J Gynecol Oncol. 2025 Mar;36(2):e96
https://doi.org/10.3802/jgo.2025.36.e96
pISSN 2005-0380·eISSN 2005-0399

JOURNAL OF GYNECOLOGIC ONCOLOGY

Practice Guideline

Practice guideline for management of endometrial cancer in Thailand: a Thai Gynecologic Cancer Society consensus statement

Nicha Assavapokee,[1] **Uraiwan Khomphaiboonkij**,[2] **Siriwan Tangjitgamol**,[3] **Surapan Khunamornpong**,[4] **Tip Pongsuvareeyakul**,[4] **Saranya Chanpanitkitchot**,[5] **Arb-aroon Lertkhachonsuk**,[6] **on behalf of the Thai Gynecologic Cancer Society**

[1]Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
[2]Department of Gynecologic Oncology, National Cancer Institute, Bangkok, Thailand
[3]Women's Health Center, MedPark Hospital, Bangkok, Thailand
[4]Department of Pathology, Chiang Mai Hospital, Faculty of Medicine, Chiang Mai University, Chiangmai, Thailand
[5]Nopparat Rajathanee Hospital, Bangkok, Thailand
[6]Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Faculty of Medicine Ramathibodi, Bangkok, Thailand

Received: Jan 13, 2025
Revised: Feb 7, 2025
Accepted: Feb 26, 2025
Published online: Mar 12, 2025

Correspondence to
Siriwan Tangjitgamol
Women's Health Center, MedPark Hospital, 3333 Rama IV Rd, Khlong Toei, Bangkok 10110, Thailand.
Email: siriwanonco@yahoo.com

ORCID iDs
Nicha Assavapokee
https://orcid.org/0009-0006-5553-1783
Uraiwan Khomphaiboonkij
https://orcid.org/0000-0003-3758-6706
Siriwan Tangjitgamol
https://orcid.org/0000-0001-5367-8884
Surapan Khunamornpong
https://orcid.org/0000-0002-5442-0188
Tip Pongsuvareeyakul
https://orcid.org/0000-0002-2922-7773
Saranya Chanpanitkitchot
https://orcid.org/0000-0003-3675-8262
Arb-aroon Lertkhachonsuk
https://orcid.org/0000-0003-3283-5064

ABSTRACT

The Thai Gynecologic Cancer Society (TGCS) continues its efforts to elevate the standard of practice of gynecologic oncologists across all regions of Thailand. A key initiative involves collaborating with the Royal Thai College of Obstetricians and Gynaecologists and the National Cancer Institute, Thailand to regularly update and release clinical practice guidelines (CPGs) for gynecologic cancer. The TGCS released the first CPG for endometrial cancer (EMC) in 2011. Following significant advancements in disease understanding and the major revision of EMC staging by the International Federation of Gynecology and Obstetrics in 2023, national experts collaborated to update the guideline for EMC. The key components of the CPG for EMC covered screening, diagnostic indications and methods, primary treatment including surgical approaches and procedures, pathological processes, adjuvant therapies, and the management of recurrent and advanced diseases through medical or surgical means. The guideline was based on scientific evidence, recommendations from international organizations, and the unique healthcare context of Thailand. The final version reflects a consensus reached through extensive discussions among TGCS members. To share our work with international organizations and healthcare professionals, an English version of the CPG was developed. While it mirrors the content of the Thai version, it differs in length and level of detail. The English version additionally included the level of evidence and a recommendation summary for each section, reflecting common domestic practices, available resources, and coverage under health reimbursement systems.

Keywords: Consensus; Endometrial Carcinoma; Practice Guideline

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

Author Contributions
Conceptualization: T.S.; Data curation: A.N., K.U., K.S., P.T., T.S.; Supervision: T.S.; Validation: A.N., K.S., P.T., C.S., L.A.A., T.S.; Visualization: A.N., K.U., P.T., C.S., L.A.A., T.S.; Writing - original draft: A.N., K.U., K.S., P.T., T.S.; Writing - review & editing: A.N., K.U., K.S., P.T., C.S., L.A.A., T.S.

INTRODUCTION

In Thailand, the incidence and mortality rates of endometrial cancer (EMC) have been increasing in recent years, ranking behind breast and cervical cancer. According to 2022 global cancer statistics from the 2024 GLOBOCAN estimates, the age-standardized incidence rate of EMC in Thailand was approximately 6.9 per 100,000 women, accounting for 4,248 new cases annually. The mortality rate was 1.9 per 100,000 women, corresponding to 1,301 deaths each year [1]. On the other hand, data collected by the National Cancer Institute (NCI) of Thailand from the hospital cancer registry in 2022 identified EMC as the third most common cancer among Thai women (5.2%), following breast (41.7%) and cervical (13.1%) cancers [2].

Unlike cervical cancer screening, which is mainly age-based, EMC screening is based on individual medical history and risk factors. Diagnosis is typically performed through an office procedure, such as an endometrial biopsy. Hysterectomy remains the cornerstone of primary treatment, with various surgical approaches depending on the hospital setting.

Surgico-pathological findings have been fundamental to staging by the International Federation of Gynecology and Obstetrics (FIGO) since 1988, with significant revisions in 2009 and again in 2023. The 2023 update presents substantial challenges for clinicians, including gynecologists, gynecologic oncologists, pathologists, and medical oncologists, particularly in incorporating molecular studies. This integration plays a critical role in the staging of early-stage disease, influencing prognosis, and guiding for adjuvant treatment. Additionally, the growing importance of targeted therapies and immunotherapies in managing recurrent or advanced disease further highlights the importance of these molecular tests. Molecular testing requires increased awareness among laboratory professionals for preparation and results interpretation, clinicians, and healthcare budget managers regarding the cost-effectiveness within the Thai healthcare system.

In Thailand, there are 3 health care coverage schemes aiming to ensure that all Thai citizens have access to healthcare services, albeit with different levels of coverage and benefits.

1) The Universal Coverage Scheme, also known as the '30-Baht Scheme,' provides healthcare coverage for all Thai citizens not covered by other government insurance programs. Funded through general taxation, the scheme is managed by the National Health Security Office.

2) Social Security Scheme, under the responsibility of Social Security Office, provides healthcare coverage for private sector employees. It is funded through contributions from employers, employees, and the government. The scheme covers medical services at designated hospitals, including outpatient and inpatient healthcare for sickness, maternity, disability, and other benefits.

3) Civil Servant Medical Benefit Scheme is designed for government employees, their dependents (parents, spouses, and children), and retirees. Fully funded by the government, this scheme offers more comprehensive healthcare coverage than other schemes, including a wider range of reimbursement for medical expenses.

This guideline summarizes the available evidence on pathology, molecular testing, clinical management recommendations for EMC, and current reimbursement policy in Thailand.

https://doi.org/10.3802/jgo.2025.36.e96

JOURNAL OF GYNECOLOGIC ONCOLOGY

METHODOLOGY

This CPG was developed using a standardized methodology for creating CPGs. Current evidence-based data were collected by national experts in gynecologic oncology and pathology, focusing on contentious issues and practical applications. The guideline covered all aspects of EMC management, including screening, diagnosis, and treatment. Detailed pathological studies were included, emphasizing their role in staging and treatment decisions. The staging system follows the 2023 FIGO guidelines, with additional remarks to fit with the situation in Thailand.

Following the TGCS working group's preparation of the draft in Thai, extensive discussions were held among committee members. The revised version was then submitted for review and endorsement by the Professional Standards Subcommittee of the Royal Thai College of Obstetricians and Gynaecologists (RTCOG) [3]. With an addition of supplement, which included expanded information on radiation therapy and palliative care, was published electronically by the NCI [4].

The English version presented here was based on the RTCOG-endorsed Thai version and was organized into 6 sections: Screening, Diagnosis, Primary treatment, Staging of Disease, Molecular Testing, Adjuvant treatment, and Treatment for metastasis and recurrence. Summarized text boxes under each section were added to enhance clarity and utility, reflecting the Thai reimbursement scheme to provide an international perspective. The level of evidence for each recommendation was categorized into 1 of 3 levels, based on the quality and quantity of evidence, as outlined in **Table 1**: A (good and consistent evidence), B (limited or inconsistent evidence), or C (consensus and opinion) [5].

CLINICAL CONSIDERATIONS AND RECOMMENDATIONS

1. Screening

Since most women with EMC present with abnormal vaginal bleeding, the disease is often diagnosed at an early stage, leading to a 5-year survival rate of 74–91 [6]. As a result, screening may not impact the mortality rates. Currently, there is no evidence to support or recommend routine screening for EMC in women with no or moderate risk factors who are asymptomatic, as it is not considered cost-effective [7]. In Thailand, the gynecologic cancer screening is recommended and covered by all health schemes for only cervical cancer, but not for EMC among women without risk factors.

High-risk women, defined by a history of genetic mutations, may be offered annual screening with transvaginal ultrasonography (TVS) and endometrial biopsy starting at ages 30–35 or sooner before the age of onset of related cancer in a family member [8]. Familial conditions with their lifetime risk of EMC are, for examples:

- Lynch syndrome. Women with mismatch repair (MMR) gene mutations have various lifetime risks of developing EMC depending on the specific gene mutation: 20%–54% for MLH1, 21%–49% for MSH2, 16%–71% for MSH6, 15% for PMS2, and 21%–57% for EPCAM.
- Cowden syndrome. Women with PTEN gene mutations have a 19%–28% risk of developing EMC by age of 70 years.
- Hereditary Breast and Ovarian Cancer Syndrome. Women with BRCA gene mutations (BRCA1/2) have a 2- to 3-fold increased risk of EMC.

https://doi.org/10.3802/jgo.2025.36.e96

Table 1. Summary of Thai recommendations for the screening, diagnosis and treatment of EMC

Recommendations	LoR
Recommendation 1: screening	
1a. Routine screening for EMC using cervical cytology, TVS, or endometrial biopsy is not recommended for the general population without abnormal vaginal bleeding.	A
1b. Annual screening with TVS and endometrial biopsy should be offered to women with a history of genetic mutations, starting at ages 30–35, following counseling on the risks, benefits, and limitations.	A
Recommendation 2: diagnosis	
2a. Endometrial pathology evaluation is warranted when clinically indicated.	A
2b. For suspected or confirmed EMC, a comprehensive preoperative evaluation is essential.	A
2c. Additional imaging may be considered for patients at high risk of extra-pelvic disease.	A
Recommendation 3: primary treatment	
3a. Total hysterectomy with bilateral salpingo-oophorectomy is the standard surgical procedure. Minimally invasive surgery should be considered for uterine-confined disease.	A
3b. Lymphadenectomy is recommended for patients with high-risk clinicopathological factors.	A
3c. SLNE can be considered as a strategy for nodal assessment in cases of low-risk/intermediate-risk EMC in experienced centers.	A
3d. Ovarian preservation can be considered in premenopausal women with early-stage I low grade-endometrioid cancer, normal-appearing ovaries, and no family history of genetic mutations. Salpingectomy is recommended.	B
3e. Full surgical staging including omentectomy, peritoneal biopsies and pelvic/para-aortic lymph node staging should be considered in high-risk endometrial carcinoma histology.	A
Recommendation 4: staging of disease and molecular testing	
4a. The histological type, FIGO grade, depth of myometrial invasion, and number of LVSI should be documented for all EMC pathology specimens.	A
4b. IHC for p53, MMR proteins, HER2 and hormonal receptors should be considered.	A
4c. Testing for *POLE* mutations is recommended particularly for stage I–II EMC.	B
Recommendation 5: adjuvant treatment	
5a. Adjuvant treatment after surgery is generally not indicated for low-risk EMC.	A
5b. Adjuvant VBT is recommended for intermediate-risk EMC to reduce vaginal recurrence.	A
5c Omission of adjuvant VBT may be considered in intermediate-risk EMC, particularly in patients under 60 years of age.	A
5d. In high-intermediate-risk EMC patients with negative LVSI and who have undergone lymphadenectomy, VBT may be considered.	A
5e. In high-intermediate-risk EMC patients with LVSI or who did not undergo lymphadenectomy, EBPRT is recommended.	A
5f. Individualized chemotherapy may be considered for grade 3 and/or substantial LVSI.	A
5g. Adjuvant chemotherapy (carboplatin with paclitaxel) with radiation therapy is recommended for high-risk patients.	A
5h. Integration of immunotherapy should be considered for dMMR/MSI-H tumors in advanced and metastatic EMC.	A
5i. Trastuzumab should be considered as part of first-line treatment in patients with HER2-positive advanced or metastatic EMC.	B
Recommendation 6: treatment for metastasis and recurrence	
6a. Treatment for advanced or recurrent EMC depends on tumor location, prior treatments, disease-free interval, and patient condition.	A
6b. Pelvic radiation with or without brachytherapy should be considered in patients who have not received prior radiation therapy or have only undergone brachytherapy.	A
6c. Systemic treatment should also be considered, starting with first-line platinum-based chemotherapy.	A
6d. For second-line treatment, doxorubicin and weekly paclitaxel have shown considerable activity.	B
6e. Hormonal therapy can be considered as a first-line option for patients with low-grade endometrioid cancer and small tumor volume.	B
6f. In patients with MSI-H/dMMR EMC who have progressed after platinum-based therapy, single-agent immune checkpoint inhibitors may be considered.	B

dMMR, mismatch repair-deficient; EBPRT, external beam radiation therapy; EMC, endometrial cancer; FIGO, International Federation of Gynecology and Obstetrics; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; LoR, level of recommendation; LVSI, lymphovascular space invasion; MMR, mismatch repair; MSI-H, microsatellite instability hypermutated; SLNE, sentinel lymph node excision; TVS, transvaginal ultrasonography; VBT, vaginal brachytherapy.

Of note, women with a strong likelihood of genetic abnormalities, especially those with a family history of Lynch syndrome in first- or second-degree relatives, are also considered as having high-risk.

Approximately 50% of women with Lynch syndrome may develop EMC before colorectal cancer, with an average interval of 11 years. Furthermore, 25% are at risk of developing colorectal cancer within 20 years following an EMC diagnosis [9]. Given these risks, various medical associations recommend specific screening guidelines for both endometrial and colorectal cancers in women with Lynch syndrome [10]. Physicians should adopt an individualized approach based on the patient's history and risk factors. The advice for high-risk women includes regular surveillance, immediate consultation for any abnormal symptoms, and discussing the option

of prophylactic hysterectomy with bilateral salpingo-oophorectomy after age of 40 or upon completion of childbearing as a preventive measure [11].

- Routine screening for endometrial cancer is not recommended for the general population and are not covered by any health insurance scheme. However, individuals are advised to seek medical attention if they experience persistent intermenstrual bleeding or irregular or heavy menstrual cycles.
- Women with history of genetic mutations should be offered annual screening with TVS and endometrial biopsy starting at age of 30–35 years after counseling about the risks, benefits and limitations of screening.

2. Diagnosis

Abnormal uterine bleeding is the most common symptom of EMC, occurring in approximately 90% of cases. It is crucial for healthcare providers to routinely ask about any unusual bleeding patterns or postmenopausal bleeding during health assessments. In premenopausal women, especially those aged 45 and older, the new onset of abnormal uterine bleeding—such as heavy or irregular bleeding—should prompt further investigation. For women younger than 45, an evaluation is advised if known risk factors are present [12].

TVS is generally the first step to assess uterine features particularly endometrium of a woman with abnormal uterine bleeding. In postmenopausal women whose endometrial thickness exceeds 4 millimeters, an endometrial biopsy should be performed during the same visit. The sensitivity of detecting endometrial pathology is 96%–98%, with a specificity of 42%–51% and a negative predictive value of 99%. Previous study suggested that an endometrial thickness below 4 millimeters carries a very low risk (0.62%) of EM [13].

An office endometrial biopsy is usually sufficient for diagnosis. However, clinicians should be aware of the 10% false-negative rate [14]. Therefore, a negative biopsy in a symptomatic patient should be followed by uterine curettage. Hysteroscopy can be valuable in identifying endometrial lesions, such as polyps, particularly in patients with persistent or recurrent bleeding. However, the routine use of hysteroscopy as an initial diagnostic tool is not cost-effective [15], and is best reserved for cases where initial evaluations, such as biopsy or ultrasound, fail to clarify symptoms or findings. All procedures for obtaining endometrial tissues including sampling biopsy, curettage, and hysteroscopy can be reimbursed by all health coverage program.

After a primary diagnosis from tissue sampling, the preoperative evaluation should begin with a thorough review of the patient's medical history, followed by a complete physical examination. Laboratory tests are crucial and should include a complete blood count and liver as well as renal function tests. Additionally, consideration should be given to the genetic evaluation of the tumor and assessment for inherited cancer risk. If clinically indicated, various imaging studies should be performed to assess the extent of cancer spread, which will aid in treatment planning. These imaging modalities may include magnetic resonance imaging (MRI), computed tomography (CT), and positron emission tomography (PET) [16]. MRI of the abdomen and pelvis is currently the most accurate method for assessing tumor invasion and disease spread, having 83% accuracy for evaluating the depth of myometrial invasion and 89% positive predictive value for detecting cancer spread to cervix [17]. CT scans of the chest, abdomen, and pelvis are indicated when there is suspicion of disease

https://doi.org/10.3802/jgo.2025.36.e96

extending beyond the pelvis, such as to the liver, lungs, or abdominal cavity. Alternatively, fluorodeoxyglucose positron emission tomography (FDG-PET) offers excellent specificity and positive predictive value for identifying cancer spread and is especially valuable in cases where recurrence is suspected. Unfortunately, the use of FDG-PET/CT scans in Thailand is limited due to its high cost and a lack of reimbursement. Under the national healthcare schemes, only CT or MRI scans are covered, while FDG-PET is not.

Measuring serum CA125 levels may be particularly useful, especially in suspected advanced cases, as elevated CA125 levels can help monitor treatment response and detect recurrence [18].

- Women who exhibit signs and symptoms suggestive of endometrial cancer should undergo TVS and office endometrial sampling for pathology. If the biopsy results are inconclusive, subsequent curettage may be performed.
- Additional imaging i.e., CT, MRI, and FDG-PET scans may be considered for patients at high risk of extra-pelvic disease. However, only CT or MRI scans but not FDG-PET scans are included in any government reimbursement schemes.
- Tissue biopsy, whether by endometrial sampling, curettage, or hysteroscopy are covered under all health insurance schemes.

3. Primary treatment

Hysterectomy with bilateral salpingo-oophorectomy is the standard surgical procedure for EMC. In cases of uterine-confined disease, minimally invasive surgery should be considered to enhance patient recovery and reduce postoperative complications. In cases of advanced or metastatic EMC, or when a patient has medical comorbidities that make them inoperable, a multi-disciplinary treatment approach involving gynecologic oncologists, radiation oncologists, and medical oncologists should be considered.

Surgical staging via laparotomy has become less common due to advancements in minimally invasive techniques. Laparoscopic hysterectomy is now the recommended standard surgical approach [19], offering benefits such as fewer complications, improved patient satisfaction, less postoperative pain, and shorter hospital stays, despite potentially longer operative times [20]. Robotic-assisted laparoscopic surgery can facilitate procedures for challenging cases, particularly in obese patients, and yields comparable outcomes with shorter operation times [21]. Vaginal hysterectomy may be suitable for older or obese patients with comorbidities, although it limits the ability to assess abdominal lesions or to perform lymphadenectomy. The choice of surgical method ultimately depends on several factors, such as disease characteristics, the patient's overall condition, surgical expertise, and hospital resources.

Lymphadenectomy does not provide additional benefits in terms of recurrence and survival for patients with stage I EMC [22]. Despite the lack of randomized comparative data for patients at high risk of recurrence, lymphadenectomy was recommended for high-intermediate and high-risk patients, including those with aggressive histologies (e.g., grade 3 endometrioid carcinoma, carcinosarcoma, serous carcinoma, clear cell carcinoma, and undifferentiated carcinoma), deep myometrial invasion (≥50%), tumor size >2 cm, or cancer that has spread to the cervix or other organs[23].

In cases where there is no evidence of enlarged pelvic lymph nodes, sentinel lymph node excision (SLNE) is strongly recommended as it is less invasive and highly effective, with a

https://doi.org/10.3802/jgo.2025.36.e96

sensitivity of up to 91% [24,25]. A study conducted at a Thai university hospital demonstrated a high detection rate of 91.2%, with an accuracy of 97.6% with SLNE [26]. However, achieving these results requires surgical expertise and experience. Recurrence rates and survival outcomes for patients undergoing SLNE are comparable to those of patients who have undergone a complete lymphadenectomy [27]. Of note, it is crucial that the sentinel lymph node is thoroughly assessed, with a comprehensive pathological examination (ultrastaging). This examination should include slicing the lymph nodes transversely every 2 mm for hematoxylin and eosin (H&E) staining along with immunohistochemistry (IHC) of cytokeratin if no cancer cells are detected in the H&E-stained sections [28].

The incidence of occult ovarian metastasis in normal-appearing ovaries is low, ranging from 0.4% to 0.8% [29]. A retrospective study with a 16-year median follow-up suggests that ovarian preservation in premenopausal patients with stage IA to IB EMC is safe and not associated with increased cancer-related mortality [30]. Systematic reviews and meta-analyses also confirm that ovarian preservation does not adversely affect survival [31]. However, in patients with grade 2–3 FIGO stage I endometrioid carcinoma, ovarian preservation is rarely practiced, despite no clear detrimental effect on overall survival (OS) [32].

Uterine serous carcinomas, clear cell carcinomas, carcinosarcomas, and undifferentiated carcinomas are aggressive histologic variants [33], with a higher incidence of extrauterine disease at diagnosis [34]. Although serous EMCs are often diagnosed at an earlier stage, they still carry a higher risk of recurrence and poorer prognosis compared to the endometrioid type at the same stage [35]. Carcinosarcomas, which are considered high-grade EMCs, are particularly aggressive, with a 5-year survival rate of only 25%–30% [36]. A multimodality approach is generally advised for these aggressive histologic tumor types. The primary treatment includes total hysterectomy with bilateral salpingo-oophorectomy, comprehensive surgical staging, and maximal tumor debulking with any gross lesions [37].

- Hysterectomy with bilateral salpingo-oophorectomy is the standard surgical procedure for endometrial cancer. Additional omentectomy, peritoneal biopsy, and pelvic/para-aortic lymph node resection should be performed for those with high-risk clinicopathological features.
- Minimally invasive surgery should be considered to reduce postoperative complication and to enhance patient recovery.
- SLNE can be considered in low- or intermediate-risk cancer in experienced center.
- Ovarian preservation can be considered in pre-menopausal women with no family history of genetic mutations, early-stage, low-grade endometrial cancer, and with normal appearance of ovaries.
- All health coverage schemes include exploratory surgical staging. Laparoscopic or robotic approaches require surcharge covered by the women themselves.

4. Staging of disease, immunohistochemical study and molecular testing

In 2023, FIGO revised the staging system for EMC to include important histopathological features, such as tumor type and grade, lymphovascular space invasion (LVSI), site of lymph node involvement as well as size of metastatic lesions, and molecular features [19].

The molecular classification of EMC, as identified by The Cancer Genome Atlas [38], has established 4 distinct molecular subtypes that significantly extend beyond traditional

https://doi.org/10.3802/jgo.2025.36.e96

histological classifications and are linked to diverse prognoses [39]. These 4 subtypes include: 1) *POLE* ultramutated, 2) microsatellite instability hypermutated (MSI-H or MMR-deficient [dMMR]), 3) copy number high (*TP53*-mutated/p53-abnormal), and 4) copy number low (no specific molecular profile). This critical stratification not only enhances the accuracy of predicting clinical outcomes but also profoundly influences treatment strategies.

The expression of molecular features highlights the need for personalized therapy. Key testing for MMR status or microsatellite instability (MSI) serves a dual purpose. It serves as a screening test for Lynch syndrome while simultaneously identifying patients with metastatic disease who could benefit from immune checkpoint inhibitors. The addition of adjuvant chemotherapy has demonstrated improved outcomes for patients with *TP53*-mutated EMC. In contrast, *POLE*-mutated cancers may present an opportunity for treatment de-escalation [40,41]. The presence of human epidermal growth factor receptor 2 (HER2) amplification in 20%–40% of non-endometrioid EMCs underscores the rationale for employing HER2-targeted therapies in combination with chemotherapy, especially for advanced and recurrent serous EMC [42,43].

In Thailand, this guideline is informed by experts from the TGCS, working in collaboration with gynecologic pathologists to ensure relevance to local practices. Key considerations include laboratory capabilities, cost-effectiveness, and clinical applicability. IHC for p53 and MMR proteins is essential for all newly diagnosed patients, regardless of histological type, to assess molecular profiles and tailor treatment approaches. Testing for *POLE* mutations is specifically recommended for patients with stage I–II EMC, as it may signify a favorable prognosis and support the potential for treatment de-escalation, particularly in endometrioid carcinoma with abnormal p53 IHC result. Hormonal receptor testing—including estrogen, progesterone, and HER2 —should be considered as they may aid in the selection of the appropriate therapeutic interventions. This is especially important in advanced-stage cases for prognostic and therapeutic purposes. Given the availability and quality of pathological tissue blocks, these tests should ideally be performed at the time of primary diagnosis. In addition, MMR testing should be prioritized in cases where Lynch syndrome is suspected, ensuring that appropriate management strategies are implemented.

Most laboratories in Thailand can perform IHC studies; however, these are only covered under the Civil Servant Medical Benefit Program. Unfortunately, only a few laboratories offer molecular testing services, and these are not covered by any health insurance schemes.

- The pathology report of endometrial cancer must include at least the histological type, FIGO grade, sites of primary and metastatic lesions, depth of myometrial invasion, and number of LVSI.
- Molecular testing for *POLE* mutations, available only in some laboratories and not reimbursable from any health benefit scheme, is particularly recommended for stage I-II endometrial cancer.
- IHC for p53, MMR proteins, and hormonal receptors status should also be performed at the time of diagnosis especially in advanced diseases.
- Immunohistochemical studies are generally provided at no cost for only patients under the Civil Servant Medical Benefit program whereas molecular studies are not covered by any health coverage schemes.

https://doi.org/10.3802/jgo.2025.36.e96

5. Adjuvant treatment

Adjuvant treatment recommendations should be tailored based on the stage of the disease, pathological findings, and molecular characteristics of the tumor. These factors collectively guide the decision-making process to optimize patient outcomes and ensure that therapies are appropriately matched to the individual risk profile. The inclusion of molecular features, such as *POLE* mutations, p53 status, and MMR deficiencies, plays an increasingly critical role in refining treatment strategies.

Low-risk group (stage IA with low grade [G1–2] endometrioid histology)

In cases of low-risk EMC, adjuvant treatment after surgery is generally not required. Studies have shown that patients in this category have a 5-year survival rate of up to 96% [44], with a 14-year recurrence rate as low as 6.3% [45]. The adjuvant therapy has not demonstrated a statistically significant benefit in improving survival for these patients. Current research also highlights the prognostic significance of molecular factors, particularly *POLE* mutations, which are associated with favorable outcomes, regardless of other pathological factors [46]. Therefore, adjuvant therapy is not necessary for stage I and II with *POLE* mutations. The analysis from the PORTEC-3 trial indicated that patients with advanced-stage or non-endometrioid histology with *POLE* mutations demonstrated an excellent prognosis, which appeared to be independent of the use of adjuvant treatment [47]. However, there is limited data regarding the safety of omitting adjuvant treatment in this group of patients.

Although IHC studies are widely available in Thailand, *POLE* mutation testing remains limited and cannot be reimbursed by any health coverage programs. In situations where molecular testing is unavailable, clinicians should rely on histologic features. For example, in the absence of *POLE* testing, adjuvant therapy for early-stage disease should be considered based on surgico-histopathologic risk factors, such as histopathologic type, grade, depth of myometrial invasion, and the extent of LVSI.

Intermediate-risk group (stage I aggressive histology or TP53 mutation without myometrial invasion, and stage IB or stage II with low-grade endometrioid histology)

Studies have demonstrated that external beam pelvic radiation therapy (EBPRT) as adjuvant therapy significantly reduces locoregional recurrence [48,49]. Subsequent research has shown that vaginal brachytherapy (VBT) alone can effectively reduce locoregional recurrence rates with fewer side effects compared to pelvic radiation, without any significant difference in OS [50]. As a result, VBT alone is recommended as adjuvant treatment for intermediate-risk patients, particularly when aiming to minimize side effects from EBPRT [51]. In younger patients under 60 years of age, where the risk of recurrence is lower, omitting adjuvant therapy may be considered [52].

For patients with non-endometrioid histologies and/or *TP53* mutations without myometrial invasion or cancer limited to polyps, studies have shown that VBT following surgery results in low recurrence rates. These patients also demonstrate high survival rates regardless of chemotherapy use [53]. Nonetheless, insufficient data exists to provide a conclusive recommendation for adjuvant treatment. Decisions regarding the use of adjuvant therapy or the option to omit it should be made on an individual basis within a multidisciplinary team setting [54].

https://doi.org/10.3802/jgo.2025.36.e96

High-intermediate-risk group (stage I with substantial LVSI, stage IB with grade 3 endometrioid or stage II)

The Norwegian trial randomized stage I EMC patients to receive either VBT alone or EBPRT with a VBT boost. Results indicated that EBPRT significantly reduced the risk of non-vaginal pelvic recurrences, but improved OS was observed only patients with FIGO stage IB grade 3 disease [55]. Similarly, one trial from the Gynecologic Oncology Group found that VBT combined with chemotherapy was not superior to EBPRT in terms of recurrence-free survival (RFS) or OS but led to greater acute toxicity and an increased rate of lymph node recurrence [56]. Consequently, for patients with FIGO stage IB grade 3 or FIGO stage II endometrioid carcinoma, only EBPRT is recommended. Although a VBT boost is commonly administered after EBPRT in patients with uterine risk factors, there are currently no randomized controlled trials supporting the routine addition of VBT to EBPRT [57].

The extent of LVSI is an important prognostic feature. The pooled analysis of the PORTEC-1 and PORTEC-2 trials emphasized substantial LVSI as the strongest independent prognostic factor for pelvic regional recurrence, distant metastasis, and OS [58]. Hence, the patients in the high intermediate-risk group, who have undergone complete lymphadenectomy and are LVSI negative may be considered for VBT as an adjuvant treatment. In contrast, adjuvant EBPRT should be prioritized for stage II disease or in presence of substantial LVSI especially when surgical nodal staging has not been conducted, due to its effectiveness in significantly reducing pelvic recurrence rates, despite not impacting OS. Additionally, chemotherapy may be warranted for patients with grade 3 tumors and/or substantial LVSI to mitigate the risk of recurrence in pelvic and para-aortic lymph nodes [59,60]. The exception is in patients with MMR-deficient tumors, who do not derive any benefit from chemotherapy [47].

High-risk group (all stages of any myometrial invasion with TP53 mutations, high risk histology and stage III–IV)

Adjuvant chemotherapy, carboplatin with paclitaxel, in conjunction with radiation therapy is recommended for high-risk patients, as it significantly enhances both 5-year progression-free survival (PFS) and OS rates compared to radiation therapy alone. This is particularly for patients diagnosed with stage III EMC or those with serous carcinoma histology and p53 abnormalities [61]. Current treatment regimens allow for the concurrent administration of chemotherapy with radiation, followed by additional chemotherapy (concomitant CMT-RT) or sequential CMT-RT). Studies indicate that chemotherapy alone can be an option without significantly impacting OS, especially for patients who may not tolerate combined modalities, even though it may lead to higher local recurrence rates in the vagina and pelvic lymph nodes [62].

The PORTEC-3 trial demonstrated a significant improvement in both RFS and OS, especially among patients with stage III disease and those with serous carcinoma whose 5-year survival rate was increased from 52.8% to 71.4% with the addition of chemotherapy [62]. Molecular analyses revealed that the only subgroup benefiting from chemotherapy was patients with p53-abnormal tumors, with a notable increase in 5-year RFS from 36% to 59% following chemotherapy. Therefore, a combined treatment approach is recommended for patients with p53-abnormal or *TP53*-mutated FIGO stage I with myometrial invasion to IIIC2 EMC [47].

https://doi.org/10.3802/jgo.2025.36.e96

- Low-risk group: adjuvant treatment is not recommended. Patients with stage I and II with *POLE* mutations should have a shared decision-making regarding the exemption of adjuvant treatment. When molecular testing is unavailable, the decision for adjuvant treatment should be based on histopathologic risk features.
- Intermediate-risk group: VBT alone is recommended, except for younger patients under 60 years of age, who may choose to omit adjuvant treatment. Thorough counseling and shared decision-making are highly recommended for both low- and intermediate-risk groups.
- High-intermediate risk group: external beam radiotherapy (EBRT) is recommended, with consideration for a VBT boost.
- High-risk group: adjuvant chemotherapy (carboplatin with paclitaxel) combined with radiation therapy is recommended.
- All healthcare coverage programs include adjuvant therapy with radiation and chemotherapy.

6. Treatment for metastasis and recurrence

In cases where the disease has significantly progressed, metastasized, and cannot be fully surgically removed, various treatment methods may help extend the disease-free interval, the progression-free interval, or even OS. The choice of treatment for advanced or recurrent EMC depends on the location of the cancer, previous treatments, the disease-free interval, and the patient's condition. Treatment decisions are typically made collaboratively between gynecologic oncologists, radiation oncologists, the patients, and their caregivers.

Patients who have locoregional recurrence following primary surgery alone

Pelvic radiation therapy with or without VBT should be considered for patients who had never received radiation therapy or had only brachytherapy. If the patient has previously received EBRT, surgery should be considered if it is expected that complete resection of the tumor can be achieved, in the absence of excessive morbidity [63,64].

Patients who have metastatic or advanced diseases

Systemic treatment should be considered. Options are hormonal therapy, chemotherapy, and/ or immunotherapy or targeted therapy.

1) Hormonal therapy

Hormonal therapy can be considered as a first-line option for patients with low-grade endometrioid cancer and a small tumor burden, particularly if the patient's condition makes them unsuitable for chemotherapy [54]. Treatment regimens may include progestins [65], tamoxifen [66], or aromatase inhibitors [67].

2) Chemotherapy

Patients who have never received platinum-based chemotherapy or who have received it with a disease-free period of at least 6 months could have carboplatin area under the curve 5–6 and paclitaxel 175 mg/m^2, administered every 21 days for a total of 6 cycles [68], or docetaxel if paclitaxel is contraindicated. Other combination regimens are:

- Cisplatin and doxorubicin with or without paclitaxel [69].
- Carboplatin and paclitaxel with or without bevacizumab [70].

There is no established standard of care for second-line chemotherapy. A combination therapy with doxorubicin with paclitaxel may be considered for the patients who have already received platinum-based chemotherapy with a short disease-free period [71].

https://doi.org/10.3802/jgo.2025.36.e96

Considering the clinical efficacy of cytotoxic drugs and hormonal agents alongside the national health budget, Thailand's healthcare coverage programs include only specific chemotherapy agents—cisplatin, carboplatin, paclitaxel, and doxorubicin—as well as certain hormonal therapies, such as progestin and megestrol acetate. Other non-listed agents may be used but are reimbursed based on the Diagnosis Related Group system (lump-sum or flat-rate payment).

3) Immunotherapy or targeted therapy

Despite advancements in chemotherapy, outcomes for treatment-naïve patients with advanced-stage and metastatic EMC remain unsatisfactory, with a 5-year mortality rate exceeding 50%. Immune checkpoint inhibitors like pembrolizumab, dostarlimab, or trastuzumab for HER-2 positive uterine serous carcinoma/carcinosarcoma are the agents which showed activity in EMC.

In EMC with dMMR/MSI-H, pembrolizumab [72] or dostarlimab [73] as monotherapy could be considered. Any of these 2 immunotherapeutic agents, combined with chemotherapy, have demonstrated promising results with significant PFS and OS improvement in patients with dMMR or MSI-H tumors [74,75].

The combination of pembrolizumab and lenvatinib may be considered in recurrent or advanced EMC irrespective of MMR status [76]. However, their combination (pembrolizumab plus lenvatinib) did not show superior PFS or OS benefits over chemotherapy as the first-line treatment, in either MMR-proficient or all comers [77].

Trastuzumab, a monoclonal antibody targeting HER2, has shown promise in the treatment of HER2-positive advanced EMC. Adding trastuzumab to standard chemotherapy in frontline settings, particularly for patients with serous carcinoma that overexpresses HER2, has demonstrated improved PFS and OS and should be considered in this group of patients [78,79].

The integration of immunotherapy in the treatment of advanced and metastatic EMC is an important consideration especially in cases of dMMR/MSI-H tumors. However, immunotherapy or targeted therapy is not currently covered by any government healthcare schemes in Thailand. Physicians should provide comprehensive counseling to patients on both standard treatment options, the benefit of immunotherapy, and the patient's financial situation.

- Loco-regional recurrences: surgery may be considered for patients who have received pelvic radiation. If the patients are not surgical candidates, pelvic radiation with or without brachytherapy should be considered for those who have never had pelvic radiation therapy, or who have only received brachytherapy. Otherwise, systemic therapy should be explored.
- Distant recurrences: systemic therapy with hormone is recommended for patients with low-grade endometrioid cancer with a small tumor burden. Chemotherapy, specifically platinum-based regimens, should be administered to patients who have had at least 6 months of disease-free intervals; otherwise, alternative regimens should be considered.
- Medication list of all healthcare coverage programs include only specific chemotherapy agents (cisplatin, carboplatin, paclitaxel, and doxorubicin) and certain hormonal therapies (progestin and megestrol acetate).
- Targeted therapy and immunotherapy are not currently covered by any national health benefit schemes.

https://doi.org/10.3802/jgo.2025.36.e96

REFERENCES

1. Ferlay J, Ervik M, Lam F, Laversanne M, Colombet M, Mery L, et al. Global cancer observatory: cancer today [Internet]. Lyon: International Agency for Research on Cancer; 2024 [cited 2024 Oct 20]. Available from: https://gco.iarc.who.int/media/globocan/factsheets/populations/764-thailand-fact-sheet.pdf.
2. National Cancer Institute. Cancer anywhere. J DMS 2022;47:5-9.
3. The Royal Thai College of Obstetricians and Gynaecologists. Clinical practice guidelines [Internet]. Bangkok: The Royal Thai College of Obstetricians and Gynaecologists; 2025 [cited 2024 Oct 20]. Available from: https://www.rtcog.or.th.
4. National Cancer Institute. Guidelines for screening, diagnosis, and treatment of endometrial cancer [Internet]. Bethesda, MD: National Cancer Institute; 2024 [cited 2024 Oct 20]. Available from: https://www.nci.go.th/th/cpg/CPG%20endometrial%20cancer%20Final.pdf.
5. Wright JD, Pawar N, Gonzalez JSR, Lewin SN, Burke WM, Simpson LL, et al. Scientific evidence underlying the American College of Obstetricians and Gynecologists' practice bulletins. Obstet Gynecol 2011;118:505-12. PUBMED | CROSSREF
6. Morice P, Leary A, Creutzberg C, Abu-Rustum N, Darai E. Endometrial cancer. Lancet 2016;387:1094-108. PUBMED | CROSSREF
7. Sroczynski G, Gogollari A, Conrads-Frank A, Hallsson LR, Pashayan N, Widschwendter M, et al. Cost-effectiveness of early detection and prevention strategies for endometrial cancer-a systematic review. Cancers (Basel) 2020;12:1874. PUBMED | CROSSREF
8. Lancaster JM, Powell CB, Chen LM, Richardson DL; SGO Clinical Practice Committee. Society of Gynecologic Oncology statement on risk assessment for inherited gynecologic cancer predispositions. Gynecol Oncol 2015;136:3-7. PUBMED | CROSSREF
9. Lu KH, Dinh M, Kohlmann W, Watson P, Green J, Syngal S, et al. Gynecologic cancer as a "sentinel cancer" for women with hereditary nonpolyposis colorectal cancer syndrome. Obstet Gynecol 2005;105:569-74. PUBMED | CROSSREF
10. Stjepanovic N, Moreira L, Carneiro F, Balaguer F, Cervantes A, Balmaña J, et al. Hereditary gastrointestinal cancers: ESMO clinical practice guidelines for diagnosis, treatment and follow-up†. Ann Oncol 2019;30:1558-71. PUBMED | CROSSREF
11. Schmeler KM, Lynch HT, Chen LM, Munsell MF, Soliman PT, Clark MB, et al. Prophylactic surgery to reduce the risk of gynecologic cancers in the Lynch syndrome. N Engl J Med 2006;354:261-9. PUBMED | CROSSREF
12. ACOG committee opinion no. 557: management of acute abnormal uterine bleeding in nonpregnant reproductive-aged women. Obstet Gynecol 2013;121:891-6. PUBMED | CROSSREF
13. Long B, Clarke MA, Morillo ADM, Wentzensen N, Bakkum-Gamez JN. Ultrasound detection of endometrial cancer in women with postmenopausal bleeding: systematic review and meta-analysis. Gynecol Oncol 2020;157:624-33. PUBMED | CROSSREF
14. Taraboanta C, Britton H, Plotkin A, Azordegan N, Clement PB, Gilks CB. Performance characteristics of endometrial sampling in diagnosis of endometrial carcinoma. Int J Gynecol Pathol 2020;39:19-25. PUBMED | CROSSREF
15. Clark TJ, Barton PM, Coomarasamy A, Gupta JK, Khan KS. Investigating postmenopausal bleeding for endometrial cancer: cost-effectiveness of initial diagnostic strategies. BJOG 2006;113:502-10. PUBMED | CROSSREF
16. Lin MY, Dobrotwir A, McNally O, Abu-Rustum NR, Narayan K. Role of imaging in the routine management of endometrial cancer. Int J Gynaecol Obstet 2018;143 Suppl 2:109-17. PUBMED | CROSSREF
17. Nagar H, Dobbs S, McClelland HR, Price J, McCluggage WG, Grey A. The diagnostic accuracy of magnetic resonance imaging in detecting cervical involvement in endometrial cancer. Gynecol Oncol 2006;103:431-4. PUBMED | CROSSREF
18. Jiang T, Huang L, Zhang S. Preoperative serum CA125: a useful marker for surgical management of endometrial cancer. BMC Cancer 2015;15:396. PUBMED | CROSSREF
19. Berek JS, Matias-Guiu X, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, et al. FIGO staging of endometrial cancer: 2023. J Gynecol Oncol 2023;34:e85. PUBMED | CROSSREF
20. Galaal K, Donkers H, Bryant A, Lopes AD. Laparoscopy versus laparotomy for the management of early stage endometrial cancer. Cochrane Database Syst Rev 2018;10:CD006655. PUBMED | CROSSREF
21. Mäenpää MM, Nieminen K, Tomás EI, Laurila M, Luukkaala TH, Mäenpää JU. Robotic-assisted vs traditional laparoscopic surgery for endometrial cancer: a randomized controlled trial. Am J Obstet Gynecol 2016;215:588.e1-588.e7. PUBMED | CROSSREF

22. Frost JA, Webster KE, Bryant A, Morrison J. Lymphadenectomy for the management of endometrial cancer. Cochrane Database Syst Rev 2017;10:CD007585. PUBMED | CROSSREF
23. Vargas R, Rauh-Hain JA, Clemmer J, Clark RM, Goodman A, Growdon WB, et al. Tumor size, depth of invasion, and histologic grade as prognostic factors of lymph node involvement in endometrial cancer: a SEER analysis. Gynecol Oncol 2014;133:216-20. PUBMED | CROSSREF
24. Persson J, Salehi S, Bollino M, Lönnerfors C, Falconer H, Geppert B. Pelvic Sentinel lymph node detection in high-risk endometrial cancer (SHREC-trial)-the final step towards a paradigm shift in surgical staging. Eur J Cancer 2019;116:77-85. PUBMED | CROSSREF
25. Rossi EC, Kowalski LD, Scalici J, Cantrell L, Schuler K, Hanna RK, et al. A comparison of sentinel lymph node biopsy to lymphadenectomy for endometrial cancer staging (FIRES trial): a multicentre, prospective, cohort study. Lancet Oncol 2017;18:384-92. PUBMED | CROSSREF
26. Khemworapong K, Jaishuen A, Srichaikul P, Inthasorn P, Viriyapak B, Achariyapota V, et al. The fluorescence imaging for laparoscopic and laparotomic endometrial sentinel lymph node biopsy (FILLES) trial: Siriraj gynecologic sentinel node of endometrial cancer (SiGN-En) study. J Surg Oncol 2024;129:403-9. PUBMED | CROSSREF
27. Daraï E, Dubernard G, Bats AS, Heitz D, Mathevet P, Marret H, et al. Sentinel node biopsy for the management of early stage endometrial cancer: long-term results of the SENTI-ENDO study. Gynecol Oncol 2015;136:54-9. PUBMED | CROSSREF
28. Euscher E, Sui D, Soliman P, Westin S, Ramalingam P, Bassett R, et al. Ultrastaging of sentinel lymph nodes in endometrial carcinoma according to use of 2 different methods. Int J Gynecol Pathol 2018;37:242-51. PUBMED | CROSSREF
29. Lee TS, Jung JY, Kim JW, Park NH, Song YS, Kang SB, et al. Feasibility of ovarian preservation in patients with early stage endometrial carcinoma. Gynecol Oncol 2007;104:52-7. PUBMED | CROSSREF
30. Wright JD, Buck AM, Shah M, Burke WM, Schiff PB, Herzog TJ. Safety of ovarian preservation in premenopausal women with endometrial cancer. J Clin Oncol 2009;27:1214-9. PUBMED | CROSSREF
31. Gu H, Li J, Gu Y, Tu H, Zhou Y, Liu J. Survival impact of ovarian preservation on women with early-stage endometrial cancer: a systematic review and meta-analysis. Int J Gynecol Cancer 2017;27:77-84. PUBMED | CROSSREF
32. Nasioudis D, Mastroyannis SA, Ko EM, Haggerty AF, Cory L, Giuntoli RL 2nd, et al. Safety of ovarian preservation for premenopausal patients with FIGO stage I grade 2 and 3 endometrioid endometrial adenocarcinoma. Int J Gynecol Cancer 2022;32:1355-60. PUBMED | CROSSREF
33. WHO Classification of Tumours Editorial Board. Female genital tumours. 5th ed. Geneva: WHO Classification of Tumours Editorial Board; 2020.
34. Mendivil A, Schuler KM, Gehrig PA. Non-endometrioid adenocarcinoma of the uterine corpus: a review of selected histological subtypes. Cancer Contr 2009;16:46-52. PUBMED | CROSSREF
35. Bogani G, Ray-Coquard I, Concin N, Ngoi NYL, Morice P, Enomoto T, et al. Uterine serous carcinoma. Gynecol Oncol 2021;162:226-34. PUBMED | CROSSREF
36. Bogani G, Ray-Coquard I, Concin N, Ngoi NYL, Morice P, Caruso G, et al. Endometrial carcinosarcoma. Int J Gynecol Cancer 2023;33:147-74. PUBMED | CROSSREF
37. Abu-Rustum N, Yashar C, Arend R, Barber E, Bradley K, Brooks R, et al. Uterine neoplasms, version 1.2023, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 2023;21:181-209. PUBMED | CROSSREF
38. Kandoth C, Schultz N, Cherniack AD, Akbani R, Liu Y, Shen H, et al. Integrated genomic characterization of endometrial carcinoma. Nature 2013;497:67-73. PUBMED | CROSSREF
39. Kim SR, Cloutier BT, Leung S, Cochrane D, Britton H, Pina A, et al. Molecular subtypes of clear cell carcinoma of the endometrium: opportunities for prognostic and predictive stratification. Gynecol Oncol 2020;158:3-11. PUBMED | CROSSREF
40. Talhouk A, McConechy MK, Leung S, Yang W, Lum A, Senz J, et al. Confirmation of ProMisE: a simple, genomics-based clinical classifier for endometrial cancer. Cancer 2017;123:802-13. PUBMED | CROSSREF
41. Casey L, Singh N. POLE, MMR, and MSI testing in endometrial cancer: proceedings of the ISGyP companion society session at the USCAP 2020 annual meeting. Int J Gynecol Pathol 2021;40:5-16. PUBMED | CROSSREF
42. Buza N. HER2 testing and reporting in endometrial serous carcinoma: practical recommendations for HER2 immunohistochemistry and fluorescent in situ hybridization: proceedings of the ISGyP companion society session at the 2020 USCAP annual meeting. Int J Gynecol Pathol 2021;40:17-23. PUBMED | CROSSREF
43. Rottmann D, Snir OL, Wu X, Wong S, Hui P, Santin AD, et al. HER2 testing of gynecologic carcinosarcomas: tumor stratification for potential targeted therapy. Mod Pathol 2020;33:118-27. PUBMED | CROSSREF

44. Poulsen HK, Jacobsen M, Bertelsen K, Andersen JE, Ahrons S, Bock J, et al. Adjuvant radiation therapy is not necessary in the management of endometrial carcinoma stage I, low-risk cases. Int J Gynecol Cancer 1996;6:38-43. CROSSREF
45. Bertelsen K, Ortoft G, Hansen ES. Survival of Danish patients with endometrial cancer in the intermediate-risk group not given postoperative radiotherapy: the Danish Endometrial Cancer Study (DEMCA). Int J Gynecol Cancer 2011;21:1191-9. PUBMED | CROSSREF
46. Church DN, Stelloo E, Nout RA, Valtcheva N, Depreeuw J, ter Haar N, et al. Prognostic significance of POLE proofreading mutations in endometrial cancer. J Natl Cancer Inst 2014;107:402. PUBMED | CROSSREF
47. León-Castillo A, de Boer SM, Powell ME, Mileshkin LR, Mackay HJ, Leary A, et al. Molecular classification of the PORTEC-3 trial for high-risk endometrial cancer: impact on prognosis and benefit from adjuvant therapy. J Clin Oncol 2020;38:3388-97. PUBMED | CROSSREF
48. Creutzberg CL, van Putten WL, Koper PC, Lybeert ML, Jobsen JJ, Wárlám-Rodenhuis CC, et al. Surgery and postoperative radiotherapy versus surgery alone for patients with stage-1 endometrial carcinoma: multicentre randomised trial. PORTEC study group. Post operative radiation therapy in endometrial carcinoma. Lancet 2000;355:1404-11. PUBMED | CROSSREF
49. Keys HM, Roberts JA, Brunetto VL, Zaino RJ, Spirtos NM, Bloss JD, et al. A phase III trial of surgery with or without adjunctive external pelvic radiation therapy in intermediate risk endometrial adenocarcinoma: a Gynecologic Oncology Group study. Gynecol Oncol 2004;92:744-51. PUBMED | CROSSREF
50. Nout RA, Smit VT, Putter H, Jürgenliemk-Schulz IM, Jobsen JJ, Lutgens LC, et al. Vaginal brachytherapy versus pelvic external beam radiotherapy for patients with endometrial cancer of high-intermediate risk (PORTEC-2): an open-label, non-inferiority, randomised trial. Lancet 2010;375:816-23. PUBMED | CROSSREF
51. Wortman BG, Creutzberg CL, Putter H, Jürgenliemk-Schulz IM, Jobsen JJ, Lutgens LCHW, et al. Ten-year results of the PORTEC-2 trial for high-intermediate risk endometrial carcinoma: improving patient selection for adjuvant therapy. Br J Cancer 2018;119:1067-74. PUBMED | CROSSREF
52. Kong A, Johnson N, Kitchener HC, Lawrie TA. Adjuvant radiotherapy for stage I endometrial cancer: an updated Cochrane systematic review and meta-analysis. J Natl Cancer Inst 2012;104:1625-34. PUBMED | CROSSREF
53. Barney BM, Petersen IA, Mariani A, Dowdy SC, Bakkum-Gamez JN, Haddock MG. The role of vaginal brachytherapy in the treatment of surgical stage I papillary serous or clear cell endometrial cancer. Int J Radiat Oncol Biol Phys 2013;85:109-15. PUBMED | CROSSREF
54. Koppikar S, Oaknin A, Babu KG, Lorusso D, Gupta S, Wu LY, et al. Pan-Asian adapted ESMO clinical practice guidelines for the diagnosis, treatment and follow-up of patients with endometrial cancer. ESMO Open 2023;8:100774. PUBMED | CROSSREF
55. Aalders J, Abeler V, Kolstad P, Onsrud M. Postoperative external irradiation and prognostic parameters in stage I endometrial carcinoma: clinical and histopathologic study of 540 patients. Obstet Gynecol 1980;56:419-27. PUBMED
56. Randall ME, Filiaci V, McMeekin DS, von Gruenigen V, Huang H, Yashar CM, et al. Phase III trial: adjuvant pelvic radiation therapy versus vaginal brachytherapy plus paclitaxel/carboplatin in high-intermediate and high-risk early stage endometrial cancer. J Clin Oncol 2019;37:1810-8. PUBMED | CROSSREF
57. Harkenrider MM, Abu-Rustum N, Albuquerque K, Bradfield L, Bradley K, Dolinar E, et al. Radiation therapy for endometrial cancer: an American Society for Radiation Oncology clinical practice guideline. Pract Radiat Oncol 2023;13:41-65. PUBMED | CROSSREF
58. Bosse T, Peters EE, Creutzberg CL, Jürgenliemk-Schulz IM, Jobsen JJ, Mens JW, et al. Substantial lymph-vascular space invasion (LVSI) is a significant risk factor for recurrence in endometrial cancer--a pooled analysis of PORTEC 1 and 2 trials. Eur J Cancer 2015;51:1742-50. PUBMED | CROSSREF
59. Hachisuga T, Kaku T, Fukuda K, Eguchi F, Emoto M, Kamura T, et al. The grading of lymphovascular space invasion in endometrial carcinoma. Cancer 1999;86:2090-7. PUBMED | CROSSREF
60. de Boer SM, Powell ME, Mileshkin L, Katsaros D, Bessette P, Haie-Meder C, et al. Adjuvant chemoradiotherapy versus radiotherapy alone for women with high-risk endometrial cancer (PORTEC-3): final results of an international, open-label, multicentre, randomised, phase 3 trial. Lancet Oncol 2018;19:295-309. PUBMED | CROSSREF
61. Hogberg T, Signorelli M, de Oliveira CF, Fossati R, Lissoni AA, Sorbe B, et al. Sequential adjuvant chemotherapy and radiotherapy in endometrial cancer--results from two randomised studies. Eur J Cancer 2010;46:2422-31. PUBMED | CROSSREF
62. de Boer SM, Powell ME, Mileshkin L, Katsaros D, Bessette P, Haie-Meder C, et al. Adjuvant chemoradiotherapy versus radiotherapy alone in women with high-risk endometrial cancer (PORTEC-3):

patterns of recurrence and post-hoc survival analysis of a randomised phase 3 trial. Lancet Oncol 2019;20:1273-85. PUBMED | CROSSREF

63. Matei D, Filiaci V, Randall ME, Mutch D, Steinhoff MM, DiSilvestro PA, et al. Adjuvant chemotherapy plus radiation for locally advanced endometrial cancer. N Engl J Med 2019;380:2317-26. PUBMED | CROSSREF
64. Shikama A, Minaguchi T, Takao W, Hosokawa Y, Nishida K, Tasaka N, et al. Predictors of favorable survival after secondary cytoreductive surgery for recurrent endometrial cancer. Int J Clin Oncol 2019;24:1256-63. PUBMED | CROSSREF
65. Singh M, Zaino RJ, Filiaci VJ, Leslie KK. Relationship of estrogen and progesterone receptors to clinical outcome in metastatic endometrial carcinoma: a Gynecologic Oncology Group study. Gynecol Oncol 2007;106:325-33. PUBMED | CROSSREF
66. van Weelden WJ, Massuger LFAG, ; ENITEC, Pijnenborg JMA, Romano A. Anti-estrogen treatment in endometrial cancer: a systematic review. Front Oncol 2019;9:359. PUBMED | CROSSREF
67. Mileshkin L, Edmondson R, O'Connell RL, Sjoquist KM, Andrews J, Jyothirmayi R, et al. Phase 2 study of anastrozole in recurrent estrogen (ER)/progesterone (PR) positive endometrial cancer: the PARAGON trial - ANZGOG 0903. Gynecol Oncol 2019;154:29-37. PUBMED | CROSSREF
68. Rubinstein M, Halpenny D, Makker V, Grisham RN, Aghajanian C, Cadoo K. Retreatment with carboplatin and paclitaxel for recurrent endometrial cancer: a retrospective study of the Memorial Sloan Kettering Cancer Center experience. Gynecol Oncol Rep 2019;28:120-3. PUBMED | CROSSREF
69. Fleming GF, Brunetto VL, Cella D, Look KY, Reid GC, Munkarah AR, et al. Phase III trial of doxorubicin plus cisplatin with or without paclitaxel plus filgrastim in advanced endometrial carcinoma: a Gynecologic Oncology Group study. J Clin Oncol 2004;22:2159-66. PUBMED | CROSSREF
70. Rose PG, Ali S, Moslemi-Kebria M, Simpkins F. Paclitaxel, carboplatin, and bevacizumab in advanced and recurrent endometrial carcinoma. Int J Gynecol Cancer 2017;27:452-8. PUBMED | CROSSREF
71. Fleming GF, Filiaci VL, Bentley RC, Herzog T, Sorosky J, Vaccarello L, et al. Phase III randomized trial of doxorubicin + cisplatin versus doxorubicin + 24-h paclitaxel + filgrastim in endometrial carcinoma: a Gynecologic Oncology Group study. Ann Oncol 2004;15:1173-8. PUBMED | CROSSREF
72. O'Malley DM, Bariani GM, Cassier PA, Marabelle A, Hansen AR, De Jesus Acosta A, et al. Pembrolizumab in patients with microsatellite instability-high advanced endometrial cancer: results from the KEYNOTE-158 study. J Clin Oncol 2022;40:752-61. PUBMED | CROSSREF
73. Oaknin A, Pothuri B, Gilbert L, Sabatier R, Brown J, Ghamande S, et al. Safety, efficacy, and biomarker analyses of dostarlimab in patients with endometrial cancer: interim results of the phase I GARNET study. Clin Cancer Res 2023;29:4564-74. PUBMED | CROSSREF
74. Eskander RN, Sill MW, Beffa L, Moore RG, Hope JM, Musa FB, et al. Pembrolizumab plus chemotherapy in advanced endometrial cancer. N Engl J Med 2023;388:2159-70. PUBMED | CROSSREF
75. Powell MA, Cibula D, O'Malley DM, Boere I, Shahin MS, Savarese A, et al. Efficacy and safety of dostarlimab in combination with chemotherapy in patients with dMMR/MSI-H primary advanced or recurrent endometrial cancer in a phase 3, randomized, placebo-controlled trial (ENGOT-EN6-NSGO/GOG-3031/RUBY). Gynecol Oncol 2025;192:40-9. PUBMED | CROSSREF
76. Makker V, Colombo N, Casado Herráez A, Santin AD, Colomba E, Miller DS, et al. Lenvatinib plus pembrolizumab for advanced endometrial cancer. N Engl J Med 2022;386:437-48. PUBMED | CROSSREF
77. Marth C, Moore RG, Bidziński M, Pignata S, Ayhan A, Rubio MJ, et al. First-line lenvatinib plus pembrolizumab versus chemotherapy for advanced endometrial cancer: a randomized, open-label, phase III trial. J Clin Oncol 2024:JCO2401326. PUBMED | CROSSREF
78. Fader AN, Roque DM, Siegel E, Buza N, Hui P, Abdelghany O, et al. Randomized phase II trial of carboplatin-paclitaxel versus carboplatin-paclitaxel-trastuzumab in uterine serous carcinomas that overexpress human epidermal growth factor receptor 2/neu. J Clin Oncol 2018;36:2044-51. PUBMED | CROSSREF
79. Nishikawa T, Hasegawa K, Matsumoto K, Mori M, Hirashima Y, Takehara K, et al. Trastuzumab deruxtecan for human epidermal growth factor receptor 2-expressing advanced or recurrent uterine carcinosarcoma (NCCH1615): the STATICE trial. J Clin Oncol 2023;41:2789-99. PUBMED | CROSSREF