The Emerging Role of Homologous Recombination Deficiency Testing and the Progress of PARP Inhibitors in Advanced Ovarian Cancer: Interviews with Three Key Opinion Leaders

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Interview Summary

Ovarian cancer is the most lethal gynaecologic malignancy worldwide because of its vague presentation, insidious nature, recurrence, and drug resistance. The most important patient factors affecting the occurrence of ovarian cancer include genetic factors, such as family history and *BRCA* gene mutations. For many years, a combination of debulking surgery and platinum-based chemotherapy has been the standard of care in first-line therapy for patients with newly-diagnosed advanced ovarian cancer. A significant breakthrough in the management of patients with advanced ovarian cancer is treatment with poly(ADP-ribose) polymerase (PARP) inhibitors.

Tumours with homologous recombination deficiency (HRD), including those in patients with *BRCA* mutation, are sensitive to base excision repair blockade via PARP inhibitors. Somatic (tumour) tests that determine HRD status in patients with ovarian cancer enable clinicians to optimise the use of PARP inhibitors and provide information on the magnitude of benefit with PARP inhibitor therapy; however, HRD testing methodologies are diverse, and the clinical application of HRD diagnostic testing remains controversial. Furthermore, although PARP inhibitors are shifting the care paradigm for patients with advanced ovarian cancer, innovative strategies are still needed to optimise treatment and improve patient outcomes.

For this article, EMJ conducted interviews in September 2022 with three key opinion leaders: Ram Ganapathi, Women's Health Institute, Cleveland Clinic, Ohio, USA; Mansoor Raza Mirza, Rigshospitalet, Copenhagen University Hospital, Denmark; and Rowan Miller, University College London Hospitals NHS Foundation Trust, UK, all of whom have a wealth of experience and expertise in the management of ovarian cancer. The experts gave valuable insights into topics such as the power of leveraging DNA damage response (DDR) pathways in the management of advanced ovarian cancer, and the evolving landscape of HRD testing. The impact of PARP inhibitors on the management of advanced ovarian cancer, the most significant clinical trials conducted with these drugs, and potential future clinical trials in this area were also explored.

INTRODUCTION

Ovarian cancer is the most lethal gynaecologic malignancy worldwide because of its vague presentation, insidious nature, recurrence, and drug resistance.[1-5] The most important patient factors affecting the occurrence of ovarian cancer include genetic factors, such as family history and *BRCA* gene mutations.[6] For many years, a combination of debulking surgery and platinum-based chemotherapy has been the standard of care in first-line therapy for patients with newly-diagnosed advanced ovarian cancer.[7-9] A significant breakthrough in the management of patients with advanced ovarian cancer is treatment with PARP inhibitors.[7,10]

Tumours with HRD, including those in patients with *BRCA* mutation, are sensitive to base excision repair blockade via PARP inhibitors.[11] Somatic (tumour) tests that determine HRD status in patients with ovarian cancer enable clinicians to optimise the use of PARP inhibitors and provide information on the magnitude of benefit with PARP inhibitor therapy; however, HRD testing methodologies are diverse, and the clinical application of HRD diagnostic testing remains controversial.[12,13] Furthermore, although PARP inhibitors are shifting the care paradigm for patients with advanced ovarian cancer, innovative strategies are still needed to optimise treatment and improve patient outcomes.

LATE DIAGNOSIS IN OVARIAN CANCER

Ganapathi described ovarian cancer as an indolent disease, with no tell-tale signs in the early stages; therefore, early detection of this cancer is elusive, and most patients are diagnosed with advanced (locally advanced or metastatic) disease,[14] which is associated with significant mortality.[2,15] He noted that platinum and taxane-based chemotherapy has been the standard of care for decades and, more recently, has included the addition of bevacizumab, which can lead to improved outcome.[16,17] Although there is an approximately 80% response rate to treatment with platinum and taxane-based chemotherapy,[17] there is a high rate of recurrence (approximately 70%), which complicates patient management.[18] Ganapathi emphasised that little is known about the approximately 20% of patients who do not respond to standard of care chemotherapy, and there is insufficient research in this area. He stated: "I feel extremely sorry for these platinum-resistant patients because we currently have very limited treatment options for them."

Ganapathi indicated that survival rates in patients with ovarian cancer have steadily improved over the last 10 years. He suggested that this impact on outcome was potentially due to better understanding of the biology of ovarian cancer, advances in surgical management of

advanced disease, more effective maintenance treatment options and, notably, the efficacy of PARP inhibitors, based on understanding of the role of *BRCA* genes and DDR pathways.

Unlike in some other cancers, the results from the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS),[19-21] an extensive screening programme, showed that even though there was a significant reduction in the diagnosis of late-stage ovarian cancer through screening, this did not translate to an increase in overall survival (OS). Furthermore, the results of the Australian Ovarian Cancer Study[22] indicated that reducing time to diagnosis did not greatly alter the stage of disease at diagnosis or improve survival outcomes.

Mirza depicted that before the PARP inhibitor era, the prognosis for patients with ovarian cancer was very poor. He reported that work has been conducted for the last 30 years to find a diagnostic test or specific biomarker to enable the early diagnosis of ovarian cancer, but to no avail. The first symptom most females with ovarian cancer experience is an inability to fit into their clothes, at which point the disease has likely spread from the ovary into the abdominal cavity (Stage III disease). Screening females aged over 50 years, or other high-risk patients, is not feasible; however, there are specific subpopulations in whom the risk of *BRCA* mutation is high, e.g., the Ashkenazi Jewish population,[23] who may benefit from a screening programme to detect *BRCA* mutations. Mirza stated that there is no effective method to enable early diagnosis of disease in most patients who may develop ovarian cancer.

Miller explained that patient outcome is directly related to disease stage, and that most patients with ovarian cancer present with Stage III or IV disease. Despite the recent advances in diagnosis and treatment, the long-term survival is poor compared with early-stage disease. She stated that in addition to driving research into new therapies, the key to improving long-term survival is to find a method to detect disease early. Miller also highlighted the importance of raising awareness of the signs and symptoms of ovarian cancer among non-oncology healthcare professionals (HCP), and among females in general to empower them to seek medical advice and investigations if they develop new and persistent symptoms that may indicate ovarian cancer. Miller explained that the symptoms of ovarian cancer are vague and non-specific; however, cancer charities in the UK, such as Ovacome, are raising awareness of four key symptoms that, when present together, may indicate ovarian cancer.[24] The four symptoms are represented by the abbreviation BEAT: Bloating that doesn't come and go; Eating difficulty and feeling full more quickly; Abdominal and pelvis pain you feel most days; and Toilet changes in urination or bowel habits.[24]

THE POWER OF LEVERAGING DNA DAMAGE RESPONSE PATHWAYS IN THE MANAGEMENT OF OVARIAN CANCER

Ganapathi, Mirza, and Miller strongly believe in the power of leveraging DDR pathways in the management of ovarian cancer, and acknowledged the importance and value of *BRCA* testing and HRD testing. They also emphasised that a better understanding of DDR pathways and all the DNA repair genes involved in the disease, not just *BRCA*, is necessary to improve the diagnosis and treatment of patients. Miller referred to a plethora of new drugs being developed to target a range of weaknesses in the DDR pathways, and suggested that these may complement PARP inhibitors or be effective in cases of PARP resistance.

THE EVOLVING LANDSCAPE OF HOMOLOGOUS RECOMBINATION DEFICIENCY TESTING

Homologous Recombination, *BRCA* Mutations, and PARP Inhibitors

Homologous recombination and base excision repair are two of the most important DDR pathways. The proteins encoded by *BRCA* genes are necessary for homologous recombination, and PARP enzymes are involved in base excision repair.[11] The *BRCA1* and *BRCA2* genes are essential for cell repair and maintaining genomic stability.[25] Germline mutations in *BRCA1* and *BRCA2* account for a substantial proportion of inherited breast and ovarian cancers.[25] PARP enzymes have essential roles in cellular processes, including the regulation of

transcription, apoptosis, and the DNA damage response.[26] Inhibition of PARP in damaged cells, such as ovarian cancer cells, prevents the DNA repair process, which leads to the disruption of cellular homeostasis and cell death. PARP inhibitors were the first approved cancer drugs that specifically target the DNA damage response in *BRCA1/2* mutated breast and ovarian cancers.[5,26-30] These drugs have transformed the management of advanced ovarian cancer.[10,31-34]

What Is Homologous Recombination Deficiency Testing, and Why is it Important?

The inability to repair DNA through homologous recombination creates a specific pattern of mutations on the genome, also known as a footprint, signature, or 'genomic scar',[35] which can be detected with molecular analysis. This genomic scar remains even if reversion mutations have occurred, or there are other resistance mechanisms. HRD testing picks up these genetic alterations, thereby revealing past mutations that remain even if they may no longer be functionally important.

Tumours with HRD, including those in *BRCA* mutation carriers, are sensitive to base excision repair blockade via PARP inhibitors.[11] Around 50% of ovarian cancers are HRD-positive, and these tumours are more sensitive to platinum-based chemotherapy and PARP inhibitor therapies.[36] Defects in one or both *BRCA1* and *BRCA2* genes, and the resulting deficiency in BRCA1 and/or BRCA2 proteins, induce profound cellular sensitivity to the inhibition of PARP activity.[37] HRD and platinum sensitivity are therefore prospective biomarkers for predicting the response to PARP inhibitors in patients with ovarian cancer.[38] HRD testing is important because it identifies patients who are specifically sensitive to platinum-based chemotherapy and PARP inhibitors.

Miller recommended HRD testing for every patient with advanced (Stage III or IV) disease to help clinicians optimise treatment; however, there are no data on whether patients with Stage II disease will benefit from PARP inhibitors, although Miller suggested they probably would. She also commented on the important prognostic and predictive information that knowledge of HRD status provides. An understanding of the magnitude of benefit is important when counselling patients who are experiencing toxicity and an impact on their quality of life. For example, there would be a greater impetus to persevere and find strategies to manage toxicities in a patient with a *BRCA* mutation struggling with a PARP inhibitor than an HRD-negative patient in the same situation, due to differences in the magnitude of benefit. Knowledge of HRD status therefore enables clinicians to consider the balance between quality of life and benefit of treatment, and to appropriately counsel the patient.

Knowledge and Understanding of Homologous Recombination Deficiency Testing and Homologous Recombination Deficiency-Positive Advanced Ovarian Cancer

Ganapathi deemed there to be considerable knowledge and understanding of HRD-positive advanced ovarian cancer among HCPs, mainly because of the impact of *BRCA* testing, which has raised awareness of the genetic aspects of ovarian cancer. Guidelines from the American Society of Clinical Oncology (ASCO),[39,40] recommendations from the European Society for Medical Oncology (ESMO),[12] and European expert consensus recommendations,[41] along with well-attended, high-profile ASCO and ESMO meetings, have contributed to the knowledge and understanding of HRD-positive advanced ovarian cancer. However, Ganapathi referred to HRD status as having a "pretty broad definition", and that other genes involved in ovarian cancer need to be defined. He declared that there are gaps in knowledge on this topic among HCPs, including how genes other than *BRCA* impact on disease progression and recurrence, and which is the best gene panel for diagnostic testing.

Mirza discussed real-world data from the US that showed only 68% of patients with ovarian cancer received any form of *BRCA* testing, and only 21% received somatic *BRCA* testing.[42] In addition, one-third of patients with a *BRCA* mutation did not receive PARP inhibitor therapy.[43] Mirza estimated that up to 80% of patients with advanced ovarian cancer are not getting testing for HRD; therefore, many patients who are potentially eligible for PARP inhibitors are not being captured. According to Mirza, these data exemplify the gaps in knowledge among HCPs, and show that the importance of performing

HRD testing has not been adequately conveyed. Evidence of this is found in Mirza's native Denmark, where university hospitals advocate HRD testing for every patient diagnosed with ovarian cancer, whereas community hospitals may not even be aware of HRD testing.

Miller thought that HRD testing was being used fairly consistently in the UK, and she regarded the importance of HRD testing to be well recognised by gynaecological cancer specialists, but there was less awareness among professionals outside the ovarian cancer field. She indicated that there is definitely work to be done in raising awareness at every level of healthcare because HRD testing impacts treatment options for patients in the first-line treatment setting.

Methods of Homologous Recombination Deficiency Testing in Current Use

Mirza explained that two commercially available tests in current use, myChoice® CDx (Myriad Oncology, Salt Lake City, Utah, USA),[44] and Foundation Medicine Inc.'s (Cambridge, Massachusetts, USA) loss of heterozygosity (LOH) test, have been prospectively validated in Phase III studies: myChoice CDx in SOLO1,[45,46] PRIMA/ENGOT-OV26/GOG-3012,[47,48] and PAOLA 1,[49-51] and LOH test in ARIEL3.[52-54] He clarified that these diagnostic tests enable stratification of patients based on sensitivity to PARP inhibitors and are not interchangeable. Mirza added that there are many other testing methods in use, but these are not validated, and he strongly advised against their usage. Miller remarked on some important efforts in the development and validation of academic HRD tests, and predicted that validated academic HRD tests might be available in the future.

More Accurate Homologous Recombination Deficiency Testing is Needed

Mirza highlighted that a key issue with myChoice CDx,[44] the most commonly used HRD test, is a lack of accuracy. This test scores three different biological changes: LOH, telomeric allelic imbalance, and large-scale state transitions; on a linear scale.[44] The total score is used to determine HRD status.[44] Patients with a genomic instability score ≥42 are defined as HRD-positive and are automatically eligible for PARP inhibitors, whereas those with a score <42 are regarded as HRD-negative and are not automatically eligible for these drugs. However, as the scoring scale is linear rather than binary, patients just below the cut-off (e.g., a score of 40) may actually be HRD-positive. Likewise, those just above the cut-off (e.g., a score of 44) may be HRD-negative. Mirza rationalised that these patients may potentially have little difference between them biologically, but are eligible for different treatment options based on their test score. Similarly, Ganapathi questioned whether the cut-off of 42 for myChoice CDx is optimal and whether sufficient research has been conducted on this topic.

In addition, Mirza estimated that ≤15% of HRD test results are inconclusive because of technical reasons or lack of tumour tissue. He hoped that HRD testing kits currently being developed within universities will be more reliable. On that theme, Mirza discussed a programme in which three institutions in Belgium, Switzerland, and Italy produced their own HRD test, and compared results from this test with those of myChoice CDx using biopsies from patients who are HRD-positive in PAOLA-1.[49,50] The Leuven test (Belgium) showed the same results as myChoice CDx.[55] Results from the other two institutions are pending.

Miller highlighted an important deficiency of HRD testing: it does not provide any information about restoration of homologous recombination repair in a tumour, e.g., as a result of *BRCA* reversion mutation. She also commented that existing HRD tests fail to consistently identify a subgroup of patients who derive no benefit from PARP inhibitors.[12] Miller described a determination throughout Europe to develop HRD testing that is more reliable than current assays; however, she acknowledged that validating new assays is challenging. She stated: "We need academic collaborations between individuals and institutions to try to provide the most practical, best-performing, and cost-effective assays."

The Importance of Homologous Recombination Deficiency Testing at Diagnosis and Recurrence

Miller explained that HRD testing is important at diagnosis (or as early as possible in the treatment pathway) in patients with advanced ovarian cancer for first-line maintenance therapy

because knowledge of HRD status helps clinicians to optimise treatment selection.

Ganapathi recommended HRD testing at diagnosis of ovarian cancer and then at every recurrence to help clinicians direct treatment and target DDR pathways as appropriate. He advocated that testing should not be limited to *BRCA* but include other genes and DDR pathways to strengthen the development of better treatment strategies and new drugs.

In Denmark, Mirza explained, somatic *BRCA* testing by the pathologist using tissue removed during surgery is automatic for patients diagnosed with ovarian cancer. Medical oncologists then request germline *BRCA* testing to check hereditary disease, and to prompt the required genetic counselling for the patient's family. He clarified that patients with *BRCA* mutation are eligible for PARP inhibitors, so they do not undergo HRD testing, whereas those for whom somatic and germline *BRCA* is negative (*BRCA* wild-type) undergo HRD testing to check eligibility.

THE IMPACT OF PARP INHIBITORS ON THE MANAGEMENT OF ADVANCED OVARIAN CANCER

Dramatic Change in Patient Prognosis Following Approval of PARP Inhibitors in Platinum-Sensitive Relapsed Ovarian Cancer

Mirza commented that the prognosis for patients with advanced ovarian cancer had changed dramatically since olaparib was approved as maintenance therapy in platinum-sensitive relapsed ovarian cancer for patients with *BRCA* mutation following Study 19 in 2012,[56] with the results of SOLO2[57] in 2017 confirming the efficacy of olaparib as maintenance therapy.[58] The regulatory approval for all populations with platinum-sensitive relapse, regardless of *BRCA* and HRD status, of niraparib following the NOVA[59] study in 2016, and rucaparib following ARIEL3[52-54] in 2017 was also instrumental in this dramatic change in prognosis in the platinum-sensitive relapse setting.

Practice-Changing Clinical Trials with PARP Inhibitors as First-Line Maintenance Treatment in Advanced Ovarian Cancer

Ganapathi, Mirza, and Miller regarded the key clinical trials with PARP inhibitors in the first-line maintenance setting to be SOLO1,[45,46] PAOLA-1,[49,51] and PRIMA,[47,48] all of which were described as 'practice changing'.

The positive results in SOLO1 in 2018[45,46] led to the approval of olaparib monotherapy as first-line maintenance treatment in patients with *BRCA* mutation. Approval for olaparib in combination with bevacizumab was based on the results of PAOLA-1,[49,51] which included all patients, regardless of biomarkers. The results indicated progression-free survival (PFS) benefit with olaparib in the HRD-positive population (patients with *BRCA* mutation, or *BRCA* wild-type if they had HRD), but did not show efficacy in the HRD-negative population. In PRIMA,[47,48] the results were positive for PFS for niraparib in all subpopulations, and led to approval in all patients regardless of *BRCA* and HRD status.

Response with PARP Inhibitors in a Patient Population with and Without Homologous Recombination Deficiency

In the ATHENA-MONO trial,[60,61] rucaparib monotherapy was effective as first-line maintenance, conferring significant benefit versus placebo in patients with advanced ovarian cancer with and without HRD. According to Ganapathi, this response in patients who are HRD-positive and HRD-negative means that the "net is broader than we think." He indicated that patients who are *BRCA* wild-type and HRD-negative might have mutations in other genes in the DDR pathways that lead to PARP inhibitor sensitivity.

Mirza discussed that patients who score below the cut-off of 42 on the linear myChoice CDx scale are categorised as HRD-negative yet may be HRD-positive; hence, they may respond to PARP inhibitors, albeit to a lesser extent than patients who scored above the cut-off. This may explain the modest efficacy of niraparib in patients with HRD-negative disease, according to HRD test results, in the PRIMA trial.[47] PARP inhibitor treatment for HRD-negative patients may be debated, as patients are given either niraparib or bevacizumab, or, in some cases, no maintenance therapy, which Mirza thinks is inappropriate.

Miller emphasised that maintenance treatment options for patients who are HRD-negative represent a huge unmet need, as there is only a small benefit with niraparib or bevacizumab and no reported benefit with olaparib in these patients. She highlighted the need to better understand the biology of these patients to enable a more targeted approach, as there are no effective standard of care therapies for these patients after platinum-based chemotherapy. Although the options are limited for these patients, Miller acknowledged "at least we are moving further and further away from the 'one-size-fits-all' approach to ovarian cancer."

Impact of PARP Inhibitors on Overall Survival

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 in patients with newly-diagnosed disease following a response to platinum-based chemotherapy;[34,62-65] however, OS data have been lacking because data have not been mature. Importantly, Mirza identified a late-breaking abstract from the ESMO 2022 meeting that 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 (5-year OS rate, 65.5% versus 48.4%; hazard ratio [HR]: 0.62; 95% confidence interval [CI]: 0.45–0.85).[66] No OS benefit was observed in patients who were HRD-negative (HR: 1.19; 95% CI: 0.88–1.63) in this study.[66]

In addition, Miller highlighted the 7-year follow-up data from SOLO1 presented at the ESMO 2022 meeting that showed a continued survival benefit for patients with newly diagnosed advanced ovarian cancer and *BRCA* mutation who were treated with maintenance olaparib for up to 2 years versus placebo.[67,68] In this trial, 67.0% of patients on olaparib were alive at 7 years versus 46.5% on placebo.[67,68] 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).[67,68] Although this result did not reach the prespecified threshold for statistical significance (p<0.0001), it was considered to be clinically meaningful, and indicated the potential for long-term remission.[67,68] Miller stated that it was reassuring that the improvements in PFS translate into OS benefits, despite many patients in the placebo group receiving PARP inhibitor at a later date.

Overall Impact of PARP Inhibitors in Advanced Ovarian Cancer

All three key opinion leaders acknowledged the substantial overall impact of PARP inhibitors in advanced ovarian cancer. Ganapathi considered PARP inhibitors to be a valuable tool for clinicians for maintenance treatment. Mirza stated that "with PARP inhibitors, we have changed history." Miller also stated that PARP inhibitors have transformed the management of ovarian cancer in the first-line maintenance setting, with the gains in PFS, and now in OS, in patients with *BRCA* mutation and HRD "so much more than anything we have seen before with other advances in ovarian cancer."

WHICH CLINICAL TRIALS ARE NEEDED IN ADVANCED OVARIAN CANCER IN THE FUTURE?

Ganapathi suggested that future studies should include more comprehensive *BRCA* and HRD testing, including testing at diagnosis, at recurrence, and in patients who do not respond. He also advocated investigating the optimal time to initiate treatment with PARP inhibitors, e.g., upfront versus maintenance and whether this impacts outcomes, and the long-term effects of PARP inhibitors. Ganapathi also specified a need to explore treatments for patients who are platinum-resistant, who were excluded from the PARP inhibitor studies, to better understand the lack of response to treatment and disease recurrence in these patients.

Mirza advocated future research to investigate why patients are relapsing and what can be done for these patients, how to best manage the HRD-negative population, and whether patients' treatment can start with PARP inhibitors at diagnosis. He described the use of targeted therapy at the time of diagnosis, thereby delaying or circumventing chemotherapy, as an ideal strategy that would provide a better quality of life for patients.

According to Miller there are two major areas of unmet need for future research. The first priority is to determine how to improve outcomes for patients who are truly HRD-negative, as they have a worse prognosis than patients who are HRD-positive, and derive little benefit from PARP inhibitors. The second priority is to improve the management of patients with advanced ovarian cancer who develop PARP inhibitor resistance.

FUTURE PROSPECTS AND CONCLUSIONS

Ganapathi concluded that the future for the treatment and management of patients with advanced ovarian cancer is promising and rapid progress is being made in this area. He highlighted that improvements in testing capability, a more comprehensive panel of genes for HRD testing, and the development of more effective inhibitors would provide a very strong diagnosis and treatment portfolio for ovarian cancer in the future. Ganapathi noted that patients with a broad background of genetic changes are responding to PARP inhibitors, but little is known about the importance of these genetic changes in disease recurrence. He described a 'continuum of progress' in which the increased understanding of *BRCA* and HRD testing and the impact of PARP inhibitors have led to remarkable changes in how clinicians treat patients with advanced ovarian cancer, and he awaits future developments with interest.

Mirza proposed that the maximum benefit with single-agent PARP inhibitors in ovarian cancer has probably been reached, and the combination of these inhibitors with anti-androgenic drugs and immunotherapy may be the way forward,[69] even though immunotherapy alone has not been efficacious in Phase III studies.[70-72] He also expressed the need for further research into patients who relapse, with PARP inhibitor combinations and antibody-drug conjugates of interest in this space.

Miller remarked that adding HRD testing to *BRCA* testing has enabled more personalised medicine in the last 2 to 3 years, and that clinicians will get better at identifying the patients who will benefit most from PARP inhibitors. Miller's hope for the future is that HRD testing will become cheaper and more widespread, and that functional real-time HRD assays will be developed to further aid clinicians in treatment decisions. She described PARP inhibitors as a 'game changer' in ovarian cancer; however, approaches to ensure they are used in the patients who will benefit most, and strategies to overcome resistance to these drugs are needed. Miller looks forward to the results of first-line trials, including ATHENA[60,61] and DUO,[73] that combined PARP inhibitors with immune checkpoint inhibitors to see whether immunotherapy adds to the benefits of PARP inhibitors. Miller concluded: "We are very good at treating ovarian cancer, but not so good at curing it; however, new maintenance PARP inhibitor therapies are substantially reducing the risk of recurrence, or are delaying it significantly, which is something positive to tell our patients."

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