anabel Ferreras (formerly of Genactis), Marie-Laure Louis (formerly of Genactis), Tony Cox (formerly of Genactis), and David Twinberrow of Genactis, for their thoughtful contributions to the manuscript. Writing and editorial support, under the direction of the authors, was funded by GSK (Waltham, MA, USA); coordinated by Chun Zhou, PhD, of GSK and Prudence Roaf, MPH, formerly of GSK; and provided by Jessica M Weems, PhD, and Jennifer Robertson, PhD, of Ashfield MedComms, an Inizio company.

Contributors Concept, design, and data interpretation: KNM, MRM, CG, SP, DL, BJM, JS, JMS, AG-M. Data acquisition and analysis: ND'E. Drafting of the manuscript: all authors. Critical revision of the paper for important intellectual content: all authors. JMS is the guarantor and accepts full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

Funding This study was funded by GSK. The funder participated in the design and conduct of the study; management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Competing interests The authors disclose the following potential conflicts of interest: KNM: Institutional research grant: Angle PLC; Consulting fees: Fujirebio Diagnostics Inc; Advisory fees: GSK. MRM: Advisory board fees: Allarity Therapeutics, AstraZeneca, Biocad, BioNTech, Boehringer Ingelheim, Clovis, Daiichi-Sankyo, Eisai, Genmab, GSK, ImmunoGen, Incyte, Karyopharm, Merck/MSD, Mersana, Novartis, Regeneron, Roche, Seagen, Takeda, Tesaro, Zailab; membership on the board of directors or stockholder/shareholder: Karyopharm Therapeutics, Sera Prognostics; Institutional research grants: Allarity, Apexigen, AstraZeneca, Boehringer Ingelheim, Clovis, GSK, Novartis, Tesaro, Ultimovacs; Trial chair: AstraZeneca, Boehringer Ingelheim, Deciphera, Daiichi-Sankyo, GSK, Merck, Mersana, NuvationBio, Tesaro. SP: Honoraria: AstraZeneca, GSK, MSD, Roche; Research funding: AstraZeneca, GSK, MSD, Pfizer, Roche. CG: Honoraria/consultancy fees: AstraZeneca, Chugai, Clovis, Cor2Ed, Eisai, GSK, MSD, Peer Voice, Takeda; Research funding: Aprea, Artios, AstraZeneca, BerGen Bio, GSK, Medannexin, MSD, Novartis, NuCana; Issued/pending patents related to predicting treatment response in ovarian cancer. DL: Grants or contracts: Alkermes, AstraZeneca, Clovis Oncology, Corcept, Genmab, GSK, ImmunoGen, Incyte, MSD, Novartis, Pharma&, Pharmamar, Roche, Seagen; Consulting fees: AstraZeneca, Clovis Oncology, Corcept, Daiichi Sankyo, Genmab, GSK, ImmunoGen, MSD, Novartis, Novocure, Oncoinvest, Seagen, Sutro; Honoraria: AstraZeneca, Corcept, Genmab, GSK, ImmunoGen, MSD, Seagen; Support for attending meetings and/or travel: AstraZeneca, GSK, Menarini, MSD; Participation on a data safety monitoring board or advisory board: AstraZeneca, Clovis Oncology, Corcept, Daiichi Sankyo, Genmab, GSK, ImmunoGen, MSD, Novocure, Oncoinvest, Seagen, Sutro; Leadership or fiduciary roles: ENGOT, GCIG, MITO. BJM: Consulting fees: Acrivon, Adaptimune, Agenus, Akeso Bio, Amgen, Aravive, AstraZeneca, Bayer, Clovis, Eisai, Elevar, EMD Merck, Genmab/Seagen, GOG Foundation, Gradalis, Heng Rui, ImmunoGen, Iovance, Karyopharm, Laekna, MacroGenics, Merck, Mersana, Myriad, Novartis, Novocure, OncoC4, Panavance, Pieris, Pfizer, Puma, Regeneron, Roche/Genentech, Sorrento, Teasro/GSK, US Oncology Research, VBL, Verastem, Zentalis; Speakers' bureau honoraria: AstraZeneca, Eisai, Myriad, Roche/Genentech, Tesaro/GSK. JS: Grants or contracts: GSK, Roche; Consulting fees: Alkermes, Amgen, AstraZeneca, Clovis Oncology, Genmab, GSK, ImmunoGen, Merck Sharp & Dohme, MSD, Novartis, Oncoinvent, Pfizer/Merck, PharmaMar, Roche; Honoraria fees: AstraZeneca, Clovis, Eisai, MSD, PharmaMar, Roche, Tesaro/GSK; Support for attending meetings: AstraZeneca, PharmaMar, Roche, Tesaro/GSK. JMS: Employee of GSK. ND'E: Employee of Genactis (the company that was contracted to perform the statistical analyses). AG-M: Fees for different educational or advisory-related activities: Alkermes, Amgen, AstraZeneca, Clovis, Eisai, Genmab, GSK, Hedera Dx, Immunogen, Illumina, Karyopharm, Macrogenics, Mersana, MSD, Novartis, Novocure, Oncoinvent, PharmaMar, Regeneron, Roche, Seagen, Sotio, Sutro, Takeda, Tubulis.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement In accordance with the journal's guidelines, we will provide our data for independent analysis by a selected team by the Editorial Team for the purposes of additional data analysis or for the reproducibility of this study in other centers if such is requested. For requests for access to anonymised subject level data, please contact the corresponding author.

ORCID iDs
Kathleen N Moore http://orcid.org/0000-0002-5803-0718
Bradley J Monk http://orcid.org/0000-0001-6985-0159
Jalid Sehouli http://orcid.org/0000-0002-5963-6623
Antonio González-Martín http://orcid.org/0000-0001-8376-9576

REFERENCES

1 Sung H, Ferlay J, Siegel RL, *et al*. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2021;71:209–49.
2 Gupta S, Nag S, Aggarwal S, *et al*. Maintenance therapy for recurrent epithelial ovarian cancer: current therapies and future perspectives - a review. *J Ovarian Res* 2019;12:103.
3 Manchana T, Phoolcharoen N, Tantbirojn P. BRCA mutation in high grade epithelial ovarian cancers. *Gynecol Oncol Rep* 2019;29:102–5.
4 Matulonis UA, Sood AK, Fallowfield L, *et al*. Ovarian cancer. *Nat Rev Dis Primers* 2016;2:16061.
5 Konstantinopoulos PA, Ceccaldi R, Shapiro GI, *et al*. Homologous recombination deficiency: exploiting the fundamental vulnerability of ovarian cancer. *Cancer Discov* 2015;5:1137–54.
6 Damia G, Broggini M. Platinum resistance in ovarian cancer: role of DNA repair. *Cancers (Basel)* 2019;11:119.
7 González-Martín A, Harter P, Leary A, *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.
8 Kehoe S, Hook J, Nankivell M, *et al*. Primary chemotherapy versus primary surgery for newly diagnosed advanced ovarian cancer (CHORUS): an open-label, randomised, controlled, non-inferiority trial. *Lancet* 2015;386:249–57.
9 Bartoletti M, Pelizzari G, Gerratana L, *et al*. Bevacizumab or PARP-inhibitors maintenance therapy for platinum-sensitive recurrent ovarian cancer: a network meta-analysis. *Int J Mol Sci* 2020;21:3805.
10 European Medicines Agency. Avastin (bevacizumab) assessment report. Available: https://www.ema.europa.eu/en/documents/variation-report/avastin-h-c-582-ii-0041-epar-assessment-report-variation_en.pdf [Accessed 28 Mar 2024].
11 Genentech Inc. Avastin (bevacizumab) prescribing information. Available: https://www.gene.com/download/pdf/avastin_prescribing.pdf [Accessed 28 Mar 2024].
12 Marchetti C, Muzii L, Romito A, *et al*. First-line treatment of women with advanced ovarian cancer: focus on bevacizumab. *Onco Targets Ther* 2019;12:1095–103.
13 Banerjee S, Gonzalez-Martin A, Harter P, *et al*. First-line PARP inhibitors in ovarian cancer: summary of an ESMO Open - Cancer Horizons round-table discussion. *ESMO Open* 2020;5:e001110.
14 Colombo N, Ledermann JA, ESMO Guidelines Committee. Updated treatment recommendations for newly diagnosed epithelial ovarian carcinoma from the ESMO Clinical Practice Guidelines. *Ann Oncol* 2021;32:1300–3.
15 Miller RE, Leary A, Scott CL, *et al*. ESMO recommendations on predictive biomarker testing for homologous recombination deficiency and PARP inhibitor benefit in ovarian cancer. *Ann Oncol* 2020;31:1606–22.
16 Bollinger JM, Sanka A, Dolman L, *et al*. BRCA1/2 variant data-sharing practices. *J Law Med Ethics* 2019;47:88–96.
17 Kurian AW, Ward KC, Howlader N, *et al*. Genetic testing and results in a population-based cohort of breast cancer patients and ovarian cancer patients. *J Clin Oncol* 2019;37:1305–15.
18 European Pharmaceutical Market Research Association. Code of conduct. Available: https://www.ephmra.org/sites/default/files/2022-08/EPHMRA%202022%20Code%20of%20Conduct.pdf [Accessed 28 Mar 2024].
19 British Healthcare Business Intelligence Association. Legal and ethical guidelines for healthcare market research. Available: https://www.bhbia.org.uk/guidelines-and-legislation/legal-and-ethical-guidelines [Accessed 28 Mar 2024].
20 Insights Association. Code of standards and ethics for market research and data analytics. Available: https://www.insightsassociation.org/Portals/INSIGHTS/IA%20Code_1_6_23_Final.pdf [Accessed 28 Mar 2024].
21 Frey MK, Ellis A, Shyne S, *et al*. Bridging the gap: a priorities assessment tool to support shared decision making, maximize appointment time, and increase patient satisfaction in women with ovarian cancer. *JCO Oncol Pract* 2020;16:e148–54.
22 Rohr I, Alavi S, Richter R, *et al*. Expectations and preferences of patients with primary and relapsed ovarian cancer to maintenance therapy: a NOGGO/ENGOT-ov22 and GCIG survey (Expression IV). *Int J Gynecol Cancer* 2020;30:509–14.
23 Goh JCH, Gourley C, Tan DSP, *et al*. Optimizing treatment selection and sequencing decisions for first-line maintenance therapy of newly diagnosed advanced ovarian cancer. *Gynecol Oncol Rep* 2022;42:101028.
24 Burger RA, Brady MF, Bookman MA, *et al*. Incorporation of bevacizumab in the primary treatment of ovarian cancer. *N Engl J Med* 2011;365:2473–83.
25 Perren TJ, Swart AM, Pfisterer J, *et al*. A phase 3 trial of bevacizumab in ovarian cancer. *N Engl J Med* 2011;365:2484–96.
26 Mirza MR, Coleman RL, González-Martín A, *et al*. The forefront of ovarian cancer therapy: update on PARP inhibitors. *Ann Oncol* 2020;31:1148–59.
27 Moore K, Colombo N, Scambia G, *et al*. Maintenance olaparib in patients with newly diagnosed advanced ovarian cancer. *N Engl J Med* 2018;379:2495–505.
28 Ray-Coquard I, Pautier P, Pignata S, *et al*. Olaparib plus bevacizumab as first-line maintenance in ovarian cancer. *N Engl J Med* 2019;381:2416–28.
29 González-Martín A, Pothuri B, Vergote I, *et al*. Niraparib in patients with newly diagnosed advanced ovarian cancer. *N Engl J Med* 2019;381:2391–402.
30 Camm AJ, Fox KAA. Strengths and weaknesses of 'real-world' studies involving non-vitamin K antagonist oral anticoagulants. *Open Heart* 2018;5:e000788.