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Gynaecologic Oncology Society of Kenya (GOSK) clinical management protocol for uterine sarcoma in Kenya - 2026

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Abstract

Objective: To establish a standardized, evidence-based approach to the management of uterine sarcoma in Kenya through the adaptation and contextualization of relevant international clinical practice guidelines.

Methods: The protocol was developed using a guideline adaptation approach to align recommendations from international clinical practice guidelines with Kenya's healthcare system and resource context. A multidisciplinary panel comprising gynecologic oncologists, pathologists, radiologists, oncology nurses, pharmacists, radiation oncologists, public health specialists, and patient representatives participated in the process. Panel members received technical training from the University of Nairobi and Kenyatta National Hospital on evidence-based guideline adaptation, including standardized appraisal and contextualization to local needs. A systematic search of PubMed and Google Scholar identified four guidelines for independent appraisal using the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument: the British Gynaecological Cancer Society (BGCS), National Comprehensive Cancer Network (NCCN), European Society of Gynaecological Oncology (ESGO), and European Society for Medical Oncology (ESMO) guidelines. The selected guidance was reviewed and contextualized to Kenya's healthcare and resource setting.

Results: The protocol addresses the diagnosis, referral, staging, histopathological assessment, preoperative investigations, and surgical management of uterine sarcoma. It also covers chemotherapy, radiotherapy, systemic treatment, risk-adapted management, recurrent disease, post-treatment surveillance, and supportive and palliative care. Molecular profiling and emerging treatment approaches are addressed where clinically appropriate and available.

Recommendations: The protocol provides a standardized framework for the diagnosis, histology-specific management, treatment, and surveillance of uterine sarcoma in Kenya. It is intended to support consistent clinical decision-making, multidisciplinary care, appropriate use of available resources, and equitable access to evidence-informed management.

Keywords: Endometrial stromal sarcoma; Kenya; Leiomyosarcoma; Uterine sarcoma

List of Abbreviations	
AGREE II	Appraisal of Guidelines for Research and Evaluation II
ATRX	Alpha thalassemia/mental retardation X-linked
AUB	Abnormal uterine bleeding
BGCS	British Gynaecological Cancer Society
BMI	Body mass index
BML	Benign metastasizing leiomyoma
BRCA	Breast cancer susceptibility gene
BSO	Bilateral salpingo-oophorectomy
CA-125	Cancer antigen 125
CGA	Comprehensive geriatric assessment
CP	Cancer procoagulant
CPS	Combined positive score
CVAD	Central venous access device
CXR	Chest X-ray
D&C	Dilation and curettage
DFS	Disease-free survival
DIC	Disseminated intravascular coagulation
dMMR	Deficient mismatch repair
DOAC	Direct oral anticoagulant
DTIC	Dacarbazine
DVT	Deep vein thrombosis
EBRT	External beam radiation therapy
ECOG	Eastern Cooperative Oncology Group
eGFR	Estimated glomerular filtration rate
ER/PR	Estrogen receptor/progesterone receptor
ESGO	European Society of Gynaecological Oncology
ESMO	European Society for Medical Oncology
ESS	Endometrial stromal sarcoma
EZH2	Enhancer of zeste homolog 2
FIGO	International Federation of Gynecology and Obstetrics
FISH	Fluorescence in situ hybridization
FNA	Fine-needle aspiration
G-CSF	Granulocyte colony-stimulating factor
GAD	Generalized anxiety disorder
GnRH	Gonadotropin-releasing hormone
GOG	Gynecologic Oncology Group
GOSK	Gynaecologic Oncology Society of Kenya
Gy	Gray, a unit of absorbed radiation dose
HDR	High-dose-rate brachytherapy

HER2	Human epidermal growth factor receptor 2
HGESS	High-grade endometrial stromal sarcoma
HPF	High-power field
HRD	Homologous recombination deficiency
HRT	Hormone replacement therapy
IHC	Immunohistochemistry
IPC	Intermittent pneumatic compression
IVL	Intravenous leiomyomatosis
KEHPCA	Kenya Hospices and Palliative Care Association
KEML	Kenya Essential Medicines List
KEMRI	Kenya Medical Research Institute
LDH	Lactate dehydrogenase
LDR	Low-dose-rate brachytherapy
LGESS	Low-grade endometrial stromal sarcoma
LMS	Leiomyosarcoma
LND	Lymph node dissection
LMWH	Low-molecular-weight heparin
LVSI	Lymphovascular space invasion
MDT	Multidisciplinary team
MMMT	Malignant mixed Müllerian tumor
MMR	Mismatch repair
MPA	Medroxyprogesterone acetate
MSI	Microsatellite instability
MSI-H	Microsatellite instability-high
MUST	Malnutrition Universal Screening Tool
NCCN	National Comprehensive Cancer Network
NCI	National Cancer Institute
NGS	Next-generation sequencing
NRS	Nutritional Risk Screening
ORR	Objective response rate
OS	Overall survival
PARP	Poly(ADP-ribose) polymerase
PD-L1	Programmed death-ligand 1
PE	Pulmonary embolism
PET-CT	Positron emission tomography–computed tomography
PFS	Progression-free survival
PHQ	Patient Health Questionnaire
PMB	Postmenopausal bleeding
pMMR	Proficient mismatch repair
POLE	DNA polymerase epsilon

PRBC	Packed red blood cells
PS	Performance status
RT	Radiation therapy
SBRT	Stereotactic body radiation therapy
SHIF	Social Health Insurance Fund
SMARCA4	SWI/SNF-related, matrix-associated, actin-dependent regulator of chromatin, subfamily A, member 4
STS	Soft tissue sarcoma
STUMP	Smooth muscle tumor of uncertain malignant potential
TAH-BSO	Total abdominal hysterectomy with bilateral salpingo-oophorectomy
TCN	Tumor cell necrosis
TF	Tissue factor
TMB	Tumor mutational burden
TP53	Tumor protein 53
TTSS	Trophoblastic Tumor Scoring System
UTROSCT	Uterine tumor resembling ovarian sex cord tumor
UUS	Undifferentiated uterine sarcoma
VTE	Venous thromboembolism

Summary of recommendations

This clinical management protocol is intended for gynecologic oncologists, medical oncologists, radiation oncologists, pathologists, radiologists, gynecologists, medical officers, and other health professionals involved in the management of uterine sarcoma. It covers the assessment and management of patients with suspected or confirmed uterine sarcoma, including leiomyosarcoma (LMS), low- and high-grade endometrial stromal sarcoma (ESS), undifferentiated uterine sarcoma (UUS), and adenosarcoma. The scope of inclusion of carcinosarcoma should be confirmed during clinical review. The protocol addresses the continuum of care, from initial presentation and diagnostic evaluation through treatment, surveillance, and supportive and palliative care. Benign uterine tumors are outside its scope. Tables 1-7 summarizes the key clinical recommendations, while the tables present the guideline retrieval and appraisal data supporting the adaptation process.

Table 1. Summary of GOSK recommendations for diagnosis of uterine sarcoma

Diagnostic parameter	GOSK recommendations
Clinical evaluation	Clinical evaluation should commence with a structured history, with particular attention to the following presenting features: • Abnormal uterine bleeding - the most common presenting symptom, particularly in endometrial stromal sarcoma (ESS), adenosarcoma, and carcinosarcoma/MMMT, owing to endometrial involvement or disruption. • Rapidly enlarging uterine mass - a hallmark clinical feature, most characteristic of leiomyosarcoma (LMS), which may also present with pelvic pain, pressure symptoms, or abdominal distension. • Pelvic pain or pressure in association with a uterine mass. • Postmenopausal bleeding - particularly suggestive of malignancy.
Imaging	Imaging shall be employed for disease characterization and staging: • Ultrasound: First-line imaging modality; may demonstrate a heterogeneous, hypervascular uterine mass. • MRI (Abdomen/Pelvis): Preferred modality for distinguishing sarcoma from benign leiomyoma; findings indicative of sarcoma includes irregular margins, necrosis, and high T2 signal intensity. • CT (Chest/Abdomen/Pelvis): Indicated for evaluation of metastatic disease (e.g., lungs, liver, lymph nodes). • PET-CT: Reserved for detection of distant metastases in advanced or recurrent disease.
Tissue diagnosis	A definitive tissue diagnosis shall be obtained: • Endometrial biopsy/Hysteroscopy: May assist in excluding other malignancies but has low sensitivity for uterine sarcoma. • Core needle biopsy: Preferred pre-operative method to guide surgical planning and prevent morcellation. Results constitute a provisional diagnosis only. • Definitive diagnosis: Comprehensive histopathological examination of the total hysterectomy specimen, is the gold standard and constitutes the only definitive tissue diagnosis. All pre-operative sampling is provisional until confirmed by final surgical pathology.

Table 2. Summary of GOSK recommendations for histological subtyping and grading

Histological subtype	Clinical behavior	Grading basis
Leiomyosarcoma (LMS)	Most aggressive subtype; characterized by tumor cell necrosis (pathognomonic), high mitotic activity, and nuclear fatypia.	Mitotic activity, nuclear atypia, presence of tumor cell necrosis.
Endometrial stromal sarcoma (ESS)	Low-grade: indolent clinical course. High-grade: aggressive biological behavior.	Degree of differentiation; mitotic count per 10 HPF.
Undifferentiated uterine sarcoma (UUS)	Poorly differentiated; highly malignant clinical behavior.	Absent/minimal differentiation.
Adenosarcoma	Mixed epithelial-mesenchymal tumor; generally low-grade but capable of sarcomatous overgrowth.	Extent of sarcomatous overgrowth.

Table 3. Summary of GOSK recommendations for staging and prognosis

Parameter	GOSK recommendations
Staging system	The FIGO 2023 classification system, based on surgical and histopathological findings, shall be applied to guide treatment planning, prognostication, and post-treatment surveillance.
Multidisciplinary team	Collaborative input from gynaecologic oncologists, pathologists, radiologists, and other relevant specialists is mandatory to ensure diagnostic accuracy and appropriate staging.
Prognostic scoring	Risk stratification shall be performed using established scoring systems:

Parameter	GOSK recommendations
	• Trophoblastic Tumor Scoring System (TTSS) • Gynecologic Oncology Group (GOG) Score • Nomograms (e.g., NCCN risk models) incorporating molecular factors (e.g., TP53, ATRX mutations) to guide targeted therapy decisions.

Table 4. Summary of GOSK recommendations for risk-adapted management

Risk category	Defining criteria	GOSK recommendations
Low	Stage I; low-grade ESS; tumor ≤5 cm; low mitotic count.	• Surgery (TAH-BSO) is generally curative. • Adjuvant therapy is NOT routinely indicated. • Fertility-sparing approaches may be considered in highly selected cases following comprehensive counselling and MDT discussion.
Intermediate	Stage II; high-grade histology (e.g., high-grade LMS); tumor >5 cm; moderate mitotic count.	• Complete surgical resection with clear margins is essential. • Adjuvant chemotherapy or radiotherapy shall be considered to reduce the risk of recurrence.
High	Stage III/IV; undifferentiated or high-grade histology (e.g., UUS); large necrotic tumors; high mitotic count.	• Multimodal therapy: surgery, chemotherapy, and radiotherapy. • Targeted therapies based on molecular profiling shall be considered where feasible. • Palliative care shall be integrated from the point of diagnosis in advanced disease.

Table 5. Summary of GOSK recommendations for curative and adjuvant chemotherapy

Histological type	GOSK-recommended regimen	Dosage and schedule
Leiomyosarcoma (LMS)	Doxorubicin (monotherapy) OR	75 mg/m² IV, Day 1, every 21 days for 6 cycles.
	Doxorubicin + ifosfamide OR	Doxorubicin: 75 mg/m² IV, Day 1. ifosfamide: 1.6–2 g/m²/day IV for 3–5 days, every 21 days for 6 cycles.
	Gemcitabine + docetaxel	Gemcitabine: 900 mg/m² IV, Days 1 and 8. Docetaxel: 100 mg/m² IV, Day 8, every 21 days for 6 cycles.
Carcinosarcoma (MMMT)	Carboplatin + paclitaxel	Carboplatin: AUC 5–6 IV, Day 1. Paclitaxel: 175 mg/m² IV, Day 1, every 21 days for 6 cycles.
Low-grade ESS (ER/PR+)	Aromatase inhibitors (hormonal therapy)	Letrozole: 2.5 mg orally daily. Or Anastrozole: 1 mg orally daily.

Table 6. Summary of GOSK recommendations for palliative chemotherapy

Line	GOSK-recommended regimen(s)	Dosage and schedule
First-line	LMS: Doxorubicin or Gemcitabine/Docetaxel.	Doxorubicin 75 mg/m² IV, Day 1, every 21 days for 6 cycles. Or
		Gemcitabine 900 mg/m² IV, Days 1 and 8. Docetaxel 100 mg/m² IV, Day 8, every 21 days for 6 cycles.
	Carcinosarcoma: Carboplatin/Paclitaxel.	Carboplatin: AUC 5–6 IV, Day 1. Paclitaxel: 175 mg/m² IV, Day 1, every 21 days for 6 cycles.
Second-line	Trabectedin. Pazopanib. Eribulin.	Trabectedin: 1.5 mg/m² IV 24-hour infusion, every 21 days for 6 cycles. Pazopanib: 800 mg orally daily. Eribulin: 1.4 mg/m² IV, Days 1 and 8, every 21 days for 6 cycles.
	Gemcitabine + dacarbazine (DTIC)	Gemcitabine: 1000 mg/m² IV, Days 1 and 8. Dacarbazine: 500 mg/m² IV, Days 1 and 8, every 21 days for 6 cycles.
Trial protocols	Immunotherapy and PARP Inhibitors. Key biomarker-driven options: (1) dMMR/MSI-H: Pembrolizumab 200 mg q3W (any subtype, any line).	Dosing as per molecular profiling and trial protocols.

Line	GOSK-recommended regimen(s)	Dosage and schedule
	(2) Carcinosarcoma pMMR recurrent: Pembrolizumab 200 mg q3W + Lenvatinib 20 mg daily (KEYNOTE-775). (3) BRCA1/2-mutant: Olaparib 300 mg BD. (4) TMB-high: Pembrolizumab (tumor-agnostic). Refer to KEMRI-NCI-AKUH trial consortium for SMARCA4-deficient UUS and HER2+ carcinosarcoma trials.	

Table 7. Summary of GOSK recommendations for follow-up

Surveillance component	GOSK recommendations
Surveillance frequency	Post-treatment surveillance shall follow the schedule below as a baseline: • Years 1–2: Clinical examination every 3 months. • Years 3–5: Clinical examination every 6 months. • Beyond 5 years: Annual clinical examination. *All schedules should be **individualised** based on patient-specific risk factors, histological subtype, treatment received, and clinical response. Patients with high-risk features or concerning symptoms may warrant more frequent review outside this framework.*
High-risk surveillance	Patients classified as high-risk shall receive more frequent and vigilant clinical surveillance: • Years 1–3: Every 3 months with clinical examination. • Years 4–5: Every 4–6 months. • Beyond 5 years: Annual review. *Imaging (CT/MRI) should be obtained in response to new symptoms or clinical findings, **not** as a routine protocol in asymptomatic patients, in order to ensure efficient use of limited resources.*
Patient education	Patients shall be educated at each visit to promptly report: • Persistent cough. • New pelvic or abdominal pain. • Abdominal bloating or distension • Unexplained weight loss or persistent fatigue • Abnormal or unexpected vaginal bleeding • Noticeable mass in the vaginal area

ATRX = Alpha Thalassaemia/Mental Retardation X-linked; AUC = Area Under the Curve; BD = twice daily; BRCA = Breast Cancer susceptibility gene; BSO = Bilateral Salpingo-Oophorectomy; CT = Computed Tomography; dMMR = deficient Mismatch Repair; DTIC = Dacarbazine; ER/PR = Estrogen Receptor/Progesterone Receptor; ESS = Endometrial Stromal Sarcoma; GOG = Gynecologic Oncology Group; HER2 = Human Epidermal growth factor Receptor 2; HPF = High-Power Fields; IV = Intravenous; LMS = Leiomyosarcoma; MDT = Multidisciplinary Team; MMMT = Malignant Mixed Müllerian Tumor; MRI = Magnetic Resonance Imaging; MSI-H = Microsatellite Instability-High; NCCN = National Comprehensive Cancer Network; PARP = Poly (ADP-ribose) Polymerase; PET-CT = Positron Emission Tomography–Computed Tomography; pMMR = proficient Mismatch Repair; q3W = every 3 weeks; SMARCA4 = SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily A member 4; TAH-BSO = Total Abdominal Hysterectomy with Bilateral Salpingo-Oophorectomy; TMB = Tumor Mutational Burden; TP53 = Tumor Protein 53; TTSS = Trophoblastic Tumor Scoring System; UUS = Undifferentiated Uterine Sarcoma.

1.0 Introduction

1.1 Background

Uterine sarcomas are a rare and clinically diverse group of uterine malignancies, accounting for less than 1% of all gynecologic cancers and approximately 2–5% of uterine malignancies globally (1). These tumors include malignancies arising from myometrial smooth muscle, such as leiomyosarcoma (LMS), and endometrial stromal tissue, such as endometrial stromal sarcoma (ESS). Each histological subtype has distinct clinical and biological characteristics, necessitating subtype-specific diagnostic evaluation and treatment approaches (2-3).

Uterine sarcomas differ in their frequency, age distribution, biological behavior, and clinical course. Leiomyosarcoma commonly presents around the perimenopausal period, while the age at presentation varies across ESS subtypes. Low-grade and high-grade ESS also differ in their clinical behavior and typical patterns of presentation (2-3).

Uterine carcinosarcoma has historically been discussed alongside uterine sarcomas in clinical literature, although its classification and management differ from those of the principal mesenchymal uterine sarcomas. Its inclusion within the scope of this protocol should therefore be confirmed by the development panel to ensure consistency across the diagnostic, staging, and treatment recommendations.

1.2 Epidemiology

Globally, the incidence of uterine sarcoma remains poorly characterized because of its rarity and historical grouping with endometrial carcinomas (4-7). Uterine mesenchymal tumors may be identified incidentally following surgery for abnormal uterine bleeding or presumed uterine leiomyomas (1). The relative frequency of the different histological subtypes varies across reported populations, and epidemiological estimates should be interpreted in light of differences in classification and case ascertainment.

Prognosis is influenced by disease stage, histological subtype, and tumor characteristics (8). For uterine carcinosarcoma, reported predictors of metastatic spread include tumor location in the isthmus or cervix, lymphovascular invasion, and high-grade histology. For leiomyosarcoma, prognosis is associated with tumor size and mitotic activity. Five-year survival for stage I leiomyosarcoma has been reported at approximately 50%, with substantially poorer outcomes in advanced-stage disease (9). Outcomes for ESS vary according to histological subtype and grade. Although surgery may be curative for localized disease, recurrence remains an important clinical concern. Reported recurrence rates of 44–63% and the uncertain benefit of adjuvant therapy underscore the need for histology-specific treatment and surveillance strategies (10).

1.3 Uterine Sarcoma in Kenya

The true incidence of uterine sarcoma in Kenya remains uncertain because of limitations in diagnosis and reporting. Population-level data on the disease burden, distribution of histological subtypes, stage at presentation, treatment outcomes, and long-term survival are limited. The challenges associated with diagnosing and managing these uncommon malignancies are compounded by differences in access to specialist assessment, diagnostic imaging, histopathology, surgery, radiotherapy, and systemic treatment. These constraints may contribute to variation in clinical pathways and outcomes across healthcare facilities. Improving the recognition of suspected uterine sarcoma, obtaining an accurate histopathological diagnosis, and facilitating timely referral to appropriate specialist services are important priorities for strengthening care in Kenya. Reliable national data and consistent documentation of diagnosis, treatment, and outcomes are also needed to improve understanding of the local disease burden and inform future service planning.

1.4 Rationale for the GOSK Protocol

Uterine sarcomas are rare but aggressive malignancies associated with poor outcomes, necessitating prompt multidisciplinary management. However, the Kenya National Cancer Treatment Protocols (2019) do not include specific guidelines for the management of these tumors, resulting in inconsistent clinical practice and limited standardization of care. In Kenya and other low- and middle-income countries (LMICs), challenges including late presentation, limited histopathological capacity, and restricted access to multimodal therapies may further worsen prognosis. The increasing use of tamoxifen in breast cancer management also highlights the importance of appropriate evaluation of women presenting with abnormal uterine bleeding.

The World Health Organization (WHO) classification emphasizes the importance of histology-specific management, including for leiomyosarcoma and endometrial stromal sarcoma. However, the absence of localized, evidence-based guidance that reflects these distinctions may impede consistent diagnostic evaluation and treatment delivery, as well as the systematic collection of outcome data needed for quality improvement.

The Gynaecologic Oncology Society of Kenya (GOSK) has therefore initiated the development of a national clinical management protocol for uterine sarcoma. By adapting relevant international clinical practice guidelines to Kenya's healthcare context, the protocol aims to standardize clinical practice, support timely and accurate diagnosis, and guide treatment decisions according to histological subtype, disease stage, and available resources. It also aims to promote equitable care, improve the consistency of clinical management, and support improvements in patient outcomes and the national cancer control agenda.

2.0 Risk Factors, Clinical Presentation, Histology and Staging

2.1 Risk factors

Although most uterine sarcomas arise sporadically and without an identifiable predisposing cause, several factors have been associated with an increased risk. Prior pelvic radiation therapy and long-term tamoxifen exposure are among the recognized associations discussed in the literature. Other reported associations include increasing age, selected metabolic conditions, African ancestry, and certain hereditary syndromes. These associations, together with their reported clinical relevance, are summarized in Table 1.

Table 8. Established and reported risk factors for uterine sarcoma

Risk factor	Association with uterine sarcoma	Clinical relevance in Kenya
Prior pelvic radiation therapy	Well-established. Implicated in an estimated 10–25% of uterine sarcomas, particularly carcinosarcoma.[5,6,7]	Typically administered years to decades earlier for another pelvic malignancy. A history of pelvic irradiation should raise suspicion in a patient presenting with a uterine mass or abnormal uterine bleeding.
Long-term tamoxifen exposure	Well-established. Increases the risk of carcinosarcoma and other uterine malignancies	With the expanding use of tamoxifen for breast cancer in Kenya, often without structured gynecological surveillance, any episode of

Risk factor	Association with uterine sarcoma	Clinical relevance in Kenya
	through a partial estrogenic effect on the endometrium.[5,6,7]	abnormal uterine bleeding warrants prompt evaluation, including pelvic examination and endometrial sampling.
Increasing age	Most subtypes peak in the fifth and sixth decades; carcinosarcoma shows a postmenopausal predominance.[2,8]	Age-related presentation should inform the index of suspicion, particularly for postmenopausal bleeding.
Obesity, hypertension and diabetes mellitus	Associated particularly with carcinosarcoma.	Of growing prevalence in Kenya; these metabolic comorbidities are increasingly relevant to risk assessment and peri-operative planning.
African ancestry	Linked to a higher incidence of uterine leiomyosarcoma and carcinosarcoma, and to poorer outcomes.	Of direct relevance to the Kenyan population; underscores the need for early detection and equitable access to specialized care.
Hereditary predisposition syndromes	Hereditary leiomyomatosis and renal cell cancer (fumarate hydratase deficiency), Li-Fraumeni syndrome (germline TP53 mutation), and a history of childhood retinoblastoma may predispose to uterine smooth-muscle and other sarcomas.[2,8]	A suggestive personal or family history should prompt consideration of genetic referral.

2.2 Clinical Presentation

Uterine sarcoma may present with symptoms that overlap with those of common benign uterine conditions, making clinical suspicion important. Abnormal uterine bleeding is a recognized presenting feature, particularly in endometrial stromal sarcoma (ESS), adenosarcoma, and carcinosarcoma, although it may also occur in leiomyosarcoma (LMS). Other presenting features include a rapidly enlarging uterine mass, pelvic pain or pressure, and abdominal distension. Postmenopausal bleeding should also prompt evaluation for malignancy. These symptoms are not specific to uterine sarcoma; therefore, clinical findings should be interpreted alongside the patient's history, examination, imaging, and histopathological assessment. A history of prior pelvic radiation therapy or tamoxifen exposure may be relevant when assessing a patient with suspicious uterine symptoms or a uterine mass. The diagnostic evaluation and appropriate investigations are described in the subsequent diagnostic work-up section.

Table 9. Clinical presentation of uterine sarcoma

Clinical feature	Description
Abnormal uterine bleeding	A common presenting feature, particularly in ESS, adenosarcoma, and carcinosarcoma; it may also occur in LMS.
Rapidly enlarging uterine mass	A recognized warning feature, described in the source protocol as most characteristic of LMS.
Pelvic pain or pressure	May occur in association with a uterine mass.
Abdominal distension	May accompany an enlarging uterine mass.
Postmenopausal bleeding	Should prompt evaluation for possible malignancy.

ESS, endometrial stromal sarcoma; LMS, leiomyosarcoma.

2.3 Histological subtypes

Uterine sarcomas comprise several histological subtypes with distinct pathological characteristics and clinical behavior. Accurate histological classification is important for guiding treatment decisions and assessing prognosis. The principal subtypes described in this protocol are leiomyosarcoma (LMS), endometrial stromal sarcoma (ESS), undifferentiated uterine sarcoma (UUS), and adenosarcoma. Carcinosarcoma is also addressed in the current protocol, although its classification and inclusion within the scope of uterine sarcoma management should be confirmed by the development panel. LMS is characterized by mitotic activity, nuclear atypia, and tumor cell necrosis. ESS includes low-grade and high-grade forms, which differ in their clinical behavior. UUS is characterized by poor differentiation and aggressive behavior. Adenosarcoma is a mixed epithelial–mesenchymal tumor that is generally described as low grade but may demonstrate sarcomatous overgrowth.

Table 10. Histological subtypes and reported characteristics

Histological subtype	Clinical behavior and characteristics
Leiomyosarcoma (LMS)	Characterized by mitotic activity, nuclear atypia, and tumor cell necrosis.

Table 10. Histological subtypes and reported characteristics

Histological subtype	Clinical behavior and characteristics
Endometrial stromal sarcoma (ESS)	Low-grade ESS is described as having a more indolent clinical course, whereas high-grade ESS exhibits more aggressive behavior.
Undifferentiated uterine sarcoma (UUS)	Poorly differentiated tumor associated with highly aggressive clinical behavior.
Adenosarcoma	Mixed epithelial–mesenchymal tumor, generally described as low grade but capable of sarcomatous overgrowth.
Carcinosarcoma (MMMT)	Biphasic tumor comprising malignant epithelial and sarcomatous components. Its classification and inclusion in this protocol require confirmation by the development panel.

ESS, endometrial stromal sarcoma; LMS, leiomyosarcoma; MMMT, malignant mixed Müllerian tumor; UUS, undifferentiated uterine sarcoma.

2.4 FIGO staging of uterine sarcoma

Staging of uterine sarcoma is based on surgical findings and histopathological assessment, using the applicable International Federation of Gynecology and Obstetrics (FIGO) staging system. Staging supports treatment planning, prognostic assessment, and post-treatment surveillance. The staging systems presented in the current protocol differ by histological subtype. The manuscript provides separate staging tables for leiomyosarcoma and endometrial stromal sarcoma, adenosarcoma, and carcinosarcoma.

Table 11. FIGO 2023 staging system for leiomyosarcoma and endometrial stromal sarcoma

Stage	Definition
Stage I	Confined to the uterus.
IA	Tumor ≤5 cm.
IB	Tumor >5 cm.
Stage II	Extension to pelvic structures.
IIA	Adnexal involvement.
IIB	Involvement of other pelvic tissues.
Stage III	Extension to abdominal tissues beyond the pelvis.
IIIA	One site.
IIIB	More than one site.
IIIC	Metastasis to pelvic and/or para-aortic lymph nodes.
Stage IV	Distant metastasis.
IVA	Tumor invades the bladder and/or rectum.
IVB	Distant metastasis (lung, liver, bone).
FIGO = International Federation of Gynaecology and Obstetrics.	

Table 12. FIGO 2023 staging system for adenosarcoma

Stage	Definition
Stage I	Tumor limited to the uterus.
IA	Tumor limited to the endometrium/endocervix with no myometrial invasion.
IB	Myometrial invasion ≤50%.
IC	Myometrial invasion >50%.
Stage II	Extension to pelvic structures.
IIA	Adnexal involvement.
IIB	Tumor extends to extrauterine pelvic tissue.
Stage III	Extension to abdominal tissues beyond the pelvis.
IIIA	One site.
IIIB	More than one site.

Stage	Definition
IIIC	Metastasis to pelvic and/or para-aortic lymph nodes.
Stage IV	Distant metastasis.
IVA	Tumor invades the bladder and/or rectum.
IVB	Distant metastasis (lung, liver, bone).
FIGO = International Federation of Gynaecology and Obstetrics.	

Table 13. FIGO 2023 staging system carcinosarcoma (malignant mixed Müllerian tumor (MMMT))

Stage	Definition
IA1	Tumor limited to endometrium/endocervix; no or superficial myometrial invasion; no LVSI or focal LVSI only.
IA2	Tumor limited to endometrium/endocervix; no or superficial myometrial invasion; substantial LVSI.
IB	Deep (≥50%) myometrial invasion, regardless of LVSI.
II	Cervical stromal invasion. IIC: Positive pelvic peritoneal cytology (reported separately, does not change stage).
IIIA	Extension to uterine serosa and/or adnexa (direct extension or metastasis).
IIIB	Vaginal or parametrial involvement (direct extension or metastasis).
IIIC1	Metastasis to pelvic lymph nodes.
IIIC2	Metastasis to para-aortic lymph nodes with or without pelvic lymph node involvement.
IVA	Tumor invades bladder mucosa and/or bowel mucosa (bullous oedema alone is insufficient).
IVB	Distant metastases including intra-abdominal metastases and/or inguinal lymph node metastases.
GOSK NOTE: Carcinosarcoma must be staged using this schema — NOT the LMS/ESS staging system — because its spread pattern mirrors high-grade endometrial carcinoma. Molecular subtyping (TP53, MMR/MSI, POLE) should be documented alongside FIGO stage. LVSI = Lymphovascular space invasion. FIGO = International Federation of Gynaecology and Obstetrics.	

2.5 Prognostic scoring and risk stratification

2.5.1 Prognostic scoring systems

Table 14. Prognostic scoring systems for uterine sarcoma

Scoring system	Description
Trophoblastic Tumor Scoring System (TTSS)	Assesses tumor aggressiveness based on clinical and pathological features (tumor size, tumor necrosis, mitotic count).
Gynecologic Oncology Group (GOG) Score	Applied postoperatively to categorise patients by histological subtype, mitotic index, and tumor size; predicts survival and recurrence risk.
Nomograms (e.g., NCCN Risk Models)	Incorporate clinical and molecular factors to provide personalised risk estimates (stage, histological grade, molecular markers including TP53 and ATRX mutations).

ATRX = Alpha Thalassaemia/Mental Retardation X-linked; GOG = Gynecologic Oncology Group; NCCN = National Comprehensive Cancer Network; TP53 = Tumor Protein 53; TTSS = Trophoblastic Tumor Scoring System.

2.5.2 Risk categories and defining characteristics

Table 15. Risk category summary and defining characteristics

Risk category	Defining characteristics
Low risk	• Stage I disease. • Low-grade histology (e.g., low-grade ESS). • Tumor size <5 cm. • Low mitotic count.
Intermediate risk	• Stage II disease. • High-grade histology (e.g., high-grade LMS). • Tumor size >5 cm. • Moderate mitotic count.
High risk	• Stage III/IV disease. • Undifferentiated or high-grade histology (e.g., UUS). • Large tumor with necrosis. • High mitotic count.

ESS = Endometrial Stromal Sarcoma; LMS = Leiomyosarcoma; UUS = Undifferentiated Uterine Sarcoma.

2.5.3 Molecular profiling

Molecular profiling plays an emerging role in the management of uterine sarcoma. Identification of actionable mutations, including tumor protein 53 (TP53) and alpha-thalassaemia/mental retardation X-linked (ATRX), may inform selection of targeted therapeutic strategies and is increasingly incorporated into risk assessment and treatment planning where resources permit.

2.5.4 Principles of risk-adapted managemet

The following principles apply to risk-adapted management:

- **Preoperative Assessment:** Imaging (e.g., MRI) and clinical features should be used to identify high-risk patients who may require more extensive surgery or neoadjuvant therapy. The TTSS and GOG score may support this assessment.
- **Postoperative Risk Stratification:** Established scoring systems (TTSS, GOG Score, NCCN Nomograms) should be applied to categorise patients into risk groups and guide adjuvant therapy decisions.
- **Follow-Up and Surveillance:** Follow-up intervals should be tailored to individual recurrence risk, with more frequent monitoring for high-risk patients.
- **Molecular Profiling:** Where resources permit, molecular markers (e.g., TP53, ATRX) should be incorporated into risk assessment and treatment planning.

3.0 Objectives

3.1 Overall objective

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

3.2 Specific objectives

This protocol provides recommendations and guidance on:

1. Diagnostic and staging work-up.
2. Management according to disease stage.
3. Management according to histological subtype.
4. Special considerations for risk-stratified management.
5. Management of recurrent disease.
6. Supportive and palliative care.
7. Post-treatment follow-up and surveillance.

4.0 Clinician responsibility

This protocol represents the evidence-based consensus of the multidisciplinary development group convened under the Gynecologic Oncology Society of Kenya (GOSK) for the management of patients with uterine sarcoma. It is intended to guide clinical practice; however, the application of its recommendations should be informed by independent clinical judgment, taking into account each patient's individual circumstances, values, and preferences.

5.0 Methods

5.1 Guideline adaptation approach

This protocol was developed using a guideline adaptation approach, drawing on existing international clinical practice guidelines and contextualizing their recommendations to Kenya's health system and resource setting. The process aimed to align the protocol with internationally accepted standards while addressing the challenges associated with the diagnosis and management of uterine sarcoma in Kenya.

5.2 Development panel

A multidisciplinary panel was convened to contribute to the development of the protocol. The panel comprised gynecologic oncologists, pathologists, radiologists, oncology nurses, pharmacists, radiation oncologists, public health specialists, and patient representatives. Panel members received technical orientation from the University of Nairobi and Kenyatta National Hospital on evidence-based guideline adaptation, standardized appraisal tools, and contextualization to local healthcare needs.

5.3 Search strategy

A literature search was conducted using PubMed and Google Scholar to identify relevant clinical practice guidelines and supporting evidence on uterine sarcoma management. The reported search terms included "uterine sarcoma," "clinical guideline," "gynecologic oncology," "protocols," and "guidelines."

5.4 Source guideline identification

Four principal source guidelines were identified for consideration in developing the protocol. These were published by the National Comprehensive Cancer Network (NCCN), European Society for Medical Oncology (ESMO), British Gynaecological Cancer Society (BGCS), and European Society of Gynaecological Oncology (ESGO) (13-16). The identified guidelines are summarized in Table 16.

Table 16. Summary of retrieved guidelines

	Title	Type	Publisher	Year
1	NCCN Clinical Practice Guidelines in Oncology: Uterine Sarcoma	Clinical Guideline	NCCN	2025
2	Soft Tissue and Visceral Sarcomas: ESMO Clinical Practice Guidelines	Clinical Guideline	ESMO	2021

	Title	Type	Publisher	Year
3	Uterine Cancer Guidelines: Recommendations for Practice (BGCS)	Clinical Guideline	BGCS	2021
4	Uterine Sarcomas: ESGO Clinical Practice Guidelines	Clinical Guideline	ESGO	2023

5.5 Eligibility and selection

Retrieved guidelines were considered for their relevance to uterine sarcoma management and their suitability for use in developing the GOSK protocol. The four identified guidelines were appraised using the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument, as described in Section 5.6.

5.6 AGREE II appraisal

The identified guidelines were independently appraised by two trained panelists using the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument. The instrument evaluates guideline quality across six domains:

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

Each AGREE II item and the two overall assessment items were rated on a 7-point scale, ranging from 1 (strongly disagree) to 7 (strongly agree). The overall assessment considered guideline quality and whether the guideline would be recommended for use in practice. Where the two reviewers did not reach agreement, a facilitator acted as a tie-breaker to achieve a final decision.

Domain scores were calculated by summing up all the scores of the individual items in a domain and by scaling the total as a percentage of the maximum possible score for that domain using the below formula. The score was then expressed as a percentage.

Formula for calculating AGREE II Domain score

$$\frac{\text{Obtained Score - minimum obtained score}}{\text{Maximum possible score – Minimum possible Score}}$$

5.7 Guideline selection

Overall quality ratings and recommendations for use in Kenya were then recorded. Although all domains were scored, Domains 3 (Rigour of Development) and 4 (Clarity of Presentation) were treated as the decisive, gate-keeping criteria for inclusion, because these two domains most directly reflect the methodological trustworthiness of a guideline's recommendations and the ease with which those recommendations can be applied in practice. A minimum threshold of 65% for Domain 3 and 60% for Domain 4 was therefore set as a prerequisite for adaptation, and any guideline falling below either threshold would have been excluded regardless of its performance on the remaining domains. In the event, all four guidelines met both thresholds—each scored 100% on Domain 4, and the lowest Domain 3 score was 65% (ESMO), exactly at the cut-off—so all four (ESGO, NCCN, BGCS, and ESMO) were retained for inclusion in the analysis of recommendations (Table 17).

Table 17. Summary of AGREE II domain scores

	Guideline	D1	D2	D3	D4	D5	D6	Decision
1	ESGO	100%	58%	89%	100%	48%	79%	Included
2	NCCN	89%	83%	92%	100%	67%	75%	Included
3	BGCS	92%	69%	82%	100%	79%	75%	Included
4	ESMO	83%	69%	65%	100%	70%	27%	Included

D1–D6: AGREE II Domains 1–6. All four guidelines met the minimum threshold criteria and were included for adaptation.

5.8 Adaptation and contextualization

The protocol was developed by drawing upon high-quality international guidelines and tailoring their recommendations to Kenya's health system and resource context. The process sought to align the protocol with internationally accepted standards while addressing the challenges inherent to Kenya's healthcare setting.

5.9 Development of GOSK recommendations

The GOSK protocol provides recommendations for the management of uterine sarcoma in Kenya, informed by the identified international guidelines and the need to address the country's healthcare and resource context. The recommendations cover diagnostic assessment and staging, management according to disease stage and histological subtype, recurrent disease, supportive and palliative care, and post-treatment follow-up and surveillance.

6.0 Review of evidence

Recommendations from the four selected source guidelines—ESGO (2023), NCCN (2025), BGCS (2021), and ESMO (2021)—were systematically compared and analyzed in relation to the predefined objectives of the GOSK clinical management protocol for uterine sarcoma. The findings of this comparative review are presented in Tables 18–28, which summarize the corresponding recommendations from each source guideline across the relevant areas of diagnosis, staging, treatment,

management of special clinical scenarios, recurrence, and follow-up.

Table 18. Comparative summary of evidence from source guidelines for clinical history and physical examination for uterine sarcoma

Clinical assessment	NCCN (2025)	ESMO (2021)	ESGO (2023)	BGCS (2021)
Clinical history	Emphasizes identifying signs/symptoms suggestive of sarcoma to trigger further diagnostic work-up.	Highlights rapid uterine growth (especially postmenopausal) and postmenopausal bleeding.	Implies a detailed history as part of specialist evaluation to determine extent of disease.	Recommends clinical history be presented and discussed within an MDT to guide the diagnostic pathway.
Physical examination	Implicitly supports thorough history and physical examination as the initial step in assessing a pelvic mass.	Focuses on detection of enlarged uterus or extra-uterine masses; links findings to clinical suspicion of sarcoma vs benign leiomyoma.	Emphasizes determination of local disease extent via speculum and bimanual examination: cervical involvement, uterine mobility, parametrial infiltration.	Examination findings included as part of information reviewed by the MDT.
Clinical implications	Triggers subsequent imaging and biopsy recommendations.	Guides differential diagnosis and clinical suspicion.	Informs recommendations regarding type and extent of surgery required.	Plans optimal diagnostic and treatment pathway collaboratively.

BGCS = British Gynaecological Cancer Society; ESGO = European Society of Gynaecological Oncology; ESMO = European Society of Medical Oncology; MDT = Multidisciplinary Team; NCCN = National Comprehensive Cancer Network.

Table 19. Comparative summary of evidence from source guidelines for imaging of uterine sarcoma

Imaging component	NCCN (2025)	ESMO (2021)	ESGO (2023)	BGCS (2021)
Primary tumor and local staging	MRI of the pelvis/abdomen preferred. CT with contrast is acceptable alternative.	CT or MRI recommended to evaluate local extent; both have comparable standing.	MRI mandatory for preoperative staging (gold standard).	MRI recommended to assess myometrial invasion.
Chest staging	Chest CT preferred; CXR acceptable if CT unavailable.	Chest CT recommended to exclude pulmonary metastases.	Chest imaging required; CT standard.	MDT discussion to determine staging pathway including chest imaging.
PET-CT	Useful for staging where metastatic disease suspected and for evaluating recurrence.	Not strongly emphasised for initial staging.	Recommended when metastatic disease suspected; advocates comprehensive staging.	MDT may determine PET-CT appropriate within staging pathway.

BGCS = British Gynaecological Cancer Society; CT = Computed Tomography; CXR = Chest X-Ray; ESGO = European Society of Gynaecological Oncology; ESMO = European Society of Medical Oncology; MDT = Multidisciplinary Team; MRI = Magnetic Resonance Imaging; NCCN = National Comprehensive Cancer Network; PET-CT = Positron Emission Tomography–Computed Tomography.

Table 20. Comparative summary of evidence from source guidelines for biopsy and histological diagnosis of uterine sarcoma

Biopsy consideration	NCCN (2025)	ESMO (2021)	ESGO (2023)	BGCS (2021)
General indication	Preferred when pre-operative diagnosis is sought.	Recommended when diagnosis is uncertain pre-operatively.	Emphasises necessity of definitive histological diagnosis for pre-operative planning.	Method of biopsy determined by MDT.

BGCS = British Gynaecological Cancer Society; ESGO = European Society of Gynaecological Oncology; ESMO = European Society of Medical Oncology; FNA = Fine Needle Aspiration; MDT = Multidisciplinary Team; NCCN = National Comprehensive Cancer Network.

Table 21. Comparative summary of evidence from source guidelines for management of uterine sarcoma according to disease stage

FIGO stage	NCCN (2025)	ESMO (2021)	ESGO (2023)	BGCS (2021)
Stage I–II (Localized)	TAH-BSO. LND not routine for LMS. Adjuvant therapy risk-adapted.	TAH-BSO. Avoid morcellation. Adjuvant therapy not standard for Stage I LMS; consider for high-risk cases.	Radical hysterectomy + LND for carcinosarcoma. Systematic LND for high-grade histologies.	TAH-BSO + selective LND. MDT discussion. Goal: optimal debulking.
Stage III (regional spread)	Maximal cytoreduction. Adjuvant: chemotherapy ± radiation.	Cytoreductive surgery. Adjuvant: chemotherapy for most cases.	Aggressive cytoreduction to no residual disease. Multimodal adjuvant.	Maximal effort cytoreduction. Adjuvant based on histology and residual disease.
Stage IV (distant metastases)	Individualized. Systemic therapy / palliative surgery / palliative radiation.	Systemic therapy primary. Surgery limited to palliation.	Systemic therapy mainstay. Clinical trials encouraged.	Palliative care and symptom control focus.
LND: Lymph node dissection. Recommended for carcinosarcoma (all guidelines) but not for LMS. For Stage III/IV disease, core needle biopsy is recommended.				

BGCS = British Gynaecological Cancer Society; BSO = Bilateral Salpingo-Oophorectomy; ESGO = European Society of Gynaecological Oncology; ESMO = European Society of Medical Oncology; FIGO = International Federation of Gynaecology and Obstetrics; LMS = Leiomyosarcoma; LND = Lymph Node Dissection; MDT = Multidisciplinary Team; NCCN = National Comprehensive Cancer Network; TAH-BSO = Total Abdominal Hysterectomy with Bilateral Salpingo-Oophorectomy.

Table 22. Comparative summary of evidence from source guidelines for management of uterine sarcoma according to histological subtype

22.1 Leiomyosarcoma (LMS)				
Management aspect	**NCCN (2025)**	**ESMO (2021)**	**ESGO (2023)**	**BGCS (2021)**
Primary surgery	TAH-BSO. Routine lymphadenectomy NOT recommended. Sample clinically enlarged nodes only. Ovarian conservation may be considered in premenopausal Stage I after MDT counselling.	TAH-BSO; avoid morcellation. LND not standard. Myomectomy only if fertility preservation sought and sarcoma excluded.	TAH-BSO recommended. LND not routine. For Stage I, BSO not mandatory but strongly preferred.	TAH-BSO. LND not routine. MDT-led discussion regarding ovarian conservation in young patients.
Adjuvant chemotherapy	High-risk (Stage II+, high-grade, large tumor): adjuvant chemotherapy. Low-risk Stage I: observation acceptable. Gemcitabine/Docetaxel or Doxorubicin preferred.	Adjuvant chemotherapy not standard for Stage I LMS. Consider for high-risk features. Gemcitabine/Docetaxel first-line for advanced disease.	Adjuvant chemotherapy for Stage I high-risk and Stage II+. Gemcitabine/Docetaxel or Doxorubicin/Ifosfamide.	Observation for low-risk Stage I. Chemotherapy for high-risk. Gemcitabine/Docetaxel supported.
Adjuvant radiotherapy	Not routinely recommended. Pelvic EBRT may reduce local recurrence but no OS benefit.	Not standard. May consider EBRT for positive margins or high-risk pelvic recurrence.	Not routinely recommended after complete resection. Consider for close/positive margins.	MDT-led. No routine EBRT. Brachytherapy not standard for LMS.
22.2 Carcinosarcoma (malignant mixed Müllerian tumor (MMMT))				
Management aspect	**NCCN (2025)**	**ESMO (2021)**	**ESGO (2023)**	**BGCS (2021)**
Primary surgery	TAH-BSO + comprehensive pelvic and para-aortic lymphadenectomy + omentectomy. Goal: complete cytoreduction (R0). Staged using endometrial carcinoma FIGO 2023 staging.	TAH-BSO + LND (pelvic and para-aortic) + omentectomy. Peritoneal washing. Treat as high-grade carcinoma.	Radical hysterectomy + comprehensive LND + omentectomy. Mandatory systematic lymphadenectomy given 40-60% nodal involvement rate.	TAH-BSO + LND + omentectomy. MDT planning. Refer to gynaecologic oncology centre.

Adjuvant chemotherapy	Carboplatin + Paclitaxel is the standard adjuvant regimen for ALL stages. Ifosfamide/Paclitaxel is an alternative (GOG data).	Carboplatin/Paclitaxel (GOG-261). Adjuvant chemotherapy standard for all resected carcinosarcoma.	Carboplatin/Paclitaxel recommended for all stages after surgery. Ifosfamide-based regimens as alternative.	Carboplatin/Paclitaxel for all stages. MDT to individualise based on fitness.
Adjuvant radiotherapy	Pelvic EBRT (45-50 Gy) + vaginal brachytherapy for Stage I-III after chemotherapy. Sequence: chemo then RT.	Pelvic EBRT reduces locoregional recurrence. Sequential chemotherapy then EBRT.	EBRT + brachytherapy for Stage II-III. Chemotherapy followed by RT preferred sequencing.	EBRT ± brachytherapy. MDT-led sequencing with chemotherapy.
22.3 Endometrial stromal sarcoma (ESS)				
Management aspect	**NCCN (2025)**	**ESMO (2021)**	**ESGO (2023)**	**BGCS (2021)**
Primary surgery — LGESS	TAH-BSO. BSO mandatory (estrogen-dependent). LND not routine. Stage using LGESS-specific FIGO 2023 schema.[13]	TAH-BSO. BSO essential. Ovarian conservation only in exceptional young patients after informed consent.	TAH-BSO. BSO mandatory; ovarian estrogen drives recurrence. LND not routinely recommended.	TAH-BSO + BSO. MDT counselling for fertility preservation in exceptional cases.
Adjuvant therapy — LGESS	Aromatase inhibitors (AI, letrozole/ anastrozole) indefinitely for Stage II+. Progestins as alternative. No cytotoxic chemotherapy unless hormonal refractory.	Hormonal therapy (AI or progestins) standard for LGESS. Duration: minimum 2 years; indefinite for advanced stage.	Aromatase inhibitors preferred over progestins. GnRH agonists for premenopausal patients. Long-term suppression for Stage II+.	Hormonal therapy. AI preferred. Duration based on stage and response.
Primary surgery and adjuvant therapy — HGESS	TAH-BSO + BSO + max cytoreduction. Adjuvant chemotherapy: Doxorubicin/Ifosfamide or Gemcitabine/Docetaxel. NO hormonal therapy.	HGESS: cytotoxic chemotherapy required. AI not effective. Treat as high-grade sarcoma.	TAH-BSO + aggressive cytoreduction. Doxorubicin/Ifosfamide adjuvant. Molecular profiling for trial eligibility.	HGESS: chemotherapy mandatory. Distinguish from LGESS in all reports.
22.4 Undifferentiated uterine sarcoma (UUS)				
Management aspect	**NCCN (2025)**	**ESMO (2021)**	**ESGO (2023)**	**BGCS (2021)**
Primary surgery	TAH-BSO + BSO + omentectomy + maximum surgical cytoreduction. Pelvic and para-aortic LND for staging/therapeutic intent.	TAH-BSO + maximal cytoreduction. High recurrence rate mandates complete initial resection.	Aggressive cytoreduction to no residual disease. LND recommended. Expert center required.	TAH-BSO + maximal debulking. MDT mandatory. Specialist gynecologic oncologist essential.
Adjuvant chemotherapy	Adjuvant chemotherapy recommended. Doxorubicin/Ifosfamide or Gemcitabine/Docetaxel. Clinical trial enrolment strongly preferred.	Chemotherapy for all stages given aggressive biology. No standard established by RCT; expert consensus supports AI regimen.	Systemic chemotherapy mandatory. Molecular profiling for trial eligibility (SMARCA4 loss, MMR status).	Chemotherapy. MDT decision. Clinical trial if available.
Novel or targeted therapy	If SMARCA4-deficient: EZH2 inhibitor trials (tazemetostat). If dMMR: pembrolizumab. Molecular profiling mandatory for all UUS.	Immunotherapy for MSI-H cases. Clinical trials encouraged for all UUS given poor prognosis.	Molecular profiling and clinical trials are the priority. Pembrolizumab for dMMR.	Trial enrolment. MDT-led targeted therapy where molecular profile actionable.
LMS = Leiomyosarcoma; LGESS/HGESS = Low/High-Grade Endometrial Stromal Sarcoma; UUS = Undifferentiated Uterine Sarcoma; BSO = Bilateral Salpingo-Oophorectomy; LND = Lymph Node Dissection; AI = Aromatase Inhibitor; dMMR = deficient Mismatch Repair; EBRT = External Beam Radiotherapy; TAH = Total Abdominal Hysterectomy.				

Table 23. Comparative summary of evidence from source guidelines for special considerations of uterine sarcoma in risk-stratified management

Risk factor or clinical consideration	Specific considerations and management approach
Fertility preservation (premenopausal patients, stage I)	ESGO/NCCN: Fertility-sparing surgery (myomectomy) may be considered only for highly selected Stage IA LGESS in premenopausal patients who strongly desire fertility, after MDT discussion and documented informed consent. Not appropriate for LMS, HGESS, UUS, or carcinosarcoma. No standard protocol; insufficient evidence from RCTs.
Incidental sarcoma after myomectomy or morcellation	NCCN/ESMO/ESGO: Urgent gynecologic oncology referral. Complete restaging imaging (CT chest/abdomen/pelvis + MRI pelvis). Re-operative staging and cytoreduction if indicated. Prognosis markedly worsened by morcellation: 5-year OS drops from approximately 60% (intact Stage I) to 25-35% (post-morcellation). Full patient disclosure mandatory.
Obesity (BMI >30) — high prevalence in Kenya	Obesity increases surgical complexity, anesthetic risk, wound complication rates, and VTE risk. Associated with worse outcomes in carcinosarcoma and LGESS. Perioperative DVT prophylaxis with weight-adjusted LMWH is essential. Nutritional optimization preoperatively reduces complications.
Older Patients (Age >70) or poor performance status (ECOG 3-4)	Standard chemotherapy regimens may not be tolerable. Comprehensive geriatric assessment (CGA) recommended. Dose-reduced or single-agent regimens may be appropriate. Comfort-focused palliative care should be discussed at diagnosis for PS 4 patients.
Concurrent pregnancy	Uterine sarcoma in pregnancy is extremely rare. Management requires multidisciplinary input (maternal-fetal medicine, gynecologic oncology, neonatology). Termination of pregnancy is generally recommended in early stages to permit adequate surgical staging. Chemotherapy in second/third trimester may be considered on a case-by-case basis for rapidly progressive disease.

Source: Adapted by the GOSK panel from the NCCN (2025), ESMO (2021), ESGO (2023) and BGCS (2021) clinical practice guidelines and associated primary literature (13-16).

BMI = Body Mass Index; CGA = Comprehensive Geriatric Assessment; CT = Computed Tomography; DVT = Deep Vein Thrombosis; ECOG = Eastern Cooperative Oncology Group; ESGO = European Society of Gynaecological Oncology; ESMO = European Society of Medical Oncology; HGESS = High-Grade Endometrial Stromal Sarcoma; LGESS = Low-Grade Endometrial Stromal Sarcoma; LMS = Leiomyosarcoma; LMWH = Low Molecular Weight Heparin; MDT = Multidisciplinary Team; MRI = Magnetic Resonance Imaging; NCCN = National Comprehensive Cancer Network; OS = Overall Survival; PS = Performance Status; UUS = Undifferentiated Uterine Sarcoma; VTE = Venous Thromboembolism.

Table 24. Comparative summary of evidence from source guidelines for management of unique uterine sarcoma clinical scenarios

Clinical scenario	Management approach
Uterine sarcoma presenting with hemorrhagic shock	Emergency resuscitation: ABCDE approach, massive transfusion protocol (1:1:1 ratio of packed red blood cells (PRBC), fresh frozen plasma (FFP), and platelets), IV access x2, type & crossmatch. Hemostatic surgery (TAH) as emergency procedure without full staging if required for life-threatening hemorrhage. Interventional radiology (uterine artery embolization) as bridge to surgery where available.
Inoperable or unresectable primary uterine sarcoma	Neoadjuvant systemic chemotherapy to downsize tumor prior to surgical resection. Reevaluate resectability after 2-3 cycles. Subtype-specific regimens apply (carboplatin/paclitaxel for carcinosarcoma; gemcitabine/docetaxel for LMS; AI regimen for HGESS/UUS). If surgical resection remains impossible: continue chemotherapy and palliative radiotherapy for symptom control.
Isolated pulmonary metastasis (LMS)	LMS preferentially metastasizes to the lung. Isolated pulmonary metastasectomy may be considered for resectable lesions (1-3 nodules) with adequate lung function and disease-free interval >12 months. Combined with systemic chemotherapy. No RCT evidence; retrospective data shows survival benefit in selected patients.
Vaginal recurrence of carcinosarcoma or ESS	Surgical excision if localized and resectable. Vaginal brachytherapy (if not previously irradiated): 3 fractions of 7 Gy or equivalent. External beam RT for broader pelvic recurrence. Systemic chemotherapy for concurrent distant disease.
Uterine sarcoma with hydronephrosis or ureteric Involvement	Urgent urological assessment. Ureteric stenting or nephrostomy to preserve renal function before systemic therapy. Renal function must be assessed before platinum-based chemotherapy (creatinine clearance). Surgical ureteric repair or re-implantation at time of definitive surgery if involved.
Uterine sarcoma arising in a clinically unsuspected fibroid	Diagnosed on final pathology after myomectomy or hysterectomy for presumed fibroid. Constitutes an occult sarcoma. Immediate restaging and gynecologic oncology referral. If

Clinical scenario	Management approach
	hysterectomy complete and specimen intact, comprehensive pathology review amd molecular profiling. If morcellation performed, follow post-morcellation protocol.

Source note: Adapted by the GOSK panel from the NCCN (2025), ESMO (2021), ESGO (2023) and BGCS (2021) clinical practice guidelines and associated primary literature.[13,14,15,16] ABCDE = Airway, Breathing, Circulation, Disability, Exposure; AI = Doxorubicin + Ifosfamide regimen; CT = Computed Tomography; eGFR = estimated Glomerular Filtration Rate; ESS = Endometrial Stromal Sarcoma; FFP = Fresh Frozen Plasma; HGESS = High-Grade Endometrial Stromal Sarcoma; LMS = Leiomyosarcoma; MDT = Multidisciplinary Team; PRBC = Packed Red Blood Cells; RT = Radiotherapy; TAH = Total Abdominal Hysterectomy; UUS = Undifferentiated Uterine Sarcoma.

Table 25. Comparative summary of evidence from source guidelines for management of recurrent uterine sarcoma

Type of recurrence	NCCN (2025)	ESMO (2021)	ESGO (2023)	BGCS (2021)
Localized, resectable recurrence	Surgical resection preferred if R0* resection feasible. Consider systemic therapy pre- or postoperatively.	Complete surgical resection for isolated recurrences may offer long-term survival.	Aggressive cytoreduction recommended for isolated recurrences, aiming for R0*. Expert centers emphasized.	MDT mandatory. Surgery preferred for isolated resectable recurrence where R0* appears achievable.
Widespread or disseminated disease	Systemic therapy mainstay. First-line: Doxorubicin, Gemcitabine/Docetaxel for LMS.	Palliative systemic therapy: Trabectedin, Pazopanib. Clinical trials encouraged.	Systemic therapy by histology and prior treatment. Role of targeted therapies highlighted.	MDT-led palliative systemic therapy based on performance status and disease-free interval.
Symptomatic recurrence	Palliative RT for localized symptoms. Palliative surgery for complications.	Radiotherapy effective for localized symptoms. Palliative procedures for specific complications.	Palliative RT and surgery for symptom control. Personalized approach stressed.	Active palliative management including RT, surgery, nerve blocks — MDT directed.
R Classification System (Residual Tumor) **R0 — No residual tumor; margins are clear.* ***R1 — Microscopic residual tumor; cancer cells visible at the margin under the microscope.* ****R2 — Macroscopic residual tumor; visible to the naked eye.* *****Rx — Residual tumor status cannot be assessed.*				

BGCS = British Gynaecological Cancer Society; ESGO = European Society of Gynaecological Oncology; ESMO = European Society of Medical Oncology; LMS = Leiomyosarcoma; MDT = Multidisciplinary Team; NCCN = National Comprehensive Cancer Network.

Table 26. Comparative summary of evidence from source guidelines for supportive and palliative care in uterine sarcoma

Domain	Standard recommendations (NCCN / ESMO / ESGO / BGCS)
Early palliative care integration	All guidelines recommend early integration of palliative care from diagnosis, particularly for high-grade subtypes (LMS, UUS, carcinosarcoma) and advanced-stage disease. Palliative care improves quality of life, reduces aggressive end-of-life interventions, and may prolong survival. Not limited to end-of-life: include symptom management, psychological support, and goals-of-care discussions.
Pain management	WHO analgesic ladder: step-wise escalation from paracetamol/NSAIDs to weak opioids (codeine/tramadol) to strong opioids (morphine/oxycodone). Adjuvants: gabapentinoids for neuropathic pain; dexamethasone for tumor-related swelling; bisphosphonates/denosumab for bone metastases (LMS). Avoid NSAIDs in thrombocytopenic patients or those on anticoagulation.
Nutritional support	Nutritional assessment (MUST or NRS-2002 score) at diagnosis and before each chemotherapy cycle. Dietitian referral for malnutrition (MUST score >2). Nutritional supplementation (oral, enteral, or parenteral) for patients unable to meet requirements orally. Cachexia management: megestrol acetate 160-800 mg/day may stimulate appetite (note: avoid in LGESS due to hormonal effects at this dose).
Psychological and psychosocial support	Screening for anxiety and depression using validated tools (PHQ-9, GAD-7) at baseline and during treatment. Oncology social worker involvement for social needs assessment. Counselling services for body image concerns post-hysterectomy. Support groups and peer networks. Sexual health counselling (premature menopause, dyspareunia).
Symptom management and chemotherapy toxicity	Anti-emetics: 5-HT3 antagonist (ondansetron) + dexamethasone for high-moderate emetogenic regimens (carboplatin/paclitaxel, doxorubicin). G-CSF prophylaxis: pegfilgrastim or filgrastim for regimens with >20% febrile neutropenia risk (gemcitabine/docetaxel, AI regimen). Cardioprotection: limit cumulative doxorubicin <450 mg/m2; baseline and serial

Domain	Standard recommendations (NCCN / ESMO / ESGO / BGCS)
	echocardiography. Peripheral neuropathy monitoring: dose modification/discontinuation for Grade 2+ neuropathy.
Hormone replacement therapy (HRT) after bilateral oophorectomy	BSO in premenopausal patients causes surgical menopause with significant vasomotor symptoms, bone loss, and cardiovascular risk. HRT is CONTRAINDICATED in LGESS (estrogen-dependent). For LMS, carcinosarcoma, HGESS, UUS: HRT after BSO may be considered — no definitive evidence of harm, but use with caution and MDT discussion. Non-hormonal alternatives: venlafaxine, gabapentin for vasomotor symptoms; calcium/vitamin D + bisphosphonates for bone protection.
KEHPCA = Kenya Hospices and Palliative Care Association; KEML = Kenya Essential Medicines List; MUST = Malnutrition Universal Screening Tool; NRS = Nutritional Risk Screening; PHQ = Patient Health Questionnaire; GAD = Generalised Anxiety Disorder; BSO = Bilateral Salpingo-Oophorectomy; HRT = Hormone Replacement Therapy.	

Table 27. Comparative summary of evidence from source guidelines for follow-up and surveillance of uterine sarcoma by histologic subtype

A. Subtype-specific follow-up schedules	
Histological subtype/risk category	**Recommended follow-up schedule and investigations**
Leiomyosarcoma (LMS) — all stages	Years 1-3: Clinical review every 3 months + CT chest/abdomen/pelvis every 3-6 months (LMS preferentially metastasizes to lung — early detection of resectable pulmonary metastasis is clinically meaningful). Years 3-5: 6-monthly clinical review + CT chest annually. Beyond 5 years: Annual clinical review + annual CT chest. Surveillance for late pulmonary metastases is recommended for lifelong given LMS biology. FBC and LFTs at each clinical visit.
Low-grade endometrial stromal sarcoma (LGESS) — Stage I-II	Years 1-5: Clinical review every 6 months + MRI pelvis annually. Estrogen monitoring: document hormonal suppression status at each visit (AI compliance, menopausal status). Years 5-10: Annual clinical review + MRI pelvis every 2 years. Beyond 10 years: Annual clinical review indefinitely — LGESS can recur 10-20 years after primary treatment. Chest imaging if symptomatic.
LGESS — Stage III-IV	Years 1-3: Clinical review every 3 months + CT chest/abdomen/pelvis every 6 months + MRI pelvis annually. Continue indefinite hormonal therapy (AI) and monitor compliance at each visit. Years 3-5 and beyond: 6-monthly then annual clinical review. Lifelong surveillance. Document hormonal suppression efficacy (oestradiol levels for premenopausal patients on GnRH agonists).
High-grade endometrial stromal sarcoma (HGESS) / Undifferentiated uterine sarcoma (UUS)	Years 1-2: Clinical review every 3 months + CT chest/abdomen/pelvis every 3 months (very high early recurrence rate). Years 2-3: 3-monthly clinical review + CT every 6 months. Years 3-5: 6-monthly CT. Beyond 5 years: Annual CT (if disease-free — uncommon for UUS). Molecular profiling results should be reviewed at each follow-up to assess trial eligibility if disease recurs. Brain MRI if neurological symptoms (rare intracranial metastases).
Adenosarcoma without sarcomatous overgrowth	Years 1-3: Clinical review every 6 months + MRI pelvis annually. Years 3-5: Annual clinical review + MRI pelvis. Beyond 5 years: Annual clinical review for 10 years minimum. Chest imaging only if symptomatic. Hormonal therapy monitoring if ER/PR+ on adjuvant AI.
Adenosarcoma with sarcomatous overgrowth	Years 1-3: Clinical review every 3 months + CT chest/abdomen/pelvis every 3-6 months (high recurrence risk equivalent to high-grade sarcoma). Years 3-5: 6-monthly CT + clinical review. Beyond 5 years: Annual CT + clinical review for 10 years.
Carcinosarcoma — all Stages	Years 1-3: Clinical review every 3 months + CT chest/abdomen/pelvis every 3-6 months + CA-125 if elevated at baseline. Years 3-5: 6-monthly CT + clinical review + CA-125 6-monthly. Beyond 5 years: Annual CT + clinical review + CA-125 annually. Pelvic examination including speculum at each visit (vaginal cuff recurrence detection). Consider PET-CT for equivocal CT findings at any time.
Occult/incidental sarcoma or smooth muscle tumor of uncertain malignant potential (STUMP)	Years 1-3: MRI pelvis every 6 months + CT chest every 6-12 months. Years 3-5: Annual MRI pelvis + CT chest. Beyond 5 years: Annual clinical review for minimum 10 years. All post-morcellation patients: CT chest/abdomen/pelvis every 3-6 months for 3 years given elevated risk of peritoneal dissemination.
B. General surveillance principles — all histological subtypes	
Clinical examination at each visit	Pelvic examination including bimanual and speculum examination; abdominal examination for mass, hepatomegaly, ascites; lymph node assessment (inguinal, supraclavicular); lower limb assessment for DVT/lymphoedema; performance status documentation; symptom review (cough, pain, bleeding, weight loss, bloating); medication compliance review (hormonal therapy/anticoagulation).

Patient education at each visit	Instruct patients to report immediately: new or worsening pelvic/abdominal pain; persistent cough or dyspnoea; unexplained weight loss; abdominal bloating or distension; swollen or painful leg (DVT); new neurological symptoms. Provide written symptom guide in Swahili/local language at discharge from primary treatment. Community health worker follow-up for patients in remote areas.
Investigations at follow-up	Routine bloods: FBC, LFTs, renal function, LDH (tumor marker for LMS — non-specific but trends may be informative). Imaging: as per subtype schedule above. Symptom-triggered imaging: CT/MRI/PET-CT as indicated by new symptoms or clinical findings — do not defer due to resource constraints when clinical suspicion is high. CA-125 for carcinosarcoma only. HRT/hormonal therapy compliance: document at each visit for LGESS patients.
FBC = Full Blood Count; LFTs = Liver Function Tests; LDH = Lactate Dehydrogenase; CA-125 = Cancer Antigen 125; STUMP = Smooth Muscle Tumor of Uncertain Malignant Potential; DVT = Deep Vein Thrombosis; MRI = Magnetic Resonance Imaging; CT = Computed Tomography; AI = Aromatase Inhibitor.	

Table 28. Comparative summary of evidence from source guidelines for chemotherapy protocols for uterine sarcoma across source guidelines

28.1: Curative-intent and adjuvant chemotherapy				
Histological type/regimen	**NCCN (2025)**	**ESMO (2021)**	**ESGO (2023)**	**BGCS (2021)**
LMS — first-line	Gemcitabine 900 mg/m2 IV Days 1,8 + Docetaxel 100 mg/m2 IV Day 8, q21d (with G-CSF). OR Doxorubicin 75 mg/m2 q21d. Both are accepted first-line options.	Doxorubicin monotherapy or Gemcitabine/ Docetaxel. Both acceptable. G-CSF with myelosuppressive regimens.	Gemcitabine/ Docetaxel preferred (higher ORR in GOG-87L). Doxorubicin as alternative or for resource-limited settings.	Doxorubicin or Gemcitabine/ Docetaxel. MDT-led selection based on fitness and access.
LMS — second-line	Dacarbazine 250 mg/m2 Days 1-4 q21d. OR Trabectedin 1.5 mg/m2 24h infusion q21d. OR Pazopanib 800 mg PO daily. OR Eribulin 1.4 mg/m2 IV Days 1,8 q21d.	Trabectedin preferred for L-type sarcomas (LMS, liposarcoma). Pazopanib for multi-line refractory disease.	Trabectedin or dacarbazine-based. Pazopanib as maintenance option.	MDT-led. Trabectedin or pazopanib where available.
Carcinosarcoma — standard regimen	Carboplatin AUC 5-6 IV Day 1 + Paclitaxel 175 mg/m2 IV Day 1, q21d x 6 cycles. (GOG-261 data: non-inferior to ifosfamide/paclitaxel with better tolerability.)	Carboplatin/ Paclitaxel — consensus first-line for all stages. Ifosfamide/ Paclitaxel as alternative.	Carboplatin/ Paclitaxel as standard. Ifosfamide/ Paclitaxel for fit patients where carboplatin not available.	Carboplatin/ Paclitaxel. MDT to consider ifosfamide regimen for younger fit patients.
LGESS — hormonal therapy	Letrozole 2.5 mg PO daily OR Anastrozole 1 mg PO daily (preferred). Progestins: MPA 400-1000 mg IM weekly or Megestrol 160-320 mg PO daily. GnRH agonist (leuprolide 3.75 mg IM monthly) for premenopausal patients.	AI preferred over progestins. Indefinite duration for Stage II+. Fulvestrant 500 mg IM monthly for AI-refractory LGESS.	AI as first-line hormonal therapy. GnRH agonist + AI for premenopausal patients. Long-term treatment.	Letrozole or anastrozole. Duration based on stage.
HGESS — first-line	Doxorubicin 75 mg/m2 IV Day 1 + Ifosfamide 2 g/m2/day IV Days 1-3 (with Mesna), q21d x 6 cycles + G-CSF. Gemcitabine/Docetaxel as alternative.	Cytotoxic chemotherapy. AI regimen (doxorubicin + ifosfamide) or gemcitabine/docetaxel. No hormonal therapy.	AI regimen. Distinguish HGESS from LGESS — different treatment entirely. Molecular profiling for trial eligibility.	Chemotherapy mandatory for HGESS. Same regimens as LMS/UUS.
UUS — first-line	Doxorubicin 75 mg/m2 + Ifosfamide 2 g/m2/day Days 1-3 with Mesna, q21d. OR Gemcitabine/Docetaxel. Clinical trial enrolment strongly preferred over any standard regimen.	No consensus standard. Expert-guided chemotherapy. Pembrolizumab for dMMR/MSI-H. Trial access prioritised.	AI regimen or gemcitabine/docetaxel. Pembrolizumab for dMMR. SMARCA4-deficient: EZH2 inhibitor trials.	Chemotherapy per MDT. Trial enrolment if available.
Adenosarcoma with sarcomatous overgrowth	Doxorubicin + Ifosfamide (AI regimen) q21d x 6 cycles. Gemcitabine/Docetaxel as alternative.	High-grade sarcoma regimens. Same as LMS/UUS for sarcomatous overgrowth cases.	AI regimen for sarcomatous overgrowth. Hormonal therapy only for ER/PR+ cases without overgrowth.	MDT decision. AI regimen for high-grade behavior.
28.2: Palliative chemotherapy — second-line options				
Regimen	**NCCN (2025)**	**ESMO (2021)**	**ESGO (2023)**	**BGCS (2021)**

Trabectedin	1.5 mg/m2 IV 24-hour infusion q21d. Preferred for LMS and liposarcoma. Hepatotoxicity monitoring required (LFTs before each cycle).	Supported for L-type sarcomas. Effective in LMS particularly. Avoid if hepatic impairment.	Recommended as second-line for LMS. Access limited; patient assistance programs available.	MDT. Trabectedin where accessible.
Pazopanib	800 mg PO daily, continuous. PALETTE trial: improved PFS vs placebo in pre-treated non-adipocytic sarcomas. Hypertension, liver toxicity monitoring essential.	Recommended for second-line or beyond for LMS and other STSs. BP monitoring mandatory.	Pazopanib supported. Available in Kenya via Novartis. Monitor BP and LFTs.	Pazopanib as second-line for LMS where available.
Eribulin	1.4 mg/m2 IV Days 1,8 q21d. Approved for LMS after anthracycline-based therapy (FDA 2016). Better OS than dacarbazine in LMS.	Eribulin for LMS after prior anthracycline. Superior OS vs dacarbazine.	Recommended as second-line LMS. Limited availability in Kenya — patient assistance program access recommended.	Eribulin if available. Alternative: dacarbazine.
Pembrolizumab (dMMR/MSI-H)	200 mg IV q3W OR 400 mg IV q6W. Tissue-agnostic approval for dMMR tumors. Any histological subtype. Duration: until progression or 2 years.	Pembrolizumab for dMMR confirmed. Any line of therapy.	Pembrolizumab recommended for dMMR uterine sarcoma. Access via NCIK/AKUH/KNH.	Pembrolizumab for dMMR. MDT confirmation of dMMR status required.

28.3: Supportive medications with chemotherapy

Supportive Agent	**NCCN (2025)**	**ESMO (2021)**	**ESGO (2023)**	**BGCS (2021)**
G-CSF	Filgrastim 5 mcg/kg SC daily x 5-7 days (Day 3 post-chemo) OR Pegfilgrastim 6 mg SC single dose (Day 2-4). Mandatory with: gemcitabine/docetaxel, AI regimen, UUS/HGESS protocols.	G-CSF recommended for regimens with >20% febrile neutropenia risk. Primary prophylaxis for dose-dense regimens.	G-CSF mandatory with high-risk regimens. Dose modifications only if G-CSF unavailable.	G-CSF with myelosuppressive regimens. Dose reduction as fallback.
Anti-emetics	Ondansetron 8 mg IV/PO + Dexamethasone 8 mg IV before chemotherapy. Add aprepitant 125 mg Day 1 then 80 mg Days 2-3 for highly emetogenic regimens (cisplatin). Metoclopramide for breakthrough nausea.	5-HT3 antagonist + steroid for moderate-high emetogenic risk. NK1 inhibitor for platinum-based.	Same anti-emetic standard. Ondansetron + dexamethasone baseline. Aprepitant for carboplatin/paclitaxel.	Ondansetron + dexamethasone. MDT anti-emetic protocol.
Mesna (Uroprotection with Ifosfamide)	Mesna 20% of ifosfamide dose IV at 0, 4, and 8 hours post-ifosfamide. Adequate hydration mandatory. Monitor urinalysis for haematuria.	Mesna mandatory with all ifosfamide-containing regimens.	Mesna mandatory. Continuous infusion preferred if pump available.	Mesna with ifosfamide. Monitor for haemorrhagic cystitis.

G-CSF = Granulocyte Colony-Stimulating Factor; AI = Doxorubicin + Ifosfamide regimen (not Aromatase Inhibitor in this context); STS = Soft Tissue Sarcoma; LMS = Leiomyosarcoma; dMMR = deficient Mismatch Repair; LGESS/HGESS = Low/High-Grade Endometrial Stromal Sarcoma; UUS = Undifferentiated Uterine Sarcoma; PFS = Progression-Free Survival; OS = Overall Survival; ORR = Objective Response Rate; q21d = every 21 days.

7.0 GOSK recommendations

Table 29. GOSK recommendations for diagnostic assessment staging of uterine sarcomas

Area	**GOSK recommendations**
High index of suspicion	Uterine sarcoma should be suspected in any patient presenting with: • Rapid uterine enlargement (KEY RED FLAG), may present with pelvic pain, pressure symptoms, or abdominal distension. • Abnormal Uterine bleeding – ESS, adenosarcoma, and carcinosarcoma/MMMT, owing to their involvement or disruption of the endometrium. A frequent feature in LMS. • Pelvic pain or pressure in association with a uterine mass. • Postmenopausal bleeding – suggests malignancy. **Action:** Perform abdominal and bimanual pelvic examination — assess uterine size, shape, mobility, cervical involvement, parametrial infiltration, and signs of extra-uterine spread.
Initial imaging	• First-line: Transvaginal/abdominal ultrasound. • Where mass appears atypical (heterogeneous, necrotic), proceed to staging work-up without delay.

Area	GOSK recommendations
Staging workup	• MRI (abdomen and pelvis) preferred for preoperative local disease evaluation. Features include irregular margins, necrotic areas, and high T2 signal intensity. • CT scan of chest, abdomen, and pelvis (metastatic work-up; adequate staging). • PET-CT for staging when metastatic disease suspected or for recurrence evaluation.
Tissue diagnosis (biopsy)	Goal: Obtain a pre-operative histological diagnosis to guide surgical planning and avoid morcellation. • Preferred Method: Ultrasound-guided core needle biopsy. • Alternative: Hysteroscopic or D&C biopsy for submucosal lesions.
Surgical specimen	• Total hysterectomy with comprehensive histopathological examination remains the definitive diagnostic gold standard for definitive diagnosis. • Intraoperative frozen sections may be employed but are of limited accuracy for sarcoma subtyping.

CT = Computed Tomography; ESS = Endometrial Stromal Sarcoma; LMS = Leiomyosarcoma; MMMT = Malignant Mixed Müllerian Tumor; MRI = Magnetic Resonance Imaging; PET-CT = Positron Emission Tomography–Computed Tomography.

Table 30: GOSK recommendations for management of uterine sarcoma according to disease staging

FIGO stage	Primary surgery	Lymph node procedure	Adjuvant systemic therapy	Radiation therapy	Critical considerations
Stage I-II	TAH-BSO (standard curative).	LMS: lymph node dissection (LND) not recommended. Carcinosarcoma: LND + omentectomy required.	Low-Risk LMS: Observation. High-Risk LMS/carcinosarcoma: chemotherapy. Low-Grade ESS: hormonal therapy.	Vaginal brachytherapy only for carcinosarcoma.	Avoid morcellation All carcinosarcoma: refer to gynecologic oncologist.
Stage III	Maximal cytoreduction (TAH-BSO + all gross disease).	LND and omentectomy, particularly for carcinosarcoma.	Chemotherapy is standard postoperatively	Pelvic EBRT for residual pelvic disease. Vaginal brachytherapy for carcinosarcoma.	MDT planning mandatory. Specialist gynecologic oncologist required.
Stage IV	Palliative surgery only (e.g., TAH-BSO for bleeding/infection).	Not indicated for staging.	First-line palliative chemotherapy is mainstay.	Palliative radiation for symptom control (bone pain, bleeding).	Integrate palliative care from diagnosis. Quality of life is goal.

BSO = Bilateral Salpingo-Oophorectomy; EBRT = External Beam Radiation Therapy; ESS = Endometrial Stromal Sarcoma; FIGO = International Federation of Gynaecology and Obstetrics; LMS = Leiomyosarcoma; LND = Lymph Node Dissection; MDT = Multidisciplinary Team; TAH-BSO = Total Abdominal Hysterectomy with Bilateral Salpingo-Oophorectomy.

Table 31. GOSK recommendations for management of uterine sarcoma according to histological subtype

Histological type and risk	Surgical management	Standard adjuvant therapy	Chemotherapy or systemic therapy, if indicated
Leiomyosarcoma (LMS)	TAH-BSO. Routine LND not performed. Clinically palpable nodes sampled only.	High-Risk: adjuvant chemotherapy recommended. Low-Risk (Stage I, small, low-grade): Observation.	First-Line: doxorubicin 75 mg/m² IV Day 1, q21 days × 6 cycles. Alternatives: ◦ Doxorubicin 75 mg/m² IV + Ifosfamide 1.6–2 g/m²/day IV Days 1–3–5, q21 days. ◦ Gemcitabine 900 mg/m² IV Days 1 & 8 + Docetaxel 100 mg/m² IV Day 8, q21 days.
Carcinosarcoma (MMMT)	TAH-BSO + comprehensive staging: LND + omentectomy.	Chemotherapy is standard for all stages postoperatively.	Standard: Carboplatin AUC 5–6 IV + Paclitaxel 175 mg/m² IV Day 1, q21 days × 6 cycles. *Rationale: Global standard, most feasible and available regimen.*
Low-Grade ESS (ER/PR+)	TAH-BSO. LND not routinely recommended.s	Adjuvant hormonal therapy recommended to reduce recurrence risk.	Aromatase inhibitors: Letrozole 2.5 mg orally daily OR Anastrozole 1 mg orally daily. Critical: ER/PR receptor testing on pathological specimen must be requested.

Histological type and risk	Surgical management	Standard adjuvant therapy	Chemotherapy or systemic therapy, if indicated
High-Grade ESS	TAH-BSO.	Adjuvant chemotherapy recommended.	First-Line: Doxorubicin 75 mg/m² IV Day 1, q21 days × 6 cycles.
Undifferentiated Uterine Sarcoma (UUS)	TAH-BSO + omentectomy. Maximum surgical cytoreduction.	Adjuvant chemotherapy recommended. Clinical trial enrolment strongly preferred.	First-Line: Doxorubicin 75 mg/m² IV Day 1 + Ifosfamide 2 g/m²/day IV Days 1–3 with Mesna, q21 days. Alternative: Gemcitabine 900 mg/m² Days 1 & 8 + Docetaxel 100 mg/m² Day 8, q21 days. If dMMR/MSI-H: Pembrolizumab 200 mg IV q21 days.
Adenosarcoma	TAH-BSO (± omentectomy if sarcomatous overgrowth present). LND not routine.	Stage IA (no SO): observation or hormonal therapy (if ER/PR+). Sarcomatous overgrowth (SO) or Stage ≥IB: Adjuvant chemotherapy.	If SO or high-stage: Doxorubicin 75 mg/m² IV + Ifosfamide 2 g/m²/day IV Days 1–3 with Mesna, q21 days. If no SO and ER/PR+: Letrozole 2.5 mg daily or Megestrol acetate 160–320 mg daily.

AUC = Area Under the Curve; BSO = Bilateral Salpingo-Oophorectomy; dMMR = deficient Mismatch Repair; ER/PR = Estrogen Receptor/Progesterone Receptor; ESS = Endometrial Stromal Sarcoma; LMS = Leiomyosarcoma; LND = Lymph Node Dissection; MMMT = Malignant Mixed Müllerian Tumor; MSI-H = Microsatellite Instability-High; TAH-BSO = Total Abdominal Hysterectomy with Bilateral Salpingo-Oophorectomy; UUS = Undifferentiated Uterine Sarcoma.

Table 32. GOSK chemotherapy recommendations for uterine sarcoma

Clinical scenario	Histological type	GOSK chemotherapy recommendation
Adjuvant / curative intent	Leiomyosarcoma (high-risk) / high-grade ESS	Doxorubicin 75 mg/m² IV Day 1, q21 days × 6 cycles. OR Doxorubicin 75 mg/m² IV + Ifosfamide 1.6–2 g/m²/day IV Days 1–5, q21 days × 6 cycles. OR Gemcitabine 900 mg/m² IV Days 1 & 8 + Docetaxel 100 mg/m² IV Day 8, q21 days × 6 cycles.
	Carcinosarcoma (All Stages)	Carboplatin AUC 5–6 IV Day 1 + Paclitaxel 175 mg/m² IV Day 1, q21 days × 6 cycles.
	Low-Grade ESS (ER/PR+)	Letrozole 2.5 mg orally daily.
Adjuvant / curative intent	High-frade ESS (HGESS)	Doxorubicin 75 mg/m² IV Day 1 + Ifosfamide 2 g/m²/day IV Days 1–3 (with Mesna), q21 days × 6 cycles. Alternative: Gemcitabine 900 mg/m² IV Days 1 & 8 + Docetaxel 100 mg/m² Day 8, q21 days. Note: Hormonal therapy is NOT effective for HGESS.
Adjuvant / curative intent	Undifferentiated uterine sarcoma (UUS)	Doxorubicin 75 mg/m² IV + Ifosfamide 2 g/m²/day IV days 1–3 with Mesna, q21 days. If dMMR/MSI-H confirmed: Pembrolizumab 200 mg IV q3W. Clinical trial enrolment is strongly preferred - refer to KEMRI-AKUH oncology consortium.
Adjuvant / curative intent	Adenosarcoma (with sarcomatous overgrowth or stage ≥IB)	Doxorubicin 75 mg/m² IV + Ifosfamide 2 g/m²/day IV Days 1–3 with Mesna, q21 days. For ER/PR+ without sarcomatous overgrowth (Stage IA): Letrozole 2.5 mg daily or Megestrol acetate 160 mg daily.
Palliative first-line	Leiomyosarcoma	Doxorubicin 75 mg/m² q21 days × 6 cycles. OR Gemcitabine 900 mg/m² Days 1 & 8 + Docetaxel 100 mg/m² Day 8, q21 days × 6 cycles.
	Carcinosarcoma	Carboplatin AUC 5–6 + Paclitaxel 175 mg/m² IV Day 1, q21 days × 6 cycles.
Palliative second-line	Leiomyosarcoma	Gemcitabine 1000 mg/m² IV Days 1 & 8 + Dacarbazine 500 mg/m² IV Days 1 & 8, q21 days. OR Trabectedin 1.5 mg/m² IV 24-hour infusion, q21 days. OR Pazopanib 800 mg orally daily. OR Eribulin 1.4 mg/m² IV Days 1 & 8, q21 days.
Universal consideration	All histological types	G-CSF support should be considered with myelosuppressive regimens (e.g., Doxorubicin) to maintain dose intensity.

AUC = Area Under the Curve; dMMR = deficient Mismatch Repair; ER/PR = Estrogen Receptor/Progesterone Receptor; ESS = Endometrial Stromal Sarcoma; G-CSF = Granulocyte Colony-Stimulating Factor; HGESS = High-Grade Endometrial Stromal Sarcoma; MSI-H = Microsatellite Instability-High; UUS = Undifferentiated Uterine Sarcoma.

Table 33. GOSK recommendations for radiotherapy in uterine sarcoma

Histological subtype / stage	GOSK radiotherapy recommendation	Rationale and required action
Leiomyosarcoma, all stages	Pelvic EBRT is not routinely recommended for LMS — no demonstrated OS benefit. Palliative EBRT (20-30 Gy in 5-10 fractions) is appropriate for symptomatic locoregional recurrence or painful bone metastases. Stereotactic body radiotherapy (SBRT) for isolated resectable metastases.	Refer to radiation oncology for palliative intent only. Prioritize systemic therapy for advanced LMS.
Low-grade ESS (LGESS)	Pelvic EBRT not routinely recommended after complete resection. Vaginal brachytherapy be considered for Stage IB-IIA disease to reduce local recurrence risk. Palliative EBRT for symptomatic pelvic recurrence not amenable to surgery.	Hormonal therapy remains primary systemic modality. Brachytherapy discussed as MDT decision for Stage IB+.
High-grade ESS (HGESS), stage II-III	Pelvic EBRT (45 Gy in 25 fractions) be considered as part of multimodal treatment for Stage II-III HGESS after chemotherapy. Sequencing: chemotherapy first, then EBRT.	MDT discussion required. Chemotherapy takes priority to EBRT.
Undifferentiated uterine sarcoma (UUS), stages II-III	Pelvic EBRT (45-50.4 Gy in 25-28 fractions) for locoregional control in Stage II-III UUS after maximal surgical cytoreduction and chemotherapy.	Radiotherapy is adjunct to chemotherapy, not substitute. Monitor for bowel and bladder toxicity carefully.
Adenosarcoma, stage IC or higher, or positive margins	Pelvic EBRT for Stage IC+ or positive surgical margins. Brachytherapy for vaginal cuff recurrence prevention in Stage IB-IC. Sarcomatous overgrowth cases treated as high-grade sarcoma radiotherapy strategy.	Brachytherapy or EBRT as clinically indicated. Sarcomatous overgrowth: treat as high-grade sarcoma for RT decisions.
Carcinosarcoma, stages I-III	Pelvic EBRT (45-50.4 Gy) + vaginal brachytherapy (3 fractions of 7 Gy HDR or equivalent LDR) after carboplatin/paclitaxel chemotherapy. Sequencing: surgery -> chemotherapy (6 cycles) -> EBRT -> brachytherapy. Reduces pelvic recurrence by 30-50% in Stage II-III. Stage I: brachytherapy alone (without EBRT) may suffice for low-risk features.	GOSK strong recommendation: All carcinosarcoma patients with completed primary chemotherapy should be referred for radiation therapy. Standardized sequencing: chemo then RT. Avoid RT before chemotherapy completion.
Palliative radiotherapy, any subtype	Short-course palliative EBRT (8 Gy x1 or 20 Gy in 5 fractions) for: bone metastases (pain control); hemostatic RT for pelvic hemorrhage (3 Gy x10 or 20 Gy in 5 fractions); brain metastases — whole brain RT 20-30 Gy in 5-10 fractions.	Palliative RT should be available at all cancer centres. Short fractionation schedules preferred in Kenya to minimise patient burden. Hemostatic RT as alternative to surgery for pelvic bleeding in unfit patients.
EBRT = External Beam Radiotherapy; HDR/LDR = High/Low Dose Rate brachytherapy; SBRT = Stereotactic Body Radiotherapy; Gy = Gray; MDT = Multidisciplinary Team.		

GOSK recommendations for occult uterine sarcomas and tumors of uncertain malignant potential

A clinically important subset of uterine sarcomas is not recognized before surgery. These occult sarcomas and tumors of uncertain malignant potential present diagnostic and management challenges in the Kenyan context, where patients may undergo myomectomy or hysterectomy for presumed benign disease. There is no reliable preoperative test to exclude occult uterine sarcoma (FDA 2014 safety communication; ESMO 2018). The rate of occult leiomyosarcoma (LMS) among women undergoing surgery for presumed fibroids is estimated at approximately 1 in 350 to 1 in 500.

Entity	Definition	Estimated prevalence	GOSK recommendations
Occult uterine sarcoma (OUS)	Sarcoma discovered incidentally on pathology after surgery for presumed benign disease (e.g., fibroids)	~1:350–1:500 hysterectomies for fibroid disease	Urgent MDT. Complete restaging (CT chest/abdomen/pelvis + MRI pelvis ± PET-CT). Re-operative staging/cytoreduction if indicated. Subtype-based systemic therapy. Full patient disclosure.
Smooth muscle tumor of uncertain	Smooth muscle tumor of uncertain malignant potential; does not meet	~1:1,000–1:2,000 hysterectomies	Total hysterectomy with intact specimen removal. No adjuvant chemotherapy after complete excision.

Entity	Definition	Estimated prevalence	GOSK recommendations
malignant potential (STUMP)	full WHO criteria for LMS or leiomyoma		Surveillance: MRI pelvis + CT chest every 6 months × 3 years, then annually to 5 years.
Post-morcellation LMS	LMS discovered after power or manual morcellation during myomectomy or hysterectomy	Estimated 1 in 350 procedures (FDA 2014 safety communication)	IMMEDIATE gynecologic oncology referral. Full restaging imaging. Re-operative cytoreduction. Subtype-based chemotherapy. Morcellation worsens 5-year OS from ~60% (Stage I intact) to 25–35% (post-morcellation). Full patient disclosure mandatory.
Intravenous leiomyomatosis (IVL)	Benign smooth muscle proliferation within veins; may extend to IVC and right atrium	Rare	Multidisciplinary surgery (gynae oncology + vascular ± cardiac surgery). Anti-estrogenic therapy (BSO + AI). Anticoagulation: Very high VTE risk — therapeutic LMWH perioperatively. Cardiac MRI pre-operatively if intracardiac extension suspected.
Benign metastasizing Leiomyoma (BML)	Histologically benign smooth muscle with distant metastases (lung most common); ER/PR-dependent	Extremely rare	BSO or GnRH agonist (surgical menopause). Aromatase inhibitors (letrozole 2.5 mg daily). Not cytotoxic chemotherapy. Surgical resection of symptomatic isolated pulmonary nodules. Annual chest CT surveillance.
Uterine tumor resembling ovarian sex-cord tumor (UTROSCT)	Uterine tumor resembling ovarian sex-cord tumor; usually benign behavior	Very rare (<100 reported cases)	Hysterectomy. Surveillance MRI pelvis 6-monthly × 2 years, then annually. Hormonal therapy for recurrence. No standard chemotherapy.
AI = Aromatase Inhibitor; BML = Benign Metastasising Leiomyoma; BSO = Bilateral Salpingo-Oophorectomy; CT = Computed Tomography; ESMO = European Society of Medical Oncology; GnRH = Gonadotropin-Releasing Hormone; IVC = Inferior Vena Cava; IVL = Intravenous Leiomyomatosis; LMS = Leiomyosarcoma; LMWH = Low Molecular Weight Heparin; MDT = Multidisciplinary Team; MRI = Magnetic Resonance Imaging; OS = Overall Survival; OUS = Occult Uterine Sarcoma; PET-CT = Positron Emission Tomography–Computed Tomography; STUMP = Smooth Muscle Tumor of Uncertain Malignant Potential; UTROSCT = Uterine Tumor Resembling Ovarian Sex-Cord Tumor; VTE = Venous Thromboembolism. Absolute prohibition: Power morcellation or any piecemeal uterine extraction technique is contraindicated where uterine sarcoma has not been reliably excluded. Catastrophic tumor spillage, upstages the malignancy, and drastically reduces survival. There is no reliable pre-operative test to exclude occult uterine sarcoma (FDA 2014; ESMO 2018). A post-morcellation occult sarcoma protocol must be in place at all gynecological surgical institutions in Kenya (GOSK Grade A).			

Table 34. GOSK recommendations for occult Uterine sarcomas and tumors of uncertain malignant potential

Table 35. GOSK recommendations for risk-stratified management of uterine sarcoma

Risk / clinical factor	GOSK recommendations for risk-stratified management	Rationale
Fertility preservation (premenopausal, stage I)	Fertility-sparing approaches not recommended *No standard protocol; insufficient evidence from RCTs.*	Mandatory thorough MDT, oncofertility counselling, documented consent, and close surveillance (MRI pelvis 3-monthly) not feasible in the Kenyan set up.
Incidental sarcoma after myomectomy or morcellation	All institutions performing uterine surgery must have a post-morcellation protocol. Urgent gynecologic oncology referral. Complete restaging imaging (CT chest/abdomen/pelvis + MRI pelvis). Re-operative staging within 2 weeks and cytoreduction if indicated. Subtype-specific systemic therapy after definitive pathology Full patient disclosure mandatory.	Prognosis markedly worsened by morcellation: 5-year Overall Survival drops from approximately 60% (intact Stage I) to 25-35% (post-morcellation).
Obesity (BMI >30); high prevalence in Kenya	Perioperative Weight-adjusted LMWH DVT prophylaxis (enoxaparin 0.5 mg/kg SC daily for BMI 30-40; 0.6 mg/kg for BMI >40). Pelvic surgery - extended VTE prophylaxis SC LMWH – postoperative for 28days Preoperative nutritional assessment. Bariatric anesthesia input for BMI >40.	Obesity increases surgical complexity, anaesthetic risk, wound complication rates, and VTE risk. Associated with worse outcomes in carcinosarcoma and LGESS. with weight-adjusted LMWH is essential.
Older patients (age >70) or poor performance status (ECOG 3-4)	Comprehensive geriatric assessment (CGA) at diagnosis for all patients >70 years. For PS 3-4: prioritize symptom control and quality of life. Consider dose-reduced doxorubicin (50 mg/m2) or trabectedin if tolerated. Integrate	Standard chemotherapy regimens may not be tolerable. Dose-reduced or single-agent regimens may be appropriate. Comfort-focused palliative

Risk / clinical factor	GOSK recommendations for risk-stratified management	Rationale
	palliative care from diagnosis. Avoid aggressive cytoreduction in unfit elderly patients.	care should be discussed at diagnosis for PS 4 patients
Concurrent pregnancy	Refer immediately to tertiary centre with combined obstetric and oncology expertise. MDT discussion including ethics committee if required. Document gestational age, tumor subtype, and patient preferences in detail. Individualized decision balancing maternal and fetal outcomes. Termination of pregnancy is recommended in early (previable) stages to permit adequate surgical staging. Chemotherapy in second/third trimester considered on a case-by-case basis for rapidly progressive disease.	Uterine sarcoma in pregnancy is extremely rare. Management requires multidisciplinary input (maternal-fetal medicine, gynecologic oncology, neonatology).
MDT = Multidisciplinary Team; LGESS = Low-Grade Endometrial Stromal Sarcoma; LMS = Leiomyosarcoma; HGESS = High-Grade ESS; UUS = Undifferentiated Uterine Sarcoma; PS = Performance Status; CGA = Comprehensive Geriatric Assessment; ART = Antiretroviral Therapy; VL = Viral Load; LMWH = Low Molecular Weight Heparin.		

Table 36. GOSK recommendations for management of unique clinical scenarios

Clinical scenario	GOSK management approach	Priority actions
Uterine sarcoma presenting with hemorrhagic shock	Stabilize at any facility; Emergency resuscitation: ABCDE approach, massive transfusion protocol (1:1:1 PRBC: FFP: platelets), IV access x2, type & crossmatch. Hemostatic surgery (TAH) as emergency procedure without full staging required for life-threatening hemorrhage. Interventional radiology (uterine artery embolization) as bridge to surgery where available. Tissue must be sent for histopathology even in emergency setting. Post-emergency MDT review within 2 weeks.	Transfer to gynecologic oncology center after hemodynamic stability. Emergency TAH by most experienced gynecologic oncologist available.
Inoperable or unresectable primary uterine sarcoma	Core needle Biopsy for definitive Histology Neo-adjuvant systemic chemotherapy to downsize tumor prior to surgical resection. Subtype-specific regimens apply (carboplatin/paclitaxel for carcinosarcoma; gemcitabine/docetaxel for LMS; AI regimen for HGESS/UUS). Re-stage with CT after 2-3 cycles. Re-evaluate resectability. If surgical resection remains impossible: continue chemotherapy + palliative radiotherapy for symptom control.	Surgery at gynecologic oncology center if resectability is achieved. Avoid prolonged chemotherapy without surgical intent reassessment.
Isolated pulmonary metastasis (LMS)	MDT discussion including thoracic surgery input. Resectability assessment at thoracic surgery unit. LMS preferentially metastasizes to lung. Isolated pulmonary metastasectomy for resectable lesions (1-3 nodules) with adequate lung function and disease-free interval >12 months. Combined with systemic chemotherapy.	CT chest for all LMS follow-up. Systemic therapy alongside surgical consideration.
Vaginal recurrence of carcinosarcoma or ESS	Surgical excision if localized and resectable. Vaginal brachytherapy (if not previously irradiated): 3 fractions of 7 Gy or equivalent. External beam RT for broader pelvic recurrence. Systemic chemotherapy for concurrent distant disease.	If prior EBRT, consider systemic therapy as primary management to avoid radiation toxicity.
Uterine sarcoma with hydronephrosis or ureteric involvement	Urgent urological assessment. Renal function baseline (eGFR/creatinine clearance) mandatory before carboplatin dosing (platinum-based chemotherapy). Ureteric stenting or nephrostomy to preserve renal function before systemic therapy. Surgical ureteric repair or re-implantation at time of definitive surgery if involved.	Urology involvement from diagnosis. Ureteric stent insertion does not require delay of chemotherapy beyond 2 weeks.
Uterine Sarcoma arising in a a clinically unsuspected fibroid	Diagnosed on final pathology after myomectomy or hysterectomy for presumed fibroid. Constitutes an occult sarcoma. Immediate restaging and gyna=ecologic oncology referral.	All hysterectomy/myomecto my specimens must be sent for pathological examination — this is

Clinical scenario	GOSK management approach	Priority actions
	If hysterectomy complete and specimen intact, comprehensive pathology review + molecular profiling. If morcellation performed, follow post-morcellation protocol.	non-negotiable even for presumed benign disease.
ABCDE = Airway, Breathing, Circulation, Disability, Exposure; PRBC = Packed Red Blood Cells; FFP = Fresh Frozen Plasma; EBRT = External Beam Radiotherapy; TAH = Total Abdominal Hysterectomy; eGFR = estimated Glomerular Filtration Rate.		

Table 37. GOSK recommendations for management of recurrent uterine sarcoma

Recurrence scenario	GOSK recommendation	Priority actions
Localized pelvic or vaginal recurrence — resectable (R0 feasible)	Complete surgical resection (R0) is the goal where achievable. This requires MDT pre-operative planning involving gynecologic oncology and colorectal/urology surgery as needed. Preoperative imaging (MRI pelvis + CT chest/abdomen/pelvis + PET-CT) is mandatory before re-operation. Systemic chemotherapy before or after re-resection depending on subtype. Pelvic EBRT if not previously irradiated.	Refer to gynecologic oncology center. Preoperative MDT with surgical, radiation oncology, and medical oncology teams. Document R-classification (R0/R1/R2) in operative note.
Isolated pulmonary metastasis — resectable (LMS predominant)	Pulmonary metastasectomy may be considered for: (1) isolated 1-3 nodules, (2) adequate pulmonary reserve, (3) disease-free interval >12 months from primary, (4) complete resection achievable. Associated with 5-year OS benefit in selected patients (retrospective data). Combine with systemic therapy. Thoracic surgery MDT essential.	Refer to cardiothoracic surgery for assessment. CT chest before each consideration of metastasectomy. Concurrent gemcitabine/docetaxel or second-line regimen recommended perioperatively.
Disseminated or widespread recurrence — LMS	Systemic palliative chemotherapy as mainstay. First-line recurrence regimen: Gemcitabine/Docetaxel or Doxorubicin (if not used previously). Second-line: Trabectedin 1.5 mg/m2 q21d; Pazopanib 800 mg PO daily; Eribulin 1.4 mg/m2 Days 1,8 q21d; Gemcitabine + DTIC. If dMMR confirmed: pembrolizumab 200 mg q3W. Clinical trial enrolment at any line.	MDT review at first recurrence. Reassess molecular profile (dMMR, BRCA, TMB) from initial specimen or rebiopsy. Consider trial enrolment at KEMRI-AKUH consortium. Palliative care integration from point of recurrence.
Disseminated or widespread recurrence — carcinosarcoma	If prior carboplatin/paclitaxel: pembrolizumab 200 mg q3W + lenvatinib 20 mg PO daily (KEYNOTE-775 — standard of care for pMMR recurrent carcinosarcoma). If dMMR: Pembrolizumab monotherapy. If HER2-amplified: Trastuzumab-based regimen (trial setting). ifosfamide/paclitaxel as alternative second-line chemotherapy.	GOSK: Pembrolizumab + Lenvatinib is the standard second-line for pMMR recurrent carcinosarcoma. Confirm pMMR status from primary specimen before initiating. Monitor lenvatinib toxicity (hypertension, proteinuria, fatigue) closely.
Recurrent LGESS	Surgical resection if localized and resectable. Intensify or change hormonal therapy if on adjuvant AI: switch to alternate AI, add progestin, or switch to GnRH agonist + AI. Fulvestrant 500 mg IM monthly for AI-refractory disease. Everolimus 10 mg + exemestane (from breast cancer data — limited LGESS evidence). Cytotoxic chemotherapy for rapidly progressive hormone-refractory disease.	Document hormonal therapy compliance at recurrence. Rebiopsy to confirm ER/PR status. Change hormonal agent before resorting to chemotherapy unless rapidly progressive. Fulvestrant available at specialist oncology units.
Recurrent UUS / HGESS	Second-line chemotherapy (opposite of first-line: if AI regimen used first, switch to gemcitabine/docetaxel and vice versa). If dMMR: Pembrolizumab. If SMARCA4-deficient: EZH2 inhibitor trial (tazemetostat). Palliative care integration essential given poor prognosis at first recurrence. Enrol in clinical trials as priority.	MDT review. Rebiopsy where feasible to confirm histology and reassess molecular markers. Clinical trial enrolment via KEMRI-NCI partnership. Palliative care involvement from first recurrence.
Symptomatic recurrence requiring palliation	Palliative EBRT for localized bone pain, pelvic hemorrhage, or symptomatic lymphadenopathy. Palliative surgery for bowel obstruction or urinary tract compression. Opioid analgesics per WHO pain ladder. Interventional pain procedures (nerve blocks, intrathecal) for refractory	Integrate palliative care team from first recurrence. KEHPCA referral for home-based palliative care. Ensure access to oral morphine. Avoid aggressive salvage surgery in PS 3-4 patients — focus on quality of life.

Recurrence scenario	GOSK recommendation	Priority actions
	pain. KEHPCA community palliative care for home management.	

LGESS = Low-Grade Endometrial Stromal Sarcoma; LMS = Leiomyosarcoma; UUS = Undifferentiated Uterine Sarcoma; HGESS = High-Grade ESS; AI = Doxorubicin + Ifosfamide regimen; MDT = Multidisciplinary Team; KEHPCA = Kenya Hospices and Palliative Care Association; dMMR = deficient Mismatch Repair; TMB = Tumor Mutational Burden; PS = Performance Status.

Table 38. GOSK recommendations for supportive and palliative care in uterine sarcoma

Area	GOSK recommendation	Rationale and required action
Early palliative care integration	Palliative care referral is mandatory for: (1) all Stage III/IV patients at diagnosis; (2) all high-grade subtypes (LMS, HGESS, UUS, carcinosarcoma) within 4 weeks of diagnosis; (3) any patient with performance status 3-4 at diagnosis. *Palliative care should run concurrently with anti-cancer treatment* — not sequentially. Goals-of-care discussions at diagnosis for high-grade/advanced disease.	Establish palliative care team at all designated oncology centres. Partner with KEHPCA for community-based and home palliative care. Document goals-of-care preferences in all patient records.
Advance care planning	Integrate Advance care planning (ACP) into clinical workflow - ACP discussions should occur at diagnosis for high-grade/advanced uterine sarcomas, given their aggressive clinical course. Document: resuscitation preferences, preferred place of care/death, proxy decision-maker (Healthcare Power of Attorney), treatment goals. Review and update ACP at each major disease transition.	Ensure family members are involved where culturally appropriate. Legal framework (Kenyan Law of Succession) for proxy decision-making should be communicated to families.
Pain control	WHO analgesic ladder: Step 1 (paracetamol/NSAIDs) -> Step 2 (weak opioids: tramadol/codeine) -> Step 3 (strong opioids: morphine/oxycodone). Adjuvant analgesics: gabapentinoids for neuropathic pain; bisphosphonates/denosumab for bone metastases; corticosteroids for tumor-oedema pain. Interventional: nerve blocks, epidural, intrathecal for refractory pain. *Avoid NSAIDs in thrombocytopenic patients or those on anticoagulation.*	Oral morphine sulphate is on KEML and must be freely prescribed for cancer pain at all cancer centres. Train clinical officers and nurses in opioid prescribing. Ensure supply chain continuity. Document pain scores (NRS 0-10) at every clinical encounter.
Psychosocial and spiritual support	Screen for anxiety, depression (PHQ-9/GAD-7) and existential distress at baseline and at disease progression. Oncology social work for financial toxicity assessment (cancer treatment costs are catastrophic in many Kenyan households). Respect cultural and religious beliefs in treatment decisions, particularly end-of-life. Address fertility loss grief, particularly in young patients. Counselling services for body image concerns post-hysterectomy. Support groups and peer networks. Sexual health counselling (premature menopause, dyspareunia).	Psychosocial and mental health screening is mandatory at baseline and at follow up visits. Social worker involvement from diagnosis. Verify SHIF registered and paid up. Cultural mediators for cross-cultural end-of-life discussions. Involve community religious leaders where appropriate and accepted by patient.
Nutritional support	Nutritional assessment (MUST/NRS-2002) at diagnosis and before each chemotherapy cycle. Dietitian referral for MUST score >2. Oral nutritional supplements preferred; enteral via NGT for inability to eat. Parenteral nutrition (PN) reserved for prolonged gut failure — not routinely recommended in terminal cancer. Cancer cachexia: megestrol acetate 160-480 mg daily (AVOID in LGESS/adenosarcoma ER/PR+); mirtazapine for combined appetite and mood benefit.	Integrate dietitian into MDT from diagnosis. Assess weight and albumin at each visit. Micronutrient supplementation for patients with documented deficiencies. Community health worker support for nutritional monitoring at home.
Symptom management: chemotherapy toxicity	Anti-emetics: 5-HT3 antagonist (ondansetron) + dexamethasone for high-moderate emetogenic regimens (carboplatin/paclitaxel, doxorubicin). G-CSF prophylaxis: pegfilgrastim or filgrastim for regimens with >20% febrile neutropenia risk (gemcitabine/docetaxel, AI regimen). Cardioprotection: limit cumulative doxorubicin <450 mg/m2; baseline and serial echocardiography. Peripheral neuropathy monitoring: dose modification/discontinuation for Grade 2+ neuropathy.	Ondansetron 8 mg IV/oral before chemotherapy is standard. Dexamethasone 8 mg IV as anti-emetic. G-CSF (filgrastim 5 mcg/kg SC daily x5 days or pegfilgrastim single dose) mandatory with gemcitabine/docetaxel and AI regimens. Echocardiography before and every 3 cycles of doxorubicin
Hormone replacement therapy (HRT) after bilateral oophorectomy	BSO in premenopausal patients causes surgical menopause with significant vasomotor symptoms, bone loss, and cardiovascular risk. *HRT is Contraindicated in LGESS (estrogen-dependent).*	Do not prescribe HRT for LGESS or adenosarcoma (ER/PR+). For LMS, HGESS, UUS, carcinosarcoma: non-hormonal management preferred; HRT only after

Area	GOSK recommendation	Rationale and required action
	For LMS, carcinosarcoma, HGESS, UUS: HRT after BSO may be considered — no definitive evidence of harm. Non-hormonal alternatives: venlafaxine, gabapentin for vasomotor symptoms; calcium/vitamin D + bisphosphonates for bone protection.	documented MDT discussion and patient-specific risk-benefit analysis. *Bone density assessment (DEXA) at 1-year post-BSO for all premenopausal patients.*
End-of-life care	When disease is no longer responding to anti-cancer treatment and performance status declines to 3-4: transition to comfort-focused care. Anticipatory prescribing for terminal symptoms (pain, dyspnoea, agitation, secretions). Preferred place of death documentation. Family support and bereavement care. Clear documentation of terminal phase recognition in clinical notes.	Recognize transition to end-of-life and communicate clearly with patient and family. KEHPCA community hospice referral. Ensure subcutaneous morphine, midazolam, haloperidol available for terminal symptom management at all referring facilities.

KEHPCA = Kenya Hospices and Palliative Care Association; KEML = Kenya Essential Medicines List; SHIF = Social Hospital Insurance Fund; MUST = Malnutrition Universal Screening Tool; NRS = Numerical Rating Scale; PHQ = Patient Health Questionnaire; GAD = Generalised Anxiety Disorder; ACP = Advance Care Planning; LGESS = Low-Grade Endometrial Stromal Sarcoma; BSO = Bilateral Salpingo-Oophorectomy; HRT = Hormone Replacement Therapy.

Table 39. GOSK recommendations for post-treatment follow-up and surveillance

A. General follow-up recommendations

Follow-up component	GOSK recommendation	Rationale and required action
Schedule	Standard schedule (individualize as needed): • Years 1–2: Every 3 months. • Years 3–5: Every 6 months. • Beyond 5 years: Annually. High-risk patients: • Years 1–3: Every 3 months. • Years 4–5: Every 4–6 months. • Beyond 5 years: Annual review. *All schedules shall be individualized based on histological subtype, stage, treatment received, and clinical response.*	Feasible at all levels of care. History and physical examination are primary surveillance tools. Frequency adjusted for patient-specific risk and resource availability.
Routine imaging	Routine CT or MRI scans should not be ordered. Imaging shall be requested only in response to new symptoms or abnormal clinical findings.	Routine imaging does not improve survival in asymptomatic patients.
Patient education	Patient education is mandatory at each clinical visit. Patients should be instructed to report: • Persistent cough. • New pelvic or abdominal pain. • Abdominal bloating or distension • Unexplained weight loss or persistent fatigue • Abnormal or unexpected vaginal bleeding • Noticeable mass in the vaginal area	In the absence of routine imaging, an informed and engaged patient serves as the most sensitive early detection system for recurrence.

B. Follow-up and surveillance by histological subtype

Histological subtype/risk category	GOSK recommendation
Leiomyosarcoma (LMS) — all Stages	Years 1-3: Clinical review every 3 months + CT chest/abdomen/pelvis every 3-6 months (LMS preferentially metastasizes to lung — early detection of resectable pulmonary metastasis is clinically meaningful). Years 3-5: 6-monthly clinical review + CT chest annually. Beyond 5 years: Annual clinical review + annual CT chest. Surveillance for late pulmonary metastases is recommended lifelong given LMS biology. FBC and LFTs at each clinical visit.
Low-grade ESS (LGESS) — stages I-II	Years 1-5: Clinical review every 6 months + MRI pelvis annually. Estrogen monitoring: document hormonal suppression status at each visit (AI compliance, menopausal status). Years 5-10: Annual clinical review + MRI pelvis every 2 years.

	Beyond 10 years: Annual clinical review indefinitely — LGESS can recur 10-20 years after primary treatment. Chest imaging if symptomatic.
Low-Grade ESS (LGESS) — stages III-IV	Years 1-3: Clinical review every 3 months + CT chest/abdomen/pelvis every 6 months + MRI pelvis annually. Continue indefinite hormonal therapy (AI) and monitor compliance at each visit. Years 3-5 and beyond: 6-monthly then annual clinical review. Lifelong surveillance. Document hormonal suppression efficacy (estradiol levels for premenopausal patients on GnRH agonists).
High-Grade ESS (HGESS) / undifferentiated uterine sarcoma (UUS)	Years 1-2: Clinical review every 3 months + CT chest/abdomen/pelvis every 3 months (very high early recurrence rate). Years 2-3: 3-monthly clinical review + CT every 6 months. Years 3-5: 6-monthly CT. Beyond 5 years: Annual CT (if disease-free — uncommon for UUS). Molecular profiling results should be reviewed at each follow-up to assess trial eligibility if disease recurs. Brain MRI if neurological symptoms (rare intracranial metastases).
Adenosarcoma without sarcomatous overgrowth	Years 1-3: Clinical review every 6 months + MRI pelvis annually. Years 3-5: Annual clinical review + MRI pelvis. Beyond 5 years: Annual clinical review for 10 years minimum. Chest imaging only if symptomatic. Hormonal therapy monitoring if ER/PR+ on adjuvant AI.
Adenosarcoma with Sarcomatous Overgrowth	Years 1-3: Clinical review every 3 months + CT chest/abdomen/pelvis every 3-6 months (high recurrence risk equivalent to high-grade sarcoma). Years 3-5: 6-monthly CT + clinical review. Beyond 5 years: Annual CT + clinical review for 10 years.
Carcinosarcoma — all stages	Years 1-3: Clinical review every 3 months + CT chest/abdomen/pelvis every 3-6 months + CA-125 if elevated at baseline. Years 3-5: 6-monthly CT + clinical review + CA-125 6-monthly. Beyond 5 years: Annual CT + clinical review + CA-125 annually. Pelvic examination including speculum at each visit (vaginal cuff recurrence detection). Consider PET-CT for equivocal CT findings at any time.
Occult/incidental sarcoma or smooth muscle tumor of uncertain malignant potential (STUMP)	Years 1-3: MRI pelvis every 6 months + CT chest every 6-12 months. Years 3-5: Annual MRI pelvis + CT chest. Beyond 5 years: Annual clinical review for minimum 10 years. All post-morcellation patients: CT chest/abdomen/pelvis every 3-6 months for 3 years given elevated risk of peritoneal dissemination.
C. General surveillance principles for all Subtypes	
Component	**GOSK recommendation**
Clinical examination at each visit	Pelvic examination including bimanual and speculum examination; abdominal examination for mass, hepatomegaly, ascites; lymph node assessment (inguinal, supraclavicular); lower limb assessment for DVT/lymphoedema; performance status documentation; symptom review (cough, pain, bleeding, weight loss, bloating); medication compliance review (hormonal therapy/anticoagulation).
Patient education at each visit	Instruct patients to report immediately: new or worsening pelvic/abdominal pain; persistent cough or dyspnoea; unexplained weight loss; abdominal bloating or distension; swollen or painful leg (DVT); new neurological symptoms. Provide written symptom guide in Swahili/local language at discharge from primary treatment. Community health worker follow-up for patients in remote areas.
Investigations at follow-up	Routine bloods: FBC, LFTs, renal function, LDH (tumor marker for LMS — non-specific but trends may be informative). Imaging: as per subtype schedule above. Symptom-triggered imaging: CT/MRI/PET-CT as indicated by new symptoms or clinical findings — do not defer due to resource constraints when clinical suspicion is high. CA-125 for carcinosarcoma only. HRT/hormonal therapy compliance: document at each visit for LGESS patients.
FBC = Full Blood Count; LFTs = Liver Function Tests; LDH = Lactate Dehydrogenase; CA-125 = Cancer Antigen 125; STUMP = Smooth Muscle Tumor of Uncertain Malignant Potential; DVT = Deep Vein Thrombosis; MRI = Magnetic Resonance Imaging; CT = Computed Tomography; AI = Aromatase Inhibitor.	

Table 40. GOSK recommendations for clinical trials, novel therapies and research participation

Area	GOSK recommendation	Implementation and access in Kenya
Molecular profiling — mandatory for trial eligibility	Comprehensive molecular profiling on the definitive hysterectomy specimen is mandatory for all high-grade uterine sarcomas (LMS, HGESS, UUS, carcinosarcoma) and should include: MMR IHC (MLH1, MSH2, MSH6, PMS2); MSI testing; PD-L1 expression (CPS score); BRCA1/2 germline and somatic testing; TMB (if NGS available); subtype-specific fusions (JAZF1-SUZ12 for LGESS; YWHAE-NUTM2 for HGESS; BCOR-CCNB3); SMARCA4/SMARCB1 IHC for UUS.	Testing platforms: KEMRI-Wellcome, AKUH Pathology Lab, Kenya Medical Research Institute. For NGS: referral to international platforms (Foundation Medicine, Caris) via GOSK research program. BRCA testing: germline blood testing at AKUH and private labs. Results must be documented before second-line therapy initiation.
Clinical trial access and referral	All patients with recurrent or refractory uterine sarcoma should be evaluated for clinical trial eligibility at first recurrence and at each subsequent line of therapy. GOSK supports the KEMRI-NCI-AKUH-KNH Gynaecologic Oncology Research Consortium as the primary trial access pathway in Kenya. Key active trial areas: immunotherapy combinations (pembrolizumab + novel agents); PARP inhibitor combinations for HRD-positive tumors; EZH2 inhibitors for SMARCA4-deficient UUS; HER2-targeted therapies for carcinosarcoma; antibody-drug conjugates (trastuzumab deruxtecan for HER2+ carcinosarcoma — NCT04042116).	GOSK Trial Referral Network: Gynecologic oncologist must document trial eligibility assessment at each MDT meeting for refractory disease. Contact GOSK secretariat for current open trials and enrolment criteria. Patient consent process must follow Kenya Medical Research Institute ethics standards.
Pembrolizumab access program	Pembrolizumab is accessible for eligible patients (dMMR/MSI-H confirmed) through: (1) MSD (Merck) Patient Assistance Programme; (2) NCIK-MSD compassionate use partnership; (3) AKUH and KNH oncology formulary for registered patients. Eligibility requires confirmed dMMR on IHC from the definitive hysterectomy specimen or biopsy. Contact oncology pharmacist at treating centre for enrolment.	GOSK: All oncology centres must be aware of the MSD patient assistance programme. dMMR testing is the gateway to pembrolizumab access — ensure MLH1/MSH2/MSH6/PMS2 IHC is routinely requested on all uterine sarcoma specimens.
Olaparib (PARP inhibitor) access program	Olaparib (AstraZeneca Lynparza) is accessible for BRCA1/2-mutant patients through the AstraZeneca Lynparza Patient Access Programme. Eligibility: pathogenic germline or somatic BRCA1/2 mutation confirmed by validated testing; prior standard chemotherapy (at least 1 line); ECOG PS 0-2; adequate hematological, renal, and hepatic function. Application via GOSK secretariat in partnership with AstraZeneca Kenya.	BRCA testing is the eligibility gateway. Ensure germline BRCA testing offered to all LMS, HGESS, UUS, and carcinosarcoma patients. Genetic counselling prior to germline testing. AstraZeneca Kenya rep contact managed through GOSK secretariat.
Kenyan Uterine Sarcoma Registry	GOSK recommends the urgent establishment of a National Kenyan Uterine Sarcoma Registry to capture: incidence and histological subtype distribution; treatment patterns and protocol adherence; treatment outcomes (OS, DFS, recurrence rates); molecular profiling data; VTE and complication rates; quality-of-life metrics. This will generate African-specific data to inform future guideline iterations.	Registry leadership: GOSK Clinical Committee + KEMRI + University of Nairobi Department of Obstetrics and Gynaecology. Data collection: electronic health records at KNH, MTRH, AKUH, Kenyatta University Teaching, Research and Referral Hospital. Funding: MoH Kenya Cancer Research Programme + NCI Africa partnerships.
Protocol review and updates	This protocol will be reviewed every two years or sooner upon publication of major practice-changing evidence. Review process: GOSK Clinical Practice Guidelines Committee convenes a multidisciplinary review panel; incorporates updated ESGO/NCCN/ESMO evidence; adapts to Kenyan health system developments; documents changes with version control and date of approval.	GOSK: Next scheduled review: December 2028. Urgent interim review if: major RCT results (e.g., SARC-040, KEYNOTE-B96, RUBY trial updates) change standard of care. Submit clinical queries and protocol improvement suggestions to GOSK secretariat.

GOSK = Gynaecologic Oncology Society of Kenya; KEMRI = Kenya Medical Research Institute; NCI = National Cancer Institute; AKUH = Aga Khan University Hospital; KNH = Kenyatta National Hospital; MTRH = Moi Teaching and Referral Hospital; MMR = Mismatch Repair; MSI = Microsatellite Instability; HRD = Homologous Recombination Deficiency; NGS = Next Generation Sequencing; BRCA = Breast Cancer susceptibility gene; TMB = Tumor Mutational Burden; OS = Overall Survival; DFS = Disease-Free Survival.

Clinical trial and novel therapy protocols

The use of immunotherapy and poly (ADP-ribose) polymerase (PARP) inhibitors in uterine sarcoma is biomarker-driven. Mismatch repair (MMR) immunohistochemistry (IHC), including MLH1, MSH2, MSH6, and PMS2, must be performed on the definitive hysterectomy specimen for all patients. BRCA1/2 testing is recommended for high-grade histological subtypes.

The following treatment protocols apply to patients who have undergone comprehensive molecular profiling of the definitive histopathological specimen obtained at total hysterectomy. The indications, regimens, eligibility criteria, and supporting evidence are summarized in Table 39.

Table 41. Immunotherapy and PARP inhibitors in uterine sarcoma: Indications, protocols, and eligibility

Biomarker	Agent/regimen	Indication/line	Evidence
dMMR/MSI-H — any subtype	Pembrolizumab 200 mg IV q3W OR 400 mg IV q6W	Any line, any uterine sarcoma subtype with confirmed dMMR or MSI-H. Continue until progression or 2 years.	KEYNOTE-158: ORR 33% dMMR solid tumors. FDA tissue-agnostic approval.
pMMR Carcinosarcoma, recurrent	Pembrolizumab 200 mg IV q3W + Lenvatinib 20 mg PO daily	Second-line+ after platinum-based chemotherapy. ECOG PS 0-1.	KEYNOTE-775: PFS 7.2 vs 3.8 months; OS 18.3 vs 11.4 months vs chemotherapy (pMMR cohort).
dMMR/MSI-H — Carcinosarcoma or UUS	Dostarlimab 500 mg IV q3W × 4 cycles, then 1000 mg IV q6W	Alternative to pembrolizumab for dMMR disease. Access via GSK programme in Kenya.	GARNET trial: ORR 44.7% dMMR endometrial cancers; applicable by extrapolation.
TMB-high (≥10 mut/Mb)	Pembrolizumab 200 mg IV q3W	Tumor-agnostic; any line after standard therapy. Requires NGS TMB assessment.	FDA tumor-agnostic approval 2020 (KEYNOTE-158 basket trial).
BRCA1/2 pathogenic mutation (germline or somatic)	Olaparib 300 mg PO BD, continuous	After ≥1 line of standard chemotherapy. Available via AstraZeneca Lynparza access programme (Kenya).	Tumor-agnostic BRCA approval. LMS-specific data: ORR ~15% in BRCA-mutant LMS (TAPISTRY).
HRD-positive (non-BRCA)	Niraparib 300 mg PO daily (200 mg if <77 kg)	Clinical trial context preferred (RUBY Part 2; BRCA/HRD gynaecological sarcoma trials).	Limited uterine sarcoma data; enrol in KEMRI-NCI trials.
SMARCA4-deficient UUS	Tazemetostat (EZH2 inhibitor) 800 mg PO BD	Clinical trial only (NCT04204941). EZH2 dependency in SWI/SNF-deficient tumors.	Phase II basket trial; preclinical data strong for SMARCA4-loss.
HER2-amplified Carcinosarcoma (~10%)	Trastuzumab + Pertuzumab ± Docetaxel	Clinical trial: NCT04042116. HER2 status requires IHC/FISH on definitive specimen.	Phase II trial ongoing; HER2 amplification confirmed in ~10% carcinosarcomas.
Nivolumab + Ipilimumab (LMS, TMB-high or dMMR)	Nivolumab 3 mg/kg IV q2W + Ipilimumab 1 mg/kg IV q6W	ALLIANCE A091401 data: DCR 40% in LMS. Reserve for TMB-high/dMMR cases.	Phase II: ORR 16%; DCR 40% in LMS. Trial access via NCI partnership.

BRCA = Breast Cancer susceptibility gene; CPS = Combined Positive Score; dMMR = deficient Mismatch Repair; ECOG = Eastern Cooperative Oncology Group; EZH2 = Enhancer of Zeste Homolog 2; FISH = Fluorescence In Situ Hybridisation; HER2 = Human Epidermal growth factor Receptor 2; HRD = Homologous Recombination Deficiency; IHC = Immunohistochemistry; LMS = Leiomyosarcoma; MMR = Mismatch Repair; MSI = Microsatellite Instability; MSI-H = Microsatellite Instability-High; ORR = Objective Response Rate; OS = Overall Survival; PARP = Poly (ADP-ribose) Polymerase; PD-L1 = Programmed Death-Ligand 1; PFS = Progression-Free Survival; pMMR = proficient Mismatch Repair; PS = Performance Status; TMB = Tumor Mutational Burden; UUS = Undifferentiated Uterine Sarcoma.

Mandatory pretreatment molecular testing on definitive hysterectomy specimen or diagnostic biopsy: MMR IHC (MLH1, MSH2, MSH6, PMS2) | MSI testing (PCR or NGS) | PD-L1 CPS score (22C3 assay) | BRCA1/2 germline and somatic testing | TMB (if NGS available) | HRD score (if platform available). Kenya access: Pembrolizumab (NCIK/AKUH/KNH); Olaparib (AstraZeneca Lynparza access programme via GOSK secretariat). irAE management protocols mandatory at all immunotherapy-administering institutions.

Complications of treatment and their management

The multimodal management of uterine sarcoma, comprising surgery, chemotherapy, and radiotherapy, carries a substantial burden of treatment-related morbidity that must be anticipated, prevented where possible, and managed promptly. Early recognition and structured management of complications are essential to preserving patients' quality of life and maintaining the intensity of curative-intent treatment. Thromboembolic complications, which are of particular importance in uterine sarcoma, are addressed separately in the following section. The principal complications associated with each treatment modality, together with recommendations for their prevention and management, are summarized in Table 40.

Table 42. Complications of uterine sarcoma treatment and their management

Treatment modality	Recognized complications	GOSK recommendations for prevention and management
Surgery (radical pelvic surgery: TAH-BSO ± lymphadenectomy and cytoreduction)	• Intra-operative hemorrhage • Injury to bladder, ureters or bowel • Wound infection and dehiscence • Lymphocele and lower-limb lymphoedema • Surgical menopause after BSO in premenopausal women	• Meticulous surgical technique with MDT operative planning • Prompt intra-operative recognition and repair of visceral injury • Broad-spectrum antibiotics and appropriate wound care for infection

Treatment modality	Recognized complications	GOSK recommendations for prevention and management
	• Tumor spillage from morcellation (preventable; markedly worsens prognosis)	• Drainage or conservative management of lymphocele; complex decongestive therapy for lymphoedema • Avoid morcellation where sarcoma is suspected (see Box 25)
Chemotherapy (doxorubicin, ifosfamide, gemcitabine/docetaxel, carboplatin/paclitaxel)	• Myelosuppression with febrile neutropenia, nausea and vomiting, mucositis, alopecia and fatigue • Anthracycline cardiotoxicity • Ifosfamide-induced haemorrhagic cystitis and encephalopathy • Taxane- or platinum-induced peripheral neuropathy	• G-CSF prophylaxis for regimens with >20% febrile-neutropenia risk; prompt treatment of neutropenic sepsis per protocol • Guideline-based antiemesis (5-HT3 antagonist plus dexamethasone; add an NK1 antagonist for highly emetogenic regimens) • Limit cumulative doxorubicin to <450 mg/m² with baseline and serial echocardiography • Mandatory Mesna uroprotection and adequate hydration with ifosfamide • Dose modification or discontinuation for grade ≥2 neuropathy; assess renal function before each platinum dose
Radiotherapy (pelvic external beam radiotherapy and vaginal brachytherapy)	• Acute radiation cystitis and proctitis, diarrhoea and skin reactions • Late effects: chronic bowel and bladder toxicity, vaginal stenosis, fistula formation and pelvic insufficiency fractures	• Careful field planning with adherence to normal-tissue dose constraints • Symptomatic treatment of acute reactions • Vaginal dilators and lubricants to reduce stenosis and preserve sexual function • Specialist referral for established late toxicity • Where feasible, chemotherapy before radiotherapy to limit overlapping toxicity (see Box 24)
All modalities (supportive care and monitoring)	• Cumulative and overlapping toxicity • Under-recognition of complications • Deterioration in performance status	• Baseline and interval assessment of full blood count, renal and liver function and performance status, with proactive symptom screening at every visit • Document and grade complications using a standardised system (e.g. CTCAE) to guide dose modification • Early palliative-care involvement for patients with high-grade or advanced disease

Table 43. GOSK recommendations for the prevention for the prevention and management of venous thromboembolism and coagulopathy in uterine sarcoma

A. VTE risk mechanisms in uterine sarcoma			
VTE risk mechanism	**Subtypes most affected**	**Estimated additive VTE risk**	**Pathophysiology**
Direct vascular invasion/intravenous leiomyomatosis (IVL)	LMS, IVL	>60% in IVL	Intraluminal tumor causing venous obstruction and thrombosis
Tumor compression of pelvic/iliac veins by bulky mass	All subtypes (esp. LMS, carcinosarcoma)	+15–20% above baseline	Extrinsic venous compression → venous stasis
Tissue factor (TF) overexpression by tumor cells	Carcinosarcoma, HGESS, UUS	+10–15%	TF activates extrinsic coagulation cascade → hypercoagulable state
Cancer procoagulant (CP) secretion	All high-grade subtypes	+10%	CP directly activates Factor X → thrombin generation independent of TF
Inflammatory cytokines (IL-6, TNF-α) from tumor microenvironment	All subtypes; highest UUS, carcinosarcoma	+5–10%	Downregulate Protein C/S; upregulate PAI-1 → impaired fibrinolysis
Major pelvic surgery (TAH-BSO ± lymphadenectomy)	All surgical patients	+15–25% (for up to 3 months post-op)	Virchow's triad: stasis + endothelial injury + hypercoagulability
Chemotherapy (paclitaxel, carboplatin, gemcitabine)	All treated patients	+4–6% per cycle	Endothelial injury, platelet activation, reduced Protein C
Prolonged immobility / hospitalisation	All patients; especially bulky disease	+8–12% per week of immobility	Venous stasis in lower extremity deep veins

Central venous access devices (CVAD / port-a-cath)	All chemotherapy patients	+2–5%	Upper extremity DVT and catheter-related thrombosis
Advanced/metastatic stage (III–IV)	All subtypes Stage III–IV	2–3× higher vs localized disease	Greater tumor burden, peritoneal involvement, ascites
Obesity (BMI ≥30)	All subtypes (high prevalence in Kenya)	+5–10%	Increased intra-abdominal pressure; reduced fibrinolytic capacity
B. VTE risk stratification and GOSK-recommended prophylaxis			
Risk level	**Criteria**	**Recommended prophylaxis**	
Very high	IVL; direct vascular invasion on imaging; Khorana score ≥3; Stage III–IV with peritoneal disease; post-surgical + active chemotherapy + immobile	Therapeutic LMWH (enoxaparin 1 mg/kg BD or 1.5 mg/kg once daily) + IPC devices + compression stockings. IVC filter only if anticoagulation absolutely contraindicated.	
High	Any uterine sarcoma post-surgery; Khorana 1–2 on chemotherapy; tumor >5 cm compressing pelvic veins	Prophylactic LMWH (enoxaparin 40 mg SC daily or dalteparin 5,000 IU SC daily) + IPC devices + GCS. Continue ≥28 days post-hysterectomy.	
Intermediate	Khorana score 1 on outpatient chemotherapy; localized disease; ambulatory	LMWH during hospitalisation/immobility. Consider extended prophylaxis ×28 days post-surgery (LMWH or rivaroxaban 10 mg daily or apixaban 2.5 mg BD).	
Low	Khorana 0; fully ambulatory; no surgery; no additional risk factors	Mechanical prophylaxis (IPC + GCS); early ambulation; patient education on VTE symptoms.	
C. Management of established VTE and DIC (DVT/PE) First-line: LMWH (enoxaparin 1 mg/kg BD or 1.5 mg/kg once daily) for minimum 6 months; continue indefinitely while cancer is active (CLOT trial: 52% reduction in VTE recurrence vs warfarin). Acceptable DOAC alternatives: Rivaroxaban (15 mg BD ×21 days, then 20 mg daily) or Apixaban (10 mg BD ×7 days, then 5 mg BD) — avoid in GI luminal involvement. Warfarin NOT recommended for cancer-associated VTE. DIC in uterine sarcoma (HGESS/UUS/Carcinosarcoma): Urgent hematology consultation. ISTH DIC Score ≥5 = overt DIC. Treat: FFP 10–15 mL/kg (PT/aPTT >1.5× normal + bleeding); Cryoprecipitate (fibrinogen <1.5 g/L; target >1.5 g/L); Platelets (<50 ×10⁹/L + bleeding). Tranexamic acid 1 g IV for hemorrhagic DIC ONLY. Definitive treatment = tumor control. **D.** Khorana score Gynecological malignancy = 1 point; platelets ≥350×10⁹/L = 1; Hb <100 g/L or ESA use = 1; WBC >11×10⁹/L = 1; BMI ≥35 = 1. Score 0 = low risk; 1–2 = intermediate; ≥3 = high risk. Assess at diagnosis, each cycle, each admission, and post-operatively.			

BMI = Body Mass Index; BSO = Bilateral Salpingo-Oophorectomy; CP = Cancer Procoagulant; CVAD = Central Venous Access Device; DIC = Disseminated Intravascular Coagulation; DOAC = Direct Oral Anticoagulant; DVT = Deep Vein Thrombosis; FFP = Fresh Frozen Plasma; GCS = Graduated Compression Stockings; HGESS = High-Grade Endometrial Stromal Sarcoma; IPC = Intermittent Pneumatic Compression; ISTH = International Society on Thrombosis and Haemostasis; IVC = Inferior Vena Cava; IVL = Intravenous Leiomyomatosis; LMS = Leiomyosarcoma; LMWH = Low Molecular Weight Heparin; PAI-1 = Plasminogen Activator Inhibitor-1; PE = Pulmonary Embolism; TAH-BSO = Total Abdominal Hysterectomy with Bilateral Salpingo-Oophorectomy; TF = Tissue Factor; UUS = Undifferentiated Uterine Sarcoma; VTE = Venous Thromboembolism.

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