

Practice Guideline



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Clinical practice guidelines for uterine corpus cancer: an update to the Korean Society of Gynecologic Oncology guidelines

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ABSTRACT

The Korean Society of Gynecologic Oncology has updated its clinical practice guidelines for endometrial cancer to incorporate advancements in recent high-quality randomized controlled trials. These guidelines address evolving treatment paradigms, and are tailored to the Korean medical context. Key updates include a strong recommendation for doxorubicin/trabectedin combination therapy in metastatic or recurrent unresectable leiomyosarcoma based on the significant survival benefits demonstrated in a randomized controlled trial. For advanced or recurrent endometrial cancer, immune checkpoint inhibitors combined with chemotherapy have received strong recommendations, owing to their proven efficacy and increased accessibility in Korea. Conditional recommendations were made for combination therapies involving durvalumab and olaparib, reflecting their potential benefits, but acknowledging regulatory and accessibility constraints. These guidelines aim to provide evidence-based, practical strategies to optimize care for patients with endometrial cancer while addressing unmet clinical needs and adapting global advancements to Korea's healthcare environment.

Keywords: Endometrial Neoplasm; Survival; Immune Checkpoint Inhibitor; PARP Inhibitors; Trabectedin; Leiomyosarcoma

INTRODUCTION

Endometrial cancer, also known as uterine corpus cancer, is a significant global health concern. In 2022, 420,368 new cases were reported worldwide, reflecting their growing impact [1]. Its incidence is rising owing to factors such as aging populations, increasing

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Conflict of Interest

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

Data Availability

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

obesity rates, and changes in reproductive patterns [2]. Advances in molecular classification and diagnostic techniques are promising for improving treatment outcomes [3]. This rising trend underscores the urgent need for updated clinical practice guidelines to optimize patient care and improve survival outcomes.

Recognizing the importance of standardized treatment protocols, the Korean Society of Gynecologic Oncology (KSGO) has been actively developing and updating practice guidelines for endometrial cancer since 2006. The previous version 5.0, published in March 2024, provided comprehensive evidence-based recommendations covering a wide range of diagnostic and therapeutic approaches [4]. However, rapid advancements in endometrial cancer research, particularly in targeted therapies, immune checkpoint inhibitors, and poly(ADP-ribose) polymerase (PARP) inhibitors, have necessitated an expedited revision of these guidelines.

The newly updated version 5.1 of the KSGO guideline incorporates the most recent high-quality evidence from randomized controlled trials (RCTs) to address critical questions in the management of endometrial cancer. This version includes the revision of key questions from version 5.0 (**Table 1**) and introduces new questions (**Table 2**) that reflect advancements in therapeutic strategies. Through this update, the KSGO aims to provide clinicians with actionable evidence-based recommendations to support decision-making in routine clinical practice.

By addressing both established and emerging therapies, updated guidelines seek to enhance the standard of care for patients with endometrial cancer in Korea. This effort reaffirms the KSGO's commitment to improving patient outcomes and advancing the field of gynecologic oncology.

Table 1. Changes in guidelines version 5.1 compared to version 5.0

#	Item	Detail	Status
KQ1	Key question	Does immune checkpoint inhibitor treatment improve survival in patients with advanced or recurrent endometrial cancer, who have failed treatment with platinum-based chemotherapy?	Maintained
	Recommendation	Immune checkpoint inhibitor-based treatment is recommended for patients with advanced or recurrent endometrial cancer who have failed treatment with platinum-based chemotherapy. (<i>Strong for</i>)	
KQ2	Key question	Does combined treatment with trastuzumab improve survival in patients with HER2/neu-positive endometrial cancer?	Maintained
	Recommendation	Chemotherapy combined with trastuzumab is recommended for patients with HER2/neu-positive advanced, recurrent serous endometrial cancer. (<i>Strong for</i>)	
KQ3	Key question	Is there a difference in the recurrence rate if lymph node dissection is omitted in the endometrial cancer staging operation for the low-risk group?	Maintained
	Recommendation	Pelvic lymph node dissection can be omitted in endometrial cancer staging operation for patients with low risk. (<i>Weak/Conditional for</i>)	
KQ4	Key question	Is there a difference in the recurrence rate between sentinel lymph node mapping and conventional lymph node dissection in early-stage endometrial cancer surgery?	Maintained
	Recommendation	Sentinel lymph node mapping can be performed during the staging operation for early-stage endometrial cancer. (<i>Weak/Conditional for</i>)	
KQ5	Key question	Does chemoradiotherapy, as a postoperative adjuvant treatment, improve the survival rate compared to chemotherapy in patients with advanced endometrial cancer?	Maintained
	Recommendation	Chemoradiotherapy or chemotherapy can be performed after surgery in patients with advanced endometrial cancer. (<i>Weak/Conditional for</i>)	
KQ6	Key question	Do immune checkpoint inhibitors plus chemotherapy improve survival in patients with advanced or first recurrent endometrial cancer?	Updated
	Recommendation	Immune checkpoint inhibitors in combination with chemotherapy as first-line therapy are recommended in patients with primary advanced or first recurrent endometrial cancer. (<i>Weak/Conditional for</i>)	

KQ, key question.

Table 2. Key questions and recommendations newly developed in guidelines version 5.1

#	Item	Detail	Status
KQ1	Key question	Does combination therapy with trabectedin improve the survival of patients with metastatic or recurrent unresectable leiomyosarcoma?	New
	Recommendation	Doxorubicin/trabectedin combination therapy is recommended as first-line treatment for patients with metastatic, recurrent, or unresectable leiomyosarcoma to improve survival outcomes. (Level of Evidence: I, Grade of Recommendation: A, Consensus)	
KQ2	Key question	Does combination therapy with immune checkpoint inhibitors and PARP inhibitors improve the survival of patients with metastatic or recurrent endometrial cancer?	New
	Recommendation	Combination therapy with immune checkpoint inhibitors and PARP inhibitors is recommended as first-line treatment for patients with advanced or recurrent endometrial cancer to improve survival outcomes. (Level of Evidence: I, Grade of Recommendation: B, Consensus)	
KQ3	Key question	Does initial treatment with immune checkpoint inhibitors improve survival in patients with advanced or recurrent endometrial cancer?	Updated
	Recommendation	Combination therapy with immune checkpoint inhibitors and chemotherapy is strongly recommended as first-line treatment for patients with advanced or recurrent endometrial cancer to improve survival outcomes. (Level of Evidence: I, Grade of Recommendation: A, Consensus)	

KQ, key question.

Author Contributions

Conceptualization: K.J.H., K.D.Y., S.D.H., K.Y.B.;
 Data curation: K.J.H.; Formal analysis: K.J.H.;
 Funding acquisition: K.Y.B.; Investigation:
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 Project administration: K.D.Y., S.D.H., K.Y.B.;
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METHODS

1. Developing the recommendations

The KSGO developed the 5.1 version of the guideline for the management of endometrial cancer based on the most recent RCTs and relevant clinical evidence. This update aimed to reflect advancements in research and clinical practice, while addressing newly emerging key questions to guide optimal patient care.

Unlike version 5.0, which included systematic reviews and meta-analyses based on comprehensive literature searches, the 5.1 guideline primarily relied on evidence from recently published RCTs. While the 5.0 guideline involved processes such as detailed literature searches, data extraction, and meta-analyses to generate recommendations, the 5.1 version focused on integrating high-quality, large-scale RCTs that directly addressed the revised and new key questions.

The updates to version 5.1 included:

1. Revising existing key questions.
2. Adding 2 new key questions to address emerging evidence in the diagnosis, treatment, and management of endometrial cancer.

2. Key question development

The KSGO Uterine Corpus Cancer Committee developed and refined the key questions through multiple discussions (**Data S1**). These key questions were formulated using the Population, Intervention, Comparison, and Outcome (PICO) framework to ensure clinical relevance and applicability. The new and revised key questions focus on addressing recent advancements in treatment modalities, including the integration of immune checkpoint inhibitors and targeted therapies.

3. Literature selection

The recommendations in version 5.1 were based on recent evidence from well-known RCTs directly addressing the updated key questions. Only peer-reviewed RCTs published in English that reported clear outcomes related to the key questions were included. Studies unrelated to endometrial cancer, case reports, observational studies, and duplicate data from overlapping patient populations were also excluded.

4. Quality of evidence

The quality of evidence supporting the recommendations of this guideline was graded using the levels defined in **Table 3**. Level I evidence represents findings from at least one large, randomized, controlled trial of good methodological quality (with low potential for bias) or meta-analyses of well-conducted randomized trials without heterogeneity. Level II evidence includes small randomized trials, large randomized trials with potential biases, or meta-analyses of such trials with demonstrated heterogeneity. Levels III, IV, and V correspond to progressively lower levels of evidence, ranging from prospective cohort studies (Level III) to retrospective studies, case reports, or expert opinions (Level V). This grading system ensures transparency and reliability in linking recommendations to the strength of underlying evidence.

5. Grades of recommendation

The grades of recommendation were assigned based on the quality of evidence, the balance of benefits and harms, and clinical relevance (**Table 3**). Grade A indicates strong evidence of efficacy with substantial clinical benefit, and such interventions are strongly recommended. Grade B signifies strong or moderate evidence of efficacy, although with limited clinical benefit, making the intervention generally recommended. Grade C is applied when there is insufficient evidence for efficacy or when benefits do not clearly outweigh risks, making the intervention optional. Grade D indicates moderate evidence against efficacy or concerns for adverse outcomes, resulting in a general recommendation against intervention. Grade E reflects strong evidence against efficacy or significant adverse outcomes, with interventions never being recommended. This grading system provides clinicians with clear evidence-based guidance for informed decision making in clinical practice.

6. Consensus process

The final recommendations were formulated and agreed upon by the KSGO Uterine Corpus Cancer Committee. Multiple rounds of discussion were conducted to resolve differences in the interpretation or application of the evidence. All recommendations were finalized during the consensus meeting of committee members.

Table 3. Level of evidence and grades of recommendation
(adapted from the Infectious Diseases Society of America—United States Public Health Service Grading System*)

Variables	Description
Level of evidence	
Level I	Evidence from at least one large, randomized, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well-conducted randomized trials without heterogeneity
Level II	Small randomized trials or large randomized trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity
Level III	Prospective cohort studies
Level IV	Retrospective cohort studies or case-control studies
Level V	Studies without a control group, case reports, expert opinions
Grades of recommendation	
Grade A	Strong evidence for efficacy with substantial clinical benefit, strongly recommended
Grade B	Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended
Grade C	Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages, optional
Grade D	Moderate evidence against efficacy or for adverse outcomes, generally not recommended
Grade E	Strong evidence against efficacy or for adverse outcomes, never recommended

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EVIDENCE

1. KQ1. Does combination therapy with trabectedin improve the survival of patients with metastatic or recurrent unresectable leiomyosarcoma?

One randomized phase 3 clinical trial was included in the analysis for this key question. The LMS-04 trial by Pautier et al. [5] in 2024 provided primary evidence to support the efficacy of trabectedin. This multicenter, randomized, open-label, phase 3 trial was conducted across 20 centers in France and compared doxorubicin monotherapy with doxorubicin plus trabectedin, followed by trabectedin maintenance therapy, in patients with metastatic or unresectable leiomyosarcoma. Randomization was stratified based on the tumor origin (uterine vs. soft tissue) and disease stage (locally advanced vs. metastatic).

Progression-free survival (PFS) & overall survival (OS)

The LMS-04 trial enrolled 150 patients, with 74 randomized to the doxorubicin–trabectedin group and 76 to the doxorubicin group. The median PFS was significantly longer in the doxorubicin-trabectedin group (12 months; 95% confidence interval [CI]=10–16) than in the doxorubicin group (6 months; 95% CI=4–7), with an adjusted hazard ratio (HR) for progression or death of 0.37 (95% CI=0.26–0.53). Similarly, the median OS was significantly improved in the doxorubicin-trabectedin group (33 months; 95% CI=26–48) compared to the doxorubicin group (24 months; 95% CI=19–31), with an adjusted HR for death of 0.65 (95% CI=0.44–0.95).

Adverse events (grade 3≤)

Adverse events of grade 3 or higher were more frequent in the doxorubicin–trabectedin group (97%) than in the doxorubicin group (56%). Common adverse events in the doxorubicin-trabectedin group included neutropenia, anemia, thrombocytopenia, and febrile neutropenia. Despite the higher toxicity, 81% of the patients in the combination group completed all 6 cycles of induction therapy. Although no treatment-related deaths were reported in the doxorubicin-trabectedin group, 1 treatment-related death occurred in the doxorubicin group, as detailed in the study.

Based on the above results, the following was recommended:

Doxorubicin/trabectedin combination therapy is recommended as first-line treatment for patients with metastatic, recurrent, or unresectable leiomyosarcoma to improve survival outcomes. (Level of Evidence: I, Grade of Recommendation: A, Consensus)

2. KQ2. Does combination therapy with immune checkpoint inhibitors and PARP inhibitors improve the survival of patients with metastatic or recurrent endometrial cancer?

One randomized phase 3 clinical trial was included in the analysis for this key question. The DUO-E trial, published by Westin et al. in 2024 [6], served as the primary evidence supporting the efficacy of combination therapy with immune checkpoint inhibitors and PARP inhibitors. This multicenter, randomized, open-label Phase 3 trial was conducted across 20 centers in France and compared doxorubicin monotherapy with doxorubicin plus durvalumab, followed by maintenance durvalumab with or without olaparib, in patients with metastatic or unresectable endometrial cancer. Randomization was stratified based on the tumor origin (uterine vs. soft tissue) and disease stage (locally advanced vs. metastatic).

PFS & OS

The DUO-E trial enrolled 718 patients, with 239 randomized to the durvalumab + olaparib arm, 238 to the durvalumab arm, and 241 to the control arm. The median PFS was significantly longer in the durvalumab + olaparib group (15.1 months; 95% CI=12.6–20.7) compared to the control group (9.6 months; 95% CI=9.0–9.9), with an adjusted hazard ratio for progression or death of 0.55 (95% CI=0.43–0.69). The trial also reported a positive trend in OS, favoring the durvalumab + olaparib arm. The HR for death was 0.59 (95% CI=0.42–0.83; $p=0.003$) compared to the control arm. However, the OS data were not fully mature at the time of the analysis. The interim results suggested a potential survival benefit with combination therapy, but further follow-up is required to confirm these findings.

Adverse events (grade 3 $\leq$)

Grade 3 $\leq$ adverse events were more frequent in the durvalumab + olaparib group (67.2%) than in the control group (56.4%). During the maintenance phase, the frequency of grade 3 or higher adverse events was notably higher in the durvalumab + olaparib group (41.1%) than that in the control group (16.6%).

The most common grade 3 or higher adverse events in the durvalumab + olaparib group included neutropenia (26.0%) and anemia (23.5%), whereas the control group reported neutropenia (23.3%) and anemia (14.4%) as the most frequent events. Serious adverse events were observed in 35.7% of patients in the durvalumab + olaparib group compared with 30.9% in the control group. Fatal adverse events occurred in 2.1% and 3.4% of patients in the durvalumab + olaparib and control groups, respectively.

Notably, rare but significant adverse events, such as pneumonitis (5.0%) and pure red cell aplasia (1.6%), were reported in the durvalumab + olaparib group, some of which led to treatment discontinuation. The rate of treatment discontinuation due to adverse events was higher in the durvalumab + olaparib group (24.4%) than that in the control group (18.6%). Most adverse events were managed with dose modifications.

Based on the above results, the following was recommended:

Combination therapy with immune checkpoint inhibitors and PARP inhibitors is recommended as first-line treatment for patients with advanced or recurrent endometrial cancer to improve survival outcomes. (Level of Evidence: I, Grade of Recommendation: B, Consensus)

3. KQ3. Does combination therapy with immune checkpoint inhibitors improve survival in patients with advanced or recurrent endometrial cancer?

Two randomized phase 3 clinical trials were included in the analysis of this key question. The NRG-GY018 trial [7] and RUBY trial [8,9] provided substantial evidence supporting the use of immune checkpoint inhibitors in combination with chemotherapy for advanced or recurrent endometrial cancer. The NRG-GY018 trial evaluated pembrolizumab combined with carboplatin and paclitaxel versus placebo plus carboplatin and paclitaxel in a global double-blind randomized trial [7]. The study enrolled 816 patients stratified according to their mismatch repair (MMR) status. The RUBY trial assessed dostarlimab in combination with carboplatin and paclitaxel compared with placebo plus carboplatin and paclitaxel in 494 patients, similarly stratified based on MMR status [8,9].

PFS & OS

In the NRG-GY018 trial, pembrolizumab plus chemotherapy demonstrated significant PFS benefits in both deficient and proficient mismatch repairs (dMMR and pMMR) subgroups [7]. Patients with dMMR tumors experienced significant PFS benefits with pembrolizumab plus chemotherapy (median PFS not reached vs. 7.6 months; HR=0.30; 95% CI=0.19–0.48) compared to the control group. In the pMMR population, the combination therapy demonstrated a median PFS of 13.1 months (95% CI=10.8–15.4) compared to 8.7 months (95% CI=7.5–10.1) in the control group (HR=0.54; 95% CI=0.41–0.71).

In the RUBY trial, dostarlimab plus chemotherapy demonstrated significant PFS improvements across the overall population and the dMMR and pMMR subgroups [8]. In the overall population, the 24-month PFS rate was 36.1% (95% CI=29.3–42.9) in the dostarlimab group compared with 18.1% (95% CI=13.0–23.9) in the placebo group, with a HR of 0.64 (95% CI=0.51–0.80; $p<0.001$). Among patients with dMMR tumors, the 24-month PFS rate was 61.4% (95% CI=46.3–73.4) in the dostarlimab group and 15.7% (95% CI=7.2–27.0) in the placebo group (HR=0.28; 95% CI=0.16–0.50; $p<0.001$). In the pMMR subgroup, the 24-month PFS rate was 28.4% (95% CI=21.2–36.0) in the dostarlimab group compared with 18.8% (95% CI=12.8–25.7) in the placebo group, with an HR of 0.76 (95% CI=0.59–0.98; $p=0.033$).

The NRG-GY018 trial did not report mature OS data at the time of publication. Although PFS results provided strong evidence for pembrolizumab efficacy, OS data were pending and are expected in future analyses [7]. In contrast, the RUBY trial provided updated OS data, demonstrating significant improvements in the dostarlimab plus chemotherapy group across the overall population and dMMR subgroup [9]. In the overall population, the 24-month OS rate was 70.1% (95% CI=63.8–75.5) in the dostarlimab group compared with 54.3% (95% CI=47.8–60.3) in the placebo group, with a HR of 0.69 (95% CI=0.54–0.89; $p=0.002$). Among patients with dMMR tumors, the 24-month OS rate was 82.8% (95% CI=69.5–90.7) in the dostarlimab group and 57.5% (95% CI=44.4–68.6) in the placebo group (HR=0.32; 95% CI=0.17–0.63; nominal $p=0.0002$). In the pMMR subgroup, the OS benefit was less pronounced, with a 24-month OS rate of 66.5% (95% CI=59.2–72.8) in the dostarlimab group compared with 53.2% (95% CI=45.6–60.2) in the placebo group (HR=0.79; 95% CI=0.60–1.04; nominal $p=0.0493$).

Adverse events (grade 3≤)

In the NRG-GY018 trial, the incidence of grade 3 or higher adverse events was higher in the pembrolizumab plus chemotherapy group than in the placebo plus chemotherapy group in both the dMMR and pMMR cohorts [7]. In the dMMR cohort, 63.3% of patients in the pembrolizumab group experienced grade 3 or higher adverse events compared to 47.2% in the placebo group. Common grade 3 or higher adverse events included anemia and neutropenia. Anemia occurred in 19.3% of patients in the pembrolizumab group compared to 10.4% in the placebo group, while neutropenia was observed at a lower rate in the pembrolizumab group (11.9%) than in the placebo group (17.0%). This unexpected trend did not appear to affect the overall safety profile of the treatment.

In the RUBY trial, the incidence of grade 3 or higher adverse events was also higher in the dostarlimab plus chemotherapy group than in the placebo group [8,9]. Among the overall population, 72.2% of patients in the dostarlimab group experienced grade 3 or higher adverse events compared with 60.2% in the placebo group. Anemia was reported in 14.9% of patients in the dostarlimab group compared to 16.7% in the placebo group, while neutropenia occurred in 9.5% of patients in the dostarlimab group compared to 9.3% in the placebo group.

Both trials showed that the addition of immune checkpoint inhibitors to chemotherapy increased the incidence of grade 3 or higher adverse events. However, these events were generally manageable with standard supportive care and no unexpected safety signals were identified.

Based on the above results, the following was recommended:

Combination therapy with immune checkpoint inhibitors and chemotherapy is strongly recommended as first-line treatment for patients with advanced or recurrent endometrial cancer to improve survival outcomes. (Level of Evidence: I, Grade of Recommendation: A, Consensus)

DISCUSSION

The updated version 5.1 of the KSGO guidelines for the management of endometrial cancer reflects significant advancements in clinical evidence and demonstrates an adaptive approach to guideline development tailored to current needs. Unlike the previous version 5.0, which incorporated systematic reviews and meta-analyses as part of its development process, version 5.1 was based primarily on high-quality RCTs. This methodological shift allowed the guidelines to incorporate the most current and robust clinical data, ensuring their relevance in a rapidly evolving therapeutic landscape. Moreover, the recommendations were carefully tailored to align with Korea's unique medical environment, considering factors such as insurance coverage and treatment accessibility to enhance feasibility.

One of the notable updates in version 5.1 is the inclusion of recommendations for trabectedin in the treatment of metastatic or recurrent unresectable leiomyosarcoma. Based on evidence from the LMS-04 trial, doxorubicin/trabectedin combination therapy demonstrated significant improvements in PFS and OS compared to doxorubicin monotherapy [5]. Although combination therapy was associated with a higher frequency of adverse events, these were manageable with supportive care, and the treatment showed substantial clinical benefits. Given its demonstrated efficacy and approval for use as a first-line therapy in Korea under specific indications, this recommendation received strong grade A. The alignment between clinical evidence and practical applicability underscores the importance of integrating this therapy into routine practice for eligible patients.

Another major update is the introduction of recommendations for combination therapies involving immune checkpoint inhibitors and PARP inhibitors for advanced or recurrent endometrial cancer. The DUO-E trial provided high-quality evidence that combining durvalumab and olaparib significantly improved PFS with early indications of potential OS benefits [6]. While OS data remain immature, the robust results from this large-scale trial qualify as level I evidence. However, this therapy has received only partial Food and Drug Administration approval for use in dMMR populations and is not yet available in Korea [10]. Consequently, the guideline assigns a grade B recommendation, reflecting the promising efficacy of this combination, while acknowledging the current regulatory and accessibility limitations. This recommendation highlights the potential of biomarker-driven therapies to optimize patient outcomes, while emphasizing the need for further validation and expanded accessibility.

Significant revisions have been made to the recommendations for immune checkpoint inhibitors in combination with chemotherapy for advanced or recurrent endometrial cancer.

While version 5.0 provided only a weak or conditional recommendation due to limited accessibility in Korea, the updated guidelines strongly recommend (Grade A) pembrolizumab or dostarlimab combined with platinum-based chemotherapy. This shift is supported by new evidence from pivotal RCTs, including the NRG-GY018 and RUBY trials, which demonstrated substantial improvements in both PFS and OS across both dMMR and pMMR populations [7-9]. The increased availability of these therapies in Korea further supports this recommendation, making them central to modern endometrial cancer treatment.

The updated guidelines underscore KSGO's commitment to integrating emerging global evidence with Korea's healthcare realities. While recommendations are grounded in high-quality RCTs, their strength was carefully adjusted to reflect domestic factors, such as insurance policies and treatment reimbursement. For instance, the strong recommendation for trabectedin acknowledges its demonstrated efficacy and current approval status in Korea, whereas the general recommendation for durvalumab and olaparib reflects limited domestic accessibility despite robust evidence.

By incorporating these updates, version 5.1 addresses critical unmet needs in the management of advanced and recurrent endometrial cancer. The emphasis on evidence-based actionable recommendations ensures that the guidelines remain practical for clinicians while advancing the standard of care. Moving forward, the KSGO remains committed to continuous updates that reflect the latest scientific advancements and adapts to the evolving needs of Korea's healthcare system.

SUPPLEMENTARY MATERIAL

Data S1

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

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