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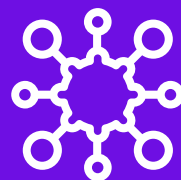
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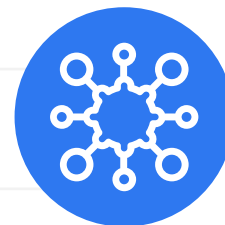
**A Review of the Latest
Advancements in
Ovarian Cancer Care
Featured at ESMO 2022**

Oncology



A Review of the Latest Advancements in Ovarian Cancer Care Featured at ESMO 2022

The sessions covered in this article took place at the European Society for Medical Oncology (ESMO) Congress 2022, 9th–13th September 2022 in Paris, France



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Abstract

Ovarian cancer is the seventh most commonly diagnosed cancer among females and the most lethal gynaecologic malignancy globally because of its vague presentation, insidious nature, recurrence, and drug resistance. There is a pressing need to improve survival and quality of life in patients with ovarian cancer in the context of rising global incidence, high risk of relapse, and poor prognosis. Presentations at the European Society for Medical Oncology (ESMO) Congress 2022 from 9th–13th September in Paris, France, showed the breadth and depth of research in ovarian cancer, including a first look at the highly anticipated data from Phase III studies on the impact on overall survival (OS) of poly(ADP-ribose) polymerase (PARP) inhibitors as first-line maintenance therapy. Clinically meaningful OS benefit was shown with olaparib at 5 years' follow-up in PAOLA-1 and at 7 years' follow-up in SOLO1. These positive results are a breakthrough in ovarian cancer treatment and are an important indicator that improvements in progression-free survival (PFS) may translate into OS benefits. Studies in which PARP inhibitors showed clinically meaningful efficacy, but OS data remain immature, include PRIMA, in which niraparib as a first-line maintenance therapy maintained clinically significant improvement in progression-free survival at 3.5 years' follow-up. Research into chemotherapy resistance using a glucocorticoid receptor modulator in combination with nab-paclitaxel as part of second-line treatment showed that glucocorticoid receptor modulation can improve the efficacy of chemotherapy. Pre-clinical and early phase clinical studies are investigating a range of approaches for the treatment of ovarian cancer such as development of a chimeric antigen receptor T cell therapy, combination of a PARP inhibitor and an immune checkpoint inhibitor, and a bispecific antibody. Developments in these areas are awaited with interest. There is considerable focus on biomarkers for prognosis and progression in ovarian cancer, including research on breast related cancer antigen and homologous recombination deficiency testing, cancer antigen 125 (CA125) decline, and circulating tumour DNA (ctDNA); however,

wider genetic testing, improved education of physicians on the importance of testing, and increased access to testing are recommended to optimise treatment and disease prevention. The research in ovarian cancer presented at ESMO 2022 marks important progress in this field.

INTRODUCTION

Ovarian cancer is the seventh most commonly diagnosed cancer among females,¹⁻³ the third most common gynaecological malignancy⁴ after cervical and endometrial (uterine) cancers,^{1,5} and the most lethal gynaecologic malignancy globally because of its vague presentation, insidious nature, recurrence, and drug resistance.^{3,4,6-8} There is currently no public health screening programme for early detection of ovarian cancer; therefore, most patients with ovarian cancer are diagnosed with advanced (locally advanced or metastatic) disease, which is associated with significant mortality.² Among the most important patient factors affecting the occurrence of ovarian cancer are genetic factors such as family history and breast-related cancer antigen (*BRCA*) mutations.¹ First-line therapy for females with newly-diagnosed, advanced ovarian cancer has for many years been a combination of debulking surgery and platinum-based chemotherapy as standard of care.⁹⁻¹¹ A major breakthrough in the treatment of patients with advanced ovarian cancer is the use of PARP inhibitors.^{9,12-14} Considering that the global incidence of ovarian cancer is expected to rise by 55% to 371,000 cases per year by 2035, newly-diagnosed patients with advanced ovarian cancer are at high-risk of relapse. Current 5-year survival rates are 30–50%, and 15% of females with ovarian cancer die within 2 months of diagnosis; therefore, urgent action is required to improve survival and quality of life in females with this disease.^{15,16} This article discusses the latest advancements in ovarian cancer care, as featured at the European Society for Medical Oncology (ESMO) Congress 2022 from 9th–13th September in Paris, France.

IMPACT OF PARP INHIBITORS ON OVERALL SURVIVAL IN PHASE III STUDIES IN PLATINUM-SENSITIVE PATIENTS WITH ADVANCED OVARIAN CANCER

The use of PARP inhibitors in the maintenance treatment of advanced ovarian cancer is reported to be associated with long-term efficacy and improved PFS compared with placebo or standard chemotherapy in patients with newly-diagnosed disease following a response to platinum-based chemotherapy;^{13,17-24} however, OS data have been lacking because data have not been mature. Several Phase III studies presented at ESMO 2022²⁵⁻²⁸ showed OS benefits with PARP inhibitors.

Olaparib

PAOLA-1: clinical meaningful overall survival benefit at 5 years' follow-up

PAOLA-1 compared olaparib with bevacizumab versus placebo plus bevacizumab in patients with advanced, high-grade, epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer after first-line platinum-based chemotherapy.^{17,29} After a median follow-up of 22.9 months, median PFS was 22.1 months with olaparib plus bevacizumab and 16.6 months with placebo plus bevacizumab (hazard ratio [HR]: 0.59; 95% confidence interval [CI]: 0.49–0.72; $p < 0.001$).¹⁷ The HR for the olaparib group versus the placebo group was 0.33 (95% CI: 0.25–0.45) in patients with homologous recombination deficiency (HRD)-positive tumours, including *BRCA* mutations (median PFS: 37.2 months versus 17.7 months), and 0.43 (95% CI: 0.28–0.66) in patients with HRD-positive tumours without *BRCA* mutations (median PFS: 28.1 months versus 16.6 months).¹⁷ The addition of maintenance olaparib, therefore, provided a significant PFS benefit, which was substantial in patients with HRD-positive tumours, including those without a *BRCA* mutation.¹⁷

A late-breaking abstract from ESMO 2022 highlighted the clinically meaningful OS benefit with olaparib plus bevacizumab as first-line maintenance treatment in patients who are HRD-positive, regardless of tumour *BRCA* status in PAOLA-1 at 5-years' follow-up (5-year OS rate: 65.5% versus 48.4%; HR: 0.62; 95% CI: 0.45–0.85; OS data maturity: 55.3%).²⁵ No OS benefit was observed in patients who were HRD-negative (HR: 1.19; 95% CI: 0.88–1.63) in this study.²⁵ Despite a high proportion of patients in the control arm receiving a PARP inhibitor post-progression (123 patients [45.7%] versus 105 patients [19.6%] in the active treatment arm), these results confirm olaparib plus bevacizumab as standard of care in this setting.²⁵

SOLO1: continued survival benefit at 7 years' follow-up

SOLO1 was a randomised, double-blind, placebo-controlled trial of olaparib as maintenance therapy in patients with newly-diagnosed, advanced, high-grade serous or endometrioid ovarian cancer, primary peritoneal cancer, or fallopian-tube cancer (or a combination thereof) with a mutation in *BRCA1* and/or *BRCA2*, who had a complete or partial clinical response after first-line platinum-based chemotherapy.^{18,30} Patients received maintenance olaparib versus placebo for up to 2 years or until disease progression.^{18,30} In the primary analysis, after a median followup of 41 months, patients in the olaparib group derived significant PFS benefit versus placebo (median not reached versus 13.8 months; HR: 0.30; 95% CI: 0.23–0.41; $p < 0.001$).³¹ Data after a 5-year follow-up showed that the benefit of olaparib versus placebo seen in the primary analysis was maintained, with median a PFS of 56.0 months versus 13.8 months (HR: 0.33; 95% CI: 0.25–0.43) after a median follow-up of 4.8 years and 5.0 years, respectively.¹⁸

The 7-year follow-up data from SOLO1,^{18,30} presented at ESMO 2022, showed a continued survival benefit for patients.^{26,27} In this trial, 67.0% of patients on olaparib were alive at 7 years versus 46.5% on placebo.^{26,27} Median OS was not reached in the olaparib arm and was 75.2 months in the placebo arm (HR: 0.55; 95% CI: 0.40–0.76; $p = 0.0004$; OS data maturity: 38.1%).^{26,27} Although this result did not reach the pre-specified threshold for statistical significance ($p < 0.0001$), it was considered to be clinically meaningful, and indicated the potential for long-term

remission.^{26,27} The improvements in PFS reported at 5 years' follow-up¹⁸ translated into OS benefits at 7 years' follow-up, despite almost half the patients in the placebo group (44.3%) receiving PARP inhibitor in a subsequent line of therapy.^{26,27}

OPINION: final overall survival data support the use of maintenance olaparib

OPINION was conducted to investigate olaparib maintenance monotherapy in patients without a deleterious or suspected deleterious germline *BRCA1/2* mutation who had platinum-sensitive, relapsed ovarian cancer and had received at least two lines of platinum-based chemotherapy.^{20,32} In the primary analysis (18 months after the last patient received their first dose), 210 PFS events had occurred and the median PFS was 9.2 months (95% CI: 7.6–10.9; data maturity: 75.3%) in the overall population.²⁰ At 12 months and 18 months, 38.5% and 24.3% of patients were progression-free, respectively.²⁰

The final OS data from OPINION,^{20,32} reported at ESMO 2022, support the use of maintenance olaparib in patients with platinum-sensitive, relapsed ovarian cancer without a germline *BRCA1/2* mutation.²⁸ Median follow-up in censored patients was 33.1 months. In this study, median OS was 32.7 months (95% CI: 29.5–35.3; data maturity: 52.3%), and 24- and 30-month Kaplan–Meier OS rates were 65.8% and 54.9%, respectively. The 30-month Kaplan–Meier OS rate was 66.7% (95% CI: 57.5–74.3) for patients who were HRD-positive (including somatic *BRCA* mutation) and 40.2% (95% CI: 29.9–50.3) for patients with partial (6–12 months) platinum sensitivity.²⁸

Rucaparib

ARIEL4: overall survival confounded by high rate of crossover from chemotherapy to rucaparib

In ARIEL4, patients with relapsed, heavily pre-treated ovarian cancer with *BRCA1/2* mutation received rucaparib or standard-of-care chemotherapy, and those with confirmed radiographic progression on chemotherapy crossed over to receive rucaparib.^{21,33} In the primary analysis, at a median follow-up of 25.0 months, the median PFS was 7.4 months (95% CI: 7.3–9.1) in the rucaparib group versus 5.7 months (95% CI: 5.5–7.3) in the chemotherapy group (HR: 0.64; 95% CI: 0.49–0.84; $p = 0.0010$) in the efficacy population.²¹

OS results from ARIEL4^{21,33} were reported at ESMO 2022.³⁴ In this study, 80 (69.0%) patients crossed over from chemotherapy to rucaparib and, overall, 313 out of 349 (89.7%) patients received rucaparib; therefore, OS was confounded by the high rate of crossover, raising important questions about the optimal sequencing of PARP inhibitors in advanced disease.³⁴

ADDITIONAL CLINICALLY MEANINGFUL EFFICACY OUTCOMES USING PARP INHIBITORS IN PLATINUM-SENSITIVE PATIENTS WITH ADVANCED OVARIAN CANCER

PARP inhibitors showed clinically meaningful efficacy in patients with relapsed, platinum-sensitive, advanced ovarian cancer in several other clinical studies presented at ESMO 2022.³⁵⁻³⁹

Niraparib

PRIMA: niraparib maintained clinically significant improvement in progression-free survival at 3.5 years' follow-up

Niraparib showed PFS benefit as a first-line maintenance therapy after a response to platinum-based chemotherapy in patients with newly-diagnosed, advanced ovarian cancer, regardless of biomarker status, in the primary analysis of the Phase III study, PRIMA/ENGOT-OV26/GOG-3012.^{22-24,40} Updated long-term efficacy data from this study, presented at ESMO 2022, showed that clinically significant improvement in PFS with niraparib was maintained at a median of 3.5 years' follow-up irrespective of HRD status.³⁵ Median PFS was significantly longer with niraparib than with placebo in patients with HRD tumours (24.5 months versus 11.2 months, respectively; HR: 0.52; 95% CI: 0.40–0.68; $p < 0.0001$) and in the overall population (13.8 months versus 8.2 months, respectively; HR: 0.66; 95% CI: 0.56–0.79; $p < 0.0001$).³⁵ The estimated probability of no progressive disease or death for at least 4 years for niraparib versus placebo was 24% versus 14%, respectively, in the overall population, and 38% versus 17%, respectively, in patients with HRD tumours.³⁵ OS data remain immature at 41% for the overall population (33%

of patients on placebo versus 9% of patients on niraparib received subsequent PARP inhibitor).³⁵

Olaparib

MEDIOLA: olaparib plus durvalumab with bevacizumab shows promising efficacy

Median PFS with olaparib plus durvalumab (O+D) and olaparib plus durvalumab with bevacizumab (O+D+B) in patients with platinum-sensitive relapsed ovarian cancer and non-germline *BRCA* mutation was 5.5 (95% CI: 3.6–7.5) months and 14.7 (95% CI: 10.0–18.1) months, respectively, in MEDIOLA, a Phase II study.^{41,42} The final analysis of OS and disease control rate at 56 weeks in these cohorts was presented at ESMO 2022.³⁶ Median follow-up for OS was 23.2 months for O+D and 31.9 months for O+D+B. Kaplan–Meier estimates of median OS (95% CI) were 26.1 (18.7–not calculable) months for O+D and 31.9 (22.1–not calculable) months for O+D+B. Probabilities of survival (95% CI) in the O+D and O+D+B cohorts, respectively, were 77.6 (58.6–88.6) and 96.8 (79.2–99.5) at 12 months, and 50.8 (32.1–66.8) and 64.5 (45.2–78.5) at 24 months.³⁶ Disease control rate at 56 weeks (90% CI) was 9.4% (2.6–22.5) for O+D and 38.7% (24.1–55.0) for O+D+B. Treatment with O+D+B in this study showed promising efficacy in these patients.³⁶

Rucaparib

ATHENA-MONO: first-line rucaparib maintenance treatment improved progression-free survival versus placebo across subgroups

In ATHENA-MONO (GOG-3020/ENGOT-ov45),^{43,44} first-line rucaparib maintenance treatment improved PFS versus placebo across subgroups in patients with newly-diagnosed, platinum-sensitive, advanced ovarian cancer, regardless of timing of surgery or prognostic disease characteristics, including International Federation of Gynaecology and Obstetrics (Fédération Internationale de Gynécologie et d'Obstétrique [FIGO]) stage or residual disease (intention-to-treat population; $p < 0.0001$ –0.0302).³⁷ These results support rucaparib as a maintenance treatment option for patients with ovarian cancer with or without high-risk factors for progression at baseline, irrespective of molecular characteristics.³⁷

PARP Inhibitors

Efficacy of PARP inhibitor monotherapy in secondary platinum-sensitive relapse

PARP inhibitor monotherapy and platinum-based chemotherapy had a comparable therapeutic effect in a retrospective study of patients with ovarian cancer and germline *BRCA1/2* mutation who received no maintenance treatment after first- and second-line platinum-therapy, and had a secondary platinum-free interval (PFI) of >6 months.³⁸ Objective response rate was 77.4% versus 84.0% for PARP inhibitor monotherapy and chemotherapy, respectively ($p=0.538$), and median PFS was 8.6 months versus 11.1 months, respectively ($p=0.679$). PARP inhibitor monotherapy significantly prolonged post-recurrent survival (HR: 0.35; 95% CI: 0.14–0.86; $p=0.022$).³⁸ Post-recurrent survival for patients on PARP inhibitors was similar to that for patients with PFI ≥ 6 months after third-line platinum chemotherapy (HR: 0.66; 95% CI: 0.19–2.24; $p=0.503$), and superior to patients with PFI <6 months after third-line platinum chemotherapy (HR: 0.14; 95% CI: 0.03–0.57; $p=0.006$).³⁸ The authors concluded that prolonged PFI with PARP inhibitor monotherapy did not negatively affect the outcome of subsequent platinum-based chemotherapy and could improve prognosis.³⁸

Potential benefit of reintroduction or continuation of PARP inhibitors after local therapy for oligometastatic progression

Reintroduction or continuation of PARP inhibitor treatment rather than initiating a new line of chemotherapy has been proposed for patients with high-grade epithelial ovarian cancer after local treatment for oligometastatic progression (i.e., progression with a limited number of metastatic sites).³⁹ A retrospective study showed that median PFS under PARP inhibitors after local therapy was 11.5 months (95% CI: 7.4–17.2), and the 1-year OS rate was 90.7% (95% CI: 79.1–96.0).²⁸ These results of almost 1 year without progression or introduction of a new line of systemic therapy indicate the potential benefit of this strategy in patients with oligometastatic progression under PARP inhibitors.³⁹

PHASE II STUDY OF GLUCOCORTICOID RECEPTOR MODULATOR IN COMBINATION WITH NAB-PACLITAXEL

Chemotherapy resistance remains a major problem in many solid tumours, including ovarian cancer.⁴⁵ Cortisol activity at the glucocorticoid receptor (GR) contributes to chemotherapy resistance by suppressing apoptotic pathways used by cytotoxic agents, and high tumour GR expression is associated with poor chemotherapy response in ovarian cancer.⁴⁶ A Phase II study of relacorilant, a selective GR modulator, in combination with nab-paclitaxel (NP) in patients with ovarian cancer showed that GR modulation with relacorilant can improve the efficacy of NP,^{46,47} including in a subgroup of patients without primary platinum-refractory disease and with 1–3 prior lines of therapy who received intermittent relacorilant plus NP.⁴⁸ Intermittent dosing in this subpopulation will be studied further in an upcoming Phase III trial (ROSELLA)⁴⁹ to evaluate whether selective GR modulation with relacorilant combined with NP promotes chemotherapy response.

PRE-CLINICAL AND EARLY PHASE CLINICAL STUDIES IN OVARIAN CANCER

In Vitro/Pre-clinical Study of Clonal Dynamics Effects

High-grade, serous ovarian cancer is characterised by extensive intra-tumoural heterogeneity, which is associated with drug resistance.⁵⁰ An investigation of clonal dynamics effects showed that resistance to carboplatin, paclitaxel, and olaparib pre-exists drug exposure in high-grade, serous ovarian cancer models, regardless of *BRCA* status and drug treatment selects for resistant phenotypes.⁵⁰ The results indicated that evolutionary dynamics are largely deterministic and hence, can be used to predict patient outcomes and personalise treatments.⁵⁰

Pre-clinical/Phase I Study of a Potential Target to Develop a Chimeric Antigen Receptor T Cell Therapy

Although immune checkpoint inhibitors have shown efficacy in several cancers, including breast and lung cancers,^{51,52} results from studies in ovarian cancer have been disappointing.⁵³⁻⁵⁵ Alkaline phosphatase, placental type (ALPP), a cell surface protein expressed only in female reproductive tissues, has been identified as a potential target to develop a chimeric antigen receptor T cell therapy against ovarian and endometrial cancers.⁵⁶ Pre-clinical and initial clinical findings indicate that anti-ALPP chimeric antigen receptor T cell immunotherapy is potentially efficacious against female reproductive cancers expressing ALPP.⁵⁶

Pilot Study of a PARP Inhibitor–Immune Checkpoint Inhibitor Combination as Neoadjuvant Therapy

Published data indicate that the efficacy of PARP inhibitors may be associated with immunomodulation.^{57,58} The potential benefit of combining PARP inhibitors with immunotherapy as maintenance treatment in patients with ovarian cancer is being explored.⁵⁹⁻⁶¹ Further research is focusing on this treatment combination in the neoadjuvant setting.⁶² Olaparib alone, or in combination with the immune checkpoint inhibitor pembrolizumab, is being evaluated as neoadjuvant therapy in a pilot study in patients with HRD-positive advanced ovarian cancer.⁶² Objective response rate for neoadjuvant olaparib monotherapy was 50% (95% CI: 18.7–81.3).⁶² The study of neoadjuvant combination treatment with olaparib plus pembrolizumab is ongoing.⁶²

Phase I Dose-Escalation Study of Bispecific Antibody

A first-in-human, Phase I, dose-escalation study was conducted to evaluate ubamatamab, a bispecific antibody that promotes T cell-mediated cytotoxicity by binding *MUC16*-expressing ovarian cancer cells and CD3+ T cells, in patients with recurrent ovarian cancer and elevated serum CA125.^{63,64} Ubamatamab had an acceptable safety profile, with evidence of durable responses across a wide dose range, in this heavily pretreated population with ovarian cancer.⁶⁴ Based on data from this Phase I study, a randomised Phase II expansion study has been initiated.⁶³

BIOMARKERS FOR PROGNOSIS AND PROGRESSION IN PATIENTS WITH OVARIAN CANCER

Homologous Recombination Deficiency Testing to Identify Predictors of Sensitivity to PARP Inhibitors

Ovarian cancer is one of the most heritable cancers.⁶⁵ Given the high prevalence of genetic variants, many organisations recommend universal genetic counselling and testing for females diagnosed with epithelial ovarian cancer.⁶⁶ Homologous recombination repair enables error-free repair of double-strand breaks and interstrand crosslinks in DNA that has replicated.⁶⁷ Tumours with homologous recombination deficiency, including those in *BRCA*-mutation carriers, are sensitive to base excision repair blockade via PARP inhibitors.⁶⁸ Tumour tests that determine HRD status in patients with ovarian cancer provide information on the magnitude of benefit for PARP inhibitor therapy. HRD testing provides an opportunity to optimise the use of PARP inhibitors in patients with ovarian cancer, but methodologies are diverse, and clinical application remains controversial.^{13,14,69-71}

Physician Behaviour and Perceptions of *BRCA* and Homologous Recombination Deficiency Testing for the Management of Patients with Newly-Diagnosed Advanced Ovarian Cancer

A survey of 300 gynaecology/oncology specialists assessed use of *BRCA* and HRD testing in the management of patients with advanced ovarian cancer and showed that most patients are tested for *BRCA*, whereas HRD testing is not yet routinely requested in clinical practice.⁷² The specialists estimated that *BRCA* testing was conducted for 72±30% (mean±standard deviation) of newly-diagnosed patients in the previous 6 months.⁷² In contrast, HRD testing was reported for 6±17% patients in Canada, 27±28% in Europe, and 33±25% in Japan.⁷² Overall, 67% of specialists were aware of HRD testing and 81% agreed that genetic counselling should be offered to patients with ovarian cancer.⁷² Although poor patient performance status and inadequate tissue

availability remain challenges in biomarker testing, efforts to improve education of physicians on the importance of testing, and to expand access to testing, may increase the numbers of patients receiving biomarker-directed and timely therapy.⁷² Indeed, wider genetic testing (including moderate susceptibility gene *BRIP1*) of patients with familial epithelial ovarian cancer has been suggested as essential to optimise treatment and disease prevention.⁷³

Assays for Genomic Instability Score in the Clinical Setting

The performance of multiple molecular assays in determining HRD-associated genomic instability score (GIS) in high-grade ovarian cancer was compared with that of MyChoice[®] CDx (Myriad Oncology, Salt Lake City, Utah, USA),⁷⁴ the most commonly used assay for HRD detection in clinical studies.⁷⁵ There was concordance between all the assays for GIS assessment.⁷⁵ As expected, high scores were significantly associated with the presence of *BRCA* mutations for all assays.⁷⁵ The authors suggested that a variety of assays could be used, in principle, to assess GIS in the clinical setting.⁷⁵

Genomic Instability Score Did Not Differentiate Between Platinum-Resistant and Platinum-Sensitive Patients

PARP inhibitors are indicated as maintenance therapy after first-line chemotherapy for patients with high-grade ovarian cancer in case of *BRCA* mutation, high GIS, or objective response to platinum.⁷⁶ The capacity of GIS (MyChoice[®] CDx Plus [Myriad Oncology, Salt Lake City, Utah, USA])⁷⁷ to detect patients who did not benefit from platinum (platinum-resistant) and had poor prognosis, was evaluated in a retrospective analysis.⁷⁶ This analysis showed that GIS at diagnosis in patients with high-grade ovarian cancer did not reliably differentiate between patients who were platinum-resistant and patients who were platinum-sensitive.⁷⁶ Whether patients with discordance between GIS and platinum response benefit from PARP inhibitors is currently being investigated.⁷⁶

CA125 Decline and *BRCA* Status

CA125 decline and *BRCA* mutations are associated with chemosensitivity.^{78,79} The correlation between CA125 decline, assessed by the CA125 elimination rate constant *K* (KELIM) model, and *BRCA* status was evaluated using registry data for patients with advanced ovarian cancer treated with neoadjuvant chemotherapy.⁸⁰ KELIM and *BRCA* status were suggested to be two complementary prognostic tools in patients with advanced ovarian cancer.⁸⁰ The distributions of KELIM and *BRCA* mutations were not superimposable, indicating that they are not interchangeable.⁸⁰ According to the authors, KELIM provides important information on tumour intrinsic chemosensitivity beyond *BRCA* status that might help guide optimal maintenance treatment; however, prospective validation is warranted.⁸⁰

Soluble forms of inhibitory immune checkpoints such as plasma programmed death protein and its ligand, butyrophilin sub-family 2 member A1 and sub-family 3 A1 (BTN3A1), pan-sBTN3As, or B and T lymphocyte attenuator, have been suggested to be potentially helpful biomarkers to increase the prognostic value of CA125 in patients with advanced high-grade serous ovarian carcinoma.⁸¹

Circulating Tumour DNA as a Potential Biomarker for Disease Progression in Patients with Ovarian Cancer

Detection of progression and recurrence in patients with ovarian cancer is crucial to improve patient prognosis. Current tests based on the CA125 biomarker and radiological imaging are insufficient for the early detection of recurrent ovarian cancer.⁸² A study to assess the feasibility of ctDNA as a biomarker for disease progression in patients with ovarian cancer undergoing debulking surgery followed by adjuvant therapy, showed that ctDNA enabled earlier detection of future progression by an average of 50.9 days (maximum 267.0 days) compared to conventional diagnostic methods.⁸² Therefore, ctDNA-based surveillance may serve an important role in the early detection of disease progression in ovarian cancer, enabling prognostic stratification and prompt clinical decision making.⁸²

CONCLUSION

There is a pressing need to improve survival and quality of life in patients with ovarian cancer in the context of rising global incidence, high risk of relapse, and poor prognosis. Studies presented at ESMO 2022 showed the breadth and depth of research in ovarian cancer, including a first look at the highly anticipated data from Phase III studies on the impact of first-line maintenance therapy with PARP inhibitors on OS. The clinically meaningful OS benefit seen with olaparib in PAOLA-1 and SOLO1 is incredibly positive, and a powerful indicator that improvements in PFS may translate into OS benefits. Studies in which OS data remain immature, including PRIMA, show additional clinically meaningful efficacy outcomes with PARP inhibitors. Phase II studies investigating chemotherapy resistance showed

that GR modulation in second-line treatment improved the efficacy of chemotherapy, and this research is expanding to Phase III. Pre-clinical and early phase clinical studies are investigating a range of approaches for the treatment of ovarian cancer, and developments in these areas are awaited with interest. Considerable research is also being conducted on biomarkers for prognosis and progression in ovarian cancer; however, wider genetic testing, improved education of physicians on the importance of testing, and increased access to testing are recommended to optimise treatment and disease prevention. The considerable research and encouraging OS results in ovarian cancer presented at ESMO 2022 mark important progress in this field, and a continuing drive to improve the management and outcomes of patients with this disease.

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