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Gynaecologic Oncology Society of Kenya (GOSK) clinical management protocol for endometrial carcinoma in Kenya - 2026

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Abstract

Objective: To establish a standardized, evidence-based approach to the management of endometrial carcinoma in Kenya.

Methods: This protocol was developed using a guideline adaptation approach that aligned high-quality international guidelines with Kenya's health system and resource context. A multidisciplinary panel comprising gynecologic oncologists, pathologists, radiologists, oncology nurses, pharmacists, radiation oncologists, public health specialists, and patient representatives led the process. Panel members received technical training from the University of Nairobi and Kenyatta National Hospital on evidence-based adaptation methods, including standardized appraisal, systematic evaluation of guidelines, and contextualization to local needs. A systematic literature search of PubMed and Google Scholar was conducted. Five guidelines were retrieved and independently appraised using the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument. Three guidelines were selected for adaptation: the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Uterine Neoplasms, Version 3.2025; the Pan-Asian adapted European Society for Medical Oncology (ESMO) Clinical Practice Guidelines for the Diagnosis, Treatment, and Follow-up of Patients with Endometrial Cancer (2022); and the European Society of Gynaecological Oncology (ESGO), European Society for Radiotherapy and Oncology (ESTRO), and European Society of Pathology (ESP) guidelines for the management of patients with endometrial carcinoma (2020). The selected guidelines were reviewed and contextualized to Kenya's resource setting and healthcare infrastructure.

Results: The protocol provides recommendations for the diagnosis, staging, pathological assessment, preoperative evaluation, surgical management, and adjuvant treatment of endometrial carcinoma. It also addresses management according to disease stage, histological subtype, and risk stratification; fertility-sparing treatment; recurrent disease; post-treatment surveillance; supportive care; and targeted therapies. Molecular classification and contemporary systemic therapies, including immunotherapy, are addressed within the Kenyan healthcare context.

Recommendations: The protocol provides a standardized, evidence-informed framework for the management of endometrial carcinoma in Kenya. It aims to improve consistency in clinical decision-making across the continuum of care, support appropriate use of available resources, and promote equitable access to evidence-based management.

Keywords: Clear-cell carcinoma; Endometrial neoplasms; Endometrical carcinoma; Serous carcinoma

List of abbreviations

AGREE II	Appraisal of Guidelines for Research and Evaluation II
AUC	Area under the concentration–time curve
BSO	Bilateral salpingo-oophorectomy
CA-125	Cancer antigen 125
CCRT	Concurrent chemoradiotherapy
CT	Computed tomography
CTNNB1	Catenin beta 1
CXR	Chest radiography
D&C	Dilatation and curettage
DNA	Deoxyribonucleic acid
EBRT	External beam radiotherapy
EC	Endometrial carcinoma
EEC	Endometrioid endometrial carcinoma
ER	Estrogen receptor
ESGO	European Society of Gynaecological Oncology
ESMO	European Society for Medical Oncology
ESP	European Society of Pathology
FIGO	International Federation of Gynecology and Obstetrics
FRα	Folate receptor alpha
GOSK	Gynaecologic Oncology Society of Kenya
HER2	Human epidermal growth factor receptor 2
HIR	High-intermediate risk
HNPCC	Hereditary nonpolyposis colorectal cancer
HPV	Human papillomavirus
HRT	Hormone replacement therapy
IHC	Immunohistochemistry
IDS	Interval debulking surgery
LNG-IUD	Levonorgestrel-releasing intrauterine device
LVSI	Lymphovascular space invasion
MDT	Multidisciplinary team
MIS	Minimally invasive surgery
MLH1	MutL homolog 1
MMR	Mismatch repair
MMRd	Mismatch repair deficient
MRI	Magnetic resonance imaging
MSH2	MutS homolog 2
MSH6	MutS homolog 6
MSI	Microsatellite instability
MSI-H	Microsatellite instability-high

NACT	Neoadjuvant chemotherapy
NCCN	National Comprehensive Cancer Network
NSMP	No specific molecular profile
p53abn	p53-abnormal
PET/CT	Positron emission tomography/computed tomography
PI3K	Phosphatidylinositol 3-kinase
Pipelle	Pipelle endometrial sampler
PMS2	PMS1 homolog 2, mismatch repair system component
POLE	DNA polymerase epsilon
POLEmut	POLE-mutated
PR	Progesterone receptor
ProMisE	Proactive Molecular Risk Classifier for Endometrial Cancer
PTEN	Phosphatase and tensin homolog
SBRT	Stereotactic body radiotherapy
SLNE	Sentinel lymph node excision
TCGA	The Cancer Genome Atlas
TH	Total hysterectomy
TH/BSO	Total hysterectomy and bilateral salpingo-oophorectomy
TP53	Tumor protein 53
TVUS	Transvaginal ultrasound
VBT	Vaginal brachytherapy
VIA	Visual inspection with acetic acid
WHO	World Health Organization

Summary of recommendations

This protocol aims to enhance diagnostic accuracy, standardize treatment approaches, improve patient outcomes, and promote the efficient use of available resources. It is intended for healthcare professionals involved in the care of patients with endometrial carcinoma, including gynecologists, gynecologic oncologists, medical oncologists, radiation oncologists, pathologists, radiologists, nurses, clinical officers, and other allied healthcare workers across all levels of the healthcare system in Kenya. The key recommendations of this protocol are summarized in Tables 1–8.

Table 1: Summary of GOSK recommendations for diagnosis of endometrial carcinoma

Diagnostic parameter	GOSK recommendations
Clinical assessment	A comprehensive history should be obtained, including abnormal uterine bleeding, abnormal vaginal discharge, pelvic pain, abdominal distension or pressure symptoms, constitutional symptoms, and relevant personal or family history suggestive of hereditary cancers. A complete pelvic examination should be performed to assess tumor extent and involvement of the cervix, vagina, parametrium, adnexa, and rectovaginal septum.
Imaging	Imaging should be employed for disease staging and assessment of disease extent: • MRI (Pelvis): Preferred modality for assessing myometrial invasion, cervical stromal involvement, and regional nodal disease. • Transvaginal ultrasound (TVUS): Alternative to MRI where unavailable or contraindicated. • CT (Chest/Abdomen/Pelvis): Recommended for evaluation of nodal and distant metastatic disease, including incompletely staged disease. • PET/CT: Consider in advanced, high-risk, recurrent, or fertility-sparing cases to evaluate extrauterine and metastatic disease.
Tissue diagnosis	Tissue diagnosis should be obtained using appropriate endometrial sampling techniques: • Pipelle biopsy: Preferred first-line method for endometrial sampling. • Dilatation and curettage (D&C): Recommended when Pipelle biopsy is negative or non-diagnostic despite persistent clinical suspicion. • Hysteroscopy with directed biopsy: Consider in patients with persistent or recurrent abnormal uterine bleeding or suspected focal intrauterine lesions. • Cervical assessment: Perform cervical cancer screening and evaluate suspicious cervical lesions as clinically indicated.

Table 2: Summary of GOSK recommendations for histological subtyping and clinical behavior of endometrial carcinoma

Histological subtype	Clinical behavior
Endometrioid carcinoma	Most common subtype; generally associated with a favorable prognosis, particularly in low-grade, early-stage disease.
Serous carcinoma	High-grade aggressive subtype with a high risk of extrauterine spread and recurrence, irrespective of myometrial invasion.
Clear-cell carcinoma	Aggressive subtype associated with increased risk of recurrence and poorer survival compared with endometrioid carcinoma.
Undifferentiated/Dedifferentiated carcinoma	Rare, highly aggressive tumors with poor prognosis and frequent advanced-stage presentation.
Carcinosarcoma	Biphasic tumor with aggressive clinical behavior; managed as a high-risk endometrial carcinoma.

Table 3: Summary of GOSK recommendations for endometrial carcinoma staging and risk stratification

Parameter	GOSK recommendations
Staging system	The FIGO 2023 staging system should be used to determine disease extent, guide treatment planning, and inform prognosis.
Multidisciplinary team (MDT)	Multidisciplinary team discussion is recommended for treatment planning, particularly in patients with high-risk histology, advanced-stage disease, recurrent disease, or complex clinical scenarios.
Molecular classification	Molecular classification should be incorporated, where available, to refine prognostic assessment and guide adjuvant and systemic treatment decisions.
Risk stratification	Patients should be stratified according to clinicopathological and molecular risk factors, including FIGO stage, histological subtype, tumor grade, depth of myometrial invasion, lymphovascular space invasion (LVSI), nodal status, and molecular classification (POLEmut, MMRd, NSMP, p53abn).

Table 4: Summary of GOSK recommendations for primary treatment of endometrial carcinoma

Clinical category	GOSK recommendations
Surgery	Total hysterectomy with bilateral salpingo-oophorectomy is the standard surgical treatment. Minimally invasive surgery is preferred for uterine-confined disease.
Nodal assessment	Sentinel lymph node excision (SLNE) is preferred where expertise is available. Systematic lymphadenectomy may be considered when SLNE is unavailable or clinically indicated.

Clinical category	GOSK recommendations
High-risk histology	Infracolic omentectomy should be performed in serous carcinoma, clear cell carcinoma, undifferentiated carcinoma and carcinosarcoma.

Table 5: Summary of GOSK recommendation for adjuvant treatment of endometrial carcinoma

Risk category	GOSK recommendations
Low risk (stage IA, grade 1–2, no/focal LVSI, POLEmut)	No adjuvant treatment.
Intermediate risk (stage IB grade 1–2, no/focal LVSI, MMRd/NSMP)	Vaginal brachytherapy (VBT).
High-intermediate risk (stage IA Grade 3, stage IB grade 3, stage II, or substantial LVSI)	VBT alone may be considered in patients with node-negative disease and no or focal LVSI. External beam radiotherapy (EBRT) is recommended for patients with substantial LVSI. EBRT plus VBT may be considered in patients with grade 3 disease or cervical stromal involvement. Sequential carboplatin (AUC 5–6) plus paclitaxel (175 mg/m² every 21 days × 6 cycles) followed by EBRT ± VBT may be considered in patients with grade 3 disease, substantial LVSI, p53-abnormal tumors, or other clinicopathological features associated with increased risk of distant recurrence.
High risk (stage III–IVA, node-positive disease, serous, clear cell, carcinosarcoma, p53abn)	Sequential adjuvant chemotherapy *(carboplatin AUC 5–6 plus paclitaxel 175 mg/m² IV every 21 days for 6 cycles)* followed by EBRT ± VBT is recommended. Eligible patients with stage III–IVA MMR-deficient (MMRd) endometrial carcinoma should receive carboplatin (AUC 5–6) plus paclitaxel (175 mg/m² IV every 21 days for 6 cycles) in combination with either dostarlimab (500 mg IV every 3 weeks during chemotherapy, followed by maintenance dostarlimab 1000 mg IV every 6 weeks for up to 3 years) OR pembrolizumab (200 mg IV every 3 weeks during chemotherapy, followed by maintenance pembrolizumab 400 mg IV every 6 weeks for up to 14 cycles).
Advanced/metastatic disease (stage IVB or unresectable disease)	Primary cytoreductive surgery is preferred where feasible. Neoadjuvant chemotherapy *(carboplatin AUC 5–6 plus paclitaxel 175 mg/m² IV every 21 days for 3 cycles)* followed by interval debulking surgery should be considered when optimal primary cytoreduction is unlikely, with completion of 6 total chemotherapy cycles. Patients with unresectable disease should receive platinum-based chemotherapy ± EBRT/VBT. Biomarker-directed therapy should be incorporated where indicated, including immune checkpoint inhibitors for MMRd/MSI-H disease, trastuzumab for HER2-positive serous carcinoma, pembrolizumab plus lenvatinib for recurrent pMMR disease, and hormonal therapy for selected ER/PR-positive endometrioid carcinoma.

Table 6: Summary of GOSK recommendations on fertility-sparing treatment in endometrial carcinoma

Component	GOSK recommendations
Eligibility	Fertility-sparing management should only be offered following multidisciplinary team (MDT) review in carefully selected patients with grade 1 endometrioid carcinoma confirmed on expert pathology, disease confined to the endometrium on MRI, a favorable molecular profile (POLEmut), no evidence of hereditary cancer syndrome or extrauterine disease, and no contraindications to pregnancy or progestin therapy. Patients should be counselled that fertility-sparing treatment is not the standard of care and requires strict surveillance.
Treatment	Patients should consult with a fertility specialist, before treatment. Hysteroscopic tumor resection should be performed where feasible, followed by continuous progestin therapy using megestrol acetate (160–320 mg/day), medroxyprogesterone acetate (400–600 mg/day), or a levonorgestrel-releasing intrauterine device (LNG-IUD). Combined oral progestin and LNG-IUD therapy may be considered in selected patients.
Surveillance	Endometrial assessment should be performed every 3–6 months using endometrial biopsy (Pipelle, D&C, or hysteroscopy with biopsy). Patients achieving a complete response by 6 months should be encouraged to conceive, with continued surveillance every 6–12 months and maintenance progestin therapy if pregnancy is deferred. Definitive TH/BSO with surgical staging is recommended for patients with persistent disease, disease progression, or no complete response by 6–12 months.
Definitive treatment	Definitive TH/BSO with appropriate surgical staging should be performed after completion of childbearing

Table 7: Summary of GOSK recommendations on endometrial carcinoma follow-up

Component	GOSK recommendations
Surveillance frequency	Low-/ontermediate-risk: Every 6 months for the first 2 years, then annually until 5 years.

Component	GOSK recommendations
	High-intermediate-/high-risk: Every 3 months for the first 3 years, every 6 months until 5 years, then annually thereafter.
Clinical assessment and imaging	Perform a comprehensive history, physical examination, and pelvic examination at each follow-up visit to assess for recurrence and treatment-related complications. Low-/intermediate-risk: Consider CT or MRI 6 months after treatment, then as clinically indicated. High-intermediate/high-risk: Consider CT or MRI 3 months after treatment, then as clinically indicated by symptoms, examination findings, or suspicion of recurrence.
CA-125 monitoring	Consider serial CA-125 monitoring in patients with an initially elevated CA-125 level or serous histology. Rising CA-125 should prompt clinical evaluation and contrast-enhanced CT imaging to exclude recurrence; treatment should not be initiated based on CA-125 elevation alone.
Patient education	Educate patients regarding symptoms concerning for recurrence, including abnormal vaginal bleeding, persistent pelvic or abdominal pain, abdominal distension, persistent cough or dyspnea, unexplained weight loss, and new pelvic or abdominal masses. Reinforce adherence to scheduled follow-up and prompt medical evaluation of new symptoms.

Table 8: Summary of GOSK recommendations for management of recurrent endometrial carcinoma

Clinical category	GOSK recommendations
Locoregional recurrence with no prior radiotherapy treatment	Surgical resection should be considered in patients with resectable disease where complete gross resection is achievable. Adjuvant radiotherapy, with or without systemic therapy, should be administered based on pathologic findings.
Locoregional recurrence with prior radiotherapy treatment	Management options may include pelvic exenteration, carefully selected re-irradiation techniques, or systemic therapy based on disease extent, prior treatment, performance status, and treatment intent.
Isolated metastasis	Management options include surgical resection, EBRT, ablative therapies, including stereotactic body radiotherapy (SBRT) or radiofrequency ablation and systemic therapy.
Disseminated disease/distant metastasis	Treatment options include; Palliative systemic chemotherapy, with or without palliative radiotherapy, hormonal therapy, immunotherapy and other targeted therapies. Enrolment into clinical trials is encouraged.

1.0 Introduction

1.1 Background

Uterine malignancies comprise two distinct pathological entities: endometrial carcinoma and uterine sarcoma, which differ substantially in their pathogenesis, histopathological characteristics, biological behavior, clinical presentation, and management strategies. Endometrial carcinoma arises from the epithelial lining of the endometrium and accounts for approximately 90% of uterine malignancies, whereas uterine sarcomas originate from the uterine mesenchyme and are considerably less common (1-2).

Endometrial carcinoma is a biologically heterogeneous malignancy comprising distinct histological and molecular subtypes that influence prognosis, patterns of recurrence, and therapeutic decision-making. Endometrioid carcinoma is the predominant histological subtype and is strongly associated with obesity, prolonged unopposed estrogen exposure, diabetes mellitus, and endometrial hyperplasia. In contrast, non-endometrioid carcinomas, including serous carcinoma, clear cell carcinoma, undifferentiated carcinoma, and carcinosarcoma are less common but generally demonstrate more aggressive biological behavior and poorer clinical outcomes (3-5).

1.2 Epidemiology

The global incidence of endometrial carcinoma continues to rise, largely driven by increasing rates of obesity, diabetes mellitus, metabolic syndrome, and population aging. It is currently the second most common gynecological malignancy worldwide, with more than 420,000 new cases and over 97,000 deaths estimated in 2022 (6). Within sub-Saharan Africa, endometrial carcinoma ranks as the third most common gynecological malignancy, accounting for approximately 14,900 new cases and 4,600 deaths annually (6).

1.3 Endometrial carcinoma in Kenya

In Kenya, an estimated 829 new cases and 257 deaths were reported in 2022 (6). However, these figures probably underestimate the true national burden because of underdiagnosis, incomplete cancer registration, and disparities in access to diagnostic and oncology services. As life expectancy increases and the prevalence of obesity and other metabolic disorders continues to rise, the incidence of endometrial carcinoma is expected to increase further in Kenya. This epidemiological transition highlights the need for evidence-based national recommendations to standardize diagnosis and management across different levels of healthcare. Abnormal uterine bleeding, particularly postmenopausal bleeding, is the most common presenting symptom of endometrial carcinoma and provides an important opportunity for early diagnosis. Nevertheless, delays in presentation, limited public awareness, restricted access to diagnostic investigations, specialist multidisciplinary services, molecular testing, radiotherapy, and newer systemic therapies contribute to significant variations in care across Kenya. Consequently, patient management frequently depends on available resources, institutional

expertise, and access to specialized services rather than standardized national recommendations. These variations may result in delayed diagnosis, inconsistent treatment approaches, and inequitable patient outcomes.

1.4 Rationale for the GOSK protocol

Over the past decade, major advances in the understanding and management of endometrial carcinoma have transformed clinical practice. The incorporation of molecular classification into routine risk stratification, wider adoption of minimally invasive surgery and sentinel lymph node mapping, together with the introduction of targeted therapies and immune checkpoint inhibitors, has enabled increasingly individualized treatment strategies (3-5). Despite these advances, Kenya currently lacks a nationally endorsed, evidence-based clinical management protocol for endometrial carcinoma. This guideline was therefore developed to adapt contemporary international evidence to the Kenyan healthcare context, promote standardized multidisciplinary care, support rational resource utilization, and improve the quality, consistency, and outcomes of care for women diagnosed with endometrial carcinoma.

2.0 Risk factors, Clinical presentation, Histology, and Staging

2.1 Risk factors

Endometrial carcinoma is a multifactorial malignancy resulting from complex interactions between hormonal, metabolic, genetic, and environmental factors. Persistent exposure to unopposed estrogen is the principal pathogenic mechanism underlying endometrioid endometrial carcinoma, whereas non-endometrioid carcinomas are generally estrogen-independent tumors that occur predominantly in older women and are characterized by TP53 abnormalities and chromosomal instability. A subset of endometrial carcinomas, particularly those with mismatch repair deficiency, may arise in association with hereditary cancer syndromes such as Lynch syndrome. Recognition of these risk factors facilitates risk stratification, appropriate counseling, early diagnosis, and implementation of preventive strategies (3-5, 7-11).

2.1.1 Hormonal factors

Persistent exposure to unopposed estrogen stimulates continuous endometrial proliferation, increasing the risk of endometrial hyperplasia and subsequent malignant transformation. Important hormonal risk factors include estrogen-only hormone replacement therapy, chronic anovulation, including polycystic ovary syndrome, early menarche (before 12 years), late menopause (after 55 years), and nulliparity (10-11).

2.1.2 Metabolic and Lifestyle Factors

Metabolic disorders promote endometrial carcinogenesis through increased peripheral aromatization of androgens to estrogens, hyperinsulinemia, chronic inflammation, and dysregulated cellular proliferation. Obesity is the single most important modifiable risk factor for endometrioid endometrial carcinoma, with risk increasing progressively with increasing body mass index (3-4, 10-11). Metabolic factors include obesity, diabetes mellitus, hypertension, and metabolic syndrome.

2.1.3 Genetic and hereditary syndromes

Approximately 3–5% of endometrial carcinomas are attributable to inherited cancer predisposition syndromes. Lynch syndrome is the most common hereditary syndrome and confers a lifetime risk of approximately 40–60%, depending on the affected mismatch repair gene (3,5,8). Lynch syndrome includes MLH1, MSH2, MSH6, or PMS2 pathogenic variants; mismatch repair deficiency; increased risk of endometrial, colorectal, and ovarian cancers. On the other hand, Cowden syndrome: PTEN pathogenic variants; PI3K/AKT pathway dysregulation.

2.1.4 Other risk Factors

Additional recognized risk factors include increasing age (peak incidence at 55–65 years), previous atypical endometrial hyperplasia/endometrial intraepithelial neoplasia (EIN), previous pelvic irradiation, diets associated with obesity and metabolic syndrome, and ethnicity, with women of African ancestry more likely to present with aggressive histological subtypes and poorer oncological outcomes (10-11).

2.2 Clinical presentation

Clinical manifestations vary according to tumor stage, histological subtype, and disease extent. Postmenopausal bleeding is the cardinal presenting symptom and should always prompt evaluation to exclude endometrial carcinoma. Early-stage disease commonly presents with abnormal uterine bleeding, whereas advanced disease may present with symptoms related to local tumor invasion or distant metastases (3-5,9).

Table 9. Clinical presentation of endometrial carcinoma

Category	Clinical features
Typical presentation	Endometrial cancer commonly presents with the following signs and symptoms: postmenopausal bleeding; abnormal uterine bleeding in premenopausal women (intermenstrual bleeding, menorrhagia, irregular cycles); and watery or blood-stained vaginal discharge.
Less common presentation	Pelvic pain or pressure; dyspareunia; palpable pelvic or abdominal mass; and incidental findings during infertility workup, abnormal Pap smear, or imaging for other reasons.
Advanced disease	Presentation varies depending on disease extent and may include: constitutional symptoms—weight loss, anorexia, and fatigue; urinary symptoms—frequency, dysuria, and hematuria (bladder invasion); gastrointestinal symptoms—constipation and rectal

Table 9. Clinical presentation of endometrial carcinoma	
Category	**Clinical features**
	bleeding (rectal involvement); lower-limb edema (lymphatic obstruction); and symptoms of distant metastases—cough, dyspnea, and bone pain.

2.3 Histology and molecular classification

Endometrial carcinoma comprises a heterogeneous group of epithelial malignancies with distinct histopathological and molecular characteristics that influence prognosis, patterns of recurrence, and treatment selection. Traditionally, classification was based primarily on histological subtype and tumor grade. Advances in molecular pathology have demonstrated that tumors with similar histological appearances may exhibit markedly different biological behavior and clinical outcomes. Consequently, contemporary classification integrates histopathological assessment with molecular profiling to improve prognostic stratification and guide individualized management (4-7,12-15).

2.3.1 Historical classification

The historical classification of endometrial carcinoma was based on the Type I and Type II model proposed by Bokhman in 1983 (8). Although this model provided a useful framework for understanding endometrial carcinoma, it does not fully capture the molecular heterogeneity of the disease and has largely been superseded by contemporary molecular classification (12).

2.3.2 WHO 2020 Histological Classification

The WHO Classification of Female Genital Tumours, fifth edition (2020), recognizes endometrial carcinoma as a heterogeneous group of epithelial malignancies comprising distinct histological subtypes with different biological behaviors, prognoses, and therapeutic implications (7).

Table 10. WHO 2020 Histological Classification of Endometrial Carcinoma

Histological Subtype	Frequency	Common molecular alterations	Key clinicopathological features / prognosis
Endometrioid carcinoma	75–80%	PTEN, PIK3CA, ARID1A, CTNNB1, KRAS, POLE, MMR deficiency	Usually low grade(grade 1-2); favourable prognosis when low grade
Serous carcinoma	10%	TP53 mutation (>90%), HER2 amplification/overexpression , PPP2R1A, FBXW7	Highly aggressive; often presents late; poor prognosis
Clear cell carcinoma	<5%	PIK3CA, ARID1A, PPP2R1A, TP53	Aggressive behavior; poor prognosis
Mixed epithelial carcinoma	<5%	Variable (depending on constituent histologies)	Depends on highest-grade component
Undifferentiated/dedifferentiated carcinoma	Rare	SWI/SNF complex deficiency (SMARCA4, SMARCB1, ARID1A/ARID1B), TP53	Very aggressive; poor prognosis
Neuroendocrine carcinoma	Rare	Variable; TP53 and RB1 alterations reported in many cases	Highly aggressive with early metastasis
Mesonephric-like adenocarcinoma	Rare	KRAS mutations; NRAS occasionally reported; typically lacks PTEN and TP53 mutations	Intermediate to aggressive; often presents at advanced stage
Carcinosarcoma	Rare	TP53, PIK3CA, PPP2R1A, FBXW7.	High-grade biphasic tumor (epithelial and mesenchymal differentiation); now regarded as a metaplastic carcinoma with poor prognosis.

Source: Modified from WHO Classification of Female Genital Tumors, 5th edition (2020).

2.3.3 Limitations of histological classification

Histological classification has limitations, including interobserver variability and limited prognostic information. These limitations have contributed to the development and adoption of molecular classification to improve prognostic assessment and treatment selection (4,12-15).

2.3.4 The Cancer Genome Atlas (TCGA)

The Cancer Genome Atlas (TCGA) classification identifies four molecular subgroups of endometrial carcinoma POLE-mutated (POLEmut), mismatch repair-deficient (MMRd), no specific molecular profile (NSMP), and p53-abnormal (p53abn) (12).

Table 11: TCGA molecular classification of endometrial carcinoma

Subtype	Frequency	Molecular features	Prognosis	Clinical implications
POLEmut	7–10%	POLE exonuclease mutation	Excellent	Consider treatment de-escalation
MMRd	25–30%	Loss of MLH1/PMS2/MSH2/MSH6	Intermediate	Evaluate for Lynch syndrome; Immunotherapy
NSMP	40–50%	No specific molecular profile	Intermediate	Clinicopathological risk guides treatment (FIGO stage, histological subtype, tumor grade, depth of myometrial invasion, LVSI, cervical stromal involvement, and nodal status)
p53abn	20–25%	Abnormal p53/copy-number high	Poor	Aggressive therapy; HER2 testing in serous carcinoma

Source: Cancer Genome Atlas Research Network. Integrated genomic characterization of endometrial carcinoma. Nature. 2013;497:67–73.

2.3.5 Proactive Molecular Risk Classifier for Endometrial Cancer (ProMisE)

Integrated molecular classification is performed sequentially using POLE sequencing, mismatch repair immunohistochemistry (MLH1, PMS2, MSH2, and MSH6), and p53 immunohistochemistry, thereby assigning each tumor to one of the four TCGA-derived molecular subgroups (4,15). The Proactive Molecular Risk Classifier for Endometrial Cancer (ProMisE) was developed to translate the TCGA molecular classification into a clinically applicable algorithm using immunohistochemistry and targeted sequencing. It enables accurate molecular classification in routine pathology practice and has been widely adopted in contemporary clinical guidelines (13-15). The figure below illustrates the ProMisE testing algorithm applicable in settings where molecular testing is available.

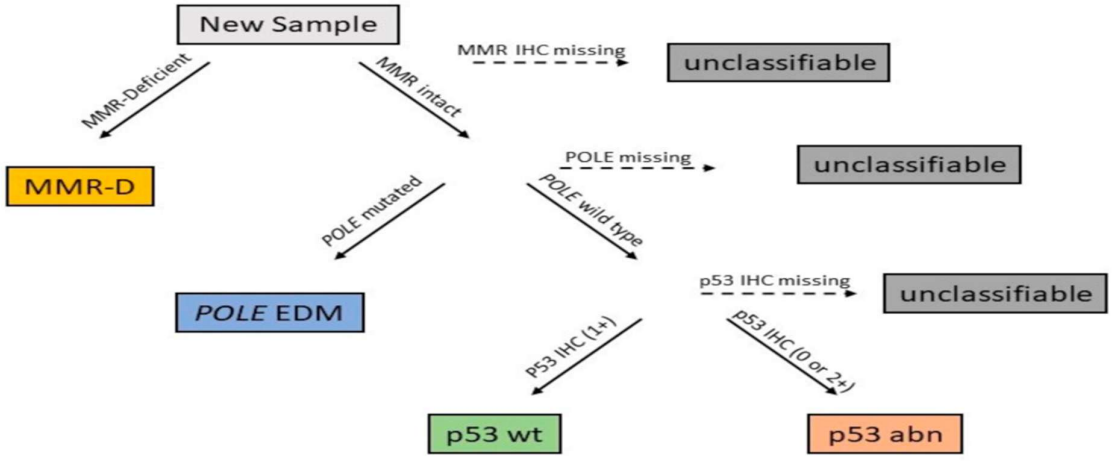


Figure 1. The Proactive Molecular Risk Classifier for Endometrial Cancer (ProMisE) Algorithm to assess a new endometrial cancer sample.

Source: Adapted from Talhouk A, McConechy MK, Leung S, et al. A clinically applicable molecular-based classification for endometrial cancers. Br J Cancer. 2015;113:299–310.

2.4 FIGO Staging Endometrial Carcinoma

Accurate surgical and pathological staging is fundamental to the management of endometrial carcinoma. Staging provides prognostic information, guides adjuvant treatment recommendations, facilitates communication among multidisciplinary teams, and enables comparison of clinical outcomes across institutions. The International Federation of Gynecology and Obstetrics (FIGO) Committee on Gynecologic Oncology transitioned from clinical to surgical staging for endometrial cancer in 1988, with subsequent updates in 2009. Endometrial cancer management guidelines have been based on the FIGO 2009 staging system for over a decade, which emphasizes both surgical and pathological parameters. While this framework provided a standardized approach to risk stratification and treatment, it did not incorporate emerging insights into the molecular heterogeneity of endometrial cancer. The 2023 FIGO staging system incorporates contemporary pathological and molecular evidence, including the prognostic significance of

molecular classification, to improve risk stratification and individualized treatment planning (5).

The tables below summarize the FIGO 2009 and 2023 staging systems for endometrial carcinoma, highlighting the key differences and updates between the two versions.

2.4.1 FIGO 2009 and 2023 staging systems

Table 12: FIGO 2009 and 2023 staging of endometrial carcinoma

Stage	2009 Staging	2023 Staging
I[a]	Tumor confined to the uterine corpus	Confined to the uterine corpus and ovary[d]
	IA[a] No or less than half myometrial invasion	Disease limited to the endometrium OR non-aggressive histological type
	IA1	Non-aggressive histological type limited to an endometrial polyp OR confined to the endometrium
	IA2	Non-aggressive histological types involving less than half myometrial invasion with no or focal LVSI
	IA3	Low-grade endometrioid carcinomas limited to the uterus and ovary[d]
	IB[a] Invasion equal to or more than half of the myometrium	Non-aggressive histological types with invasion of half or more of the myometrium, and with no or focal LVSI[e]
II[a]	Tumor invades cervical stroma, but does not extend beyond the uterus[b]	Invasion of cervical stroma without extrauterine extension OR with substantial LVSI OR aggressive histological types with myometrial invasion
	IIA	Invasion of the cervical stroma of non-aggressive histological types
	IIB	Substantial LVSI[e] of non-aggressive histological types
	IIC	Aggressive histological types[f] with any myometrial involvement
III[a]	Local and/or regional spread of the tumor	
	IIIA[a] Tumor invades the serosa of the corpus uteri and/or adnexa[c]	Invasion of uterine serosa, adnexa, or both by direct extension or metastasis.
	IIIA1	Spread to ovary or fallopian tube (except when meeting Stage IA3 criteria)[d]
	IIIA2	Involvement of uterine subserosa or spread through the uterine serosa
	IIIB[a] Vaginal involvement and/or parametrial involvement	Metastasis or direct spread to the vagina and/or to the parametria or pelvic peritoneum.
	IIIB1	Metastasis or direct spread to the vagina and/or the parametria.
	IIIB2	Metastasis to the pelvic peritoneum
	IIIC[a] Metastases to pelvic and/or para-aortic lymph nodes[c]	
	IIIC1[a] Positive pelvic nodes	
	IIIC1i	Micrometastasis[g]
	IIIC1ii	Macrometastasis[h]
	IIIC2[a] Positive para-aortic nodes ± positive pelvic lymph nodes	
	IIIC2i	Micrometastasis[g]
	IIIC2ii	Macrometastasis[h]
IV[a]	Tumor invades bladder and/or bowel mucosa, and/or distant metastases	
	IVA[a] Tumor invasion of bladder and/or bowel mucosa	
	IVB[a] Distant metastasis, including intra-abdominal metastases and/or inguinal nodes	Abdominal peritoneal metastasis beyond the pelvis
	IVC[a]	Distant metastasis, including metastasis to any extra- or intra-abdominal lymph nodes above the renal vessels, lungs, liver, brain, or bone

Stage	2009 Staging	2023 Staging

Abbreviations: FIGO: International Federation of Gynecology and Obstetrics, LVSI: lymphovascular space involvement.

[a] Either G1, G2, or G3 for the FIGO 2009 classification.

[b] Endocervical glandular involvement only should be considered as Stage I and no longer as Stage II.

[c] Positive cytology has to be reported separately without changing the stage.

[d] Low-grade endometrioid endometrial carcinoma (EEC) involving both the endometrium and the ovary is considered to have a good prognosis, and no adjuvant treatment is recommended if the criteria listed below are met. Disease limited to low-grade endometrioid carcinoma involving the endometrium and ovaries (Stage IA3) must be distinguished from extensive spread of the endometrial carcinoma to the ovary (Stage IIIA1), by the following criteria: (1) no more than superficial myometrial invasion is present (<50%); (2) absence of extensive/substantial LVSI; (3) absence of additional metastases; and (4) the ovarian tumor is unilateral, limited to the ovary, without capsule invasion/rupture (equivalent to pT1a).

[e] Focal LVSI is defined as involvement of fewer than five lymphovascular spaces surrounding the tumor, whereas substantial (extensive) LVSI is defined as diffuse or multifocal involvement of five or more lymphovascular spaces surrounding the tumor.

[f] Grade and histological type:

Serous adenocarcinomas, clear cell adenocarcinomas, mesonephric-like carcinomas, gastrointestinal-type mucinous endometrial carcinoma, undifferentiated carcinomas, and carcinosarcomas are considered high-grade by definition. For EEC, grade is based on the proportion of solid areas: low grade = grade 1 (≤5%) and grade 2 (6%–50%); and high grade = grade 3 (>50%). Nuclear atypia excessive for the grade raises the grade of a grade 1 or 2 tumor by one. The presence of unusual nuclear atypia in an architecturally low-grade tumor should prompt the evaluation of p53 and consideration of serous carcinoma. Adenocarcinomas with squamous differentiation are graded according to the microscopic features of the glandular component.

Non-aggressive histological types are composed of low-grade (grades 1 and 2) EEC. Aggressive histological types are composed of high-grade EEC (grade 3), serous, clear cell, undifferentiated, mixed, mesonephric-like, gastrointestinal mucinous type carcinomas, and carcinosarcomas.

It should be noted that high-grade EEC (grade 3) is a prognostically, clinically, and molecularly heterogeneous disease, and the tumor type that benefits most from applying molecular classification for improved prognostication and for treatment decision-making. Without molecular classification, high-grade EEC cannot be allocated appropriately to a risk group and thus molecular profiling is particularly recommended in these patients. For practical purposes, and to avoid undertreatment of patients, if the molecular classification is unknown, high-grade EEC is grouped together with the aggressive histological types in the actual FIGO classification.

[g] Micrometastases 0.2–2 mm

[h] Macrometastases >2 mm in size

Source: Adapted from Berek JS, Matias-Guiu X, Creutzberg CL, et al. FIGO staging of endometrial cancer: 2023. Int J Gynaecol Obstet. 2023;162:383–394.

2.4.2 Major changes introduced in FIGO 2023

Table 13: FIGO 2023 staging with molecular classification

Stage	Molecular findings (Stage I & II after surgical staging)
Stage $IAm_{POLEmut}$	*POLEmut* endometrial carcinoma, confined to the uterine corpus or with cervical extension, regardless of the degree of LVSI or histological type.
Stage $IICm_{p53abn}$	p53abn endometrial carcinoma confined to the uterine corpus with any myometrial invasion, with or without cervical invasion, and regardless of the degree of LVSI or histological type.

FIGO Stages I and II are based on surgical/anatomical and histological findings. In case the molecular classification reveals *POLEmut* or p53abn status, the FIGO stage is modified in the early stage of the disease. This is depicted in the FIGO stage by the addition of "m" for molecular classification, and a subscript is added to denote *POLEmut* or p53abn status, as shown above.

MMRd or NSMP status do not modify early FIGO stages; however, these molecular classifications should be recorded for the purpose of data collection. When molecular classification reveals MMRd or NSMP, it should be recorded as Stage Im_{MMRd} or Stage Im_{NSMP} and Stage IIm_{MMRd} or Stage IIm_{NSMP}.

FIGO Stages III and IV are based on surgical/anatomical findings. The stage category is not modified by molecular classification; however, the molecular classification should be recorded if known. When the molecular classification is known, it should be recorded as Stage IIIm or Stage IVm with the appropriate subscript for the purpose of data collection. For example, when molecular classification reveals p53abn, it should be recorded as Stage $IIIm_{p53abn}$ or Stage IVm_{p53abn}.

Source: Adapted from Berek JS, Matias-Guiu X, Creutzberg CL, et al. FIGO staging of endometrial cancer: 2023. Int J Gynaecol Obstet. 2023;162:383–394.

Table 14: Major changes in FIGO 2023 staging of endometrial carcinoma

FIGO 2009	FIGO 2023
No molecular classification	Molecular subtype incorporated
Single Stage IA	IA1, IA2 and IA3 introduced

FIGO 2009	FIGO 2023
Ovarian involvement is always IIIA	Low-grade endometrioid carcinomas with simultaneous low-grade unilateral ovarian involvement staged IA3. Other ovarian involvement remains Stage IIIA.
Single stage II	Stage IIA, IIB and IIC introduced
Conventional nodal staging	Nodal staging refined to distinguish micrometastases (i) and macrometastases (ii) in pelvic (IIIC1) and para-aortic (IIIC2) lymph nodes.
Stage IVB included all distant metastases	Stage IVC introduced for widespread distant metastases

2.4.3 Molecular classification and FIGO 2023

Following assignment of the anatomical stage, tumors with confirmed POLEmut or p53abn status may receive the suffix mPOLEmut or mp53abn to reflect their distinct prognostic implications. Molecular classification complements, but does not replace, anatomical staging (5).

2.4.4 Sentinel lymph node assessment

Sentinel lymph node mapping is the preferred approach for nodal assessment in uterine-confined disease where expertise is available. Ultrastaging improves the detection of isolated tumor cells and micrometastases, which are recognized within the FIGO 2023 staging system.

2.5 Risk stratification of endometrial carcinoma

Risk stratification in endometrial carcinoma has traditionally been based on clinicopathological factors, including histological subtype, tumor grade, depth of myometrial invasion, and the presence or extent of lymphovascular space invasion (LVSI). One of the earliest evidence-based prognostic models was established by the Gynecologic Oncology Group (GOG)-99 trial, which defined the high-intermediate-risk (HIR) group to guide the use of adjuvant pelvic radiotherapy to reduce locoregional recurrence (3,16).

The GOG-99 criteria define high-intermediate-risk (HIR) disease using a combination of patient age and three adverse clinicopathological factors: grade 2–3 histology, at least 50% myometrial invasion, and lymphovascular space invasion (LVSI). HIR disease is classified as follows age 70 years or older with one risk factor age 50–69 years with two risk factors, and Any age with all three risk factors present (16). With advances in molecular diagnostics, risk assessment has evolved to incorporate genomic features. The European Society of Gynaecological Oncology (ESGO), European Society for Radiotherapy and Oncology (ESTRO), and European Society of Pathology (ESP) introduced a revised 2021 risk stratification system that integrates traditional histopathological parameters with molecular profiling (4). The integration of molecular and clinicopathological parameters enhances prognostic accuracy and facilitates more personalized treatment planning by guiding adjuvant therapy decisions while minimizing overtreatment (4,14-15).

The ESGO/ESTRO/ESP 2021 risk stratification is summarized in the table below.

Table 15: ESGO/ESTRO/ESP risk stratification of endometrial carcinoma

Risk Category	Molecular profiling unavailable	Molecular profiling available
Low risk	Low-grade stage IA endometrioid with no or focal LVSI	Stage I-II POLEmut with no residual disease Low-grade Stage IA endometrioid MMRd/NSMP with no or focal LVSI
Intermediate risk	High-grade stage IA endometrioid with no or focal LVSI Low-grade stage IB endometrioid with no or focal LVSI Stage IA non-endometrioid without myometrial invasion	Low-grade stage IB endometrioid MMRd/NSMP with no or focal LVSI High-grade Stage IA endometrioid MMRd/NSMP with no or focal LVSI Stage IA p53 abn and/or non-endometrioid without myometrial invasion
High intermediate risk	Stage I endometrioid with substantial LVSI regardless of grade and depth of invasion. High-grade stage IB endometrioid regardless of LVSI status. Stage II endometrioid carcinoma.	Stage I endometrioid MMRd/NSMP with substantial LVSI regardless of depth of invasion. High-grade stage IB endometrioid MMR/NSMP regardless of LVSI status Stage II MMRd/NSMP endometrioid carcinoma
High risk	Stage III – IVA without residual disease Stage I - IVA non-endometrioid with myometrial invasion and no residual disease	Stage III-IVA endometrioid MMRd/NSMP with no residual disease Stage I – IVA endometrioid p53 abn + myometrial invasion with no residual disease Stage I – IVA serous, undifferentiated, carcinosarcoma MMRd/NSMP + myometrial invasion with no residual disease.

Risk Category	Molecular profiling unavailable	Molecular profiling available
Advanced/metastatic disease	Stage III – IVA with residual disease Stage IVB	Stage III – IVA with residual disease, any molecular type Stage IVB any molecular type
According to FIGO binary grading, grades 1 and 2 carcinomas are considered low-grade, and grade 3 carcinomas are considered high-grade.		

Source: Adapted from Concin N, Matias-Guiu X, Vergote I, et al. ESGO/ESTRO/ESP Guidelines for the Management of Patients with Endometrial Carcinoma. Int J Gynecol Cancer. 2021;31(1):12–39.

3.0 Objectives

3.1 Overall objective

To establish a standardized, evidence-based approach to the management of endometrial carcinoma in Kenya.

3.2 Specific objectives

This management protocol for endometrial carcinoma provides recommendations and guidance on:

1. The diagnostic workup, including clinical assessment, imaging, and histopathological methods.
2. Surgical staging procedures for endometrial carcinoma.
3. Special considerations in incomplete surgical staging and fertility-sparing options.
4. Adjuvant treatment according to stage, histological type, and risk stratification.
5. Management of recurrent disease.
6. Post-treatment surveillance.
7. Supportive and palliative care.

4.0 Clinician responsibility

This protocol represents the evidence-based consensus of the multidisciplinary development group under the Gynecologic Oncology Society of Kenya (GOSK) for the management of patients with endometrial carcinoma. It is intended to provide guidance to clinicians; however, application of these recommendations should always be informed by independent clinical judgment, considering each patient's individual circumstances.

5. Methods

5.1 Guideline adaptation approach

This protocol was developed through an adaptation approach, drawing on high-quality existing international guidelines and tailoring them to Kenya's health system and resource context. A multidisciplinary protocol development panel was convened, comprising gynecologic oncologists, pathologists, radiologists, gynecologic oncology nurses, onco-pharmacists, radiation oncologists, public health specialists, and patient representatives. The panel received technical orientation from experts at the University of Nairobi and Kenyatta National Hospital on the principles of evidence-based guideline adaptation. The training emphasized the use of standardized appraisal tools, systematic methods for evaluating published guidelines and protocols, and approaches for contextualizing recommendations to local realities. This process aimed to ensure alignment with internationally accepted standards while addressing the unique challenges of Kenya's healthcare setting (17-19).

5.2 Search strategy and identification of source guidelines

A comprehensive search was conducted through PubMed and Google Scholar to identify relevant evidence-based guidelines, systematic reviews, and best practice statements on the management of endometrial carcinoma. Search terms included "endometrial carcinoma," "clinical guideline," "gynecologic oncology," "protocol," and "guideline." Five primary reference guidelines were identified, as summarized in Table 16 (3-4, 17-22).

Table 16: Summary of retrieved endometrial carcinoma guidelines

	Title	Publisher	Year of last update
1.	Clinical Practice Guidelines in Oncology: Uterine Neoplasms Version 3.2025.[3]	National Comprehensive Cancer Network (NCCN)	2025
2.	ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma.[4]	European Society of Gynaecological Oncology (ESGO), the European Society for Radiotherapy and Oncology (ESTRO), and the European Society of Pathology (ESP)	2021
3.	Pan-Asian adapted ESMO Clinical Practice Guidelines for the diagnosis, treatment and follow-up of patients with endometrial cancer.[20]	European Society for Medical Oncology (ESMO) Open Journal	2022
4.	British Gynaecological Cancer Society (BGCS) Uterine Cancer Guidelines: Recommendations for Practice.[21]	BGCS	2021
5.	Prescribed Minimum Benefits (PMB) definition guideline: Endometrial cancer.[22]	The Council for Medical Schemes (CMS) South Africa	2019

5.3 AGREE II appraisal

All retrieved guidelines were appraised independently by two trained panelists using the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument, which evaluates quality across six domains (17):

1. Scope and purpose.
2. Stakeholder involvement.
3. Rigour of development.
4. Clarity of presentation.
5. Applicability.
6. Editorial independence.

Each domain was scored on a 7-point Likert scale. Scores were converted to percentages using the AGREE II recommended formula. Overall quality ratings and recommendations for use in Kenya were recorded (17).

5.4 Guideline selection

Although all domains were assessed, particular emphasis was placed on Rigour of Development (Domain 3) and Clarity of Presentation (Domain 4). Guidelines scoring below 75% for Domain 3 or below 60% for Domain 4 were excluded. Three guidelines—the NCCN, ESGO/ESTRO/ESP, and Pan-Asian ESMO guidelines—were selected for detailed analysis of recommendations (17,19).

Table 17: Summary of AGREE II domain scores for each source guideline

	Title	Domain 1	Domain 2	Domain 3	Domain 4	Domain 5	Domain 6	Overall Decision
1	NCCN Clinical Practice Guidelines in Oncology: Uterine Neoplasms Version 3.2025.[3]	85%	85%	90%	92%	83%	90%	Included
2	Pan-Asian adapted ESMO Clinical Practice Guidelines for the diagnosis, treatment and follow-up of patients with endometrial cancer.[20]	89%	80%	89%	92%	85%	88%	Included
3	British Gynaecological Cancer Society (BGCS) Uterine Cancer Guidelines: Recommendations for Practice.[21]	88%	80%	86%	92%	80%	89%	Included
4	ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma.[4]	90%	88%	86%	92%	85%	85%	Included
5	Prescribed Minimum Benefits (PMB) definition guideline: Endometrial cancer.[22]	75%	70%	60%	65%	80%	70%	Excluded

6.0 Review of evidence

Recommendations from the three selected guidelines: NCCN 2025, ESGO/ESTRO/ESP 2021, and Pan-Asian ESMO 2022 were systematically compared and analyzed in relation to each of the predefined objectives of the adapted national guideline for the management of endometrial carcinoma.

Table 18: Comparative evidence from source guidelines for diagnostic workup for endometrial carcinoma

Category	**Guideline**		
	NCCN[3]	**ESGO/ESTRO/ESP[4]**	**Pan-Asian Adapted ESMO[20]**
Clinical assessment	Comprehensive history and physical exam, including pelvic exam. Pipelle endometrial biopsy. D & C (where the endometrial biopsy is negative in a symptomatic patient). Hysteroscopy (patients with persistent or recurrent AUB)	Comprehensive history including inventory of co-morbidities and physical exam, including pelvic exam. Pipelle endometrial biopsy or D & C.	Comprehensive history and physical exam, including gynaecological exam. Pipelle endometrial biopsy or D & C.
Imaging	Chest X-ray (Chest CT where CXR is abnormal). Pelvic MRI – assessment of origin of tumor (endometrial vs	Expert transvaginal or transrectal ultrasound Pelvic MRI	Expert transvaginal ultrasound Pelvic MRI

Category	Guideline		
	endocervical) and local disease extent. Chest/abdomen/pelvic CT – high grade carcinoma to assess for metastasis, incompletely staged disease or suspected metastatic disease. Neck/chest/abdomen/pelvis/groin fluorodeoxyglucose (FDG)-PET/CT – assess metastasis.	Chest/abdomen/pelvic CT or PET-CT - Depending on clinical and pathologic risk to assess ovarian, nodal, peritoneal, and other sites of metastatic disease.	Additional imaging tests in patients at high risk of extrapelvic disease, e.g., abdominal and thoracic CT scan and/or FDG PET.
Histopathology	Pathological assessment of hysterectomy/staging specimens by expert pathologist. Comprehensive molecular profiling is strongly encouraged on the initial biopsy or D&C material or the final hysterectomy specimen. ER/PR testing for stage III-IV and recurrent endometrioid carcinoma. HER 2 IHC testing for advanced/recurrent serous carcinoma, carcinosarcoma and p53 aberrant carcinomas regardless of histotype.	Histopathologic tumor type and grade in endometrial biopsy is required. The decision to use molecular classification depends on availability of resources.	Histologic type, FIGO grade, myometrial invasion and LVSI reported for all pathology specimens. Molecular classification of all pathology specimens regardless of histology.

Table 19: Comparative evidence from source guidelines for surgical staging of endometrioid endometrial carcinoma

Tumor stage	Tumor grade	Guideline		
		NCCN[3]	ESGO/ESTRPO/ESP[4]	Pan-Asian ESMO[20]
1A	1 & 2 (low grade)	TH/BSO/Peritoneal cytology Ovarian preservation in premenopausal women with endometrioid histology, grade 1 and normal appearing ovary (bilateral salpingectomy recommended) *. Pelvic nodal dissection or SLNE, where available. Nodal dissection can be omitted in cases with no myometrial invasion**. Visual evaluation of peritoneal, diaphragmatic and serosal surfaces with biopsy of any suspicious lesions.	TH/BSO SLNE, where available. Systematic LND is not recommended for low- or intermediate-risk disease. Surgical lymph node staging should be performed in patients with high–intermediate–risk/high-risk disease. When a systematic lymphadenectomy is performed, pelvic and para-aortic infrarenal lymph node dissection is suggested. If pelvic lymph node involvement is found intra-operatively, further systematic pelvic lymph node dissection should be omitted. However, debulking of enlarged lymph nodes and para-aortic staging can be considered. Ovarian preservation can be considered in pre-menopausal patients aged <45 years with low-grade endometrioid endometrial carcinoma with myometrial invasion <50%. In cases of ovarian preservation, salpingectomy is recommended.	TH/BSO. Ovarian preservation can be considered in premen opausal women with stage IA, G1 endometrioid-type endometrial cancer. SLNE can be considered in cases of low-risk/intermediate-risk disease in experienced. It can be omitted in cases without myometrial invasion. When SLNE is not available, systematic lymphadenectomy can be carried out. Surgical lymph node staging should be carried out in patients with high-intermediate-risk/high-risk disease.
	3 (high grade)	TH/BSO/Peritoneal cytology. Pelvic + para-aortic lymphadenectomy***. SLNE acceptable		
1B		TH/BSO Pelvic + para-aortic lymphadenectomy SLNE where available		
II		TH/BSO/peritoneal cytology. Or	Total hysterectomy with bilateral salpingo-	

Tumor stage	Tumor grade	Guideline		
		NCCN[3]	ESGO/ESTRPO/ESP[4]	Pan-Asian ESMO[20]
		Radical hysterectomy (to achieve free surgical margins) Pelvic + paraaortic lymphadenectomy. SLNE is acceptable. If unsuitable for surgery, consider neoadjuvant RT or chemotherapy****.	oophorectomy and lymph node staging. More extensive procedures should be performed only if necessary to achieve free surgical margins. SLNE is acceptable.	
III – IV*****	Abdominal/Pelvic-confined disease	TH/BSO/Omentectomy Maximal effort cytoreduction (to no measurable residual disease), where feasible with acceptable morbidity. Or Consider NACT Or Definitive RT with or without systemic therapy.	Surgical tumor debulking, including enlarged lymph nodes, should be considered when complete macroscopic resection is feasible with an acceptable morbidity and quality-of-life profile, following full pre-operative staging and multidisciplinary team discussion. Primary systemic therapy should be used if upfront surgery is not feasible or acceptable. In cases of a good response to systemic therapy, delayed surgery can be considered. Only enlarged lymph nodes should be resected. Systematic lymphadenectomy is not recommended. For unresectable tumors, a multi-disciplinary team discussion should consider definitive radiotherapy with EBRT and intra-uterine brachytherapy, or neoadjuvant chemotherapy prior to surgical resection or definitive radiotherapy, depending on response.	When feasible, and with acceptable morbidity, cytoreductive surgery to the maximal surgical extent.
	Distant metastasis	Systemic therapy with or without EBRT with or without SBRT TH/BSO Or Systemic therapy, then reassess for the feasibility of surgery	Individualised approach with either RT or chemotherapy, or a combination of both, after MDT discussion. Patients with oligometastatic disease (1-5 mets) should be considered for radical local therapy: Surgery, radiation therapy, including stereotactic radiotherapy, and local ablating techniques.	
Surgical approach		Laparotomy or MIS (uterine confined disease) Laparotomy for extra-uterine disease.	MIS for uterine confined disease. Laparotomy for disease outside the uterus and cervix (excluding LN metastasis).	MIS for uterine confined disease. Laparotomy for disease outside the uterus and cervix.

BSO: Bilateral salpingo-oophorectomy; EBRT: External beam radiotherapy; MIS: Minimally invasive surgery; NACT: Neo-adjuvant chemotherapy; SBRT: Stereotactic body radiotherapy SLNE: Sentinel lymph node excision; TH: Total hysterectomy; VBT: Vaginal Brachytherapy

Tumor stage	Tumor grade	Guideline		
		NCCN[3]	ESGO/ESTRPO/ESP[4]	Pan-Asian ESMO[20]
* Ovarian preservation is not recommended for patients with ovarian cancer family history, BRCA mutations or Lynch syndrome. Absence of p53 abnormality, mismatch repair (MMR) deficiency, LVSI, and positive cytology are preferred. ** Criteria suggested as indicative of low risk for nodal metastases where nodal dissection may be omitted: ≤ 50% myometrial invasion, tumor < 2cm, well or moderately differentiated histology. *** Infra-renal para-aortic lymphadenectomy is recommended where there is deeply invasive disease or high-grade histology or Serous, Clear cell, and Carcinosarcoma histology. **** Definitive radiotherapy can be considered for primary tumors where surgery is contraindicated for medical reasons. The combination of EBRT and brachytherapy should be used for high-grade tumors and/or deep myometrial invasion. For low-grade tumors, brachytherapy alone can be considered. ***** ER/PR testing is recommended in the setting of stage III or IV endometrioid tumors. Consider CA 125. Vaginal hysterectomy, with bilateral salpingo-ophorectomy if feasible, can be considered in patients unfit for the recommended standard surgical therapy. In medically unfit patients unsuitable for curative surgery or radiotherapy, systemic treatment (including hormonal therapy) can be considered.				

Table 20: Comparative evidence from source guidelines for surgical staging non-endometrioid endometrial carcinoma

Histology	Guideline			
	NCCN[3]		ESGO/ESTRO/ESP[4]	ESMO[20]
Serous/Clear cell/Carcinosarcoma/Undifferentiated/de-differentiated Carcinomas	Suitable for surgery	TH/BSO/peritoneal cytology. Omentectomy. Peritoneal biopsies. Pelvic and para-aortic lymphadenectomy. Fertility-sparing is not recommended.	Total hysterectomy with bilateral salpingo-oophorectomy without vaginal cuff resection. Staging infracolic omentectomy should be performed in clinical stage I serous endometrial carcinoma, carcinosarcoma, and undifferentiated carcinoma. It can be omitted in clear cell and endometrioid carcinoma in stage I disease. Surgical lymph node staging. In stage III-IV surgical tumor debulking, including enlarged lymph nodes, should be considered when complete macroscopic resection is feasible with an acceptable morbidity and quality of life profile, following full pre-operative staging and discussion by a multi-disciplinary team.	Full surgical staging including omentectomy, peritoneal biopsies and lymph node staging.
	Not suitable for surgery (Disease is not amenable to resection or patient is not suitable for surgery based on comorbidities)	EBRT with or without brachytherapy with or without systemic therapy.		

Table 21: Comparative evidence from source guidelines for management of incompletely staged endometrial carcinoma

Imaging report	Stage	Guideline		
		NCCN[3]	ESGO/ESTRO/ESP[4]	ESMO*
Imaging negative	IA	Grade 1 & 2 – observation or VBT if substantial LVSI and/or patient is ≥ 60 yrs. Grade 3 – VBT or observation if no myoinvasion Or EBRT if substantial LVSI or patient is ≥ 70 yrs	Surgical restaging can be considered in patients with previously incompletely staged high–intermediate–risk/high-risk disease if the outcome might affect the adjuvant treatment strategy.	
	IB or myoinvasive with LVSI	Surgical restaging where feasible. Or		

Imaging report	Stage	Guideline		
		NCCN[3]	ESGO/ESTRO/ESP[4]	ESMO*
		EBRT and/or VBT with or without systemic therapy where surgical restaging is not feasible.		
Imaging suspicious	Resectable	Surgical re-staging.		
	Unresectable	Perform a biopsy if it has not yet been done, then treat based on stage.		
≥ II		Biopsy as indicated. EBRT and/or VBT with or without systemic therapy.		
* No guidance				

Table 22: Comparative evidence from source guidelines for fertility-sparing management in endometrial carcinoma

	Guideline		
	NCCN[3]	ESGO/ESTRO/ESP[4]	Pan-Asian ESMO*(no guidance)
Criteria	Grade 1 endometrioid on D&C confirmed by an expert pathologist. Disease limited to the endometrium. Molecular evaluation of tumor and evaluation for inherited cancer risk. No suspicious or metastatic disease on imaging. No contraindications to medical therapy or pregnancy. Counselling that the fertility-sparing option is NOT standard of care for the treatment of endometrial carcinoma.	AH/EIN or grade 1 endometrioid endometrial carcinoma without myometrial invasion and without genetic risk factors Endometrial biopsy, preferably hysteroscopy. Confirmed/diagnosed by a pathologist experienced in gynecological pathology. Radiologic imaging to assess the extension of the disease. Patients counseling that fertility-sparing treatment is not a standard treatment.	
Treatment options	Consultation with a fertility expert before therapy. Continuous progestin-based therapy: Megestrol Acetate Medroxyprogesterone Levonorgestrel IUD Dual progestin therapy (megestrol acetate/ medroxyprogesterone + levonorgestrel IUD). Weight management/ lifestyle modification counseling. TH/BSO with surgical staging is recommended after childbearing is complete.	Evaluation at fertility center. Hysteroscopic resection prior to progestin. Continuous progestin therapy: Medroxyprogesterone acetate (400–600 mg/day) or megestrol acetate (160–320 mg/day) - Levonorgestrel IUD + oral progestins ± GnRHa Continuous hormonal treatment in responders who wish to delay pregnancy	
Surveillance	Endometrial evaluation every 3–6 months (via D &C or Pipelle endometrial biopsy). If complete response by 6 months – encourage conception, continue surveillance every 6-12 months, and maintain therapy if not actively trying to conceive. If endometrial carcinoma is present at 6-12 months, perform TAH/BSO with staging (preferred by 12 months). Perform TAH/BSO with staging after completion of childbearing.	Hysteroscopy-guided biopsy and imaging at 3–4 and 6 months. No response after 6 months - standard surgical treatment TVUS and physical examination every 6 months. Hysteroscopic and endometrial biopsy in case of AUB or atypical ultrasound findings TAH/BSO after childbearing.	

Table 23: Comparative evidence from source guidelines for adjuvant treatment of endometrioid endometrial carcinoma by stage

Stage		Grade	Guideline		
			NCCN[3]	ESGO/ESTRO/ESP[4]	Pan-Asian Adapted ESMO[20]
I	IA	G1, G2	Observation Or Brachytherapy if substantial LVSI and/or ≥ 60 yrs.	No adjuvant treatment if no or focal LVSI or stage I–II pathogenic POLE mutation or p53abn carcinomas restricted to a polyp or without myometrial invasion. Or EBRT if substantial LVSI	No adjuvant treatment if no or focal LVSI Or EBRT if substantial LVSI
		G3	Brachytherapy Or Consider observation if there is no myoinvasion Or EBRT if LVSI and/or ≥ 70 yrs.	Brachytherapy Or EBRT if substantial LVSI ± adjuvant chemotherapy	Brachytherapy Or EBRT if substantial LVSI ± adjuvant chemotherapy (concomitant and/or sequential).
	IB	G1	Brachytherapy Or Observation if < 60 yrs and no LVSI.	Brachytherapy Or EBRT if substantial LVSI ± adjuvant chemotherapy. Or Observation if < 60 years and no or focal LVSI.	Brachytherapy Or EBRT if substantial LVSI ± adjuvant chemotherapy. Or Observation if < 60 years and no or focal LVSI.
		G2	Brachytherapy Or EBRT if ≥ 60 yrs and/or LVSI Or Observation if < 60 yrs no LVSI.		
		G3	EBRT and/or Brachytherapy ± systemic therapy	Brachytherapy Or EBRT if substantial LVSI ± adjuvant chemotherapy	EBRT± adjuvant chemotherapy for substantial LVSI Or Consider VBT + chemotherapy if no LVSI and EBRT not feasible.
II			EBRT preferred and/or brachytherapy ± systemic therapy	Brachytherapy Or EBRT if substantial LVSI ± adjuvant chemotherapy	Brachytherapy for grade 1 with no or focal LVSI Or EBRT ± adjuvant chemotherapy (G3 and/or substantial LVSI)
III & IV			Systemic therapy ± EBRT ± Brachytherapy	III-IVA with no residual disease after surgical staging: EBRT with concurrent and adjuvant chemotherapy Or sequential chemotherapy and RT Or Chemotherapy alone Residual disease after surgical staging: MDT discussion and individualised management. Residual lymph node disease should be treated with a combination of chemotherapy and EBRT or chemotherapy alone. Unresectable disease: MDT discussion and individualised treatment.	EBRT with concurrent and adjuvant chemotherapy Or sequential chemotherapy and RT Or Chemotherapy alone

Stage	Grade	Guideline		
		NCCN[3]	ESGO/ESTRO/ESP[4]	Pan-Asian Adapted ESMO[20]
			Primary systemic therapy with delayed surgery if good response. Or Definitive EBRT and intrauterine brachytherapy. Or Systemic therapy alone.	

Table 24: Comparative evidence from source guidelines for adjuvant treatment of high-risk histological types of endometrial carcinoma

Histology**	Stage*	Guideline		
		NCCN[3]	ESGO/ESTRO/ESP[4]	Pan-Asian ESMO[20]
Serous	Non-invasive IA	Negative Washings: VBT ± systemic therapy or Observe Positive Washings: Systemic therapy and VBT	Manage as High-risk***	Manage as High-risk***
	Invasive IA - II	Systemic therapy ± EBRT ± VBT Or EBRT ± VBT		
	III & IV	Systemic therapy ± EBRT ± VBT		
	Unsuitable for primary surgery	EBRT ± brachytherapy ± systemic therapy, then re-evaluate for surgery Or Systemic therapy, then re-evaluate for surgery and/or RT based on response.		
Clear-Cell	Non-invasive IA	Negative Washings: VBT ± systemic therapy or Observe. Positive Washings: Systemic therapy and VBT.	Manage as High-risk***	Manage as High-risk***
	Invasive IA - II	Systemic therapy ± EBRT ± VBT Or EBRT ± VBT		
	III & IV	Systemic therapy ± EBRT ± VBT		
	Unsuitable for primary surgery	EBRT ± brachytherapy ± systemic therapy then re-evaluate for surgery Or Systemic therapy then re-evaluate for surgery and/or RT based on response		
Undifferentiated/de differentiated	Adjuvant treatment after surgery	Systemic therapy ± EBRT ± VBT	Manage as High-risk***	Manage as High-risk***
	Unsuitable for primary surgery	Systemic therapy ± EBRT ± vaginal		

Histology**	Stage*	Guideline		
		NCCN[3]	ESGO/ESTRO/ESP[4]	Pan-Asian ESMO[20]
		brachytherapy re-evaluate for surgical resection and/or RT based on response		
Carcinosarcoma	IA	Systemic therapy + VBT ± EBRT (high-grade epithelial component or > 50% sarcoma dominant)	Manage as High-risk***	Manage as High-risk***
	IB - IV	Systemic therapy ± EBRT ± VBT		
	Unsuitable for primary surgery	Uterine confined ± pelvic nodal disease: EBRT ± brachytherapy± systemic therapy then re-evaluate for surgical resection Or Systemic therapy then re-evaluate for surgical resection and/or RT based on response Other metastatic disease: Systemic therapy± EBRT or Best supportive care		
* Surgically staged ** Consider CA 125 for all high-risk histologies *** EBRT with concurrent and adjuvant chemotherapy (Pelvic EBRT 45–50.4 Gy with weekly cisplatin 40 mg/m², followed by carboplatin (AUC 5–6) and paclitaxel (175 mg/m²) every 21 days for 4–6 cycles) Or sequential chemotherapy and RT (Six cycles of carboplatin/paclitaxel administered before, after, or in a "sandwich" sequence with EBRT ± VBT) Or Chemotherapy alone.				

Table 25: Comparative evidence from source guidelines for adjuvant treatment of endometrial carcinoma by risk stratification

Risk category	Guideline		
	NCCN*	ESGO/ESTRO/ESP[4]	Pan-Asian ESMO[20]
Low risk Low-grade stage IA endometrioid with no or focal LVSI OR Stage I-II POLEmut with no residual disease Low-grade Stage IA endometrioid MMRd/NSMP with no or focal LVSI		No adjuvant treatment For the rare patients with stage III–IVA and a pathogenic POLE mutation, there are no outcome data on the omission of adjuvant treatment.	No adjuvant treatment
Intermediate risk High-grade stage IA endometrioid with no or focal LVSI Low-grade stage IB endometrioid with no or focal LVSI Stage IA non-endometrioid without myometrial invasion OR Low-grade stage IB endometrioid MMRd/NSMP with no or focal LVSI High-grade Stage IA endometrioid MMRd/NSMP with no or focal LVSI		VBT Or Observation if <60 years For p53abn carcinomas restricted to a polyp or without myometrial invasion, adjuvant therapy is generally not recommended	VBT Or Observation if <60 years

Risk category	Guideline		
Stage IA p53 abn and/or non-endometrioid without myometrial invasion			
High-intermediate risk Stage I endometrioid with substantial LVSI regardless of grade and depth of invasion High-grade stage IB endometrioid regardless of LVSI status. Stage II endometrioid OR Stage I endometrioid MMRd/NSMP with substantial LVSI regardless of depth of invasion. High-grade stage IB endometrioid MMR/NSMP regardless of LVSI status Stage II MMRd/NSMP endometrioid carcinoma		pN0 after LN staging: VBT (no or focal LVSI) Or EBRT (substantial LVSI or stage II) ± Adjuvant chemo (high grade and/or substantial LVSI)	EBRT ± concomitant or sequential chemotherapy Or VBT alone if no substantial LVSI Or VBT + chemotherapy for stage IB, G3, no LVSI and EBRT not feasible
High risk Stage III – IVA without residual disease Stage I - IVA non-endometrioid with myometrial invasion and no residual disease OR Stage III-IVA endometrioid MMRd/NSMP with no residual disease Stage I – IVA endometrioid p53 abn + myometrial invasion with no residual disease Stage I – IVA serous, undifferentiated, carcinosarcoma MMRd/NSMP + myometrial invasion with no residual disease.		EBRT with concurrent and adjuvant chemotherapy** Or sequential chemotherapy and RT*** Or Chemotherapy alone	EBRT with concurrent and adjuvant chemotherapy** Or sequential chemotherapy and RT*** Or Chemotherapy alone
Advanced/Metastatic Stage III – IVA with residual disease Stage IVB Stage III – IV any molecular type		Maximal cytoreduction if macroscopic complete resection is feasible with acceptable morbidity. Or Primary systemic therapy with delayed surgery if good response. Unresectable tumors due to local extent: MDT, Definitive EBRT and intrauterine brachytherapy Or NACT Image-guided brachytherapy to boost intrauterine, parametrial, or vaginal disease Consider chemo after definitive RT Residual pelvic or para-aortic nodes: Chemo and EBRT Or Chemotherapy alone Residual pelvic disease (positive resection margin, vaginal disease, pelvic side wall disease): Individualized approach: CCRT then chemotherapy Or Chemotherapy then EBRT	

Risk category	Guideline
* No risk stratification ** PORTEC 3 Protocol: EBRT (48.6 Gy in 27 fractions of 1.8Gy each), Cisplatin 50mg/m^2 on days 1 and 29 followed by Carboplatin AUC 5 + Paclitaxel 175mg/m^2 every 21 days for 4 cycles *** Sequential RT: EBRT then 6 cycles carboplatin + paclitaxel or 6 cycles carboplatin + paclitaxel then EBRT or 'Sandwich ': 3 cycles carboplatin + paclitaxel followed by EBRT then another 3 cycles carboplatin + paclitaxel .	

Table 26: Comparative evidence from source guidelines for post-treatment surveillance of endometrial carcinoma

Guideline	Surveillance
NCCN[3]	Physical exam (including pelvis) every 3–6 mo for 2–3 y, then every 6–12 months for up to year 5, then annually. CA-125 surveillance if initially elevated or serous histology. Imaging is indicated based on symptoms or examination findings suspicious for recurrence. Clinical evaluation and management of potential long-term and late effects of treatment.
ESGO/ESTRO/ESP[4]	Not included in the guidelines.
Pan-Asian ESMO[20]	Low risk disease – 6-monthly assessment (physical and gynaecological exam) for 2 years, then annually for 5 years. High risk disease – 3 monthly assessment (physical and gynaecological exam) for 3 years, then 6 monthly for 5 years. Consider CT scan or PET-CT if node extension was present. Regular exercise, a healthy diet and weight management.

Table 27: Comparative evidence from source guidelines for management of recurrent endometrial carcinoma

Recurrence site	Prior treatment	Guideline		
		NCCN[3]	ESGO/ESTRO/ESP[4]	Pan-Asian ESMO[20]
Locoregional without distant metastasis	No prior RT to site of metastasis	EBRT ± VBT ± systemic therapy Or Surgical exploration + resection ± intraoperative RT (IORT) Disease confined to vagina or paravaginal soft tissue EBRT ± VBT ± systemic therapy Pelvic or para-aortic nodes EBRT ± systemic therapy Upper abdomen microscopic residual Systemic therapy ± EBRT Upper abdomen macroscopic Systemic therapy ± palliative EBRT or best supportive care if progression.	MDT with consideration of patient wishes. Surgical resection if complete removal of macroscopic disease can be achieved with acceptable morbidity ± RT and/or systemic therapy depending on the extent and pattern of relapse and the amount of residual disease Palliative surgery in select cases to alleviate symptoms (bleeding, fistula, bowel obstruction) EBRT± chemo with brachytherapy Vaginal cuff recurrence - Pelvic EBRT+intracavitary (±interstitial) image-guided brachytherapy Or Intracavitary only for superficial tumors	EBRT ± VBT±systemic therapy.
	Prior RT	Surgical exploration + resection ± IORT and/or Systemic therapy ± palliative EBRT Or Brachytherapy ± systemic therapy	Radical surgery, including exenteration when the intention is complete resection with clear margins Intraoperative electron radiation therapy Radical re-irradiation options (SBRT,	Surgery only if complete debulking with acceptable morbidity ± systemic therapy. .

Recurrence site	Prior treatment	Guideline		
		NCCN[3]	ESGO/ESTRO/ESP[4]	Pan-Asian ESMO[20]
			permanent seed implants, or proton therapy). Limited volume irradiation with EBRT and VBT. In patients where re-irradiation with EBRT is not an option, image-guided interstitial brachytherapy only is recommended	
Isolated metastasis		Resection and/or EBRT Or Ablative therapy Or Systemic therapy	Oligometastatic disease: - Surgery - RT including SBRT - Local ablating techniques	
Disseminated metastasis		Systemic therapy ± palliative EBRT Or Best supportive care.	Hormone therapy for patients with low-grade carcinomas without rapidly progressive disease. Systemic therapy. In patients with a long platinum- free interval, reintroduction of platinum can be considered. Anti- PD1- based immune therapy with pembrolizumab could be considered for second-line therapy of MSI/MMRd carcinomas. The combination of pembrolizumab and lenvatinib could be considered for second-line treatment of microsatellite-stable carcinomas. Clinical trial participation should be offered to all patients with relapse disease.	Hormonal therapy as front-line systemic therapy for low-grade endometrioid histology with low-volume disease. Immune checkpoint inhibitors after platinum failure in dMMR/MSI-H tumors

Table 28: Comparative evidence from source guidelines for supportive and palliative care in endometrial carcinoma

Guideline	Supportive care
NCCN[3]	Regular general medical review (managing chronic disease, monitoring cardiovascular risk factors, vaccinations, and encouraging adoption of a healthy lifestyle) All patients, whether sexually active or not, should be asked about genitourinary symptoms, including vulvovaginal dryness and referred to appropriate speciality providers (eg, physical therapy, pelvic floor therapy, sexual therapy, psychotherapy) Psychosocial support. Post-radiation use of vaginal dilators and moisturisers. HRT for treatment-related menopause.
ESGO/ESTRO/ESP[4]	Continuous evaluation for psychological distress, sexual dysfunction, and psychiatric co-morbidity, as well as identification of psychosocial needs. Interventions such as counselling, individual or group psychotherapy, psychoeducational interventions, art therapies, or relaxation techniques. Discussion and treatment of sexual problems. Personalised survivorship care plan including information and education on lifestyle and prevention of secondary malignancies and other diseases. Contact with advocacy groups should be offered to all patients

Guideline	Supportive care
Pan-Asian ESMO[20]	Promote Regular exercise, a healthy diet and weight management.

7.0 GOSK recommendations

Table 29: GOSK recommendations for the diagnostic workup of endometrial carcinoma

Diagnostic parameter	GOSK recommendations
Clinical assessment	A comprehensive history should be obtained, including abnormal uterine bleeding (onset, duration, frequency, pattern, and volume), abnormal vaginal discharge, pelvic pain, abdominal distension or pressure symptoms, constitutional symptoms, and relevant personal or family history of uterine, colorectal, breast, or ovarian malignancies suggestive of hereditary cancer syndromes. A complete physical and pelvic examination should be performed, including speculum, bimanual, and digital rectal examination, to assess tumor extent, vaginal or cervical involvement, parametrial extension, adnexal masses, and possible rectovaginal involvement. Office endometrial sampling should be performed using a Pipelle. Dilatation and curettage (D&C) should be performed under anaesthesia when endometrial biopsy results are negative or nondiagnostic despite persistent symptoms or ongoing clinical suspicion. Hysteroscopy with directed biopsy should be considered in patients with persistent or recurrent abnormal uterine bleeding, particularly where focal intrauterine pathology is suspected. Cervical cancer screening using HPV DNA testing, cytology (Pap smear), or visual inspection with acetic acid (VIA) should be performed according to prior cervical screening history and in the presence of abnormal cervical appearance or suspicious clinical findings.
Imaging	Pelvic MRI should be the preferred imaging modality for assessing the depth of myometrial invasion, cervical stromal involvement, and regional nodal disease. Transvaginal ultrasound (TVUS) may be used to assess myometrial invasion and cervical stromal involvement where MRI is unavailable or contraindicated. Chest CT should be performed as the preferred imaging modality for evaluation of pulmonary metastases. Contrast-enhanced CT of the abdomen and pelvis should be performed for assessment of nodal involvement and distant metastatic disease. Chest radiography (CXR) may be used to assess pulmonary metastases when chest CT is unavailable or contraindicated. Chest, abdominal, and pelvic CT imaging should be performed in patients with incompletely staged endometrial carcinoma diagnosed incidentally following hysterectomy. PET/CT may be considered for detecting distant metastases, particularly in advanced-stage, high-risk, or recurrent disease. PET/CT should be performed in patients being considered for fertility-sparing management to exclude extrauterine disease and assess for metastatic involvement.
Histopathology and molecular testing	The pathology report for the endometrial biopsy specimen should include the histologic subtype, FIGO grade, and presence or absence of lymphovascular space invasion (LVSI), where assessable. The pathology report following total hysterectomy and bilateral salpingo-oophorectomy (TH/BSO) should also include the depth of myometrial invasion, cervical stromal involvement, the presence or absence of LVSI, and the status of surgical margins. Molecular testing should be performed, where available, on either the endometrial biopsy or hysterectomy specimen to enable accurate prognostic stratification and inform adjuvant and systemic treatment decisions. Recommended molecular testing includes mismatch repair (MMR) protein immunohistochemistry (IHC) or microsatellite instability (MSI) testing, polymerase epsilon exonuclease (POLE) mutation analysis, and p53 immunohistochemistry. Estrogen receptor (ER) and progesterone receptor (PR) testing should be performed in patients with stage III–IV or recurrent endometrioid carcinoma to guide potential hormonal therapy. HER2 immunohistochemistry (IHC), with reflex confirmatory testing where indicated, should be performed in advanced or recurrent serous carcinoma, carcinosarcoma, and p53-abnormal endometrial carcinomas to identify candidates for HER2-directed therapy.
BSO, bilateral salpingo-oophorectomy; CT, computed tomography; CXR, chest radiography; D&C, dilatation and curettage; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; HPV, human papillomavirus; IHC, immunohistochemistry; LVSI, lymphovascular space invasion; MMR, mismatch repair; MRI, magnetic resonance imaging; MSI, microsatellite instability; PET/CT, positron emission tomography/computed tomography; POLE, polymerase epsilon exonuclease domain; PR, progesterone receptor; TH, total hysterectomy; TVUS, transvaginal ultrasound; VIA, visual inspection with acetic acid.	

Source: Adapted from National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Uterine Neoplasms. Version 3.2025; Concin N, Matias-Guiu X, Vergote I, et al. ESGO/ESTRO/ESP Guidelines for the Management of Patients with Endometrial Carcinoma. Int J Gynecol Cancer. 2021;31(1):12–39; Pan-Asian adapted ESMO Clinical Practice Guidelines. ESMO Open. 2022.

Table 30: GOSK recommendations for the management of endometrial carcinoma by stage and histology

Category	GOSK recommendations
Surgical principles	Total hysterectomy (TH) with bilateral salpingo-oophorectomy (BSO) should be performed in medically fit patients with operable endometrial carcinoma. Minimally invasive surgery (MIS) is the preferred approach for patients with apparent uterine-confined disease. Laparotomy should be considered in patients with suspected extra-uterine disease, bulky tumor burden, or where minimally invasive surgery is not feasible. A thorough intraoperative assessment should include visual inspection of the peritoneal, diaphragmatic, and serosal surfaces, with biopsy of any suspicious lesions. Peritoneal cytology, consisting of peritoneal washings or aspiration of free peritoneal fluid for cytologic examination, should be obtained at the time of surgical staging. Sentinel lymph node excision (SLNE) with pathologic ultra-staging should be performed where expertise and resources are available. Systematic pelvic with or without para-aortic lymphadenectomy may be performed where SLNE is unavailable or not feasible. Routine pelvic lymphadenectomy may be omitted in patients with low-risk disease defined by stage IA tumors, grade 1–2 histology, <50% myometrial invasion, and tumor size <2 cm. Further systematic pelvic lymph node dissection may be omitted when pelvic nodal metastases are identified intraoperatively. In advanced-stage disease, only clinically enlarged or suspicious lymph nodes should be selectively resected for staging and cytoreduction. Infracolic omentectomy should be performed in serous, clear cell, undifferentiated, and carcinosarcoma histologies due to the increased risk of occult extrauterine spread.
Endometrioid carcinoma stage IA grade 1–2	Extrafascial hysterectomy with BSO and peritoneal cytology should be performed. Ovarian preservation may be considered in carefully selected young patients with grade 1 endometrioid endometrial carcinoma who have normal-appearing ovaries, no evidence of hereditary cancer predisposition, and no high-risk pathologic or molecular features, including p53 abnormality, mismatch repair deficiency (MMRd), lymphovascular space invasion (LVSI), or positive peritoneal cytology. Bilateral salpingectomy should be performed when ovarian preservation is undertaken. Pelvic lymph node dissection should be performed for surgical nodal assessment where SLNE is unavailable; SLNE with ultra staging may be performed where available and feasible. Routine lymphadenectomy may be omitted in patients with <50% myometrial invasion and tumor size <2 cm. Adjuvant therapy may be omitted in patients with no Lymphovascular space invasion (LVSI) or only focal LVSI*. Adjuvant vaginal brachytherapy (VBT) should be considered in patients with substantial LVSI* or age ≥60 years to reduce the risk of vaginal recurrence.
Endometrioid carcinoma stage IA grade 3	Extrafascial hysterectomy with BSO and peritoneal cytology should be performed. Pelvic lymphadenectomy should be performed for nodal assessment and staging. Infra-renal para-aortic lymphadenectomy may be considered in patients with additional high-risk features such as substantial LVSI* or suspicious nodal disease. Adjuvant vaginal brachytherapy (VBT) should be administered in patients with no LVSI* or focal LVSI* to reduce the risk of vaginal recurrence. Adjuvant external beam radiotherapy (EBRT), administered alone or sequentially with platinum-based chemotherapy (carboplatin AUC 5–6 plus paclitaxel 175 mg/m² administered intravenously every 21 days for 6 cycles)**, should be considered in patients with substantial LVSI*** or age ≥60 years because of the increased risk of locoregional and distant recurrence.
Endometrioid carcinoma stage IB	Extrafascial hysterectomy with bilateral salpingooophorectomy and peritoneal cytology should be performed as part of surgical staging. Pelvic lymphadenectomy should be performed for nodal assessment and staging. Infra-renal para-aortic lymphadenectomy should be considered in patients with grade 3 tumors, particularly when additional risk factors such as substantial LVSI* or suspicious lymph nodes are present. Adjuvant VBT should be administered to patients with grade 1–2 disease and no LVSI*, or only focal LVSI*. Adjuvant EBRT, with or without VBT, should be administered in patients with grade 3 disease and no LVSI* or focal LVSI*. Adjuvant EBRT, administered alone or sequentially with platinum-based chemotherapy (carboplatin AUC 5–6 plus paclitaxel 175 mg/m² administered intravenously every 21 days for 6 cycles)**, should be considered in patients with grade 1–2 disease and substantial LVSI* or age ≥60 years.

Category	GOSK recommendations
	Adjuvant EBRT and/or VBT followed sequentially by platinum-based chemotherapy (carboplatin AUC 5–6 plus paclitaxel 175 mg/m² administered intravenously every 21 days for 6 cycles)**should be administered in patients with grade 3 disease and substantial LVSI* because of the increased risk of locoregional and distant recurrence. For patients with uterine-confined disease who are medically unfit for surgery, definitive EBRT and/or VBT may be considered as alternative treatment modalities. Hormonal therapy may be considered in carefully selected patients with ER/PR-positive disease who are unfit for surgery.
Endometrioid carcinoma stage II	Radical hysterectomy with bilateral salpingo-oophorectomy, pelvic and infra-renal para-aortic lymphadenectomy, and peritoneal cytology should be performed as part of surgical staging. Neoadjuvant radiotherapy or systemic chemotherapy (carboplatin AUC 5-6 plus paclitaxel 175 mg/m² administered intravenously every 21 days for 3 cycles)** may be considered in patients with initially unresectable disease or those not suitable candidates for primary surgery because of medical comorbidities or poor performance status, followed by reassessment for interval surgical management. Definitive EBRT with or without brachytherapy should be administered to patients with persistent medically inoperable disease or unresectable tumors not amenable to subsequent surgical management. Adjuvant EBRT and/or VBT should be administered after surgery. In patients with high-risk features, including grade 3 histology, substantial LVSI*, deep myometrial invasion, or p53 abnormality, sequential platinum-based chemotherapy (carboplatin AUC 5–6 plus paclitaxel 175 mg/m² administered intravenously every 21 days for 6 cycles) followed by EBRT and/or VBT should be considered because of the increased risk of locoregional and distant recurrence.
Endometrioid carcinoma stage III–IV	Where available, multidisciplinary team (MDT) discussion is encouraged to inform individualized management, taking into account disease characteristics, patient factors, and local resources. Extrafascial hysterectomy with bilateral salpingo-oophorectomy, omentectomy, and maximal effort cytoreductive surgery should be performed in patients with locoregional disease who are suitable surgical candidates. Cytoreductive surgery should aim to achieve no gross residual disease whenever feasible. Only clinically enlarged or suspicious lymph nodes should be selectively resected in advanced-stage disease. Neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS) should be considered in patients with bulky extra-uterine disease, diffuse peritoneal carcinomatosis, extensive nodal involvement, or other factors that make optimal primary cytoreduction unlikely. The preferred regimen is carboplatin AUC 5–6 plus paclitaxel 175 mg/m² administered intravenously every 21 days. Response should be assessed after 3 cycles using clinical evaluation and imaging. Patients with responding or stable, resectable disease should proceed to IDS, preferably within 3–6 weeks of the last chemotherapy cycle, followed by completion of chemotherapy to a total of 6 cycles. Patients with progressive disease or persistent unresectable disease should be discussed in a multidisciplinary team meeting and considered for alternative systemic therapy, radiotherapy, chemoradiotherapy, or palliative management as appropriate. Radical local therapies, including surgical metastasectomy, stereotactic body radiotherapy (SBRT), or other ablative techniques, may be considered in carefully selected patients with oligometastatic disease, defined as a limited number of metastatic lesions (typically 1–5) at one or a limited number of anatomical sites, where all known sites of disease are amenable to curative-intent local treatment In patients who are poor surgical candidates, definitive EBRT with or without VBT should be considered for locoregional disease control. Platinum-based chemotherapy (carboplatin AUC 5–6 plus paclitaxel 175 mg/m² administered intravenously every 21 days for 6 cycles) should be administered prior to radiotherapy, unless contraindicated, to treat systemic disease and reduce the risk of disease progression.Adjuvant treatment in patients with advanced-stage endometrial carcinoma and no gross residual disease following surgery should consist of either sequential platinum-based chemotherapy (carboplatin AUC 5–6 plus paclitaxel 175 mg/m² administered intravenously every 21 days for 6 cycles followed by EBRT), or concurrent chemoradiotherapy (EBRT with concurrent cisplatin) followed by adjuvant platinum-based chemotherapy. Chemotherapy alone may be considered in selected patients. In patients with residual disease, adjuvant treatment should be individualised and may include chemotherapy with or without radiotherapy based on residual disease burden, disease distribution, prior treatment, histologic subtype, molecular profile, and patient performance status.
Serous, Clear cell, Undifferentiated / Dedifferentiated carcinoma	Where available, multidisciplinary team (MDT) discussion is encouraged to inform individualized management, taking into account disease characteristics, patient factors, and local resources. Fertility-sparing treatment should not be offered because of the aggressive biologic behavior and high risk of extra-uterine spread associated with these histologic subtypes. Comprehensive surgical staging should include Extrafascial hysterectomy with bilateral salpingooophorectomy, omentectomy, peritoneal biopsies, pelvic lymphadenectomy, and infra-renal para-aortic lymphadenectomy.

Category	GOSK recommendations
	In patients who are not suitable surgical candidates, radiotherapy with or without systemic therapy, or systemic therapy alone, may be administered, followed by reassessment for surgery and/or definitive radiotherapy based on treatment response and performance status. Adjuvant VBT, with or without systemic therapy (carboplatin AUC 5–6 plus paclitaxel 175 mg/m² administered intravenously every 21 days for 6 cycles)**, should be administered in patients with stage IA non-invasive disease and negative peritoneal washings. Adjuvant systemic therapy with VBT should be administered in patients with stage IA non-invasive disease and positive peritoneal washings. Adjuvant systemic therapy (carboplatin AUC 5–6 plus paclitaxel 175 mg/m² administered intravenously every 21 days for 6 cycles)** with EBRT, with or without VBT, should be administered in patients with stage IA invasive disease and stage IB–IV disease because of the high risk of locoregional and distant recurrence.
Carcinosarcoma	Where available, multidisciplinary team (MDT) discussion is encouraged to inform individualized management, taking into account disease characteristics, patient factors, and local resources. Fertility-sparing treatment should not be offered because of the aggressive nature and high risk of extra-uterine spread associated with this histological subtype. Comprehensive surgical staging should include Extrafascial hysterectomy with bilateral salpingo-oophorectomy, omentectomy, pelvic and para-aortic lymphadenectomy, and peritoneal biopsies. In patients who are not suitable surgical candidates, radiotherapy with or without systemic therapy, or systemic therapy alone, may be administered, followed by reassessment for surgery and/or definitive radiotherapy based on treatment response and performance status. Adjuvant systemic therapy (carboplatin AUC 5–6 plus paclitaxel 175 mg/m² administered intravenously every 21 days for 6 cycles)** with VBT, with or without EBRT, should be administered in patients with stage IA disease. Adjuvant systemic therapy (carboplatin AUC 5–6 plus paclitaxel 175 mg/m² administered intravenously every 21 days for 6 cycles)** with EBRT, with or without VBT, should be administered in patients with stage IB–IV disease because of the increased risk of locoregional and distant recurrence. In advanced disease, best supportive and palliative care should be offered where appropriate, based on disease status, symptoms, performance status, and patient preferences.

AUC, area under the concentration–time curve; BSO, bilateral salpingo-oophorectomy; CCRT, concurrent chemoradiotherapy; EBRT, external beam radiotherapy; ER, estrogen receptor; IDS, interval debulking surgery; LVSI, lymphovascular space invasion; MDT, multidisciplinary team; MIS, minimally invasive surgery; MMRd, mismatch repair deficiency; NACT, neoadjuvant chemotherapy; PR, progesterone receptor; SBRT, stereotactic body radiotherapy; SLNE, sentinel lymph node excision; TH, total hysterectomy; VBT, vaginal brachytherapy.

* No LVSI = absence of lymphovascular space invasion; Focal LVSI = involvement of one or a few lymphovascular spaces adjacent to the tumor or tumor involvement of <5 lymphovascular spaces; Substantial LVSI = diffuse or multifocal involvement of lymphovascular spaces surrounding the tumor or tumor involvement of ≥5 lymphovascular spaces.

** Cisplatin (50–75 mg/m² intravenously every 21 days) in combination with paclitaxel 175 mg/m² may be used as an alternative when carboplatin is unavailable, contraindicated, or not tolerated, provided the patient has adequate renal function and performance status. Carboplatin remains the preferred platinum agent because of its more favorable toxicity profile.

Source: Adapted from National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Uterine Neoplasms. Version 3.2025; Concin N, Matias-Guiu X, Vergote I, et al. ESGO/ESTRO/ESP Guidelines for the Management of Patients with Endometrial Carcinoma. Int J Gynecol Cancer. 2021;31(1):12–39; Pan-Asian adapted ESMO Clinical Practice Guidelines. ESMO Open. 2022.

Table 31: GOSK recommendations for adjuvant treatment of endometrial carcinoma by risk stratification

Risk category	Definition	GOSK recommendations
Low risk	Stage IA endometrioid carcinoma, grade 1–2, <50% myometrial invasion, no or focal LVSI, node-negative, with a favourable molecular profile (POLE-mutated)	Adjuvant therapy may be omitted in patients with low-risk disease following complete surgical staging.
Intermediate risk	Stage IB endometrioid carcinoma, grade 1–2, no or focal LVSI, node-negative, and mismatch repair-deficient (MMRd) or no specific molecular profile (NSMP) molecular subtype.	Adjuvant vaginal brachytherapy (VBT) should be administered to reduce the risk of vaginal recurrence.
High intermediate risk	Stage IA grade 3 endometrioid carcinoma; stage IB grade 3 disease; stage II disease; substantial LVSI; or MMRd/NSMP tumors with additional	Adjuvant external beam radiotherapy (EBRT) should be administered to reduce the risk of locoregional recurrence.

Risk category	Definition	GOSK recommendations
	adverse features including deep myometrial invasion, substantial LVSI, grade 3 histology, cervical stromal involvement, or advanced age.	Adjuvant VBT alone may be considered in patients with pathologically node-negative (pN0) disease and no LVSI or only focal LVSI
High risk	Stage III–IVA disease; non-endometrioid histologies (serous, clear cell, undifferentiated/de-differentiated carcinoma, carcinosarcoma); nodal involvement; or aggressive molecular profile including p53-abnormal tumors.	Adjuvant EBRT with concurrent cisplatin-based chemoradiotherapy, followed by adjuvant platinum-based chemotherapy (carboplatin AUC 5–6 plus paclitaxel 175 mg/m² administered intravenously every 21 days for 6 cycles)**, should be administered because of the increased risk of locoregional and distant recurrence. Adjuvant chemotherapy with carboplatin (AUC 5–6) and paclitaxel (175 mg/m² intravenously every 21 days for 6 cycles) combined with an immune checkpoint inhibitor should be considered for patients with stage IIIm–IVAm MMR-deficient (MMRd) endometrial carcinoma. Acceptable immune checkpoint inhibitors include dostarlimab (500 mg intravenously every 3 weeks with chemotherapy for 6 cycles, followed by maintenance dostarlimab 1000 mg intravenously every 6 weeks for up to 3 years) or pembrolizumab (200 mg intravenously every 3 weeks with chemotherapy, followed by maintenance pembrolizumab 400 mg intravenously every 6 weeks for up to 14 cycles). EBRT may be added based on individual risk factors.
Advanced/metastatic disease	Stage IVB disease, unresectable locoregional disease, residual nodal disease, positive surgical margins, pelvic sidewall involvement, or recurrent macroscopic disease, irrespective of molecular subtype.	Where available, multidisciplinary team (MDT) discussion is encouraged to inform individualized management, taking into account disease characteristics, patient factors, and local resources. Maximal cytoreductive surgery should be performed where feasible, with the goal of achieving complete gross resection while maintaining acceptable surgical morbidity. Neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS) should be considered in patients with bulky extra-uterine disease, diffuse peritoneal carcinomatosis, extensive nodal involvement, or other factors that make optimal primary cytoreduction unlikely. The preferred regimen is carboplatin AUC 5–6 plus paclitaxel 175 mg/m² administered intravenously every 21 days. Response should be assessed after 3 cycles using clinical evaluation and imaging. Patients with responding or stable, resectable disease should proceed to IDS, preferably within 3–6 weeks of the last chemotherapy cycle, followed by completion of chemotherapy to a total of 6 cycles. Patients with progressive disease or persistent unresectable disease should be discussed in a multidisciplinary team meeting and considered for alternative systemic therapy, radiotherapy, chemoradiotherapy, or palliative management as appropriate. Definitive radiotherapy, consisting of pelvic EBRT with or without VBT, or primary systemic therapy (carboplatin AUC 5–6 plus paclitaxel 175 mg/m² administered intravenously every 21 days for 6 cycles)** should be considered in patients with persistently inoperable or unresectable tumors not amenable to subsequent surgical management. Treatment selection should be individualized based on disease extent, histologic subtype, molecular profile, performance status, comorbidities, and patient preferences.

Risk category	Definition	GOSK recommendations
		Adjuvant EBRT with concurrent and/or sequential platinum-based chemotherapy (carboplatin AUC 5–6 plus paclitaxel 175 mg/m² administered intravenously every 21 days for 6 cycles)**, or chemotherapy alone, should be considered in patients with advanced-stage endometrial carcinoma and no gross residual disease following surgery. Adjuvant chemotherapy (carboplatin AUC 5–6 plus paclitaxel 175 mg/m² administered intravenously every 21 days for 6 cycles)** may be considered following definitive radiotherapy in selected patients at high risk of systemic relapse. In patients with residual disease, adjuvant treatment should be individualized and may include chemotherapy with or without radiotherapy based on residual disease burden, disease distribution, prior treatment, histologic subtype, molecular profile, and patient performance status. Best supportive and palliative care should be offered where appropriate, based on disease status, symptoms, performance status, and patient preferences.

AUC, area under the concentration–time curve; EBRT, external beam radiotherapy; IDS, interval debulking surgery; LVSI, lymphovascular space invasion; MMRd, mismatch repair deficiency; MDT, multidisciplinary team; NACT, neoadjuvant chemotherapy; NSMP, no specific molecular profile; pN0, pathologically node-negative; POLE, DNA polymerase epsilon; VBT, vaginal brachytherapy.

* No LVSI - absence of lymphovascular space invasion; Focal LVSI - involvement of one or a few lymphovascular spaces adjacent to the tumor or tumor involvement of <5 lymphovascular spaces; Substantial LVSI - diffuse or multifocal involvement of lymphovascular spaces surrounding the tumor or tumor involvement of ≥5 lymphovascular spaces.

** Cisplatin (50–75 mg/m² intravenously every 21 days) in combination with paclitaxel 175 mg/m² may be used as an alternative when carboplatin is unavailable, contraindicated, or not tolerated, provided the patient has adequate renal function and performance status. Carboplatin remains the preferred platinum agent because of its more favorable toxicity profile.

Source: Concin N, Matias-Guiu X, Vergote I, et al. ESGO/ESTRO/ESP Guidelines for the Management of Patients with Endometrial Carcinoma. Int J Gynecol Cancer. 2021;31(1):12–39; Pan-Asian adapted ESMO Clinical Practice Guidelines. ESMO Open. 2022.

Table 32: GOSK recommendations for the management of incompletely surgically staged endometrial carcinoma

Category	GOSK recommendations
Initial evaluation	Where available, multidisciplinary team (MDT) discussion is encouraged to inform individualized management, taking into account disease characteristics, patient factors, and local resources. Postoperative contrast-enhanced CT imaging of the chest, abdomen, and pelvis should be performed to assess for residual, nodal, or metastatic disease and to guide decisions regarding completion staging or adjuvant therapy.
Imaging negative	In patients with stage IA grade 1–2 endometrioid carcinoma without substantial LVSI*, observation with regular clinical follow-up should be considered. Adjuvant VBT should be administered in patients with substantial LVSI* and/or age ≥60 years to reduce the risk of vaginal recurrence. In patients with stage IA grade 3 endometrioid carcinoma without substantial LVSI*, adjuvant VBT should be administered to reduce the risk of vaginal recurrence. Adjuvant EBRT should be considered in patients with substantial LVSI and/or age ≥60 years. In patients with stage IB or stage II endometrioid carcinoma in whom nodal assessment was not previously performed, surgical restaging may be considered where feasible. Alternatively, adjuvant EBRT with or without VBT should be administered, and chemotherapy may be considered based on tumor grade, LVSI, molecular profile, and other high-risk features.
Imaging suspicious and resectable disease	In patients with imaging findings suspicious for residual, nodal, or metastatic disease, restaging surgery should be considered where feasible, followed by stage-appropriate adjuvant therapy based on final pathologic and radiologic findings.
Imaging suspicious but unsuitable for surgery/unresectable disease	Tissue biopsy confirmation should be obtained if histopathologic diagnosis has not already been established. Patients with stage II endometrioid carcinoma who are not surgical candidates should receive definitive treatment with EBRT and systemic chemotherapy, with or without VBT.

Category	GOSK recommendations
	Patients with stage III–IV endometrioid carcinoma who are unsuitable for surgery should be managed as high-risk disease with adjuvant EBRT with concurrent cisplatin-based chemoradiotherapy, followed by adjuvant platinum-based chemotherapy.
Non-endometrioid Histology	Surgical restaging should be considered when technically feasible, when associated morbidity is acceptable, and when the findings are likely to alter adjuvant treatment decisions. Patients with non-endometrioid histology should be managed as high-risk disease with adjuvant EBRT with concurrent cisplatin-based chemoradiotherapy, followed by adjuvant platinum-based chemotherapy.
CT, computed tomography; EBRT, external beam radiotherapy; LVSI, lymphovascular space invasion; MDT, multidisciplinary team; VBT, vaginal brachytherapy. * No LVSI - absence of lymphovascular space invasion; Focal LVSI - involvement of one or a few lymphovascular spaces adjacent to the tumor or tumor involvement of <5 lymphovascular spaces; Substantial LVSI - diffuse or multifocal involvement of lymphovascular spaces surrounding the tumor or tumor involvement of ≥5 lymphovascular spaces.	

Source: Adapted from National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Uterine Neoplasms. Version 3.2025; Concin N, Matias-Guiu X, Vergote I, et al. ESGO/ESTRO/ESP Guidelines for the Management of Patients with Endometrial Carcinoma. Int J Gynecol Cancer. 2021;31(1):12–39; Pan-Asian adapted ESMO Clinical Practice Guidelines. ESMO Open. 2022.

Table 33: GOSK recommendations for fertility-sparing in endometrial carcinoma

Category	GOSK recommendations
Eligibility criteria	Grade 1 endometrioid on D&C confirmed by an expert pathologist. The disease is limited to endometrium on MRI. The disease has a favourable molecular profile (POLE mutated). There is no inherited cancer risk. There is no suspicious or metastatic disease on imaging. There are no contraindications to medical therapy or pregnancy. The patient should be willing and able to comply with the intensive surveillance schedule, including regular follow-up visits, clinical assessments, imaging, and endometrial sampling as required.
Treatment options	All candidates for fertility-sparing treatment should undergo multidisciplinary team evaluation involving, at a minimum, a gynecologic oncologist and a fertility specialist. Patients considering fertility-sparing management should be counselled by a multidisciplinary team, including consultation with a fertility specialist, before initiation of therapy. Offer patient counselling that the fertility-sparing option is NOT standard of care for the treatment of endometrial carcinoma. Hysteroscopic tumor resection should be performed before initiation of progestin-based therapy where feasible. Continuous progestin-based therapy should be prescribed using one of the following regimens: Megestrol acetate 160–320 mg daily, or Medroxyprogesterone acetate 400–600 mg daily, or Levonorgestrel-releasing intrauterine device (LNG-IUD). Combined progestin therapy using oral megestrol acetate or medroxyprogesterone acetate together with a levonorgestrel-releasing intrauterine device may be considered. Patients should receive counselling regarding weight management, lifestyle modification, and optimization of metabolic comorbidities during fertility-sparing treatment. Definitive surgical management with total hysterectomy and bilateral salpingo-oophorectomy (TH/BSO) with appropriate surgical staging should be performed once childbearing is complete.
Surveillance	Endometrial evaluation should be performed every 3–6 months during fertility-sparing treatment using dilatation and curettage (D&C), hysteroscopy with biopsy, or Pipelle endometrial biopsy. In patients with a complete response by 6 months, conception should be encouraged, and surveillance should be continued every 6–12 months. Maintenance progestin therapy should be prescribed in patients who are not actively attempting conception. In patients with no response, incomplete response, disease progression, or persistent endometrial carcinoma at 6–12 months, definitive surgical management with TH/BSO with surgical staging should be performed. Definitive TH/BSO with appropriate surgical staging should be performed after completion of childbearing, even in patients with an initial complete response to fertility-sparing therapy.

Category	GOSK recommendations
BSO, bilateral salpingo-oophorectomy; D&C, dilatation and curettage; LNG-IUD, levonorgestrel-releasing intrauterine device; MRI, magnetic resonance imaging; POLE, polymerase epsilon exonuclease domain mutation; TH, total hysterectomy.	

Source: Adapted from National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Uterine Neoplasms. Version 3.2025; Concin N, Matias-Guiu X, Vergote I, et al. ESGO/ESTRO/ESP Guidelines for the Management of Patients with Endometrial Carcinoma. Int J Gynecol Cancer. 2021;31(1):12–39.

Table 34: GOSK recommendations for post-treatment surveillance in endometrial carcinoma

Risk category / Component	GOSK recommendations
Low / Intermediate risk	Patients with low- and low-intermediate-risk endometrial carcinoma should undergo follow-up every 6 months for the first 2 years, and annually thereafter up to 5 years. A comprehensive history, physical examination, and pelvic examination should be performed at each follow-up visit to assess for disease recurrence and treatment-related complications. Post-treatment imaging may be performed 6 months after completion of therapy and subsequently only as clinically indicated by symptoms, examination findings, or suspicion of recurrence.
High intermediate risk / High risk	Patients with high-intermediate-risk (HIR) and high-risk endometrial carcinoma should undergo follow-up every 3 months for the first 3 years, every 6 months until 5 years, and annually thereafter. A comprehensive history, physical examination, and pelvic examination should be performed at each follow-up visit to assess for recurrence and treatment-related complications. Post-treatment imaging may be performed 3 months after completion of therapy and subsequently as clinically indicated by symptoms, examination findings, or suspicion of recurrence.
CA-125 Monitoring	Serum CA-125 testing may be performed during follow-up in patients with an initially elevated CA-125 level or serous histology to assist in the detection of disease recurrence. In patients with a rising or newly elevated CA-125 level, clinical assessment and appropriate imaging (preferably contrast-enhanced CT of the chest, abdomen, and pelvis) should be performed to evaluate for recurrent disease. Treatment should not be initiated solely based on an elevated CA-125 level in the absence of radiologic, histologic, or clinically demonstrable recurrence.

Source: Adapted from National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Uterine Neoplasms. Version 3.2025; Concin N, Matias-Guiu X, Vergote I, et al. ESGO/ESTRO/ESP Guidelines for the Management of Patients with Endometrial Carcinoma. Int J Gynecol Cancer. 2021;31(1):12–39; Pan-Asian adapted ESMO Clinical Practice Guidelines. ESMO Open. 2022.

Table 35: GOSK recommendations for the management of recurrent endometrial carcinoma

Extent of disease	GOSK recommendations
Locoregional recurrence	Surgical resection should be considered in patients with resectable recurrent disease who have not previously received radiotherapy and for whom complete gross resection is achievable. Adjuvant radiotherapy, with or without systemic therapy, should be administered based on pathologic findings. Isolated vaginal cuff recurrence should be treated with pelvic EBRT combined with VBT where feasible. In patients with prior pelvic irradiation, management options may include pelvic exenteration, carefully selected re-irradiation techniques, or systemic therapy based on disease extent, prior treatment, performance status, and treatment intent.
Isolated metastasis	Surgical resection and/or EBRT should be considered in patients with localized or oligometastatic recurrent disease where durable local control is achievable. Ablative therapies, including stereotactic body radiotherapy (SBRT) or radiofrequency ablation, may be considered in carefully selected patients. Systemic therapy should be administered based on histologic subtype, molecular profile, prior treatment, disease burden, and patient performance status.
Disseminated / metastatic disease	Palliative systemic chemotherapy, with or without palliative radiotherapy, should be administered. Hormonal therapy may be considered in patients with low-grade, low-volume, hormone receptor-positive endometrioid carcinoma. Available options include oral progestins (medroxyprogesterone acetate or megestrol acetate), aromatase inhibitors (letrozole,

Extent of disease	GOSK recommendations
	anastrozole, or exemestane), tamoxifen-based regimens, and levonorgestrel-releasing intrauterine systems in appropriately selected patients. Immunotherapy and other targeted therapies should be considered based on molecular profile, prior treatment exposure, and treatment eligibility. Enrollment in clinical trials should be encouraged where available and appropriate. Best supportive and palliative care should be offered where appropriate, taking into account disease status, symptom burden, performance status, and patient preferences.

Source: Adapted from National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Uterine Neoplasms. Version 3.2025; Concin N, Matias-Guiu X, Vergote I, et al. ESGO/ESTRO/ESP Guidelines for the Management of Patients with Endometrial Carcinoma. Int J Gynecol Cancer. 2021;31(1):12–39; Pan-Asian adapted ESMO Clinical Practice Guidelines. ESMO Open. 2022.

Table 36: GOSK recommendations for targeted therapy in endometrial carcinoma

Therapeutic strategy	GOSK recommendations
HER2-directed therapy	HER2 immunohistochemistry (IHC), with reflex confirmatory testing where indicated, should be performed in advanced or recurrent serous carcinoma, carcinosarcoma, and p53-abnormal endometrial carcinomas to identify candidates for HER2-directed therapy. Trastuzumab in combination with carboplatin–paclitaxel should be administered for the primary treatment of HER2-positive endometrial carcinoma. Maintenance trastuzumab may be continued following completion of chemotherapy in patients who tolerate treatment and derive ongoing clinical benefit.
Checkpoint inhibitors	Pembrolizumab or dostarlimab in combination with carboplatin–paclitaxel should be administered in patients with recurrent or metastatic mismatch repair-deficient (MMRd) or microsatellite instability-high (MSI-H) endometrial carcinoma. Pembrolizumab in combination with lenvatinib should be administered in patients with proficient mismatch repair (pMMR) endometrial carcinoma following progression after prior platinum-based chemotherapy.
Hormonal therapy	Hormonal therapy may be considered in patients with low-grade, low-volume, estrogen receptor (ER)- and/or progesterone receptor (PR)-positive endometrioid endometrial carcinoma, particularly in recurrent, metastatic, medically inoperable, or fertility-sparing settings. Recommended hormonal agents include progestins (e.g., medroxyprogesterone acetate or megestrol acetate), levonorgestrel-releasing intrauterine system (LNG-IUS), aromatase inhibitors, and tamoxifen.
Emerging Therapies	Enrollment in clinical trials should be encouraged whenever available and appropriate. mTOR inhibitors (e.g., everolimus) in combination with letrozole may be considered in patients with estrogen receptor (ER)-positive recurrent endometrioid endometrial carcinoma where available. Molecular testing for alterations in the PI3K/AKT/PTEN pathway, including *PIK3CA*, *PTEN*, and *AKT* mutations, may be considered in recurrent endometrioid carcinoma where available to guide targeted therapeutic options. Antibody–drug conjugates, including trastuzumab deruxtecan, may be considered in patients with HER2-positive endometrial carcinoma where available and clinically appropriate. Folate receptor alpha (FRα)-targeted therapies may be considered in patients with FRα-expressing endometrial tumors where available.

Source: Adapted from National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Uterine Neoplasms. Version 3.2025; Concin N, Matias-Guiu X, Vergote I, et al. ESGO/ESTRO/ESP Guidelines for the Management of Patients with Endometrial Carcinoma. Int J Gynecol Cancer. 2021;31(1):12–39; Pan-Asian adapted ESMO Clinical Practice Guidelines. ESMO Open. 2022.

Table 37: GOSK recommendations for supportive and palliative care in endometrial carcinoma

Component	GOSK recommendations
Chronic disease and cardiovascular health	Women with endometrial carcinoma commonly have underlying cardiovascular and metabolic risk factors, including obesity, hypertension, diabetes, and dyslipidemia. Regular follow-up should include assessment and management of chronic medical conditions, including monitoring and optimization of cardiovascular and metabolic risk factors.

Component	GOSK recommendations
Sexual and pelvic health	Women treated for endometrial carcinoma may experience sexual dysfunction, pelvic floor dysfunction, and vulvovaginal atrophy, particularly following surgery, radiotherapy, or menopause-inducing treatment. These concerns should be routinely assessed and appropriately managed during follow-up. Vaginal dilators and moisturizers should be recommended following pelvic radiotherapy to reduce the risk of vaginal stenosis and improve sexual health and quality of life.
Lymphedema	Women treated for endometrial carcinoma, particularly following lymph node assessment or pelvic radiotherapy, are at risk of lower-limb lymphedema and associated functional impairment. Patients should be routinely assessed for lymphedema during follow-up and offered appropriate management, supportive care, and referral to physiotherapy or lymphedema rehabilitation services, as indicated.
Treatment-induced menopause	Women treated for endometrial carcinoma may experience treatment-induced menopause and are at increased risk of bone loss, osteopenia, and osteoporosis, particularly following bilateral oophorectomy or pelvic radiotherapy. Hormone replacement therapy (HRT) may be offered to appropriately selected patients following individualized assessment of oncologic risk, menopausal symptoms, comorbidities, and patient preferences. Available options include oral or transdermal estrogen therapy for women who have undergone hysterectomy, combined estrogen–progestogen therapy for women with an intact uterus, and low-dose vaginal estrogen preparations for isolated genitourinary symptoms. Bone health should be routinely assessed and managed during follow-up care, including evaluation of osteoporosis risk and implementation of preventive and therapeutic measures where indicated.
Psychosocial support	Women treated for endometrial carcinoma may experience psychosocial distress, anxiety, depression, and fear of cancer recurrence during survivorship. Psychosocial and mental health support should be routinely offered, with referral for specialist psychological or psychiatric care where indicated. Patients should also be educated on the symptoms and signs of recurrence to promote timely presentation, evaluation, and intervention.
Symptom management	Patients with endometrial carcinoma may experience pain, nausea and vomiting, constipation, fatigue, and other disease- or treatment-related symptoms throughout the course of illness. Individualized supportive and palliative care should be integrated throughout the disease course to assess, prevent, and manage physical, psychological, social, and symptom-related needs, with the goal of optimizing quality of life.

Source: Adapted from National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Uterine Neoplasms. Version 3.2025; Concin N, Matias-Guiu X, Vergote I, et al. ESGO/ESTRO/ESP Guidelines for the Management of Patients with Endometrial Carcinoma. Int J Gynecol Cancer. 2021;31(1):12–39; Pan-Asian adapted ESMO Clinical Practice Guidelines. ESMO Open. 2022.

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