REVIEW

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Impact of Olaparib, Niraparib, Rucaparib therapies on Newly Diagnosed and Relapsed Ovarian Cancer -Systematic Review and Meta-Analysis

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Abstract

Objective: This review aims to examine the effect of PARP inhibitors on PFS, OS, and adverse events in women with advanced ovarian cancer (OC). **Methods:** The PRISMA 2020 guidelines are followed while conducting this comprehensive review. Data from 17 randomized control trails (RCT) published between 2014 and June 2024 were included. These trials compared PARPi maintenance therapy to placebo women with newly diagnosed and recurrent advanced OC. The specific keywords were used to search relevant studies in databases including PubMed, SCOPUS, Cochrane library, and WoS. The main outcomes were the Progression free survival (PFS), overall survival (OS), or adverse events (AEs). The combined hazard ratios (HRs) and risk ratios (RRs) were determined, together with 95% confidence intervals (CIs). Each of the analyses were conducted using a model with random effects. **Results:** Despite high heterogeneity, the meta-analysis found that poly (ADP-ribose) polymerase inhibitors (PARPi) maintenance therapy ominously improved PFS compared to placebo, with a combined HR of 1.33 (95% CI: 1.10-1.61) in newly diagnosed cases and 0.88 (95% CI: 0.59-1.30) in relapsed cases. However, the OS improvement was not significantly substantial, with a collective HR of 1.06 (95% CI: 0.99–1.13). AEs are considerably higher in the PARPi groups, notably hematologic toxicities including anaemia, thrombocytopenia, and neutropenia. However, these adverse effects may be controlled with dosage modifications, and therapy was discontinued only in few cases. Conclusion: PARPi are an effective therapy in both newly discovered and relapsed. Although there is a modest rise in the frequency of severe adverse reactions, they are usually handled well.

Keywords: Olaparib- Niraparib- Rucaparib- PARPi- newly diagnosed OC- Relapsed OC

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Introduction

Ovarian cancer is a leading cause of death among gynecological cancers and the third most common gynecologic malignancy. Globally, it ranks as the ninth leading cause of cancer-related deaths in women. In 2020, approximately 313,959 new ovarian cancer patients were detected, with 207,252 deaths reported worldwide [1, 2, 3]. Epithelial ovarian malignancies account for 90% of all ovarian cancer cases, with around 75% categorized as high-grade serous carcinoma (HGSC) [4, 5]. The disease often appears without symptoms, and due to ineffective screening procedures, more than 75% of cases are identified at a later stage (stage III or IV) [6, 7]. Additionally, approximately 13% of HGSC cases exhibit genetic BRCA1/2 mutations, while roughly 50% show somatic homologous recombination deficiency (HRD).

Chemotherapy remains the primary treatment for metastatic ovarian cancer, despite significant relapse rates [8]. Over the last decade, treatment options have expanded with the introduction of novel agents such as bevacizumab and PARPi, which have shown enhanced progression-free survival (PFS) when combined with chemotherapy. However, various therapeutic options, including platinum-based chemotherapy with or without bevacizumab, dose-dense platinum regimens, and intraperitoneal chemotherapy, have yielded unsatisfactory OS rates. Consequently, researchers have shifted focus toward improving survival outcomes in these patients.

PARPi enzymes play a crucial role in DNA repair, making PARP inhibitors essential for treating HRD-related malignancies. BRCA1/2 proteins facilitate the repair of double-strand DNA breaks through homologous recombination. PARP inhibitors block this repair process in cancers with BRCA1/2 mutations, leading to cell death and enhancing the effectiveness of cytotoxic therapy [9,

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10]. Currently, three PARP inhibitors olaparib, rucaparib, and niraparib have received global approval for the treatment of ovarian cancer, including malignancies of the uterine tubes and peritoneal cavity [11].

Latest research findings have identified four primary mechanisms by which PARP inhibitors exert their effects: (1) blocking base excision repair, inhibiting PARP activity; (2) trapping PARP on damaged DNA, disrupting its catalytic cycle, impairing DNA repair, and inducing double-strand breaks; (3) preventing BRCA1 recruitment to damaged DNA, thereby inhibiting PARP; and (4) stimulating non-homologous end joining to suppress PARP function [12]. These inhibitors also prevent malignant cells from repairing damaged DNA, leading to persistent DNA damage and cell death. Additionally, PARP inhibitors cause replication fork stalling, resulting in chromatin bridges, cytokinesis failure, multinucleation, and apoptosis during mitosis [13]. However, their efficacy in patients without BRCA1/2 mutations or HRD remains uncertain [14].

Several RCTs have demonstrated that PARP inhibitor maintenance therapy significantly improves PFS and OS in ovarian cancer patients, regardless of BRCA mutation or HRD status. Moreover, two recent RCTs have suggested that PARP inhibitors provide a survival advantage in terms of OS for newly diagnosed advanced epithelial ovarian cancer (EOC) patients with BRCA mutations or HRD [15]. Given the high relapse rates associated with conventional therapies and the growing body of evidence supporting PARP inhibitors, an in-depth review of their role in the treatment of newly diagnosed advanced ovarian cancer is warranted.

This analysis differs from earlier ones in that it particularly examines the effect of PARP inhibitors on both newly diagnosed and recurrent ovarian cancer, utilizing data from 17 RCTs published between 2014 and June 2024. Unlike previous meta-analyses, which examined a variety of treatment settings and patient subgroups, this study focuses on a single population and compares the effects of olaparib, niraparib, and rucaparib. It also assesses progression-free survival (PFS), overall survival (OS), and adverse events, addressing important clinical issues such as hematologic toxicities. The findings provide a more comprehensive knowledge of PARP medications' benefits and limitations in various ovarian cancer groups.

This review aims to investigate the impact of PARP inhibitors on improvement of PFS, OS, and adverse events in newly diagnosed and relapsed OC

Materials and Methods

The researchers adhered to the standards delineated in the Cochrane Handbook for Systematic Reviews of Interventions for conducting the review and followed the PRISMA guidelines for the reporting reviews and meta-analysis [16,17]

Search strategy

A comprehensive search strategy was developed and used electronic databases including SCOPUS, PubMed, the Cochrane Library, and Web of Science using a specific set of keywords: parp AND inhibitors; AND therapy; AND ovarian AND cancer; AND outcome, niraparib AND inhibitors; AND therapy; AND ovarian AND cancer; AND outcome, olaparib AND inhibitors; AND therapy; AND ovarian AND cancer; AND outcome, rucaparib AND inhibitors; AND therapy; AND ovarian AND cancer; AND outcome, veliparib AND inhibitors. The systematic review included the trails were published between 2014-June 30, 2024. The relevant papers that were not found through database explorations were located by analyzing the references to the chosen RCTs and review articles.

Eligibility, Selection criteria and data extraction

This analysis comprised RCTs which could meet the eligibility requirements: (1) patients diagnosed with advanced OC and relapsed OC were involved; (2) data was provided on PFS, OS, and AEs such as anemia, thrombocytopenia, neutropenia, leukopenia, vomiting, fatigue, and nausea in newly diagnosed and recurrent cases; (3) PARPi such as olaparib, niraparib, olaparib and durvalumab used as combination therapies. Exclusion criteria included: (1) phase I RCTs; (2) seminar papers without credible information on trial strategy; and (3) studies investigating PARP inhibitors in combination with other targeted therapy medicines.

After exclusion of duplicates, two researchers (SD and GM) used a checklist to independently extract significant data from the trials. Cohen's kappa coefficient was calculated at each stage of the selection procedure with any differences dealt with by a third reviewer (RC) [18]. Any disagreements were settled by conversation between the reviewers. Mostly differences are resolved by the third reviewer. The eligible population was separated into two groups: those treated with a PARP inhibitor and those given a placebo.

The data gathered from the studies included the clinical trial registration number, disease setting, study design and phase, sample size, histologic types, experimental and control treatments, median follow-up duration in months, median PFS in months, OS in months, AEs, and HRD status for disease progression. The major end measure was PFS, which is demarcated as the time from randomization until illness development or demise from any reason. The OS is analysed as the period between from the point of randomization (such as in a clinical trial) until any cause of death occurs [19].

Risk of bias and quality evaluation of included studies

Two authors (SD and GM) evaluated the article's quality individually employing a measuring tool available in the RevMan webtool for RCTs. As Figure 1 depicts, bias was assessed in following major fields: randomization, assessed the bias in the selection process, distribution disguise, performance bias, which was assessed by examining the participant and personnel blinding, detection bias was evaluated by checking the blinding of outcome calculation, an attrition bias was evaluated by checking if there is any inadequate infromation outcome, reporting bias was assessed by checking the process of selective reporting, and we also assessed for possible prejudices. Any disputes among the assessors

were determined by discussion and, if essential, the involvement of a second assessor (GM). The reliability was determined using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) method. SD and GM separately assessed each assessment criterion for all outcomes and associations, resolving any discrepancies with the help of a neutral third-party mediator [20. 21].

Statistical analysis

In case of Progression-free survival events in the entire population of newly diagnosed and relapsed cases, for binary outcomes, we used the exact Mantel-Haenszel technique to generate random effects estimates of RRs with 95% confidence intervals [22-24] To determine the impact of PARPi in subgroups of newly diagnosed and recurrent OC, Cediranib plus Olaparib, Olaparib vs Niraparib, Olaparib plus Bevacizumab, for PFS, OS , AEswe have we have used HRs with 95% CIs, using log HR estimates and SEs [24].

To estimate the between-study variance tau2, we applied restricted maximum-likelihood estimator [23]. The heterogeneity variance measure tau2 was estimated using the Paule-Mandel technique [25]. When there were more than five studies, we applied the Hartung-Knapp adjustment [26]; no adjustment was made for fewer than five studies. When relevant, prediction intervals (the anticipated range of effects in future studies) were provided following the guidelines of Int Hout et al. [27]

Data were examined with the Cochrane web packages. Meta-analysis findings were shown for both individual and aggregated forest plots. A p-value of <0.05 was judged statistically significant. Employing the statistical methods I^2 statistics and χ^2 tests , heterogeneity was evaluated, with a p-value < 0.1 representing substantial heterogeneity [28]. Each outcome necessitated at least three studies for inclusion in the meta-analysis

Results

Search and selection

Our search approach produced 5,254 records. Following a thorough screening process, 44 articles, including approximately 17 RCTs, were found appropriate for systematic review and meta-analysis. Figure 2 depicts a PRISMA flowchart that describes the selecting procedure.

Supplementary Table 1 highlights the characteristics of the study. PARP inhibitors utilized as a conservation therapy following chemotherapy in ten trials including patients with newly diagnosed ovarian cancer [28, 30-37] and seven trials involving recurrent cases [31, 38-43] Veliparib was used in one study [41], Olaparib in four studies [32, 34, 39, 43] Niraparib in five studies [28, 29, 34, 37, 40] and Rucaparib in one [44]. In addition, four studies combined Olaparib and Bevacizumab [31, 33, 35, 36] while two trials combined Cediranib and Olaparib [38, 42] The data for all seventeen investigations obtained from full-length publications, and all were the randomized controlled trials [39]. Each of the seventeen trials reported a median PFS in months.

Progression Free Survival (PFS) analysis

PFS in overall population

According to six clinical trials for newly diagnosed ovarian cancer [28-33, 40] and three for recurrent ovarian cancer [41, 38, 37] PARP inhibitors suggestively increased PFS compared to placebo. Patients in the experimental group had an average PFS of approximately 18.44 months, while those in the placebo group had an average of 12.66 months.

Table 1. Abbreviations

Symbol	Description	Symbol	Description
AEs	Adverse Events	HRs	Hazard Ratios
CIs	Confidence Intervals	OC	Ovarian Cancer
EOC	Epithelial Ovarian Cancer	PARPi	Poly (ADP-iibose) Polymerase Inhibitors.
GRADE	Grading of Recommendations, Assessment, Development, And Evaluation	PFS	Progression-Free Survival
HGSC	High-Grade Serous Carcinoma	RCTs	Randomized Controlled Trials
HRD	Homologous Recombination Deficit	RRs	Risk Ratios

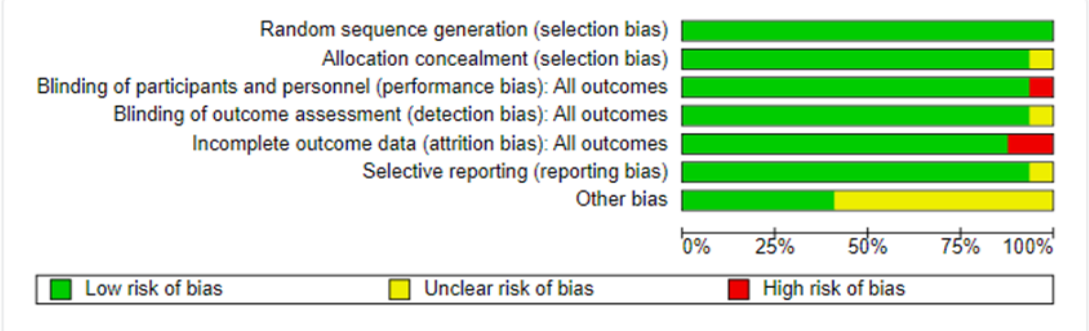

Figure 1. Risk of Bias and Quality Assessment in RCT

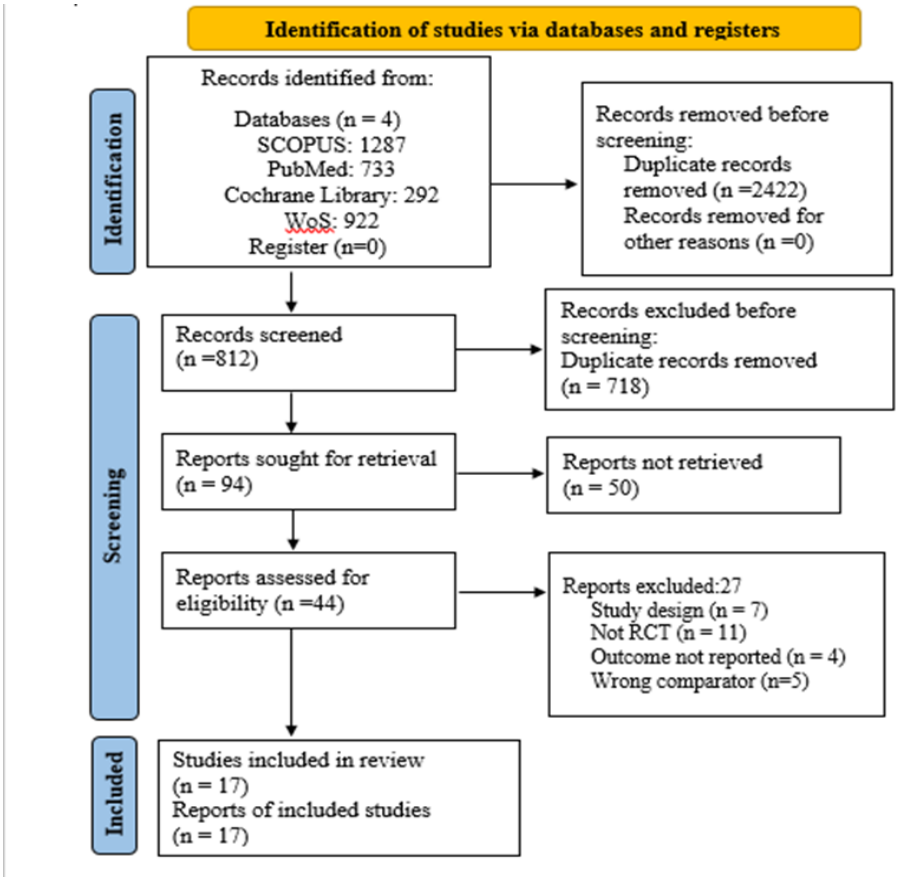

Figure 2. Effective Strategies for Identifying Relevant Studies in Databases

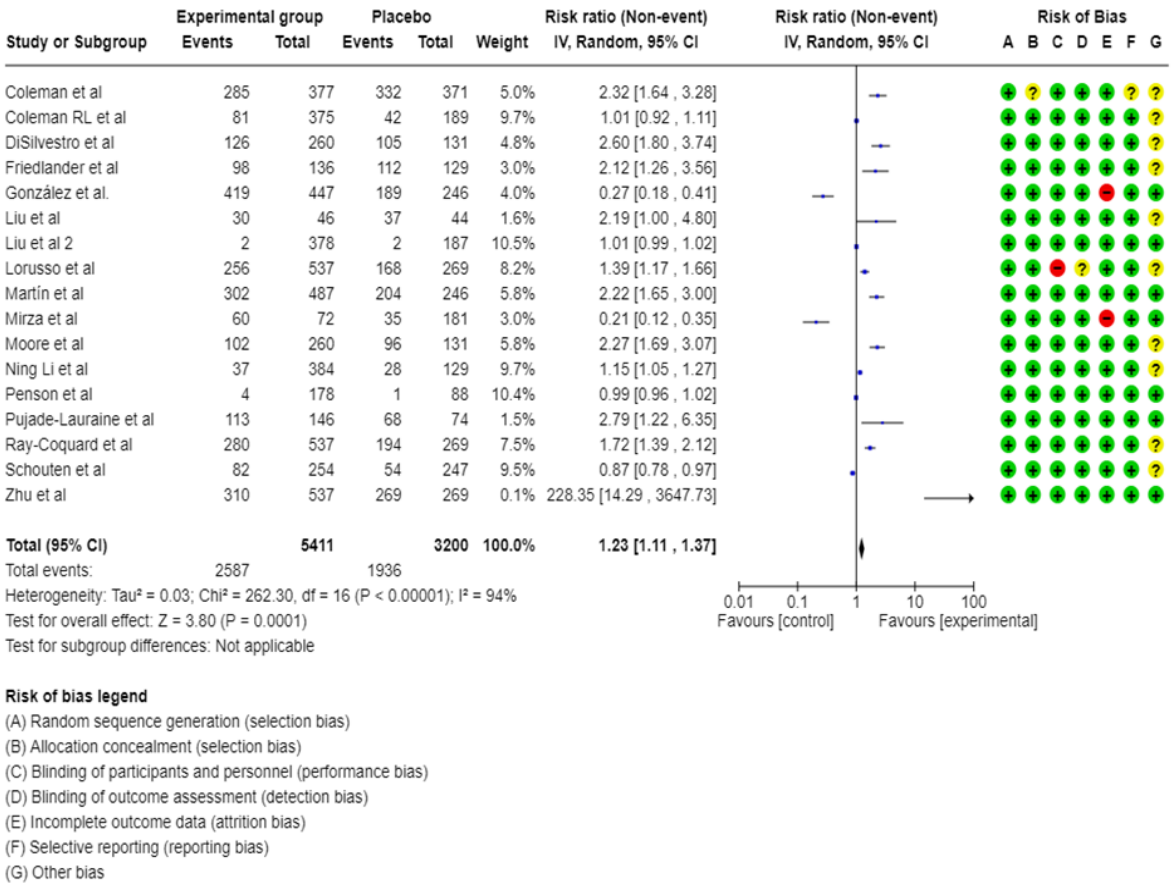

Figure 3. Progression-Free Survival Events in Experimental and Placebo

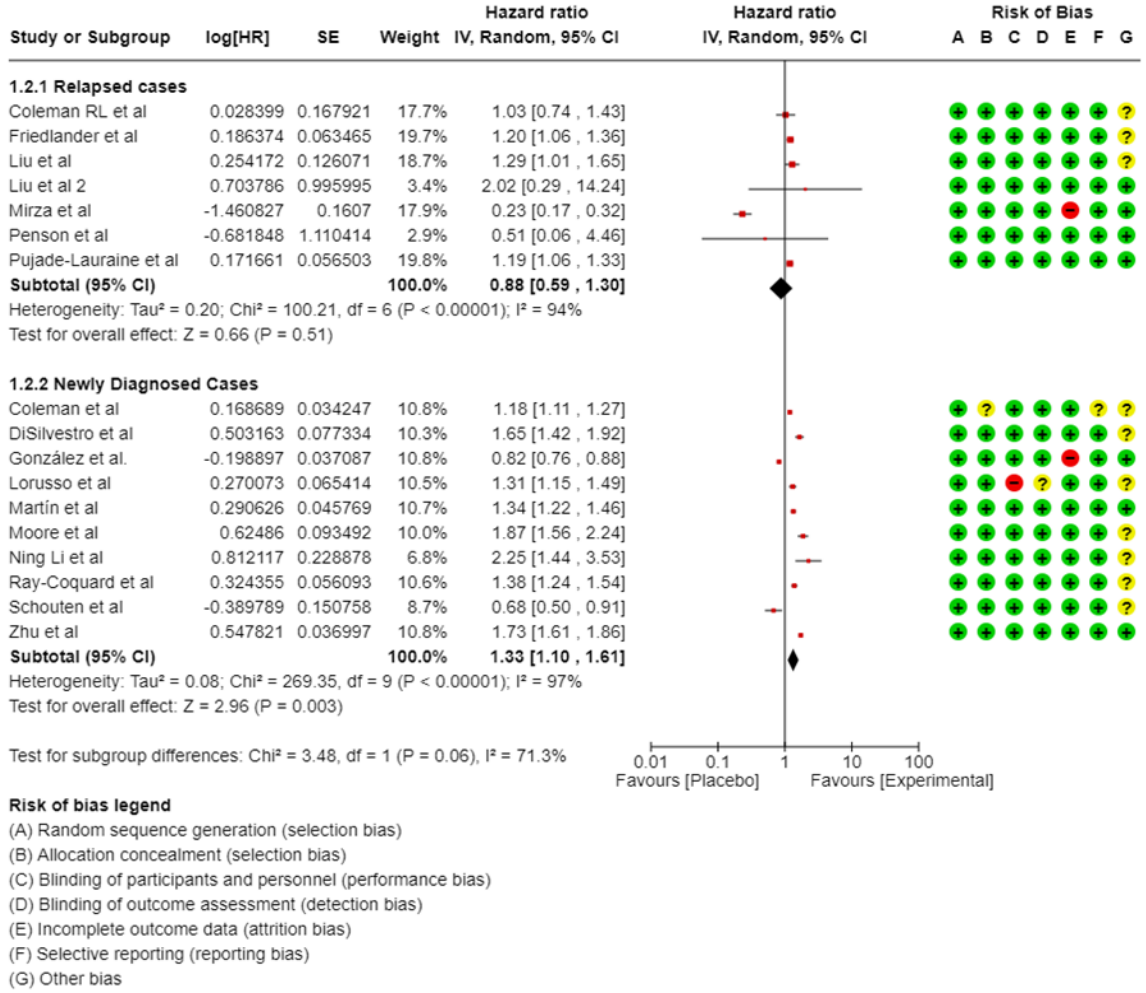

Figure 4. Impact of PARP Inhibitors on PFS in Ovarian Cancer Subgroups

The forest plot (Figure 3) shows a significant improvement in PFS for the experimental group (RR, 1.23; 95% CI, 1.11–1.37) compared to placebo. However, high heterogeneity (I^2 = 94%, Tau^2 = 0.03, Chi^2 = 262.30; $p < 0.00001$) indicates variability in the intervention's impact across studies.

The impact of PARP inhibitors on PFS in newly diagnosed and recurrent OC

Figure 4 illustrates the effect of PARPi on newly diagnosed and relapsed OC cases. Friedlander et al. [38] reported an HR of 1.20, while Liu et al. [42] found HRs of 1.29 and 2.02, showing significant benefits in experimental groups. Penson et al. [40] reported an HR of 1.42, and Pujade-Lauraine et al. [43] reported 1.19 (95% CI: 1.05–1.35), indicating improved PFS. However, for relapsed cases, the combined HR of 0.88 (95% CI: 0.59–1.30) showed no meaningful advantage over placebo despite heterogeneity.

In newly diagnosed cases, Coleman et al. [44] reported HR 1.18, DiSilvestro et al. [34] 1.65 (95% CI: 1.42–1.92), González et al. [28] 1.53 (95% CI: 1.18–2.00), Lorusso et al. [36] 1.45 (95% CI: 1.14–1.85), and Martin et al. (2023) 1.49. Moore et al. [32] reported HR 1.53, Liu et al. [42] HR 2.28 (95% CI: 1.44–3.55), Ray-Coquard et al. [31] HR 1.15 (95% CI: 1.06–1.26), Schouten et al. [33] HR 0.68 (95% CI: 0.58–0.81), and Zhu et al. [35] HR 2.35 (95% CI: 1.45–3.80). The combined HR for newly diagnosed cases is 1.33 (95% CI: 1.10–1.61), demonstrating a significant overall effect despite heterogeneity.

The impact of PARP inhibitors on PFS in newly diagnosed and recurrent OC

Cediranib plus Olaparib

Figure 5 illustrates that the combination of Cediranib and Olaparib provides a significant advantage in OC therapies. Liu et al. [38]. stated 0.35 HR (95% CI: 0.13-0.97, weight 79.1%), indicating a significant benefit over placebo. The heterogeneity measurements (Tau^2 = 0.00; Chi^2 = 0.08, df = 1, P = 0.77; I^2 = 0%) showed no variability, confirming consistent results. The overall effect test generated a Z score of 2.11 (P = 0.03), indicating that Cediranib + Olaparib outperformed the control in terms of treatment efficacy.

Olaparib vs Niraparib

DiSilvestro et al. [34]. reported HR 0.23, Friedlander et al.[39]. HR 0.39 (95% CI: 0.21-0.74), Moore et al. [32]. HR 0.24 (95% CI: 0.15-0.37), and Pujade-Lauraine et al. [43]. reported HR 0.33 (95% CI: 0.27-0.39), suggesting

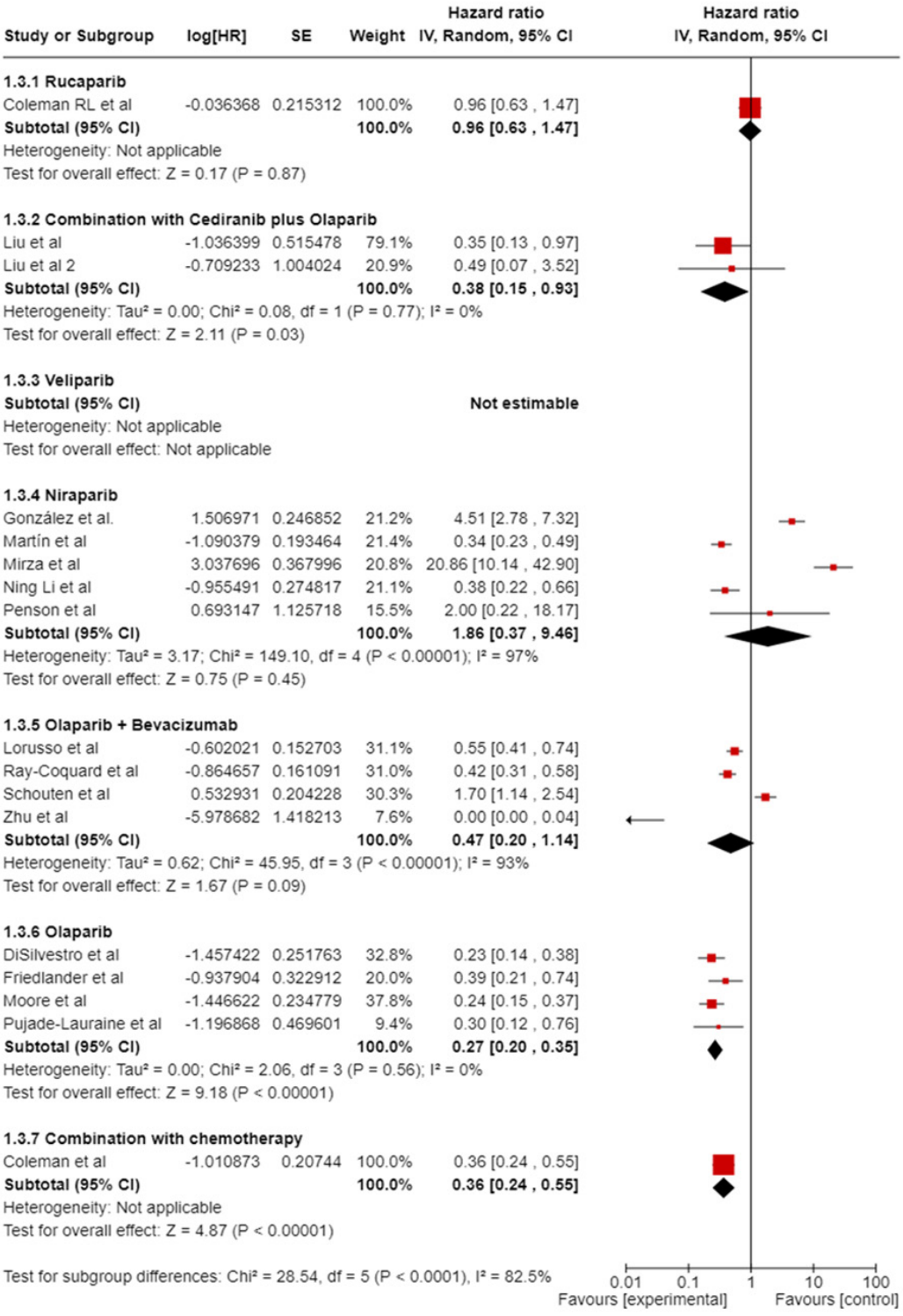

Figure 5. PARPi Impact on PFS in Ovarian Cancer Subgroups of Various Therapies

olaparib's efficacy in improving PFS compared to placebo.

The hazard ratios (HR) for the niraparib treatment subgroup are as follows: González et al. [28] (HR = 4.51 [2.78, 7.32]), Martin et al (2019). (HR = 4.04 [2.03, 8.49]), Mirza et al. [41]. (HR = 86.10 [14.10, 42.90]), Ning Liu et al (2022). (HR = 3.08 [0.22, 0.66]), and Penson et al. [40].

Olaparib plus Bevacizumab

The examination of the olaparib plus bevacizumab treatment subgroup had mixed results. Lorusso et al. [36]. (HR = 0.55 [0.41, 0.74]) and Ray-Coquard et al. [31]. (HR = 0.42 [0.31, 0.58]) discovered substantial benefits. However, Schouten et al. [33]. (HR = 1.70 [1.14, 2.54]) and Zhu et al. [35]. (HR = 1.39 [0.02, 0.04]) discovered no significant benefits.

Coleman et al. [44]. found an HR of 0.36 (95% CI: 0.24 to 0.55) for the combination treatment with chemotherapy, with no relevant heterogeneity. The total effect test (Z = 4.87, P < 0.0001) shows that the combo treatment outperformed the control.

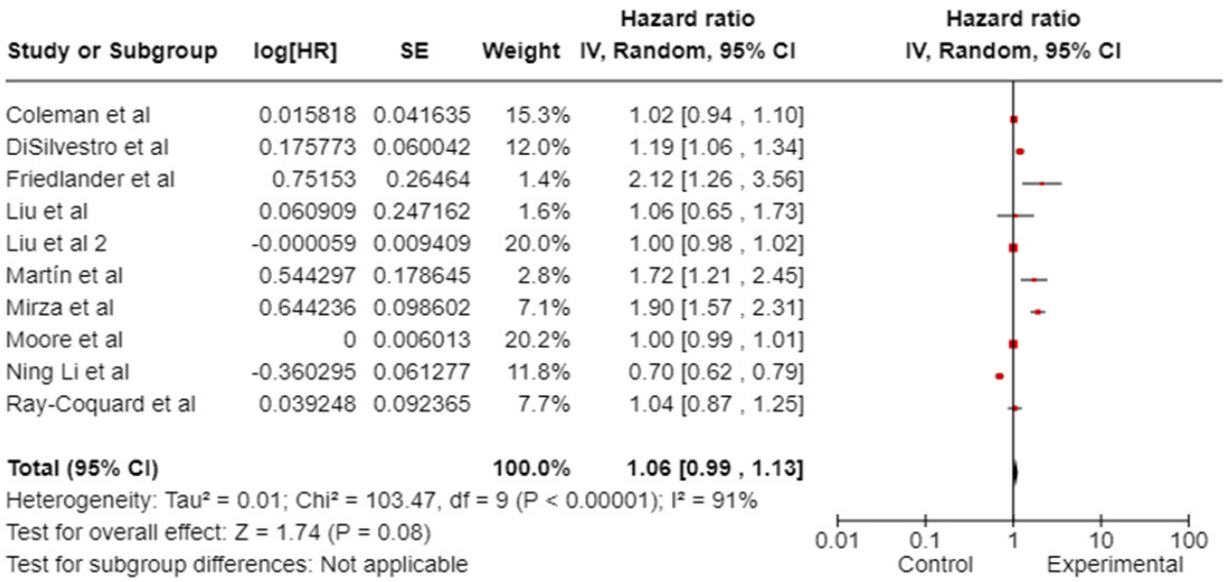

Figure 6. Impact of PARPi on Overall Survival (OS) for Five Years

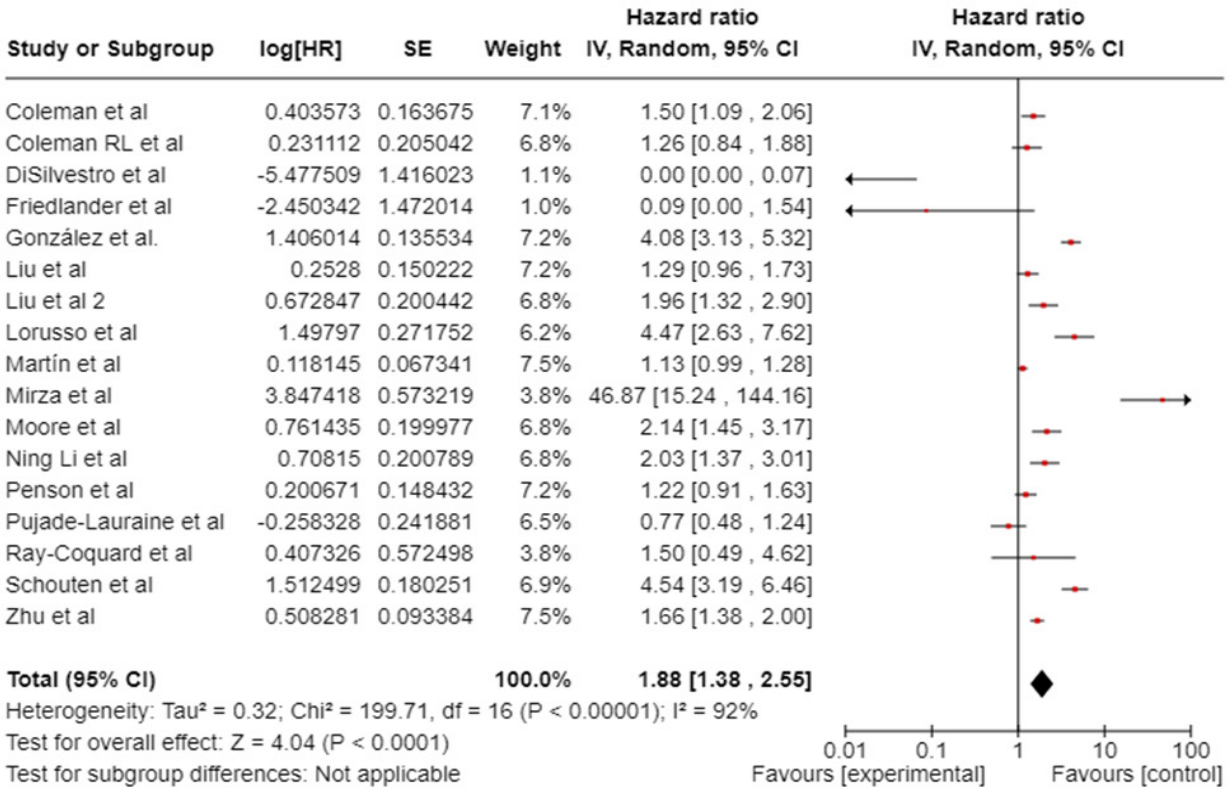

Figure 7. Impact of PARPi on Adverse Effects

Overall survival (OS) analysis

Only ten of the 17 trials included data on overall survival (OS), while the remaining investigations are still in their early stages. Figure 6 shows the hazard ratios (HRs) for OS from various studies on OC. Coleman et al. [44], DiSilvestro et al. [34], and Ning Li et al. [37]. discovered HRs close to one, meaning that the control and experimental groups had similar survival rates. The pooled HR is 1.06 (95% CI: 0.99–1.13), indicating no noteworthy change in survival.

Overall survival (OS) analysis

Table 1 compares the incidences of anemia, thrombocytopenia, and neutropenia in experimental and placebo groups across multiple trials. The experimental

groups had high frequencies of these disorders, particularly anemia (86.96%), thrombocytopenia (91.30%), and neutropenia (65.22%), as reported by Liu et al. [38]. Martín et al. [29] reported 44.97% anemia and 19.51% neutropenia. González et al. [28]. found that placebo groups had considerably reduced rates of anemia (1.63%), thrombocytopenia (0.41%), and neutropenia (1.22%). This highlights the increased risk of serious disorders with experimental therapies compared to placebos.

Figure 7 is a forest plot that evaluates the impact of PARPi on adverse effects across 17 trials. The majority of studies found hazard ratios (HRs) greater than one, indicating that PARPi-treated groups are more likely to experience negative outcomes. The pooled hazard ratio is 1.88, showing an 88% greater risk of adverse events with PARPi. The overall pooled HR is 1.88 (95% confidence interval: 1.38 to 2.55), indicating an 88% higher incidence of adverse events among PARPi-treated subjects.

Discussion

Our meta-analysis found that PARP inhibitor therapies significantly enhanced PFS compared to placebo in patients with recurrent and newly diagnosed OC. PARPi maintenance therapy improved PFS, it was also associated with an increase in grade 3 and 4 adverse events. Although PARP inhibitors' safety profile was not considerably worse than that of chemotherapy, their OS advantage in this treatment context decreased. The majority of AEs were controllable with dose changes, allowing treatment to continue with only a few patients having to quit the medication. Patients getting PARPi maintenance medication, independent of BRCA mutation status, had considerably slower disease progression than those receiving placebos.

Our meta-analysis also found that when PARPi therapy administered as maintenance treatment, could provide momentous PFS benefits over to a placebo in women with recurring conditions [38-44] and newly diagnosed advanced OC [28-32, 34-37]. Women with OC in the experimental groups reports an average PFS of 18.44 months, while those in the placebo group had an average of 12.66. This study implies that PARPi can slow disease development and lower risk of death in OC patients receiving the medication. Furthermore, our review demonstrates the distinct impact of PARPi on PFS in relapsed versus newly diagnosed OC patients. While the advantages in relapsed instances are less consistent, newly diagnosed patients exhibit strong and significant improvements in PFS with PARPi therapy.

Furthermore, our meta-analysis shows that the efficiency of various PARPi therapies in ovarian cancer differs significantly between subgroups. Using combination of Cediranib plus Olaparib shown significant effect in increasing PFS, with a median of 16.5 months associated to 8.2 months for olaparib solely [39-42]. In contrast, Niraparib's results are highly variable, with a total HR of 1.86, indicating no significant overall benefit over placebo [28, 41, 37, 40]. Nonetheless, Mirza et al. [41] study demonstrates the potent effect of niraparib on slowing disease progression in a specific patient population [41].

The combination of olaparib and bevacizumab shows mixed results, with a combined HR of 0.47 and high heterogeneity, indicating inconsistent efficacy [31, 33, 35]. In HRD-positive patients, combination therapy achieved a PFS of 31.3 months versus 15.9 months for control plus bevacizumab (HR, 0.33; 95% CI, 0.25–0.45), suggesting improved PFS with anti-angiogenic drugs and PARP inhibitors [39]. Coleman et al. [44] demonstrated the efficacy of PARPi combined with chemotherapy, showing significant benefits (HR, 0.36) over controls [30]. Friedlander et al. [39] confirmed olaparib's benefits as maintenance therapy in BRCA-mutated, platinum-sensitive relapsed OC, extending median PFS [39]. González et al. [28] reported improved PFS in HRD-positive patients treated with niraparib (21.9 months vs. 10.4 months for control) [28]. Coleman et al. [44] also highlighted veliparib's efficacy in improving PFS across BRCA-mutated, HRD, and intention-to-treat groups, with median PFS of 16.5 months versus 8.2 months for olaparib alone (HR, 0.50; 95% CI, 0.30–0.83) [44].

The current meta-analysis of ten studies demonstrates no statistically significant improvement in OS between experimental and placebo groups (HR, 1.06; 95% CI, 0.99–1.13; $p = 0.08$), with substantial heterogeneity ($I^2 = 91\%$). Consistent findings were observed by Coleman et al. (HR, 1.02) [30], Liu et al. (HR, 1.06) [38], and Moore et al. (HR, 1.00) [32]. DiSilvestro et al. [34] reported an HR of 1.19 (95% CI, 1.06–1.34; weight, 12.0%) [34], while Ning Li et al. [37] found an HR of 0.70 (95% CI, 0.62–0.79; weight, 11.8%) [37], indicating improved OS. Conversely, Friedlander et al. (HR, 2.12) [28], Martin et al. (HR, 1.72) [28], and Mirza et al. (HR, 1.90) [41] observed negative effects.

Evaluating adverse effects in clinical trials is vital for assessing treatment safety. Moore et al. [32] reported most AEs as grade 1–2, with serious AEs in 21% of olaparib users versus 12% in controls [32]. Anemia affected 7% in the olaparib group, with no cases in the placebo group. No treatment-related mortality occurred, and dose interruption or reduction was preferred over discontinuation. AML and other rare events, including pneumonitis and new malignancies, were observed in 1%. Pujade-Lauraine et al. [43] noted AEs in 86% of BRCA-mutated and 92% of non-BRCA-mutated cohorts, with grade ≥3 AEs in 15% and 21%, respectively. Furthermore, Schouten et al. [33] reported frequent treatment-emergent adverse events requiring dose adjustments, consistent with Pujade-Lauraine et al. [43] and Ray-Coquard et al. [31].

Liu et al. [38] demonstrated higher adverse events (AEs) with cediranib-olaparib combination therapy versus olaparib alone, including fatigue (68% vs. 45%), diarrhea (41% vs. 8%), and hypertension (32% vs. 8%). González-Martín et al. [28] observed thrombocytopenia, anemia, and neutropenia as prevalent AEs of niraparib maintenance therapy in PRIMA RCT, consistent with ARIEL3 results, where rucaparib induced nausea, fatigue, and anemia (22%) [44]. In PAOLA-1, olaparib-bevacizumab led to anemia (41% vs. 17%), neutropenia (18%), and thrombocytopenia (8%) [35]. SOLO1 and SOLO2 trials reported anemia (39%), fatigue (63%), and nausea

(77%). Ning Li et al. [37] noted similar AEs, including thrombocytopenia, anemia (25%), and neutropenia (20%) [34, 37]. Daily blood and liver function monitoring is recommended. The above results are similar to those of previous meta-analysis studies [45, 46].

This meta-analysis highlights that combination therapy significantly improves PFS and OS but are associated with adverse effects like hematologic toxicity and hypertension. Effective interventions, including dose adjustments and supportive care, can mitigate side effects. Further clinical trials are needed to optimize the therapeutic index of OC treatment.

One of our study's limitations was the clinical diversity between the selected RCTs, which included variances in PARP inhibitors utilized, prior therapies, and surgical results. To counteract this, we created consistent subgroups based on treatment settings and used a random effects model. Furthermore, our research relied on published data rather than individual patient data, limiting our capacity to stratify results by specific characteristics.

Despite these limitations, our study had several strengths. We only included phase II and phase III RCTs, allowing us to do relevant statistical analysis in key clinical subgroups. We also included data from the last decade to ensure the inclusion of recent investigations. Finally, the overall risk of bias was rather low, which increased the reliability of our findings.

Clinical Implications: Our meta-analysis demonstrates the considerable advantages of PARP inhibitors (PARPi) in lengthening progression-free survival (PFS) in ovarian cancer patients, particularly in newly diagnosed cases. Despite the lack of a significant OS benefit, PARPi treatment remains an important tool for slowing disease progression. The research emphasizes the need of controlling adverse events, particularly hematologic toxicities, by adjusting doses to ensure treatment adherence. Combination therapy, such as Cediranib-Olaparib and Olaparib-Bevacizumab, show potential but require close monitoring. Further trials should enhance treatment procedures to maximize efficacy while avoiding toxicity, assuring the best possible results for ovarian cancer patients.

Author Contribution Statement

Data Collection: S.D., and R.C., Conceptualization: R.C. and S.D., Funding Acquisition: G.M, and S.D., Project Administration: S.D. and G.M., Experiment Conduction: G.M. and S.D., Result Analysis: S.D, and G.M., Original Draft Preparation: R.C. and S.D., Writing-Review and Editing: R.C. and S.D., All authors reviewed the manuscript. Additional information The authors have no conflicts of interest to declare.

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Approval

This review is approved by Institutional research review committee of Symbiosis College of Nursing, Symbiosis International Deemed University, Pune, Maharashtra, India.

Conflict of Interest

Nil.

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