

Practice Guideline



Clinical guidelines for ovarian cancer: the Korean Society of Gynecologic Oncology guidelines

Banghyun Lee ,¹ Suk-Joon Chang ,² Byung Su Kwon ,³ Joo-Hyuk Son ,² Myong Cheol Lim ,⁴ Yun Hwan Kim ,⁵ Shin-Wha Lee ,⁶ Chel Hun Choi ,⁷ Kyung Jin Eoh ,⁸ Jung-Yun Lee ,⁹ Dong Hoon Suh ,¹⁰ Yong Beom Kim ¹⁰

OPEN ACCESS

Received: Oct 25, 2023

Revised: Dec 10, 2023

Accepted: Dec 13, 2023

Published online: Dec 27, 2023

Correspondence to

Suk-Joon Chang

Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Ajou University School of Medicine, 164 Worldcup-ro, Yeongtong-gu, Suwon 16499, Korea.
Email: drchang@ajou.ac.kr

¹Department of Obstetrics and Gynecology, Inha University Hospital, Inha University College of Medicine, Incheon, Korea

²Department of Obstetrics and Gynecology, Ajou University School of Medicine, Suwon, Korea

³Department of Obstetrics and Gynecology, Kyung Hee University Medical Center, School of Medicine, Kyung Hee University, Seoul, Korea

⁴Center for Gynecologic Cancer, Research Institute and Hospital, National Cancer Center, Goyang, Korea

⁵Department of Obstetrics and Gynecology, Ewha Womans University Mokdong Hospital, Ewha Womans University College of Medicine, Seoul, Korea

⁶Department of Obstetrics and Gynecology, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea

⁷Department of Obstetrics and Gynecology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

⁸Department of Obstetrics and Gynecology, Yongin Severance Hospital, Yonsei University College of Medicine, Yongin, Korea

⁹Department of Obstetrics and Gynecology, Yonsei University College of Medicine, Seoul, Korea

¹⁰Department of Obstetrics and Gynecology, Seoul National University Bundang Hospital, Seongnam, Korea

© 2024. Asian Society of Gynecologic Oncology, Korean Society of Gynecologic Oncology, and Japan Society of Gynecologic Oncology

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ORCID iDs

Banghyun Lee <https://orcid.org/0000-0003-1036-3828>
Suk-Joon Chang <https://orcid.org/0000-0002-0558-0038>
Byung Su Kwon <https://orcid.org/0000-0002-9586-0200>
Joo-Hyuk Son <https://orcid.org/0000-0002-3712-8409>
Myong Cheol Lim <https://orcid.org/0000-0001-8964-7158>
Yun Hwan Kim <https://orcid.org/0000-0001-9498-2938>
Shin-Wha Lee <https://orcid.org/0000-0002-5088-1905>
Chel Hun Choi <https://orcid.org/0000-0002-0199-6669>



ABSTRACT

Since the latest practice guidelines for ovarian cancer were developed by the Korean Society of Gynecologic Oncology (KSGO) in 2021, many studies have examined the efficacy and safety of various treatments for epithelial ovarian cancer (EOC). Therefore, the need to develop recommendations for EOC treatments has been raised. This study searched the literature using 4 key items and the Population, Intervention, Comparison, and Outcome: the efficacy and safety of poly-ADP ribose polymerase inhibitors in newly diagnosed advanced EOC; the efficacy and safety of intraperitoneal plus intravenous chemotherapy in optimally debulked advanced EOC; the efficacy and safety of secondary cytoreductive surgery in platinum-sensitive recurrent ovarian cancer; and the efficacy and safety of the addition of bevacizumab to platinum-based chemotherapy in first platinum-sensitive recurrent EOC patients who received prior bevacizumab. The evidence for these recommendations, according to each key question, was evaluated using a systematic review and meta-analysis. The committee of ovarian cancer of the KSGO developed updated guidelines for treatments of EOC.

Keywords: Epithelial Ovarian Cancer; Survival; Poly (ADP-ribose) Polymerase Inhibitor; Intraperitoneal Chemotherapy; Cytoreductive Surgery; Bevacizumab

INTRODUCTION

Ovarian cancer is the second most common gynecologic cancer and the most common cause of death from gynecologic cancers [1,2]. Epithelial ovarian cancer (EOC) occurs in more than

Kyung Jin Eoh 
<https://orcid.org/0000-0002-1684-2267>
 Jung-Yun Lee 
<https://orcid.org/0000-0001-7948-1350>
 Dong Hoon Suh 
<https://orcid.org/0000-0002-4312-966X>
 Yong Beom Kim 
<https://orcid.org/0000-0003-1196-369X>

Funding

This work was supported by Research fund of National Cancer Center, Korea, Republic of (NCC-2112570-3).

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Data Availability Statement

All data used for this guideline are available in each published study included in this paper. References of all studies are listed in the appropriate section.

Author Contributions

Conceptualization: L.B., C.S.J., K.B.S., S.J.H., L.M.C., K.Y.H., L.S.W., C.C.H., E.K.J., L.J.Y.; Data curation: L.B., K.B.S.; Formal analysis: L.B., C.S.J.; Funding acquisition: K.Y.B.; Methodology: L.B., C.S.J.; Project administration: C.S.J.; Resources: L.B., S.J.H.; Supervision: S.D.H., K.Y.B.; Visualization: L.B.; Writing - original draft: L.B., C.S.J.; Writing - review & editing: L.B., C.S.J., K.B.S., S.J.H., L.M.C., K.Y.H., L.S.W., C.C.H., E.K.J., L.J.Y., S.D.H., K.Y.B.

90% of ovarian cancers, with high-grade serous carcinoma being the most common EOC subtype [2,3]. Most EOC (75%) presents as an advanced disease (stage III or IV), which shows a more than 80% response rate for the standard of care (cytoreductive surgery and platinum-based chemotherapy) [4]. On the other hand, recurrence occurs in almost 80% of advanced EOCs [5]. In most patients with advanced EOC, cancer reoccurs repeatedly with progressively shorter progression-free intervals and repeated chemotherapy. Treatment after recurrence is ineffective, with a median survival of 2 years after recurrence [2,6].

Currently, targeted therapies are included in the standard treatment of ovarian cancer. Many EOCs have homologous recombination deficiency (HRD) with or without a BRCA1/2 mutation [7]. Poly-ADP ribose polymerase (PARP) inhibitors cause double-strand breaks in DNA, which causes cancer cell death because the cancer cells cannot perform a homologous recombination [2]. Many randomized controlled trials (RCTs) have reported that PARP inhibitors improve the survival in newly diagnosed advanced EOC and platinum-sensitive recurrent EOC [8-18]. Vascular endothelial growth factor (VEGF) and angiogenesis promote the progression of ovarian cancer [19]. Bevacizumab, an anti-VEGF monoclonal antibody, inhibits angiogenesis [19]. In many RCTs, bevacizumab has improved the survival of newly diagnosed advanced EOC patients and recurrent EOC patients [20-25].

Many RCTs have reported that intraperitoneal (IP) plus intravenous (IV) chemotherapy in newly diagnosed advanced EOC improved survival compared to IV chemotherapy [26-34]. On the other hand, IP chemotherapy has not been accepted widely as the standard of care because of more adverse events, catheter complications, and inconvenience compared with IV chemotherapy [35].

Secondary cytoreductive surgery is one of the factors associated with the 5-year survival after recurrence [2,6]. Recently, 3 RCTs have reported inconsistent survival outcomes of secondary cytoreductive surgery in platinum-sensitive recurrent EOC patients predicted to have potentially resectable disease [36-38]. These results might be attributed to different criteria for potentially resectable disease in each trial.

The committee of ovarian cancer of the Korean Society of Gynecologic Oncology (KSGO) provided and updated the practice guideline for ovarian cancer in 2006, 2010, 2016 and 2021 [39-42]. Many studies have recently reported the effects of PARP inhibitors and bevacizumab on survivals in newly diagnosed advanced EOC or platinum-sensitive recurrent EOC. The survival benefit of IP plus IV chemotherapy in newly diagnosed advanced EOC has been continuously reported in recent studies. In addition, the effects of secondary cytoreductive surgery on survivals in platinum-sensitive recurrent EOC are controversial. Therefore, updated guidelines for ovarian cancer are required.

METHODS

1. Developing the recommendations

The key questions, the Population, Intervention, Comparison, and Outcome (PICO), and the scope of the guidelines were derived through meetings of the committee of ovarian cancer and the other gynecologic cancer committees to develop the KSGO guidelines (**Data S1**). The committee of ovarian cancer developed guidelines based on a systematic review of the literature and meta-analysis.

2. Strategy of literature search

The PubMed, Cochrane Library, Embase, and KoreaMed databases were searched for relevant studies in October 2022 using a combination of keywords according to each key question and its PICO (**Data S2**). Additional relevant studies not identified by these database searches were found by examining the references from the selected clinical studies and review articles.

3. Selection criteria

Two investigators selected and excluded the literature independently according to the inclusion and exclusion criteria of each key question. Discrepancies between investigators were resolved by discussion. Only studies with the most comprehensive data were selected to avoid including duplicate information when studies included overlapping groups of patients (**Data S3**).

4. Data extraction, outcomes of interest, and risk of bias

Two investigators extracted the data of interest from studies independently using the checklist of each key question. Discrepancies between investigators were resolved by discussion.

The primary outcome variable was the progression-free survival (PFS), defined as the time between randomization and disease progression or death from any cause. The overall survival (OS), the secondary outcome, was defined as the time between randomization and death from any cause. Adverse outcomes ≥ 3 were evaluated for the safety assessment.

The qualities of the included studies were appraised separately by the 2 investigators using the revised Cochrane risk of bias tool for randomized trials (RoB 2.0 version) [43]. Any discrepancies between investigators were resolved by discussion.

5. Meta-analyses

The meta-analysis was performed using Review Manager Version 5.4.1 software (The Nordic Cochrane Centre, Copenhagen, Denmark). The p-values < 0.05 were considered significant. Random-effects models were performed using the Inverse Variance method for survival analysis. Random-effects models were also implemented in the Mantel-Haenszel method to analyze the adverse events. The hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated for survival, and the odds ratios (ORs) were calculated for adverse events. The heterogeneities of the HRs and ORs across studies were assessed using the I^2 statistic and Cochran's Q statistic. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) evidence profiles were produced using GRADEpro GDT.

6. Quality of evidence

The guidelines of the GRADE system were used to evaluate the quality of evidence for the outcomes [44]. In this guidelines, the qualities of evidence are reported as follows: high quality, indicating that further research is unlikely to change the confidence in the estimation of effect; moderate quality, indicating that further research is likely to have a significant impact on confidence in the estimate of effect and may change the estimation; low quality, indicating further research is highly likely to have a substantial impact on confidence in the estimate of effect and is likely to change the estimation; very low quality, indicating little confidence in the estimate of effect. The GRADE guidelines involve the sequential assessment of evidence quality, evaluation of the risk–benefit balance, and subsequent appraisal of the strengths of recommendations.

Table 1. Strength of recommendation

For	Strong For Weak/Conditional For
Against	Weak/Conditional Against Strong Against

7. Strength of recommendation

The strength of a recommendation was determined using the GRADE approach (**Table 1**) [45]. In the GRADE guidelines, the strength of a recommendation is defined as the extent to which one can be confident that the desirable consequences of an intervention outweigh its undesirable consequences. In strong recommendations, all or almost all informed people would make the recommended choice for or against an intervention. In weak/conditional recommendations, most informed people would choose the recommended course of action, but a substantial number would not.

EVIDENCE

1. Key question 1: Does PARP inhibitor maintenance therapy improve survival in newly diagnosed advanced EOC patients who showed a response to chemotherapy after surgery?

Search results and characteristics and assessments of the risk of bias of the included studies

The literature search identified 3,227 potentially relevant studies, and 7 studies [8-14] that met the eligibility criteria were selected (**Data S3**). **Data S4** lists the characteristics of these studies. The PAOLA-1 trial provided 2 studies [10,11] that reported the PFS and OS individually. The SOLO1 trial also provided 2 studies [12,13] that reported the PFS and OS, respectively. **Data S5** presents the results of the risk of the bias assessments. The PFS was evaluated using 5 studies: the OS using 2 studies and adverse events of \geq grade 3 using 4 studies (**Data S6**).

Two-year PFS

The PARP inhibitors improved the PFS significantly compared with the placebo (HR=0.53; 95% CI=0.41–0.68; $p<0.00001$; I^2 , 84%; 3,071 patients; moderate-quality evidence) (**Data S6** and **S7**).

Five-year OS

The OSs of the PARP inhibitors and placebo were similar (HR=0.73; 95% CI=0.44–1.20; $p=0.21$; I^2 , 86%; 1,197 patients; low-quality evidence) (**Data S6** and **S7**). On the other hand, when analyzed in patients with a BRCA1/2 mutation, the PARP inhibitors improved the OS significantly compared to the placebo (HR=0.57; 95% CI=0.44–0.74; $p<0.0001$; I^2 , 0%; 2 studies; 628 patients).

Adverse events \geq grade 3

The PARP inhibitors increased adverse events of \geq grade 3 significantly compared to the placebo (OR=2.94; 95% CI=1.13–7.63; $p=0.03$; I^2 , 96%; 2,668 patients; moderate-quality evidence) (**Data S6** and **S7**).

Based on the above results, the following was recommended:

PARP inhibitor maintenance therapy is recommended in newly diagnosed advanced EOC patients showing a response to chemotherapy after surgery (Strong For).

2. Key question 2: Does IP plus IV chemotherapy improve survival in optimally debulked advanced EOC patients?

Search results and characteristics and assessments of the risk of bias of the included studies

The literature search identified 1,166 potentially relevant studies; only 9 RCTs [26-34] that met the selection criteria were included (**Data S3**). **Data S4** lists the characteristics of these studies, and **Data S5** presents the results of the risk of bias assessments for each study. Walker et al. [32] reported data from the IP-Carboplatin, IP-Cisplatin, and IV-Carboplatin groups. Therefore, this study considered 2 studies: the IP-Carboplatin group vs. the IV-Carboplatin group and the IP-Cisplatin group vs. the IV-Carboplatin group. Eight studies were used to evaluate the PFS: 10 to evaluate the OS and 2 to evaluate adverse events of \geq grade 3 (**Data S6**).

Two-year PFS

IP plus IV chemotherapy improved the PFS significantly compared to IV chemotherapy (HR=0.89; 95% CI=0.82–0.96; p=0.004; I^2 , 11%; 4,144 patients; high-quality evidence) (**Data S6** and **S7**).

Five-year OS

IP plus IV chemotherapy improved the OS significantly compared to the IV chemotherapy (HR=0.85; 95% CI=0.74–0.96; p=0.01; I^2 , 55%; 4,808 patients; high-quality evidence) (**Data S6** and **S7**).

Adverse events \geq grade 3

The rate of adverse events of \geq grade 3 was significantly lower in the IP plus IV chemotherapy group than the IV chemotherapy group (OR=0.59; 95% CI=0.36–0.97; p=0.04; I^2 , 0%; 858 patients; high-quality evidence). When leukopenia (grade \geq 3) was analyzed, the OSs were similar in the IP plus IV chemotherapy group and the IV chemotherapy group (HR=1.39; 95% CI=0.97–2.00; p=0.08; I^2 , 82%; 5 studies; 3,439 patients) (**Data S6** and **S7**).

Based on the above results, the following was recommended:

IP plus IV chemotherapy can be used in optimally debulked advanced EOC patients (Conditional for).

3. Key question 3: Does secondary cytoreductive surgery improve the survival of patients with platinum-sensitive recurrent ovarian cancer?

Search results and characteristics and assessments of the risk of bias of the included studies

The literature search identified 2,301 potentially relevant studies, but only 3 RCTs [36-38] that met the selection criteria were eventually included (**Data S3**). **Data S4** lists the characteristics of these studies, and **Data S5** presents the results of risk of bias assessments for each study. Three studies were used to evaluate the PFS and OS (**Data S6**).

Two-year PFS

The PFS was significantly improved in the group of secondary cytoreductive surgery followed by platinum-based chemotherapy than in the platinum-based chemotherapy-alone group (HR=0.58; 95% CI=0.39–0.87; p=0.008; I², 89%; 1,249 patients; moderate-quality evidence) (**Data S6** and **S7**).

Five-year OS

The OSs were similar in the secondary cytoreductive surgery group followed by the platinum-based chemotherapy and the platinum-based chemotherapy alone group (HR=0.93; 95% CI=0.66–1.32; p=0.68; I², 76%; 1,249 patients; low-quality evidence) (**Data S6** and **S7**).

Adverse events ≥ grade 3

Meta-analysis could not be performed because there were no adequate data. Shi et al. [38] reported that the adverse events of ≥ grade 3 during platinum-based chemotherapy occurred in 25% and 20% in the groups with and without secondary cytoreductive surgery, respectively. Moreover, surgical complications of ≥ grade 3 at 30 days after secondary cytoreductive surgery occurred in 5%. There were no deaths 60 days after receiving the assigned treatment and no treatment-related deaths (**Data S4**).

Based on the above results, the following was recommended:

Secondary cytoreductive surgery is recommended in patients with platinum-sensitive recurrent ovarian cancer who are predicted to have potentially resectable disease (Strong For).

4. Key question 4: Does bevacizumab/platinum-based chemotherapy followed by bevacizumab maintenance therapy improve survival in patients with platinum-sensitive recurrent ovarian cancer who had previously received first-line platinum-based chemotherapy, including bevacizumab?

Search results and characteristics and assessments of the risk of bias of the included studies

The literature search identified 474 potentially relevant studies, but only one RCT [25] met the selection criteria (**Data S3**). **Data S4** lists the characteristics of these studies, and **Data S5** presents the results of risk of bias assessments for each study. One study was used to evaluate the PFS and OS (**Data S6**). The heterogeneities of the HRs were not assessed because only one study was included in meta-analyses.

Two-year PFS

The PFS was improved significantly in the group of platinum-based chemotherapy with bevacizumab followed by maintenance therapy than in the group of the platinum-based chemotherapy without bevacizumab (HR=0.52; 95% CI=0.41–0.65; p<0.00001; 406 patients; high-quality evidence) (**Data S6** and **S7**).

Five-year OS

The OSs were similar in the groups of the platinum-based chemotherapy with and without bevacizumab (HR=1.01; 95% CI=0.73–1.39; p=0.96; 406 patients; moderate-quality evidence) (**Data S6** and **S7**).

Adverse events \geq grade 3

Meta-analysis cannot be performed because there were no adequate data. Adverse events of \geq grade 3 occurred in 79% and 69% of the groups of the platinum-based chemotherapy with and without bevacizumab, respectively. Treatment-related deaths occurred in <1% and 1% of these groups.

The following was recommended based on the above results:

Platinum-based chemotherapy plus bevacizumab can be used in patients with platinum-sensitive recurrent ovarian cancer who had previously received first-line platinum-based chemotherapy including bevacizumab (Weak/Conditional for).

DISCUSSION

The presented recommendations for the treatments of EOC patients were based on evidence supported by a systematic review and meta-analysis. The critical RCTs reported recently were included in the meta-analyses.

Recently, 5 phase 3 RCTs [8-10,12,14] showed that PARP inhibitor maintenance therapy improved the PFS in a BRCA mutation cohort, BRCA wild cohort, HRD cohort, homologous-recombination proficiency (HRP) cohort, and the overall population of newly diagnosed advanced EOC patients with a complete or partial response to platinum-based chemotherapy. On the other hand, only 2 phase 3 RCTs [11,13] reported that the PARP inhibitor improved the OS in a BRCA mutation cohort and a HRD cohort but not in a HRP cohort and overall population. In this meta-analysis, including these studies, the PARP inhibitor improved the PFS significantly but not the OS in the overall population. On the other hand, PARP inhibitors improved the OS in a BRCA mutation cohort. The effects of the PARP inhibitor on OS require clarification based on further research. Nevertheless, in this meta-analysis, PARP inhibitors increased adverse events of \geq grade 3 significantly. Although PARP inhibitors are associated with a high risk of serious adverse events, the survival benefit of PARP inhibitors has greater clinical significance than adverse events because of the poor prognosis of advanced EOC. Therefore, the current guidelines recommend PARP inhibitors in newly diagnosed advanced EOC patients who show a response to platinum-based chemotherapy after primary surgery.

Previous RCTs reported that IP plus IV chemotherapy improved the survival in newly diagnosed advanced EOC patients with optimally or suboptimally debulked disease (**Data S4**) [26-30]. These reports were continued in recent RCTs (**Data S4**) [31-34]. In South Korea, however, IP plus IV chemotherapy has rarely been performed because of the disadvantages of IP chemotherapy. The current guidelines handle this issue to encourage using IP plus IV chemotherapy. In this meta-analysis, including 9 RCTs, IP plus IV chemotherapy improved the PFS and OS significantly compared to IV chemotherapy. Moreover, IP plus IV chemotherapy was associated with a lower rate of adverse events of \geq grade 3 (2 RCTs analysis) and a similar rate of leukopenia of \geq grade 3 (5 RCTs analysis) compared to IV chemotherapy. Although the significance of analysis is limited to the few studies included a meta-analysis of adverse events of \geq grade 3 provided high-quality evidence. Based on the meta-analyses, the current guideline recommends IP plus IV chemotherapy in optimally debulked advanced EOC patients.

Secondary cytoreductive surgery and a favorable response to second-line chemotherapy are factors associated with 5-year survival after recurrence [2,6]. The response rates to second-line chemotherapy in platinum-sensitive recurrent EOC patients are 30%–70% [46]. Therefore, secondary cytoreductive surgery may help extend survival. Recently, 3 phase 3 RCTs [36–38] reported different survival outcomes of secondary cytoreductive surgery in first platinum-sensitive recurrent EOC patients who are predicted to have potentially resectable disease (**Data S4**). Although inconsistent survivals of the studies might be attributed to different eligibility criteria, the effects of secondary cytoreductive surgery on survivals need to be clarified. In this meta-analysis, including these 3 RCTs, secondary cytoreductive surgery significantly improved the PFS but not the OS. On the other hand, one RCT [38] reported similar rates of adverse events of \geq grade 3 between the patients with and without secondary cytoreductive surgery. Moreover, secondary cytoreductive surgery was associated with a low rate of surgical complications of \geq grade 3 [38]. Therefore, the current guidelines recommend secondary cytoreductive surgery in platinum-sensitive recurrent EOC patients who are predicted to have potentially resectable disease.

The previous phase 3 RCT [20] reported a prolonged PFS by adding bevacizumab to platinum-based chemotherapy in the first platinum-sensitive recurrent EOC patients not previously treated with bevacizumab. Recently, one phase 3 RCT [25] reported that adding bevacizumab to platinum-based chemotherapy improved the PFS significantly but not the OS in the first platinum-sensitive recurrent EOC patients previously treated with bevacizumab. In this RCT, the rates of adverse events of \geq grade 3 and treatment-related death were similar in the patients with and without bevacizumab (**Data S4**). The survival outcomes of this RCT were identical to those of the meta-analyses, including only this RCT. Although only one study provided evidence, the survival benefit of adding bevacizumab to platinum-based chemotherapy has clinical significance based on the poor prognosis of recurrent EOC. Therefore, the current guidelines recommend the addition of bevacizumab to platinum-based chemotherapy in platinum-sensitive recurrent EOC patients who had previously received first-line platinum-based chemotherapy, including bevacizumab.

The present recommendation will be updated once further studies on the 4 key questions are published. These recommendations will be distributed to all members of the KSGO and members of the relevant association who use it for patient care.

ACKNOWLEDGEMENTS

We thank the Korean Cancer Management Guideline Network (KCGN) for the technical support.

SUPPLEMENTARY MATERIALS

Data S1

The Population, Intervention, Comparison, and Outcome (PICO) for key questions

[Click here to view](#)

Data S2

Search strategy

[Click here to view](#)**Data S3**

Flow chart of study selection

[Click here to view](#)**Data S4**

Characteristics of the included studies

[Click here to view](#)**Data S5**

Risk of bias

[Click here to view](#)**Data S6**

Meta-analysis

[Click here to view](#)**Data S7**

Grading of Recommendations Assessment, Development, and Evaluation (GRADE) evidence profiles

[Click here to view](#)**REFERENCES**

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. *CA Cancer J Clin* 2020;70:7-30.
[PUBMED](#) | [CROSSREF](#)
2. Kwolek DG, Gerstberger S, Tait S, Qiu JM. Ovarian, uterine, and vulvovaginal cancers: screening, treatment overview, and prognosis. *Med Clin North Am* 2023;107:329-55.
[PUBMED](#) | [CROSSREF](#)
3. Torre LA, Trabert B, DeSantis CE, Miller KD, Samimi G, Runowicz CD, et al. Ovarian cancer statistics, 2018. *CA Cancer J Clin* 2018;68:284-96.
[PUBMED](#) | [CROSSREF](#)
4. Hennessy BT, Coleman RL, Markman M. Ovarian cancer. *Lancet* 2009;374:1371-82.
[PUBMED](#) | [CROSSREF](#)
5. Pignata S, Cecere SC, Du Bois A, Harter P, Heitz F. Treatment of recurrent ovarian cancer. *Ann Oncol* 2017;28:viii51-6.
[PUBMED](#) | [CROSSREF](#)
6. Soyama H, Takano M, Miyamoto M, Yoshikawa T, Aoyama T, Goto T, et al. Factors favouring long-term survival following recurrence in ovarian cancer. *Mol Clin Oncol* 2017;7:42-6.
[PUBMED](#) | [CROSSREF](#)

7. Cancer Genome Atlas Research Network. Integrated genomic analyses of ovarian carcinoma. *Nature* 2011;474:609-15.
[PUBMED](#) | [CROSSREF](#)
8. González-Martín A, Pothuri B, Vergote I, DePont Christensen R, Graybill W, Mirza MR, et al. Niraparib in patients with newly diagnosed advanced ovarian cancer. *N Engl J Med* 2019;381:2391-402.
[PUBMED](#) | [CROSSREF](#)
9. Coleman RL, Fleming GF, Brady MF, Swisher EM, Steffensen KD, Friedlander M, et al. Veliparib with first-line chemotherapy and as maintenance therapy in ovarian cancer. *N Engl J Med* 2019;381:2403-15.
[PUBMED](#) | [CROSSREF](#)
10. Ray-Coquard I, Pautier P, Pignata S, Pérol D, González-Martín A, Berger R, et al. Olaparib plus bevacizumab as first-line maintenance in ovarian cancer. *N Engl J Med* 2019;381:2416-28.
[PUBMED](#) | [CROSSREF](#)
11. Ray-Coquard IL, Leary A, Pignata S, Cropet C, Martin AJ, Bogner G, et al. LBA29 Final overall survival (OS) results from the phase III PAOLA-1/ENGOT-ov25 trial evaluating maintenance olaparib (ola) plus bevacizumab (bev) in patients (pts) with newly diagnosed advanced ovarian cancer (AOC). *Ann Oncol* 2022;33:S1396-7.
[CROSSREF](#)
12. Banerjee S, Moore KN, Colombo N, Scambia G, Kim BG, Oaknin A, et al. 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. *Lancet Oncol* 2021;22:1721-31.
[PUBMED](#) | [CROSSREF](#)
13. DiSilvestro P, Banerjee S, Colombo N, Scambia G, Kim BG, Oaknin A, et al. Overall survival with maintenance olaparib at a 7-year follow-up in patients with newly diagnosed advanced ovarian cancer and a BRCA mutation: The SOLO1/GOG 3004 Trial. *J Clin Oncol* 2023;41:609-17.
[PUBMED](#) | [CROSSREF](#)
14. Li N, Zhu J, Yin R, Wang J, Pan L, Kong B, et al. Efficacy and safety of niraparib as maintenance treatment in patients with newly diagnosed advanced ovarian cancer using an individualized starting dose (PRIME Study): a randomized, double-blind, placebo-controlled, phase 3 trial (LBA 5). *Gynecol Oncol* 2022;166:S50-1.
[CROSSREF](#)
15. Pujade-Lauraine E, Ledermann JA, Selle F, GebSKI V, Penson RT, Oza AM, et al. Olaparib tablets as maintenance therapy in patients with platinum-sensitive, relapsed ovarian cancer and a BRCA1/2 mutation (SOLO2/ENGOT-Ov21): a double-blind, randomised, placebo-controlled, phase 3 trial. *Lancet Oncol* 2017;18:1274-84.
[PUBMED](#) | [CROSSREF](#)
16. Coleman RL, Oza AM, Lorusso D, Aghajanian C, Oaknin A, Dean A, et al. Rucaparib maintenance treatment for recurrent ovarian carcinoma after response to platinum therapy (ARIEL3): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet* 2017;390:1949-61.
[PUBMED](#) | [CROSSREF](#)
17. Mirza MR, Monk BJ, Herrstedt J, Oza AM, Mahner S, Redondo A, et al. Niraparib maintenance therapy in platinum-sensitive, recurrent ovarian cancer. *N Engl J Med* 2016;375:2154-64.
[PUBMED](#) | [CROSSREF](#)
18. Ledermann J, Harter P, Gourley C, Friedlander M, Vergote I, Rustin G, et al. Olaparib maintenance therapy in platinum-sensitive relapsed ovarian cancer. *N Engl J Med* 2012;366:1382-92.
[PUBMED](#) | [CROSSREF](#)
19. Lim D, Do Y, Kwon BS, Chang W, Lee MS, Kim J, et al. Angiogenesis and vasculogenic mimicry as therapeutic targets in ovarian cancer. *BMB Rep* 2020;53:291-8.
[PUBMED](#) | [CROSSREF](#)
20. Aghajanian C, Blank SV, Goff BA, Judson PL, Teneriello MG, Husain A, et al. OCEANS: a randomized, double-blind, placebo-controlled phase III trial of chemotherapy with or without bevacizumab in patients with platinum-sensitive recurrent epithelial ovarian, primary peritoneal, or fallopian tube cancer. *J Clin Oncol* 2012;30:2039-45.
[PUBMED](#) | [CROSSREF](#)
21. Pujade-Lauraine E, Hilpert F, Weber B, Reuss A, Poveda A, Kristensen G, et al. Bevacizumab combined with chemotherapy for platinum-resistant recurrent ovarian cancer: the AURELIA open-label randomized phase III trial. *J Clin Oncol* 2014;32:1302-8.
[PUBMED](#) | [CROSSREF](#)
22. Burger RA, Brady MF, Bookman MA, Fleming GF, Monk BJ, Huang H, et al. Incorporation of bevacizumab in the primary treatment of ovarian cancer. *N Engl J Med* 2011;365:2473-83.
[PUBMED](#) | [CROSSREF](#)

23. Perren TJ, Swart AM, Pfisterer J, Ledermann JA, Pujade-Lauraine E, Kristensen G, et al. A phase 3 trial of bevacizumab in ovarian cancer. *N Engl J Med* 2011;365:2484-96.
[PUBMED](#) | [CROSSREF](#)
24. Coleman RL, Brady MF, Herzog TJ, Sabbatini P, Armstrong DK, Walker JL, et al. Bevacizumab and paclitaxel-carboplatin chemotherapy and secondary cytoreduction in recurrent, platinum-sensitive ovarian cancer (NRG Oncology/Gynecologic Oncology Group study GOG-0213): a multicentre, open-label, randomised, phase 3 trial. *Lancet Oncol* 2017;18:779-91.
[PUBMED](#) | [CROSSREF](#)
25. Pignata S, Lorusso D, Joly F, Gallo C, Colombo N, Sessa C, et al. Carboplatin-based doublet plus bevacizumab beyond progression versus carboplatin-based doublet alone in patients with platinum-sensitive ovarian cancer: a randomised, phase 3 trial. *Lancet Oncol* 2021;22:267-76.
[PUBMED](#) | [CROSSREF](#)
26. Alberts DS, Liu PY, Hannigan EV, O'Toole R, Williams SD, Young JA, et al. Intraperitoneal cisplatin plus intravenous cyclophosphamide versus intravenous cisplatin plus intravenous cyclophosphamide for stage III ovarian cancer. *N Engl J Med* 1996;335:1950-5.
[PUBMED](#) | [CROSSREF](#)
27. Gadducci A, Carnino F, Chiara S, Brunetti I, Tanganelli L, Romanini A, et al. Intraperitoneal versus intravenous cisplatin in combination with intravenous cyclophosphamide and epidoxorubicin in optimally cytoreduced advanced epithelial ovarian cancer: a randomized trial of the Gruppo Oncologico Nord-Ovest. *Gynecol Oncol* 2000;76:157-62.
[PUBMED](#) | [CROSSREF](#)
28. Markman M, Bundy BN, Alberts DS, Fowler JM, Clark-Pearson DL, Carson LF, et al. Phase III trial of standard-dose intravenous cisplatin plus paclitaxel versus moderately high-dose carboplatin followed by intravenous paclitaxel and intraperitoneal cisplatin in small-volume stage III ovarian carcinoma: an intergroup study of the Gynecologic Oncology Group, Southwestern Oncology Group, and Eastern Cooperative Oncology Group. *J Clin Oncol* 2001;19:1001-7.
[PUBMED](#) | [CROSSREF](#)
29. Yen MS, Juang CM, Lai CR, Chao GC, Ng HT, Yuan CC. Intraperitoneal cisplatin-based chemotherapy vs. intravenous cisplatin-based chemotherapy for stage III optimally cytoreduced epithelial ovarian cancer. *Int J Gynaecol Obstet* 2001;72:55-60.
[PUBMED](#) | [CROSSREF](#)
30. Armstrong DK, Bundy B, Wenzel L, Huang HQ, Baergen R, Lele S, et al. Intraperitoneal cisplatin and paclitaxel in ovarian cancer. *N Engl J Med* 2006;354:34-43.
[PUBMED](#) | [CROSSREF](#)
31. Provencher DM, Gallagher CJ, Parulekar WR, Ledermann JA, Armstrong DK, Brundage M, et al. OV21/PETROC: a randomized Gynecologic Cancer Intergroup phase II study of intraperitoneal versus intravenous chemotherapy following neoadjuvant chemotherapy and optimal debulking surgery in epithelial ovarian cancer. *Ann Oncol* 2018;29:431-8.
[PUBMED](#) | [CROSSREF](#)
32. Walker JL, Brady MF, Wenzel L, Fleming GF, Huang HQ, DiSilvestro PA, et al. Randomized trial of intravenous versus intraperitoneal chemotherapy plus bevacizumab in advanced ovarian carcinoma: an NRG Oncology/Gynecologic Oncology Group study. *J Clin Oncol* 2019;37:1380-90.
[PUBMED](#) | [CROSSREF](#)
33. Shi T, Jiang R, Pu H, Yang H, Tu D, Dai Z, et al. Survival benefits of dose-dense early postoperative intraperitoneal chemotherapy in front-line therapy for advanced ovarian cancer: a randomised controlled study. *Br J Cancer* 2019;121:425-8.
[PUBMED](#) | [CROSSREF](#)
34. Fujiwara K, Nagao S, Yamamoto K, Tanabe H, Okamoto A, Takehara K, et al. A randomized phase 3 trial of intraperitoneal versus intravenous carboplatin with dose-dense weekly paclitaxel in patients with ovarian, fallopian tube, or primary peritoneal carcinoma (a GOTIC-001/JGOG-3019/GCIG, iPocc Trial) (LBA 3). *Gynecol Oncol* 2022;166:S49-50.
[CROSSREF](#)
35. Monk BJ, Chan JK. Is intraperitoneal chemotherapy still an acceptable option in primary adjuvant chemotherapy for advanced ovarian cancer? *Ann Oncol* 2017;28:viii40-5.
[PUBMED](#) | [CROSSREF](#)
36. Harter P, Sehouli J, Vergote I, Ferron G, Reuss A, Meier W, et al. Randomized trial of cytoreductive surgery for relapsed ovarian cancer. *N Engl J Med* 2021;385:2123-31.
[PUBMED](#) | [CROSSREF](#)
37. Coleman RL, Spirtos NM, Enserro D, Herzog TJ, Sabbatini P, Armstrong DK, et al. Secondary surgical cytoreduction for recurrent ovarian cancer. *N Engl J Med* 2019;381:1929-39.
[PUBMED](#) | [CROSSREF](#)

38. Shi T, Zhu J, Feng Y, Tu D, Zhang Y, Zhang P, et al. Secondary cytoreduction followed by chemotherapy versus chemotherapy alone in platinum-sensitive relapsed ovarian cancer (SOC-1): a multicentre, open-label, randomised, phase 3 trial. *Lancet Oncol* 2021;22:439-49.
[PUBMED](#) | [CROSSREF](#)
39. Committee of Ovarian Cancer, Korean Society of Gynecologic Oncology. Practice guideline for ovarian cancer: Korean Society of Gynecologic Oncology guidelines. Seoul: Korean Society of Gynecologic Oncology; 2006.
40. Committee of Ovarian Cancer, Korean Society of Gynecologic Oncology. Practice guideline for ovarian cancer: Korean Society of Gynecologic Oncology guidelines. Seoul: Korean Society of Gynecologic Oncology; 2010.
41. Committee of Ovarian Cancer, Korean Society of Gynecologic Oncology. Practice guideline for ovarian cancer: Korean Society of Gynecologic Oncology guidelines. Seoul: Korean Society of Gynecologic Oncology; 2016.
42. Committee of Ovarian Cancer, Korean Society of Gynecologic Oncology. Practice guideline for ovarian cancer: Korean Society of Gynecologic Oncology guidelines. Seoul: Korean Society of Gynecologic Oncology; 2021.
43. Higgins JP, Sterne JA, Savovic J, Page MJ, Hróbjartsson A, Boutron I, et al. A revised tool for assessing risk of bias in randomized trials. *Cochrane Database Syst Rev* 2016;10:29-31.
44. Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, et al. Grading quality of evidence and strength of recommendations. *BMJ* 2004;328:1490.
[PUBMED](#) | [CROSSREF](#)
45. Andrews J, Guyatt G, Oxman AD, Alderson P, Dahm P, Falck-Ytter Y, et al. GRADE guidelines: 14. Going from evidence to recommendations: the significance and presentation of recommendations. *J Clin Epidemiol* 2013;66:719-25.
[PUBMED](#) | [CROSSREF](#)
46. Garzon S, Laganà AS, Casarin J, Raffaelli R, Cromi A, Franchi M, et al. Secondary and tertiary ovarian cancer recurrence: what is the best management? *Gland Surg* 2020;9:1118-29.
[PUBMED](#) | [CROSSREF](#)