EFFECTIVENESS OF VARIOUS MAINTENANCE THERAPY IN OVARIAN CANCER: A SCOPING REVIEW

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ABSTRACT

Ovarian cancer is highly lethal with a lifetime risk of up to 1.1%. Despite advances in treatment like cytoreductive surgery and chemotherapy, high recurrence rates challenge disease management. Maintenance therapy is crucial for extending progression-free survival (PFS) and delaying recurrence. This study aims to evaluate the effectiveness of various maintenance therapies published in the last 10 years, focusing on PARP inhibitors, angiogenesis inhibitors, monoclonal antibodies, and combination therapies. A scoping review was conducted following the PRISMA ScR Protocol. The search was conducted in PubMed, ScienceDirect, and Springer databases. After removing duplicates and applying inclusion and exclusion criteria, 208 articles were screened and 22 articles were selected for final review and critically appraised using the Cochrane RoB 2 tool. This review found that maintenance treatment with PARP inhibitors (e.g., olaparib, niraparib, rucaparib) showed significant improvements in PFS, especially in patients with BRCA mutations and homologous recombination deficiency (HRD). Combination therapies, such as olaparib with bevacizumab, also enhanced PFS. Angiogenesis inhibitors like pazopanib showed variable effectiveness, while monoclonal antibodies like gatipotuzumab had limited success. The combination of pegylated liposomal doxorubicin (PLD) with carboplatin showed potential in improving PFS. These findings highlight the effectiveness of personalized maintenance therapies in extending PFS in ovarian cancer patients.

Keywords: Ovarian Cancer, Maintenance Therapy

INTRODUCTION

One of the illnesses that kills women the most is ovarian cancer. By the age of 95, a woman may have a 1.1% lifetime chance of ovarian cancer (Burke et al., 2023). In the United States, ovarian cancer claimed the lives of over 12,000 people in 2022, with over 19,000 new cases reported to the medical community. The age ranges for each subtype of ovarian cancer affect the incidence, with high-grade serous ovarian cancer peaking in women 60–65, low-grade endometrioid ovarian cancer peaking in women 45–50, and clear cell ovarian cancer most common in women 55–60 (Phung et al., 2023). The stage at which ovarian cancer is diagnosed also affects survival chances and recurrence rates; more than half of these individuals had metastases at

diagnosis. For ovarian cancer in its early stages, the 5-year survival rate is 93.1%; for late stages, it is 30.8% (Burke et al., 2023)

With a 30% to 40% 5-year survival rate, epithelial ovarian carcinoma (EOC) is the most deadly gynecological malignancy in the world. Because of its asymptomatic nature, it is frequently diagnosed at an advanced stage, requiring intensive therapy (Allemani et al., 2015). The main treatment for EOC is cytoreductive surgery (CRS) and systemic chemotherapy with carboplatin and paclitaxel. Neoadjuvant chemotherapy and interval CRS have emerged as a crucial strategy for the management of advanced-stage EOCs in recent times (Kehoe et al., 2015). While 90% of stage IV instances of ovarian cancer have recurrence, the probability of recurrence for stage I cases is less than 10% (Burke et al., 2023). In order to prevent the course of the illness or its return following first-line treatment, regardless of residual disease, there is a growing emphasis on molecularly targeted medicines and maintenance treatments due to the high recurrence rates (Nag et al., 2022).

LITERATURE REVIEW

Advanced ovarian cancer is usually treated with platinum-based chemotherapy, such as paclitaxel and carboplatin, and cytoreductive surgery. Approximately 70% of patients experience a recurrence within three years after starting therapy, despite the fact that these medicines are effective in shrinking tumors (du Bois et al., 2014).

To manage the high recurrence rate, maintenance therapy is needed as an additional strategy. Various approaches have been tested, including PARP inhibitors like olaparib, which has shown an increased PFS with a median of 19.1 months compared to placebo (Pujade-Lauraine et al., 2017), and niraparib, which reported an increased median PFS with a HR of 0.66 (González-Martín et al., 2023). Additionally, rucaparib and veliparib also demonstrated benefits in improving PFS with HRs of 0.36 and 0.68 respectively (Coleman et al., 2017, 2019). Fuzuloparib showed an improvement in median PFS compared to placebo with a HR of 0.25 (Li et al., 2022), while the combination of PLD and carboplatin increased median PFS with a HR of 0.40 (Lai et al., 2020).

Currently, research in the field of maintenance therapy for ovarian cancer has undergone significant advancements. As mentioned above, right now various new therapeutic agents, including PARP inhibitors, angiogenesis inhibitors, monoclonal antibodies, and other drugs, have been the subject of clinical trials to be evaluated as potential maintenance therapy options. However, to date, there has not been a comprehensive review of the various agents used for maintenance therapy in ovarian cancer. Therefore, the aim of this study is to identify all maintenance therapy agents published in the last 10 years for ovarian cancer management, as a basis for further systematic review. The research questions posed are: What maintenance therapy agents have been investigated for ovarian cancer? What are the effects of these maintenance therapies on PFS?

RESEARCH METHODOLOGY

Following the framework outlined by Tricco et al. (2018), this thorough review employed a scoping review methodology, incorporating references from multiple articles. An evidence-based approach guided the review process to ensure a

comprehensive examination of the relevant literature, which consists of six stages: first, identifying the research question; second, searching for relevant articles; third, selecting the articles; fourth, organizing the data; fifth, compiling and summarizing the findings; and sixth, presenting the results (Tricco et al., 2018).

To identify the relevant articles, an efficient search method is required. The search method used in this review is PEO, which stands for Population, Exposure (intervention), and Outcome. The population in this review is women with ovarian cancer, the intervention investigated is maintenance therapy, and the expected outcome is the PFS rate of therapy.

The inclusion and exclusion criteria used to determine the eligibility of articles are described in Table 1. In this study, the authors used several journal data-base, including PubMed, ScienceDirect, and Springer as search engines to find studies on the impact of maintenance therapy in women with ovarian cancer. To focus the search, the Boolean operator is used with the keywords "Maintenance Therapy" AND ("ovarian cancer" or "ovarian carcinoma" or "epithelial ovarian cancer").

Following a search of previous articles in the Zotero bibliographic software and removal of duplicates, two reviewers independently evaluated the titles and abstracts of the articles. then reviewers conducted a more detailed review of the selected abstracts. If there were any uncertainties about including an article in the next selection phase, the authors reviewed the entire paper. If needed, they resolved issues through discussions with another evaluator.

Table 1. Inclusion and Exclusion Criteria

Inclusion	Exclusion
1. Studies with a population of woman diagnosed with ovarian cancer. 2. Studies investigating maintenance therapy. 3. Studies with control groups. 4. Studies in the last 10 years	1. Literature review. 2. Studies without control groups 3. Studies conducted on animals. 4. Studies without a control group.

RESULT RESEARCH

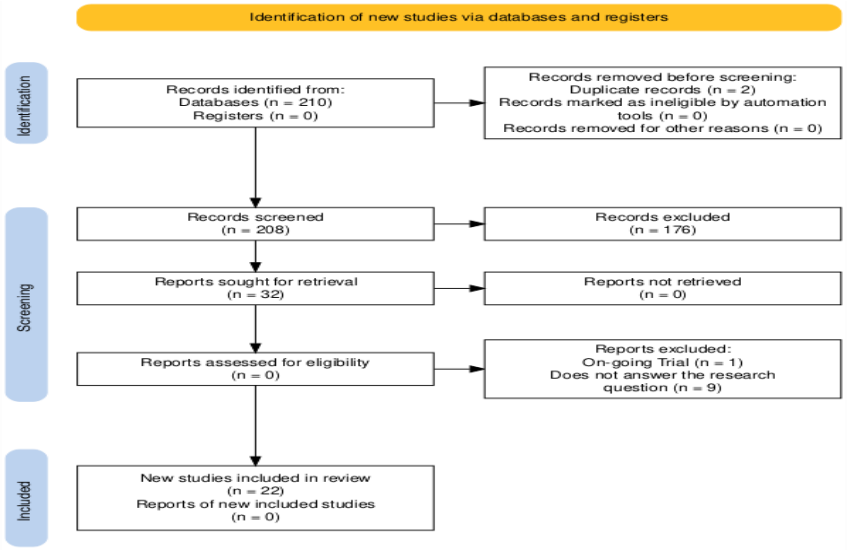

Figure 1. PRISMA Flowchart

This scoping review identified 70 articles from the PubMed database, 92 articles from ScienceDirect, and 48 articles from Springer. All searches were conducted on July 18, 2024. Next, all articles obtained, with the total number of articles, were imported into Zotero software, and 2 duplicate articles were found. After removing the duplicates, the article review began by selecting titles and reading abstracts to find articles relevant to the study and in line with the inclusion and exclusion criteria. "We found 176 studies that did not meet the inclusion criteria or had at least one exclusion criterion. After filtering based on title and abstract, 32 articles were obtained and were further screened for completeness. Of 32 articles found, 32 had full texts available And 10 articles were not included because they were not relevant to the research question. Finally, 22 articles were included in this study.

Critical Appraisal

Critical appraisal involves a meticulous, systematic, and precise evaluation of articles. The authors employed the Cochrane RoB 2 critical appraisal tool to assess each article. Researchers reviewed the articles independently to decide their suitability as references for further research. This detailed evaluation process resulted in the final scores, which are presented in Table 2.

Table 2. Chart of Data Studied

No	Author, Year	Country	Aim	Study Population	Measurement	Rob 2
1	(Li et al., 2022)	36 sites in China	evaluating the safety and efficacy of fuzuloparib in comparison to a placebo as an ovarian cancer maintenance medication.	The study has a total sample size of 252, divided into 167 in the treatment group and 85 in the control group.	The results of this study show that fuzuloparib can improve the PFS in ovarian cancer, as demonstrated by a HR of 0.25. In the subgroup analysis, the study also showed consistent results, with a HR of 0.14 in patients with germline BRCA1 or BRCA2 mutations and a HR of 0.46 in patients without mutations.	Low Risk of Bias
2	(du Bois et al., 2014)	17 nations in Australia, Asia, Europe, and North America	evaluating pazopanib's safety and efficacy as an ovarian cancer maintenance treatment.	A total of 940 patients were included, with 472 in the treatment group (receiving pazopanib) and 468 in the control group (receiving placebo).	The results of this study indicate that pazopanib can improve PFS with a HR of 0.77.	Some Concern

3	(Lai et al., 2020)	Multicenter	evaluating the efficacy of carboplatin plus PLD as maintenance treatment for ovarian cancer.	Pada penelitian ini terdapat 2 kelompok penelitian yaitu kelompok treatment sebesar 45 pasien (penerima PLD + carbloplatin) dan kelompok control sebesar 21 pasien (Observasi)	The results show that the group receiving PLD + carboplatin had better PFS compared to the control group, with a HR of 0.40.	Some Concern
4	(Lederma nn et al., 2022)	Multicenter	evaluating gatipotuzumab's safety and efficacy as a maintenance treatment for TA-MIC positive recurrent ovarian cancer.	There were 216 patients in all; 65 received a placebo and 151 received gatipotuzumab.	The results indicate that patients receiving gatipotuzumab did not show a significant difference compared to those receiving a placebo, as evidenced by a HR of 0.96 and the same median PFS of 3.5 months (3.3 – 4.6 months) in the gatipotuzumab group and 3.5 months (3.0 – 4.7 months) in the placebo group.	Low Risk of Bias

5	(X. H. Wu et al., 2021)	30 centers in China	evaluating niraparib's safety and efficacy as a maintenance treatment for platinum-sensitive ovarian cancer that has returned.	There were a total of 265 samples, divided into two groups: 177 patients in the treatment group and 88 patients in the control group.	The results show that niraparib significantly improved median PFS compared to placebo, with a HR of 0.30.	Low Risk of Bias
6	(del Campo et al., 2019)	Multicenter	assessing niraparib's efficacy and safety in the treatment of platinum-sensitive recurrent ovarian cancer.	There are 553 patients in all; 367 of them are on niraparib while 179 are on placebo	This study consists of two cohort studies. In the cohort with a population of patients with BRCA mutations, niraparib demonstrated a beneficial effect on median PFS with a HR of 0.24. Similarly, in the cohort with a population of patients without BRCA mutations, a positive effect was also observed, with a HR of 0.58.	Some Concern
7	(Mirza et al., 2016)	107 sites in the country that were enlisted	evaluating niraparib's safety and efficacy as a maintenance treatment	A total of 553 patients were included, consisting of 203 patients	This study consists of two cohort studies. In the study with a	Low Risk of Bias

		in ENGOT, including the US, Canada, and Hungary	for platinum-sensitive ovarian cancer that has returned.	from the gBRCA cohort and 350 patients from the non-gBRCA cohort.	population of patients with BRCA mutations, niraparib showed better results compared to the cohort with a population of patients without BRCA mutations, with a HR of 0.27 versus 0.45. In the non-BRCA cohort study, further sub-analysis was conducted, and it was found that in patients with HRD, niraparib was effective in improving PFS, with a HR of 0.38.	
8	(L. Wu et al., 2021)	China	evaluating Olaparib's efficacy and safety in the Chinese population as a maintenance treatment for ovarian cancer with a platinum-sensitive BRCA mutation.	There were total of 64 patients, with 44 patient in treatment group (receiving Olaparib) and 20 patients in control group receiving placebo.	This study demonstrated that Olaparib can reduce the risk of disease progression or death by 54%, with a HR of 0.46. However, the median PFS in the Olaparib	Low Risk of Bias

					group has not yet been reached and requires further observation.	
9	(Ray-Coquard et al., 2019)	11 country	evaluating the safety and efficacy of bevacizumab with olaparib as a maintenance treatment for platinum-sensitive ovarian cancer.	In total, 806 individuals participated in the research; 537 of them received olaparib with bevacizumab, while 269 patients received a placebo plus bevacizumab.	This study demonstrated that the combination of Olaparib and bevacizumab has a better effect on PFS, with a HR of 0.59. Even better results were observed in patients with HRD, indicated by a HR of 0.33. A deeper analysis of patients with HRD but without BRCA mutations revealed a HR of 0.43.	Low Risk of Bias
10	(Fujiwara et al., 2021)	7 centers in Japan, sub-group of PAOLA-1/ENGOT-ov25	evaluating the safety and efficacy of bevacizumab with olaparib as a maintenance treatment for advanced ovarian cancer in the	There were twenty-four patients in all, fifteen of whom received bevacizumab and olaparib, and nine of whom received	The results of the study indicate that Olaparib and bevacizumab are effective in improving PFS, as shown by a	Low Risk of Bias

			Japanese population.	bevacizumab and a placebo.	HR of 0.34. In the analysis of the population with HRD, bevacizumab was also effective, with a HR of 0.57.	
11	(Kim et al., 2018)	East Asia	evaluating pazopanib's safety and efficacy in the East Asian population as a maintenance treatment for ovarian cancer that has not progressed following first-line therapy.	354 individuals total were included in the trial; 145 were from the East Asia study and 209 from AGO-OVAR16. A 1:1 ratio of patients underwent randomization.	This study states that pazopanib does not have a beneficial effect and may even have a detrimental effect on the East Asian population, as reported in the AGO-OVAR16 study. The current study replicates the AGO-OVAR16 research with an East Asian population and the result is pazopanib, when used as maintenance therapy, showed a HR of 1.114.	Low Risk of Bias
12	(González-Martín et al., 2023)	Multicentre	assessing the overall niraparib survival rate	There were 733 individuals in all, of	This study shows that niraparib can reduce	Low Risk of Bias

			in patients with advanced, platinum-sensitive ovarian cancer.	whom 487 received niraparib and 246 received a placebo.	PFS with a HR of 0.66. Niraparib is also more effective in patients with HRD, as indicated by a HR of 0.52.	
13	(Coleman et al., 2017)	Multicenter across 11 Countries with 87 Hospitals and Cancer Centers.	evaluating rucaparib's efficacy in treating platinum-sensitive ovarian cancer as a maintenance treatment.	Out of 564 patients, 375 were given rucaparib, and 189 were given a placebo.	The results show that patients receiving rucaparib have higher PFS with a HR of 0.36. Rucaparib also has a better effect on PFS in patients with BRCA mutations and HRD, as demonstrated by HR of 0.23 and 0.32, respectively.	Low Risk of Bias
14	(X. Wu et al., 2024)	41 Centers in China	evaluating senaparib's safety and efficacy as a maintenance treatment for advanced ovarian cancer after first-line chemotherapy.	There were total of 404 patients, with 271 patient receiving senaparib and 133 patient receiving placebo	Senaparib has been shown to improve PFS with a HR of 0.43. However, overall survival (OS) data in this study is not yet mature for presentation and requires further observation.	Low Risk of Bias

15	(Li et al., 2023)	China	evaluating niraparib at a modified dosage for use as a maintenance treatment for a sizable patient group with advanced ovarian cancer that is sensitive to platinum.	There were total of 384 patients randomized into 225 patients receiving niraparib and 129 patients receiving placebo	Niraparib improves PFS with a HR of 0.45. The effect of increasing PFS with niraparib is better in patients with germline BRCA mutations compared to those without germline BRCA mutations, with HRs of 0.40 and 0.48, respectively.	Low Risk of Bias
16	(Coleman et al., 2019)	Multicentre at 202 sites in 10 Country	evaluating veliparib's efficacy as an advanced serous ovarian cancer treatment for both induction and maintenance.	In this study, there was a total sample size of 1,140 patients, divided into three groups: the treatment group receiving chemotherapy with veliparib and veliparib as maintenance treatment, consisting of 383 patients; the treatment group	This study shows that veliparib can improve PFS in populations of patients with BRCA mutations or HRD, proofen by HR of 0.44 and 0.57, respectively.	Low Risk of Bias

				receiving chemotherapy without veliparib and veliparib as maintenance treatment; and the control group of 375 patients receiving chemotherapy with a placebo and placebo as maintenance treatment.		
17	(Mizuno et al., 2023)	24 institution in Japan	evaluating the safety and efficacy of veliparib in combination with paclitaxel and carboplatin as a maintenance treatment for high-grade serous ovarian cancer.	In this study, the sample size was 78 patients, divided into three groups: 25 patients in the treatment group receiving chemotherapy with added veliparib and veliparib as maintenance therapy; 30 patients in the treatment group receiving chemotherapy with added veliparib and placebo	This study demonstrates that veliparib can improve PFS in ovarian cancer with a HR of 0.46.	Low Risk of Bias

				as maintenance treatment; and 23 patients in the control group receiving chemotherapy with placebo and placebo as maintenance treatment.		
18	(Pujade-Lauraine et al., 2017)	123 sites in 16 country	evaluating the efficacy of olaparib tablets as a maintenance treatment for ovarian cancer that has returned after platinum-sensitive treatment and has BRCA1 or BRCA2 mutations.	Out of total 295 sample involved in the research, They were divided into two groups: 196 patients in the treatment group (receiving Olaparib) and 99 patients in the control group (receiving placebo).	Olaparib shows an improvement in PFS in ovarian cancer with a HR of 0.30.	Low Risk of Bias
19	(Poveda et al., 2021)	123 sites in 16 country	Assessing the efficacy of Olaparib tablets in the treatment of platinum-sensitive recurrent ovarian cancer in patients who have mutations in either BRCA1 or BRCA2.	There were 295 patients in all, of whom 196 received olaparib and 99 received a placebo.	With longer data follow-up, Olaparib continues to show consistent improvement on making longer PFS in ovarian cancer, with a HR of 0.74.	Low Risk of Bias

20	(Moore et al., 2018)	118 pusat di 15 negara	assessing Olaparib's effectiveness as a maintenance treatment for ovarian cancer with BRCA mutations that is platinum-sensitive.	In this study, the total sample size was 391, with 260 patients in the treatment group (receiving Olaparib) and 131 patients in the control group (receiving placebo).	This study states that Olaparib can reduce the risk of disease progression and death by 70%, as demonstrated by the analysis showing a HR of 0.30 for PFS.	Low Risk of Bias
21	(Banerjee et al., 2021)	118 pusat di 15 negara	assessing Olaparib's effectiveness as a maintenance treatment for ovarian cancer with BRCA mutations that is platinum-sensitive.	There were total of 391 patients with 260 patiens receiving olaparib and 131 patiens receiving placebo	With longer follow-up data, Olaparib continues to show consistent results with previous studies. Olaparib can improve PFS, as evidenced by a HR of 0.33.	Low Risk of Bias
22	(DiSilvestro et al., 2023)	118 pusat di 15 negara	assessing Olaparib's effectiveness as a maintenance treatment for ovarian cancer with BRCA mutations that is platinum-sensitive.	There were a total of 391 patients with 260 patiens receiving olaparib and 131 patiens receiving a placebo	After the data matured, the effect of Olaparib on OS was analyzed and showed positive results. Olaparib can improve OS, as demonstrated by a HR of 0.55.	Low Risk of Bias

DISCUSION

For each publication included in this review, details such as the authors' names, publication year, country, objectives, methodology, population, and findings were recorded, as outlined in Table 2. The review focused on identifying key themes, including the characteristics of women receiving maintenance therapy and the effects of such therapy. The findings from these articles are summarized in the chart below, with articles categorized by drug class and type. Eighteen articles examined PARP inhibitors as maintenance therapy, with 8 focused on olaparib, 5 on niraparib, 1 on rucaparib, 2 on veliparib, 1 on fuzuloparib, and 1 on senaparib. Additionally, 2 articles investigated angiogenesis inhibitors, specifically pazopanib; 1 article explored monoclonal antibodies, specifically gatipotuzumab; and 1 article studied PLD. This review encompasses research from various institutions and countries.

Poly (ADP-ribose) Polymerase (PARP) Inhibitors

In DNA repair, there are two crucial factors: PARP enzymes and BRCA1/2 genes. When PARP is inhibited in ovarian cancer patients with BRCA1/2 mutations, the tumor cells lose these two essential factors for DNA repair, leading to increased DNA damage and apoptosis. Currently, several PARP inhibitors have been approved for use by the FDA (Food Drug Administration) for use as monotherapy in the treatment of ovarian cancer that recurs: rucaparib (Rubraca, Clovis Oncology), olaparib (Lynparza, AstraZeneca), and niraparib (Zejula, Tesaro) (Ringley et al., 2018). There are also several new PARP inhibitors such as veliparib, fuzuloparib, and senaparib.

Olaparib

The results of the SOLO2/ENGOT Ov-21 study indicate that the administration of olaparib can increase the median PFS and OS, as evidenced by a HR of 0.30 for median PFS and 0.74 for median OS.(Poveda et al., 2021; Pujade-Lauraine et al., 2017).

There are three articles analyzing the SOLO1/GOG 3004 study over a 7-year period. This research demonstrates that olaparib can significantly improve median PFS and OS, as indicated by a hazard ratio (HR) of 0.33 for median PFS and 0.55 for OS (Banerjee et al., 2021; DiSilvestro et al., 2023; Moore et al., 2018). There is also a research that replicated the SOLO1 design in a Chinese population provided additional support for these findings, indicating that olaparib lowered progression or mortality by 54% when compared to a placebo, with a HR of 0.46 (L. Wu et al., 2021).

Bevacizumab and Olaparib Combination

When bevacizumab is combined with olaparib, it has a greater effect on improving PFS compared to when bevacizumab is used as a single maintenance therapy in ovarian cancer. This is demonstrated in the PAOLA-1 trial, which showed that the treatment group receiving the combination therapy had a higher median PFS compared to the control group (receiving bevacizumab + placebo), with 22.1 months versus 16.6 months and a HR of 0.59. This effect is also more pronounced in populations with BRCA mutations and HRD. The HR for patients with BRCA mutations was 0.33, and for patients with HRD mutations but without BRCA mutations, the HR was 0.43. (Ray-Coquard et al., 2019).

This drug combination has also been proven effective in the Japanese population. A subgroup analysis conducted on Japanese patients showed that this combination could increase the median PFS in the treatment group to 27.4 months, compared to 19.4 months in the control group, with a hazard ratio (HR) of 0.34. In Japanese patients with HRD, this combination had an HR of 0.57.(Fujiwara et al., 2021).

Niraparib

Niraparib showed better median PFS compared to placebo across all groups (13.8 months versus 8.2 months) in a 3.5-year follow-up of the PRIMA/ENGOT-OV26/GOG-3012 trial, with a HR of 0.66. In the HRD and HRP groups, the niraparib group also demonstrated improved PFS: 24.5 months compared to 11.2 months with a HR of 0.52 in the HRD group, and 8.4 months compared to 5.4 months with a HR of 0.65 in the HRP group (González-Martín et al., 2023).

Niraparib increased median PFS in patients with gBRCA mutations, non-gBRCA patients with HRD, and patients without gBRCA mutations, according to the ENGOT-OV16/NOVA study. The HRs for the gBRCA group was 0.27, the overall non-gBRCA group was 0.45, and the non-gBRCA with HRD group was 0.38 (Mirza et al., 2016). Niraparib also improved the median PFS for both partial and full responders among patients with gBRCA mutations and those without, according to further data from this trial. Following platinum-based chemotherapy, the HR was 0.24 for gBRCA patients who had a partial response (PR) and 0.30 for those who had a complete response (CR). The HR for patients without a gBRCA mutation was 0.35 for PR and 0.58 for CR (del Campo et al., 2019).

According to the NOVA Trial, thrombocytopenia forced 73% of patients with recurrent ovarian cancer to lower their niraparib dosage from 300 mg/day within the first three months of treatment. According to the RADAR study, individuals who were under 77 kg in weight or had platelets < 150 x 10^3/ml may receive a dosage of 207 mg/day without experiencing any side effects (Berek et al., 2018). As a result, the NORA Trial modified its protocol to include an individualized starting dosage (ISD). This led to a longer median PFS of 18.3 months for the ISD niraparib group as opposed to 5.4 months for the placebo group, with a HR of 0.32 (X. H. Wu et al., 2021)

Additionally, the PRIME research demonstrated that niraparib, with a HR of 0.45, increased PFS in the ISD group as compared to a placebo (24.8 months versus 8.3 months). With a PFS HR of 0.40 in the BRCA group and 0.48 in patients without BRCA mutations, niraparib proved to be advantageous for both BRCA-positive and BRCA-negative groups (Li et al., 2023).

Rucaparib

With a HR of 0.36, the ARIEL3 Trial showed that the rucaparib group's median PFS was longer than that of the placebo group (10.8 months versus 5.4 months). Subsequent investigation revealed that, with a HR of 0.23, individuals with BRCA mutations in the rucaparib group had a substantially longer median PFS (16.6 months versus 5.4 months) than those in the placebo group. Furthermore, the rucaparib group showed better PFS (13.6 months versus 5.4 months) with a HR of 0.32 in patients with HRD when compared to the placebo group (Coleman et al., 2017).

Veliparib

Patients with advanced serous ovarian cancer receiving veliparib as maintenance treatment exhibited a longer median PFS (23.5 months versus 17.3 months) than the control group (HR : 0.68), according to VELIA/GOG-3005 research. Further examination of individuals with HRD showed that the veliparib-treated group had a longer PFS (31.9 months versus 20.5 months) with a HR of 0.57 compared to the control group. The veliparib group showed a higher median PFS (34.7 months versus 22 months) among individuals with BRCA mutations than the control group (HR of 0.44) (Coleman et al., 2019). In a related study assessing the effectiveness of veliparib in a Japanese population, the intention-to-treat group receiving veliparib had a higher median PFS (27.4 months versus 19.1 months) than the control group, with a HR of 0.46; however, the p-value of 0.1 meant that the results were not statistically significant (Mizuno et al., 2023).

Fuzuloparib

According to Li et al. (2022), fuzuloparib therapy resulted in a substantial improvement in median PFS with a HR of 0.25 when compared to the placebo group (12.9 months versus 5.5 months). Fuzuloparib consistently increased PFS in individuals with germline BRCA 1/2 mutations (HR 0.14) as well as those without these mutations (HR 0.46), according to subgroup analysis (Li et al., 2022).

Senaparib

Senaparib's efficacy and safety as a maintenance treatment for advanced ovarian cancer were assessed in the FLAMES trial. The results showed that the median PFS in the senaparib group was not yet reached, while the placebo group's PFS was 13.6 months with a HR of 0.43 (X. Wu et al., 2024).

Angiogenesis Inhibitor (Pazopanib)

According to a study by du Bois et al. (2014), pazopanib improved median PFS in maintenance treatment (17.9 vs. 12.3 months) when administered as monotherapy, with a HR of 0.77 when compared to placebo (du Bois et al., 2014). In contrast, pazopanib did not increase median PFS in a different research that focused on an East Asian population; in fact, PFS in the pazopanib group was worse than in the placebo group (17.9 vs. 21.5 months) with a HR of 1.114 (Kim et al., 2018).

Monoclonal Antibodies

According to research by Ledermann et al. (2022), patients with TA-MUC1-positive primary high-grade serous peritoneal cancer, fallopian tube, or recurrent ovarian cancer did not see an improvement in their median PFS when given gatipotuzumab compared to placebo (both 3.5 months), with a HR of 0.96 (Ledermann et al., 2022).

Pegylated Liposomal Doxorubicin and Carboplatin

Pegylated liposomal doxorubicin (PLD) and carboplatin were used as maintenance treatment in a research by Lai et al. (2020); carboplatin was chosen based on the patients' positive response to platinum-based chemotherapy. The results showed that, with a HR of 0.40, the combination of PLD plus carboplatin considerably increased the median PFS in comparison to placebo (55.5 vs. 9.2 months) (Lai et al., 2020).

CONCLUSION

This study highlights the effectiveness of various ovarian cancer treatments, particularly those involving PARP inhibitors, angiogenesis inhibitors, monoclonal antibodies, and combination therapies. When compared to placebo, PARP inhibitors such as niraparib, olaparib, veliparib, rucaparib, senaparib, and fuzuloparib have continuously demonstrated substantial increases in PFS, particularly in patients with HRD and BRCA mutations. The combination of olaparib and bevacizumab further improves PFS for specific patient groups, underscoring the benefits of combined treatment approaches.

Angiogenesis inhibitors, such as pazopanib, hold promise in maintenance therapy, though their effectiveness can vary across different patient populations. Monoclonal antibodies like gatipotuzumab have shown limited success in enhancing PFS, indicating the need for more research in this field. Furthermore, it has been demonstrated that adding PLD to carboplatin as a maintenance therapy can improve PFS, indicating its usefulness in treatment regimens for patients who perform well with platinum-based chemotherapy.

In summary, these results underscore the need for personalized treatment approaches that consider the molecular and genetic characteristics of ovarian cancer to achieve the best therapeutic outcomes.

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Conflict of Interest

There are no competing interests among the authors.

Author Contribution

The planning, article search, drafting, and manuscript approval for publishing were all completed by the authors.

REFERENCE

Allemani, C., Weir, H. K., Carreira, H., Harewood, R., Spika, D., Wang, X.-S., Bannon, F., Ahn, J. V, Johnson, C. J., Bonaventure, A., Marcos-Gragera, R., Stiller, C., Azevedo e Silva, G., Chen, W.-Q., Ogunbiyi, O. J., Rachet, B., Soeberg, M. J., You, H., Matsuda, T., … Coleman, M. P. (2015). Global surveillance of cancer survival 1995–2009: analysis of individual data for 25 676 887 patients from 279 population-based registries in 67 countries (CONCORD-2). *The Lancet*, *385*(9972), 977–1010. https://doi.org/10.1016/S0140-6736(14)62038-9

Banerjee, S., Moore, K. N., Colombo, N., Scambia, G., Kim, B.-G., Oaknin, A., Friedlander, M., Lisyanskaya, A., Floquet, A., Leary, A., Sonke, G. S., Gourley, C., Oza, A., González-Martín, A., Aghajanian, C., Bradley, W. H., Holmes, E., Lowe, E. S., & DiSilvestro, P. (2021). Maintenance olaparib for patients with newly diagnosed advanced ovarian cancer and a BRCA mutation (SOLO1/GOG 3004): 5-year follow-up of a randomised, double-blind, placebo-controlled, phase 3 trial. *The Lancet Oncology*, *22*(12), 1721–1731. https://doi.org/10.1016/S1470-2045(21)00531-3

Burke, W., Barkley, J., Barrows, E., Brooks, R., Gecsi, K., Huber-

Keener, K., Jeudy, M., Mei, S., O'Hara, J. S., & Chelmow, D. (2023). Executive Summary of the Ovarian Cancer Evidence Review Conference. *Obstetrics & Gynecology*, *142*(1), 179–195. https://doi.org/10.1097/AOG.0000000000005211

du Bois, A., Floquet, A., Kim, J.-W., Rau, J., del Campo, J. M., Friedlander, M., Pignata, S., Fujiwara, K., Vergote, I., Colombo, N., Mirza, M. R., Monk, B. J., Kimmig, R., Ray-Coquard, I., Zang, R., Diaz-Padilla, I., Baumann, K. H., Mouret-Reynier, M.-A., Kim, J.-H., … Harter, P. (2014). Incorporation of Pazopanib in Maintenance Therapy of Ovarian Cancer. *Journal of Clinical Oncology*, *32*(30), 3374–3382. https://doi.org/10.1200/JCO.2014.55.7348

Fujiwara, K., Fujiwara, H., Yoshida, H., Satoh, T., Yonemori, K., Nagao, S., Matsumoto, T., Kobayashi, H., Bourgeois, H., Harter, P., Mosconi, A. M., Vazquez, I. P., Reinthaller, A., Fujita, T., Rowe, P., Pujade-Lauraine, E., & Ray-Coquard, I. (2021). Olaparib plus bevacizumab as maintenance therapy in patients with newly diagnosed, advanced ovarian cancer: Japan subset from the PAOLA-1/ENGOT-ov25 trial. *Journal of Gynecologic Oncology*, *32*(5). https://doi.org/10.3802/jgo.2021.32.e82

González-Martín, A., Pothuri, B., Vergote, I., Graybill, W., Lorusso, D., McCormick, C. C., Freyer, G., Backes, F., Heitz, F., Redondo, A., Moore, R. G., Vulsteke, C., O'Cearbhaill, R. E., Malinowska, I. A., Shtessel, L., Compton, N., Mirza, M. R., & Monk, B. J. (2023). Progression-free survival and safety at 3.5 years of follow-up: results from the randomised phase 3 PRIMA/ENGOT-OV26/GOG-3012 trial of niraparib maintenance treatment in patients with newly diagnosed ovarian cancer. *European Journal of Cancer*, *189*, 112908. https://doi.org/10.1016/j.ejca.2023.04.024

Kehoe, S., Hook, J., Nankivell, M., Jayson, G. C., Kitchener, H., Lopes, T., Luesley, D., Perren, T., Bannoo, S., Mascarenhas, M., Dobbs, S., Essapen, S., Twigg, J., Herod, J., McCluggage, G., Parmar, M., & Swart, A.-M. (2015). Primary chemotherapy versus primary surgery for newly diagnosed advanced ovarian cancer (CHORUS): an open-label, randomised, controlled, non-inferiority trial. *The Lancet*, *386*(9990), 249–257. https://doi.org/10.1016/S0140-6736(14)62223-6

Kim, J.-W., Mahner, S., Wu, L.-Y., Shoji, T., Kim, B.-G., Zhu, J.-Q., Takano, T., Park, S.-Y., Kong, B.-H., Wu, Q., Wang, K.-L., Ngan, H. Y., Liu, J.-H., Wei, L.-H., Mitrica, I., Zhang, P., Crescenzo, R., Wang, Q., Cox, C. J., … du Bois, A. (2018). Pazopanib Maintenance Therapy in East Asian Women With Advanced Epithelial Ovarian Cancer: Results From AGO-OVAR16 and an East Asian Study. *International Journal of Gynecologic Cancer*, *28*(1), 2–10. https://doi.org/10.1097/IGC.0000000000000602

Lai, C.-H., Vallikad, E., Lin, H., Yang, L.-Y., Jung, S.-M., Liu,

H.-E., Ou, Y.-C., Chou, H.-H., Lin, C.-T., Huang, H.-J., Huang, K.-G., Qiu, J., Hung, Y.-C., Wu, T.-I., Chang, W.-Y., Tan, K.-T., Lin, C.-Y., Chao, A., & Chang, C.-J. (2020). Maintenance of pegylated liposomal doxorubicin/carboplatin in patients with advanced ovarian cancer: randomized study of an Asian Gynecologic Oncology Group. *Journal of Gynecologic Oncology*, *31*(1). https://doi.org/10.3802/jgo.2020.31.e5

Ledermann, J. A., Zurawski, B., Raspagliesi, F., De Giorgi, U., Arranz Arija, J., Romeo Marin, M., Lisyanskaya, A., Póka, R. L., Markowska, J., Cebotaru, C., Casado Herraez, A., Colombo, N., Kutarska, E., Hall, M., Jacobs, A., Ahrens-Fath, I., Baumeister, H., Zurlo, A., & Sehouli, J. (2022). Maintenance therapy of patients with recurrent epithelial ovarian carcinoma with the anti-tumor-associated-mucin-1 antibody gatipotuzumab: results from a double-blind, placebo-controlled, randomized, phase II study. *ESMO Open*, *7*(1), 100311. https://doi.org/10.1016/j.esmoop.2021.100311

Li, N., Zhang, Y., Wang, J., Zhu, J., Wang, L., Wu, X., Yao, D., Wu, Q., Liu, J., Tang, J., Yin, R., Lou, G., An, R., Zhang, G., Xia, X., Li, Q., Zhu, Y., Zheng, H., Yang, X., … Wu, L. (2022). Fuzuloparib Maintenance Therapy in Patients With Platinum-Sensitive, Recurrent Ovarian Carcinoma (FZOCUS-2): A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Phase III Trial. *Journal of Clinical Oncology*, *40*(22), 2436–2446. https://doi.org/10.1200/JCO.21.01511

Li, N., Zhu, J., Yin, R., Wang, J., Pan, L., Kong, B., Zheng, H., Liu, J., Wu, X., Wang, L., Huang, Y., Wang, K., Zou, D., Zhao, H., Wang, C., Lu, W., Lin, A., Lou, G., Li, G., … Wu, L. (2023). Treatment With Niraparib Maintenance Therapy in Patients With Newly Diagnosed Advanced Ovarian Cancer. *JAMA Oncology*, *9*(9), 1230. https://doi.org/10.1001/jamaoncol.2023.2283

Mirza, M. R., Monk, B. J., Herrstedt, J., Oza, A. M., Mahner, S., Redondo, A., Fabbro, M., Ledermann, J. A., Lorusso, D., Vergote, I., Ben-Baruch, N. E., Marth, C., Mądry, R., Christensen, R. D., Berek, J. S., Dørum, A., Tinker, A. V., du Bois, A., González-Martín, A., … Matulonis, U. A. (2016). Niraparib Maintenance Therapy in Platinum-Sensitive, Recurrent Ovarian Cancer. *New England Journal of Medicine*, *375*(22), 2154–2164. https://doi.org/10.1056/NEJMoa1611310

Mizuno, M., Ito, K., Nakai, H., Kato, H., Kamiura, S., Ushijima, K., Nagao, S., Takano, H., Okadome, M., Takekuma, M., Tokunaga, H., Nagase, S., Aoki, D., Coleman, R. L., Nishimura, Y., Ratajczak, C. K., Hashiba, H., Xiong, H., Katsumata, N., … Okamoto, A. (2023). Veliparib with frontline chemotherapy and as maintenance in Japanese women with ovarian cancer: a subanalysis of efficacy, safety, and antiemetic use in the phase 3 VELIA trial. *International Journal of*

Clinical Oncology, *28*(1), 163–174. https://doi.org/10.1007/s10147-022-02258-x

Nag, S., Aggarwal, S., Rauthan, A., & Warrier, N. (2022). Maintenance therapy for newly diagnosed epithelial ovarian cancer– a review. *Journal of Ovarian Research*, *15*(1), 88. https://doi.org/10.1186/s13048-022-01020-1

Phung, M. T., Pearce, C. L., Meza, R., & Jeon, J. (2023). Trends of Ovarian Cancer Incidence by Histotype and Race/Ethnicity in the United States 1992–2019. *Cancer Research Communications*, *3*(1), 1–8. https://doi.org/10.1158/2767-9764.CRC-22-0410

Poveda, A., Floquet, A., Ledermann, J. A., Asher, R., Penson, R. T., Oza, A. M., Korach, J., Huzarski, T., Pignata, S., Friedlander, M., Baldoni, A., Park-Simon, T.-W., Tamura, K., Sonke, G. S., Lisyanskaya, A., Kim, J.-H., Filho, E. A., Milenkova, T., Lowe, E. S., … Vergote, I. (2021). Olaparib tablets as maintenance therapy in patients with platinum-sensitive relapsed ovarian cancer and a BRCA1/2 mutation (SOLO2/ENGOT-Ov21): a final analysis of a double-blind, randomised, placebo-controlled, phase 3 trial. *The Lancet Oncology*, *22*(5), 620–631. https://doi.org/10.1016/S1470-2045(21)00073-5

Wu, L., Zhu, J., Yin, R., Wu, X., Lou, G., Wang, J., Gao, Y., Kong, B., Lu, X., Zhou, Q., Wang, Y., Chen, Y., Lu, W., Li, W., Cheng, Y., Liu, J., Ma, X., & Zhang, J. (2021). Olaparib maintenance therapy in patients with newly diagnosed advanced ovarian cancer and a BRCA1 and/or BRCA2 mutation: SOLO1 China cohort. *Gynecologic Oncology*, *160*(1), 175–181. https://doi.org/10.1016/j.ygyno.2020.10.005

Wu, X. H., Zhu, J. Q., Yin, R. T., Yang, J. X., Liu, J. H., Wang, J., Wu, L. Y., Liu, Z. L., Gao, Y. N., Wang, D. B., Lou, G., Yang, H. Y., Zhou, Q., Kong, B. H., Huang, Y., Chen, L. P., Li, G. L., An, R. F., Wang, K., … Mirza, M. R. (2021). Niraparib maintenance therapy in patients with platinum-sensitive recurrent ovarian cancer using an individualized starting dose (NORA): a randomized, double-blind, placebo-controlled phase III trial☆. *Annals of Oncology*, *32*(4), 512–521. https://doi.org/10.1016/j.annonc.2020.12.018

Wu, X., Liu, J., Wang, J., Wang, L., Lin, Z., Wang, X., Zhu, J., Kong, B., Fei, J., Tang, Y., Xia, B., Liang, Z., Wang, K., Huang, Y., Zheng, H., Lin, A., Jiang, K., Wang, W., Wang, X., … Zeng, L. (2024). Senaparib as first-line maintenance therapy in advanced ovarian cancer: a randomized phase 3 trial. *Nature Medicine*, *30*(6), 1612–1621. https://doi.org/10.1038/s41591-024-03003-9