Review article

Poly(ADP-ribose) polymerase inhibitor olaparib in the treatment of ovarian cancer: a comprehensive review of current literature

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ABSTRACT

Purpose of the review: This comprehensive review aims to provide a summary of current research on the utilization of olaparib, a poly(ADP-ribose) polymerase (PARP) inhibitor, in the treatment of ovarian cancer. The review aims to highlight the key findings from recent clinical trials and assess the potential of olaparib as a targeted therapy for improving the prognosis of ovarian cancer patients.

Recent findings: Ovarian cancer remains a significant global health concern with high mortality rates. While optimal debulking surgery and platinum-based chemotherapy are the standard treatments, the recurrence rates remain substantial. The emergence of PARP inhibitors, particularly olaparib, has introduced a novel therapeutic approach that targets the genomic instability and DNA repair mechanisms in cancer cells. Notable clinical trials, such as SOLO1, SOLO2, and PAOLA-1, have demonstrated the effectiveness of olaparib in significantly improving progression-free survival, particularly in patients with BRCA mutations or homologous recombination deficiency. Additionally, combination therapies involving olaparib, such as those with bevacizumab or entinostat, have shown promising results.

Summary: The utilization of olaparib has brought about a paradigm shift in the treatment of ovarian cancer. Notably, it has shown significant improvements in progression-free survival and overall survival, particularly in patients with BRCA mutations or homologous recombination deficiency. The exploration of olaparib through various clinical trials and combination therapies continues to provide valuable insights and offer new prospects for ovarian cancer patients. Moreover, the growing understanding of PARP inhibitors holds the potential for further advancements in the prognosis of patients with this formidable condition.

Key words: olaparib, PARP inhibitor, ovarian cancer, targeted therapy, poly(ADP-ribose) polymerase, cancer therapy

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INTRODUCTION

Based on the 2020 statistics from the Global Cancer Observatory [1], ovarian cancer is ranked as the third most common gynecological cancer worldwide in terms of incidence (6.6/100,000, following cervical cancer and uterine corpus cancer), and as the second highest in terms of mortality (4.2/100,000) [1, 2].

Diagnosing ovarian cancer poses significant challenges due to its often asymptomatic nature, nonspecific symptoms, and the lack of a reliable screening method [3]. As a result, the disease is frequently detected at an advanced stage [4], leading to 5-year survival rates below 45% [5].

The primary treatment approach for ovarian cancer involves optimal debulking surgery and platinum-based chemotherapy, which are considered the cornerstone of therapy [6–8]. However, despite these interventions, the recurrence rate remains high [6], highlighting the continuous need for exploring new molecular targets and innovative drugs. In response to this challenge, the development of oncologic therapies targeting poly(ADP-ribose) polymerase (PARP), an enzyme involved in repairing single-strand DNA breaks and protecting the replication fork, has emerged as a promising solution.

OVARIAN CANCER

Ovarian cancer poses a significant global health concern, contributing to a substantial number of cancer-related deaths among women. It ranks as the eighth most common cancer in women and represents the second leading cause of mortality related to reproductive cancers, second only to cervical cancer [1].

Ovarian cancer originates from the epithelial cells that line the ovaries and is typically diagnosed at an advanced stage, resulting in a poor prognosis. The complexity of ovarian cancer arises from its various histological subtypes, each exhibiting distinct molecular characteristics, clinical behaviors, and responses to treatment. The five subtypes of ovarian cancer include high-grade serous (HGSC), low-grade serous (LGSC), endometrioid (EC), clear cell (CCC), and mucinous cancers (MC) [2, 9, 10]. Additionally, ovarian epithelial cancer, fallopian tube cancer, and primary peritoneal cancer stem from similar tissue types and are managed using similar treatment approaches [11].

The exact cause of ovarian cancer remains elusive, although several risk factors have been associated with its development. Age is a significant risk factor, as the incidence of ovarian cancer rises with increasing age, particularly after menopause. Other factors include a family history of ovarian or breast cancer, inherited gene mutations (such as *BRCA1* and *BRCA2* genes mutations), endometriosis, obesity, and nulliparity [2, 12, 13].

The clinical manifestation of ovarian cancer often lacks specificity, posing challenges in diagnosis and leading to delayed detection. Common symptoms may include abdominal pain or bloating, urinary urgency, pelvic discomfort, and gastrointestinal disturbances [14]. Regrettably, these symptoms are frequently attributed to other benign conditions, resulting in missed or delayed diagnoses.

Early detection of ovarian cancer is crucial for improving patient outcomes. However, there is currently no effective screening method available for the general population. Serum biomarkers like CA-125 (cancer antigen 125) have been utilized, but their sensitivity and specificity are not optimal, leading to a high rate of false-positive and false-negative results [15]. Transvaginal ultrasound imaging can assist in identifying ovarian masses, but it lacks the ability to reliably differentiate between benign and malignant lesions [15, 16].

The treatment of ovarian cancer usually involves a comprehensive approach that combines surgery, chemotherapy, and targeted therapies [11]. Surgical intervention is performed with the goal of achieving optimal tumor debulking, while chemotherapy, commonly utilizing platinum agents in combination with taxanes, is administered in both the neoadjuvant and adjuvant settings [8]. In recent times, targeted therapies have emerged as a significant development in the field, specifically those targeting angiogenesis and PARP activity. These advancements have introduced new treatment possibilities and improved outcomes for specific subgroups of ovarian cancer patients [8, 17].

GENOMIC INSTABILITY

Genomic instability is a distinctive hallmark of cancer and assumes a pivotal role in the initiation, progression, and therapeutic response of tumors. It refers to the heightened propensity of malignant cells to accumulate genetic alterations, encompassing DNA mutations, chromosomal rearrangements, and copy number variations, thereby amplifying the intricacies of their genomic landscape [18]. Underlying this genomic instability are deficiencies in the mechanisms responsible for maintaining the integrity of the genome, including DNA repair pathways and cell cycle checkpoints. This inherent instability fuels the incessant evolution and heterogeneous nature of tumors. Moreover, it contributes significantly to the development of drug resistance and enables cancer cells to elude immune surveillance [19–21].

POLY(ADP-RIBOSE) POLYMERASE INHIBITORS

The function of poly(ADP-ribose) polymerase

The poly(ADP-ribose) polymerase (PARP) family encompasses 17 enzymes that assume a critical role in safeguarding DNA replication forks and orchestrating DNA repair processes through various pathways, including single-strand DNA breaks repair, homologous recombination, nucleotide excision repair (NER), and alternative nonhomologous end joining (NHEJ) [22, 23].

Upon detection of single-strand DNA damage, PARP undergoes activation and binds to the impaired DNA strand using its N-terminal zinc finger domain. This interaction augments the enzymatic activity of the catalytic center, allowing PARP to utilize NAD+ as a substrate and generate poly(ADP-ribose) polymers through the process of poly-ADP-ribosylation (PARylation). These generated polymers function as a scaffold, recruiting additional DNA repair enzymes and initiating the assembly of a repair complex. Subsequently, PARP undergoes conformational changes that facilitate its dissociation from DNA, thus enabling access for subsequent repair enzymes responsible for excising damaged DNA bases. The dynamic interplay between PARP and DNA repair enzymes assumes paramount significance in the efficient restoration of single-strand DNA breaks [24–26].

The mechanism of action of poly(ADP-ribose) polymerase inhibitors

Poly(ADP-ribose) polymerase inhibitors (PARPi) have emerged as a promising class of targeted cancer therapies that exploit the inherent genomic instability of cancer cells [27].

PARPi block the PARylation process of PARP and, by binding to the NAD+-binding site (NAD+ – oxidized nicotinamide adenine dinucleotide), allosterically enhances the affinity of the N-terminal zinc finger domain for DNA (deoxyribonucleic acid). These effects prevent the repair of single-strand DNA breaks. In the absence of PARP function, unrepaired single-strand breaks in double-stranded DNA lead to replication fork stalling during DNA replication, resulting in double-strand DNA breaks [28].

PARylation is essential for the dissociation of PARP from DNA. In the event of blocking the PARylation process, the resulting trapped PARP-DNA complex hinders further DNA repair. This also prevents the protection of replication forks by PARP, leading to accumulating replication stress, which in turn leads to mitotic catastrophe and cell death [29, 30].

In normal cells, double-strand DNA breaks are repaired through homologous recombination or NHEJ. Various proteins, including BRCA1 or BRCA2, participate in homologous recombination. However, in individuals with mutations in *BRCA1* or *BRCA2*, the resulting homologous recombination deficiency (HRD) leads to a dependence on PARP-mediated homologous recombination and increased sensitivity to PARP inhibitors [31]. In patients with HRD, blocking PARP leads to the collapse of replication forks, ultimately resulting in cell death through mitotic catastrophe.

HRD extends beyond tumors with *BRCA* mutations and is observed in approximately 50% of high-grade serous ovarian tumors [32, 33]. The genetically driven DNA repair impairments and genomic instability are enhanced by the action of a PARPi in order to cause cancer cell death. This phenomenon is an example of synthetic lethality – two genetic events combine to induce cell death [34].

OLAPARIB

Olaparib made history in 2014 as the inaugural PARPi to receive approval for cancer treatment [22, 35]. Olaparib is used in the treatment of ovarian, breast [36, 37], pancreatic [38, 39], and prostate cancer [38, 40].

The drug is administered orally, with a median time to reach maximum serum concentration usually within 1.5 h after dosing. In vitro binding to plasma proteins at maximum concentration is approximately 82%. In vitro studies have also shown that CYP3A4/5 (members of cytochrome P450 superfamily of enzymes) are the main enzymes responsible for olaparib metabolism [41].

The use of olaparib is associated with the occurrence of generally mild or moderate adverse reactions that usually do not require discontinuation of the drug. The most commonly observed adverse reactions include anemia, neutropenia, leukopenia, nausea, fatigue/asthenia, vomiting, diarrhea, headache, decreased appetite, taste disturbance, cough, dizziness, dyspnea, and dyspepsia. Higher grade adverse reactions include anemia, neutropenia, leukopenia, thrombocytopenia, and fatigue/asthenia. The adverse reactions that most commonly led to discontinuation or dose reduction of the drug are anemia, neutropenia, nausea, fatigue/asthenia, and vomiting [41].

The clinical use of olaparib in ovarian cancer treatment has been extensively examined in various studies, including multicenter randomized controlled trials. These studies have assessed the effectiveness and safety of olaparib in different patient populations, considering factors such as disease history, tumor stage and subtype, sensitivity to treatment, and the presence of *BRCA1*

or *BRCA2* gene mutations. The combined therapy of olaparib with other medications has also been investigated.

STUDIES ON THE USE OF OLAPARIB IN THE TREATMENT OF OVARIAN CANCER

SOLO1 trial

SOLO1/GOG3004 (ClinicalTrials.gov identifier: NCT01844986) [42] is the study with the longest follow-up for the use of PARPi in newly diagnosed ovarian cancer [43]. It is an international phase III trial that was randomized, double-blind, and placebo-controlled. The study aimed to assess the effectiveness of maintenance therapy with olaparib in patients with newly diagnosed advanced ovarian cancer and a *BRCA1/2* mutation.

Included in the study were individuals aged 18 years or older, with an Eastern Cooperative Oncology Group (ECOG) performance status of 0-1, who had newly diagnosed, advanced, high-grade serous or endometrioid ovarian cancer with a complete or partial clinical response following platinum-based chemotherapy. Between September, 2013, and March, 2015, the patients were randomly assigned in a 2 : 1 ratio (260 patients in olaparib group and 131 patients in placebo group) to receive either orally administered olaparib or placebo as maintenance monotherapy for a duration of up to 2 years. The primary endpoint of the study was progression-free survival (PFS), with overall survival (OS) as the secondary endpoint [42–44].

In the initial analysis with data cut-off in May 2018, maintenance olaparib demonstrated a significant improvement in progression-free survival (PFS) compared to placebo (hazard ratio [HR], 0.30; 95% confidence interval [CI], 0.23 to 0.41; $p < 0.001$) [42]. In the analysis conducted after a 5-year follow-up, the median progression-free survival was 56.0 months (95% CI 41.9 – not reached) for patients receiving olaparib, compared to 13.8 months (95% CI 11.1–18.2) for those receiving placebo (HR 0.33 [95% CI 0.25–0.43]) [44]. After 7 years of follow-up the OS data is still not mature enough to assess OS definitely [43].

SOLO2 trial

SOLO2/ENGOT Ov-21 trial (ClinicalTrials.gov identifier: NCT01874353) [45], a phase III clinical randomized, double-blind trial compared olaparib as a maintenance therapy to placebo in patients with relapsed serous or endometrial ovarian, fallopian tube, or primary peritoneal cancer that was platinum-sensitive and harbored a *germline BRCA1/2* mutation. The trial evaluated the efficacy of olaparib as maintenance treatment until disease progression in patients (196 patients in olaparib group, 99 patients in placebo group, enrolled between 2013 and 2014) who had achieved a complete or partial response to platinum-based chemotherapy. The primary endpoint of the study was PFS, which was assessed by investigators using RECIST 1.1 criteria [41, 45, 46].

The study demonstrated a significant improvement in investigator-assessed PFS with olaparib compared to placebo, with a HR of 0.30 (95% CI 0.22–0.41; $p < 0.0001$). The median PFS was 19.1 months for olaparib vs. 5.5 months for placebo. This finding was further supported by an independent central radiographic assessment, which confirmed the investigator-assessed PFS with an HR of 0.25 (95% CI 0.18–0.35; $p < 0.0001$) and a median PFS of 30.2 months for olaparib vs. 5.5 months for placebo. At the 2-year mark, 43% of patients treated with olaparib experienced no disease progression, compared to only 15% of patients in the placebo group [41, 45].

However, a post-hoc analysis [47] of the SOLO2 data revealed that in patients with platinum-sensitive relapsed ovarian cancer and *BRCA1/2* mutations who experienced disease progression after maintenance olaparib, the effectiveness of subsequent platinum-based chemotherapy appears to be diminished compared to patients who had not previously received PARPi. The optimal management approach for patients who relapse following PARPi treatment is currently being investigated as an active area of research.

Analysis from 2021 revealed no statistically significant difference in OS between olaparib and placebo group. Nevertheless, olaparib demonstrated a median improvement in overall survival of 12.9 months compared to placebo [48].

SOLO3 trial

In the randomized, controlled, open-label phase III trial SOLO3 (ClinicalTrials.gov identifier: NCT00628251) [49], patients with platinum-sensitive relapsed ovarian cancer and a germline *BRCA1/2* mutation, received either olaparib (178 patients initially) or single-agent nonplatinum chemotherapy (pegylated liposomal doxorubicin, paclitaxel, gemcitabine, or topotecan; 88 patients initially) according to the physician's choice. The primary objective was to assess the objective response rate (ORR) in the measurable disease analysis set, as evaluated by blinded independent central review. The key secondary objective was to evaluate the PFS in the intent-to-treat population [49].

Among patients with measurable disease (151 in the olaparib group, 72 in the chemotherapy group), the ORR was significantly higher in olaparib group (72.2% vs. 51.4%; OR 2.53 [95% CI 1.40–4.58]; $p = 0.002$). Furthermore, the PFS was also longer in the olap-

arib group (HR 0.62 [95% CI 0.43–0.91]; p = 0.013); median PFS: 13.4 months for olaparib vs. 9.2 months for chemotherapy) [49].

L-MOCA trial

L-MOCA (ClinicalTrials.gov identifier: NCT03534453) [50] is an open-label, single-arm trial designed to assess the efficacy of olaparib maintenance monotherapy in Asian patients with platinum-sensitive relapsed high-grade epithelial ovarian cancer. Other inclusion criteria included: at least 18 years of age and an ECOG performance status score of 0–1.

During the period from 2018 to 2020, a total of 225 patients were included in the study, with 224 of them receiving olaparib treatment. As of the primary data analysis conducted on December, 2020, the median PFS for the entire group was 16.1 months. Within the subgroup analysis, the median PFS was found to be 21.2 months for patients with *BRCA* mutations and 11.0 months for those with wild-type BRCA status [50].

Study 19

The Study 19 (ClinicalTrials.gov identifier: NCT00753545) [51–53] evaluated the safety and efficacy of olaparib as maintenance therapy in patients with platinum-sensitive relapsed ovarian, fallopian tube, or primary peritoneal cancer who had received two or more platinum-containing regimens. The trial was a randomized, double-blind phase II study comparing olaparib to placebo. The primary endpoint was median progression-free survival (mPFS). The study included 265 patients (136 in the olaparib group and 129 in the placebo group) who had previously achieved a response to platinum-based chemotherapy [51].

The primary analysis demonstrated a statistically significant improvement in PFS for olaparib compared to placebo (HR 0.35; 95% CI 0.25–0.49; p < 0.00001; median of 8.4 months for olaparib vs. 4.8 months for placebo). The study also showed a favorable overall survival trend for olaparib. The adverse events were generally manageable, with 9.4% of patients discontinuing therapy due to treatment-related adverse events. These findings highlight the efficacy and tolerability of olaparib as maintenance therapy in platinum-sensitive relapsed ovarian cancer patients [51].

OPINION trial

The OPINION trial (ClinicalTrials.gov identifier: NCT03402841) [54] evaluated the efficacy of olaparib maintenance monotherapy in patients with platinum-sensitive relapsed ovarian cancer who did not have a deleterious or suspected deleterious germline *BRCA1/BRCA2* mutation and had received at least two previous lines of platinum-based chemotherapy.

In the single-arm, open-label study, patients who had responded to platinum-based chemotherapy received olaparib as maintenance therapy until disease progression or unacceptable toxicity. The study enrolled a total of 279 patients. The primary endpoint was investigator-assessed PFS using modified RECIST version 1.1 criteria [46].

At the data cutoff, the median PFS in the overall population was 9.2 months. The median PFS varied across biomarker subgroups, ranging from 7.3 to 16.4 months [54].

The study concluded that maintenance olaparib showed clinical benefit in patients without a germline *BRCA* mutation, including various subgroups. No new safety concerns were observed [54].

PAOLA-1 trial

The PAOLA-1/ENGOT-ov25 (ClinicalTrials.gov identifier: NCT02477644) [32, 55] study was a randomized, double-blind, international phase III trial that aimed to evaluate the effect of combining maintenance olaparib and bevacizumab in patients with newly diagnosed advanced ovarian cancer, regardless of their *BRCA* mutation status.

The study included patients with newly diagnosed, advanced, high-grade ovarian cancer who had responded to first-line platinum-taxane chemotherapy plus bevacizumab. Patients were eligible regardless of their surgical outcome or *BRCA* mutation status. They were randomly assigned in a 2 : 1 ratio to receive either olaparib (537 patients) or placebo (269 patients) for up to 24 months. Both groups additionally received bevacizumab for 15 months. The primary endpoint of the study was defined as the time from randomization to either investigator-assessed disease progression or death [32].

After a median follow-up of 22.9 months, the study found that the median progression-free survival was 22.1 months in the olaparib group and 16.6 months in the placebo group. The HR for disease progression or death was 0.59 (95% CI 0.49–0.72; p < 0.001), indicating a significant benefit in favor of the olaparib group. The benefit was particularly pronounced in patients with tumors positive for HRD, including those with *BRCA* mutations, as well as in patients with HRD-positive tumors without *BRCA* mutations [32].

The final analysis of OS [55] was presented after a median follow-up was 61.7 and 61.9 months in the olaparib and placebo arms, respectively. The median OS was 56.5 vs. 51.6 months in the intention-to-treat population, but the difference was not

statistically significant (HR 0.92; 95% CI 0.76–1.12; p = 0.4118). In the HRD-positive population, the combination of olaparib plus bevacizumab resulted in longer OS (HR 0.62; 95% CI 0.45–0.85; 5-year OS rate, 65.5% vs. 48.4%). Updated PFS data at 5 years also showed a higher proportion of patients in the olaparib group without relapse (HR 0.41; 95% CI 0.32–0.54; 5-year PFS rate, 46.1% vs. 19.2%). The incidence of certain adverse events remained low and balanced between the treatment arms [55].

In conclusion, in patients with advanced ovarian cancer receiving first-line standard therapy including bevacizumab, the addition of maintenance olaparib significantly improved PFS and caused a clinically meaningful improvement in overall survival for patients with HRD-positive cancer. These results highlight the potential of this combination therapy to enhance curative outcomes especially in patients with HRD-positive tumors, including those without a *BRCA* mutation [32, 55].

Combination of olaparib with durvalumab

The phase II trial (ClinicalTrials.gov identifier: NCT02484404) [56] investigated the combination of olaparib with durvalumab, an anti-PD-L1 agent, in patients with recurrent ovarian cancer. The objective of the study was to test the hypothesis that PARPi induce an immunostimulatory microenvironment in ovarian cancer, thereby enhancing the effectiveness of immune checkpoint blockade. The primary goal was to assess the ORR, while secondary objectives included evaluating safety, PFS, and the immunomodulatory effects of the treatment.

A total of 35 patients with recurrent ovarian cancer participated in the trial. The ORR was 14%, indicating a modest clinical activity of the olaparib/durvalumab combination. The disease control rate (partial response + stable disease) was 71%. Notably, the treatment resulted in an immunostimulatory microenvironment, as evidenced by increased expression of IFN-γ (interferon γ) and CXCL9/10 (chemokine [C-X-C motif] ligand 9/10), systemic production of TNF-α (tumor necrosis factor α), and tumor-infiltrating lymphocytes. Higher levels of IFN-γ were associated with improved PFS, while elevated VEGFR3 (vascular endothelial growth factor receptor 3) levels were linked to worse PFS [56].

In conclusion, the combination of olaparib and durvalumab showed limited but notable clinical activity in recurrent ovarian cancer. The study findings suggest immunomodulatory effects of the treatment and indicate that blockade of the VEGF/VEGFR (vascular endothelial growth factor/receptor) pathway may be necessary to enhance the combination's efficacy [56].

CAPRI trial

In the single-arm CAPRI (ClinicalTrials.gov identifier: NCT03462342) [57] trial, the combination of olaparib and ceralasertib (ataxia telangiectasia and Rad3-related kinase inhibitor, ATRi) showed promising results in patients with recurrent, platinum-sensitive *BRCA1/2* mutated or homologous recombination deficient high-grade serous ovarian cancer who had acquired resistance to PARPi. Out of the 13 patients enrolled, 12 were evaluated for efficacy. The ORR was 50% (95% CI 0.15–0.72), with 6 patients showing partial responses. The treatment was well-tolerated, with manageable toxicities. Grade 3/4 toxicities were observed in 5 patients, but no patients discontinued treatment due to toxicity. These findings may suggest that ceralasertib may re-sensitize PARPi-resistant HGSC to olaparib, indicating the need for further investigation of this combination therapy [57].

EPIK-O trial

Patients diagnosed with platinum-resistant high-grade serous epithelial ovarian cancer lacking germline BRCA mutation often experience unfavorable survival outcomes. To address this, the ongoing EPIK-O/ENGOT-OV61 (ClinicalTrials.gov identifier: NCT04729387) [58], a randomized (1 : 1), open-label, phase III trial, aims to investigate the effectiveness and safety of alpelisib and olaparib compared to cytotoxic chemotherapy in platinum-resistant or refractory HGSC without germline *BRCA* mutation. The primary focus is on evaluating PFS, while OS serves as a significant secondary objective. The estimated primary completion date of the trial is December 2023 [59].

Combination of olaparib with entinostat

Entinostat, a histone deacetylase inhibitor (HDACi), may enhance the effectiveness of olaparib in homologous recombination-proficient ovarian cancer. Preclinical studies demonstrate that the combination of olaparib and entinostat reduces cell viability and clonogenicity in homologous recombination-proficient ovarian cancer cells. It also decreases peritoneal metastases and extends survival in animal models. Entinostat enhances olaparib-induced DNA damage, disrupts replication fork progression, leading to irreparable DNA damage and cell death. These findings may offer preclinical evidence supporting the potential investigation of combining olaparib and entinostat in homologous recombination-proficient ovarian cancer [60].

LIGHT trial

The multicenter, non-randomized, open-label phase II study known as LIGHT (ClinicalTrials.gov identifier: NCT02983799) [61] aimed to evaluate the effectiveness of olaparib treatment in patients with platinum-sensitive relapsed ovarian cancer who had

known *BRCA1/BRCA2*-mutated (BRCAm) status and HRD. The primary objective of the study was to assess the ORR, while secondary endpoints included the disease control rate (DCR) and PFS [61].

A total of 272 patients were enrolled in the study, with 270 of them included in the efficacy analysis. These patients were divided into four cohorts based on their BRCAm and HRD status. Cohort 1 consisted of patients with a germline BRCAm, Cohort 2 included patients with a somatic BRCAm, Cohort 3 comprised HRD-positive patients without a BRCAm (defined as having a genomic instability score of ≥ 42), and Cohort 4 consisted of HRD-negative patients (with a genomic instability score of < 42). The objective response rates in Cohorts 1–4 were 69.3%, 64.0%, 29.4%, and 10.1%, respectively. The disease control rates were 96.0%, 100.0%, 79.4%, and 75.3% in each cohort, respectively. The median progression-free survival was 11.0, 10.8, 7.2, and 5.4 months, respectively [61].

Combination of olaparib with prexasertib

In a phase I study [62], the combination of the checkpoint kinase 1 (CHK1) inhibitor prexasertib and a modified regimen of olaparib was found to be well-tolerated and showed promising initial antitumor activity. Pharmacodynamic assessments confirmed that prexasertib compromised homologous recombination, leading to the induction of DNA damage and replication stress [62].

CONCLUSIONS

The article compiles and summarizes current research on the use of olaparib in the treatment of ovarian cancer. In conclusion, olaparib has revolutionized the treatment landscape for ovarian cancer. It has demonstrated significant improvements in progression-free survival and overall survival, particularly in patients with *BRCA* mutations or homologous recombination deficiency. The exploration of olaparib in various clinical trials and combination therapies continues to provide valuable insights and offer new hope for ovarian cancer patients. Moreover, there are ongoing investigations exploring the application of olaparib in other malignancies, as well as studies focusing on other PARPi. The growing understanding of PARPi has the potential to lead to further advancements in the prognosis of patients suffering from the formidable condition of ovarian cancer.

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