JOGECA

Journal of Obstetrics
and Gynaecology of
Eastern and Central Africa

Clinical Protocol

Gynecologic Oncology

Gynaecologic Oncology Society of Kenya (GOSK) clinical management protocol for malignant ovarian sex cord stromal tumors in Kenya - 2026

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DOI:

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Abstract

Objective: To establish a standardized evidence-based approach to the management of malignant ovarian sex cord-stromal tumors (MOSCSTs) in Kenya.

Methods: This protocol was developed by adapting high-quality international clinical practice guidelines to 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 led the development process. Panel members received technical training from the University of Nairobi and Kenyatta National Hospital on evidence-based guideline adaptation, including standardized appraisal, systematic evaluation of guidelines, and contextualization to local needs. A systematic literature search was conducted in PubMed and Google Scholar. Five guidelines were identified and independently appraised using the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument. Four guidelines were selected for adaptation: the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology on ovarian cancer, including fallopian tube cancer and primary peritoneal cancer; the European Society for Medical Oncology (ESMO) clinical practice guidelines on non-epithelial ovarian cancer; the European Society of Gynaecological Oncology (ESGO) guidelines on non-epithelial ovarian cancers in adolescents and young adults; and the Japan Society of Gynecologic Oncology guidelines on ovarian cancer, fallopian tube cancer, and primary peritoneal cancer. The selected guidelines were reviewed, and their recommendations were contextualized to Kenya's healthcare infrastructure and available resources.

Results: The protocol provides recommendations on clinical evaluation, histopathological assessment, staging, laboratory investigations, imaging, and the management of MOSCSTs. It addresses surgery as the primary treatment approach, the role of adjuvant and systemic therapies, and fertility-sparing management in selected patients with early-stage disease. It also covers the multidisciplinary management of advanced, recurrent, and treatment-resistant disease, post-treatment surveillance, survivorship, and supportive and palliative care.

Recommendations: The protocol provides a standardized framework for the diagnosis, staging, treatment, and follow-up of MOSCSTs in Kenya. It emphasizes appropriate surgical management, individualized fertility-preserving approaches, multidisciplinary care, long-term surveillance, and referral for clinical trials where available, taking into account the patient's clinical circumstances and the resources available.

Keywords: Kenya; Malignant ovarian sex cord-stromal tumors

List of abbreviations

AFP	Alpha-fetoprotein
AGCT	Adult granulosa cell tumor
AGREE II	Appraisal of Guidelines for Research and Evaluation II
AMH	Anti-Müllerian hormone
AUC	Area under the curve
BEP	Bleomycin, etoposide, and cisplatin
BRCA	Breast cancer susceptibility gene (BRCA1/BRCA2)
BSO	Bilateral salpingo-oophorectomy
CA-125	Cancer antigen 125
CEA	Carcinoembryonic antigen
CECT	Contrast-enhanced computed tomography
CrCl	Creatinine clearance
CT	Computed tomography
DICER1	DICER1 ribonuclease III
ESGO	European Society of Gynaecological Oncology
ESMO	European Society for Medical Oncology
FDG-PET	Fluorodeoxyglucose positron emission tomography
FIGO	International Federation of Gynecology and Obstetrics
FOXL2	Forkhead box L2
FSS	Fertility-sparing surgery
G-CSF	Granulocyte colony-stimulating factor
GnRH	Gonadotropin-releasing hormone
GOSK	Gynaecologic Oncology Society of Kenya
hCG	Human chorionic gonadotropin
HRT	Hormone replacement therapy
IHC	Immunohistochemistry
JGCT	Juvenile granulosa cell tumor
JSGO	Japan Society of Gynecologic Oncology
KNH	Kenyatta National Hospital
LDH	Lactate dehydrogenase
MDT	Multidisciplinary team
MOSCSTs	Malignant ovarian sex cord-stromal tumors
MRI	Magnetic resonance imaging
NACT	Neoadjuvant chemotherapy
NCCN	National Comprehensive Cancer Network
OMT	Omentectomy
PALND	Para-aortic lymphadenectomy
PEI	Cisplatin, etoposide, and ifosfamide
PET-CT	Positron emission tomography–computed tomography

PLND	Pelvic lymph node dissection
PRO	Patient-reported outcomes
REI	Reproductive endocrinology and infertility
SCCOHT	Small cell carcinoma of the ovary, hypercalcemic type
SCTAT	Sex cord tumor with annular tubules
SEER	Surveillance, Epidemiology, and End Results
SLCT	Sertoli-Leydig cell tumor
SMARCA4	SWI/SNF-related, matrix-associated, actin-dependent regulator of chromatin, subfamily A, member 4
STK11	Serine/threonine kinase 11
TAH	Total abdominal hysterectomy
TH	Total hysterectomy
TVS	Transvaginal ultrasound scan
UON	University of Nairobi
USO	Unilateral salpingo-oophorectomy
VAC	Vincristine, actinomycin D, and cyclophosphamide
VIP	Etoposide, ifosfamide, and cisplatin
WHO	World Health Organization
WT1	Wilms tumor 1

Summary of recommendations

This guideline has been adapted to the Kenyan healthcare system to inform clinical decision-making across the continuum of care for patients with suspected or confirmed malignant ovarian sex cord-stromal tumors (MOSCSTs), from initial suspicion and diagnosis through treatment, surveillance, and long-term survivorship. It is intended for multidisciplinary teams and specialist clinicians, while also supporting primary care providers and allied health professionals in delivering coordinated, patient-centered oncologic care. The guideline emphasizes multidisciplinary team (MDT) management and referral to specialist gynecologic oncology centers to support the delivery of high-quality cancer care.

Table 1: Summary of GOSK recommendations for clinical evaluation and diagnostic workup of MOSCSTs

Clinic domain	**GOSK recommendations**
Clinical history and physical examination	Take a comprehensive history and perform a physical examination focusing on features of pelvic mass like abdominal pain, bloating, and abdominal distension, as well as hormonal effects such as menstrual irregularities, post-menopausal bleeding, precocious puberty, or signs of virilization/defeminization like hirsutism and voice deepening
Pelvic ultrasound	Pelvic ultrasound is the preferred first-line imaging modality: assess size, laterality, solid/cystic components, septations, papillary projections, vascularity
Cross-sectional and chest imaging	Abdomino-pelvic Computed Tomography (CT) scan, chest X-ray or CT scan, and Positron Emission Tomography (PET) scan are recommended to evaluate suspected advanced/metastatic disease.
Tumor markers	Evaluation of tumor markers is recommended as part of the diagnostic workup and to rule out other ovarian tumors, especially germ cell tumors. The tumor marker panel should include Inhibin B, Cancer Antigen 125 (CA 125), Antimüllerian Hormone (AMH), human Chorionic Gonadotropin (hCG), Alpha Foetal Proteins (AFP), and Lactate Dehydrogenase (LDH).
Hormonal assessment	A hormonal profile panel, guided by the presence of corresponding signs of tumor-related hormonal production, is recommended. The panel may include Estrogen, dehydroepiandrosterone, testosterone, luteinizing hormone, and follicle-stimulating hormone.
Karyotyping	Karyotype is recommended in all premenarcheal girls with suspected gonadoblastomas.

Table 2: Summary of GOSK recommendations for management of early-stage (FIGO stage I) MOSCSTs

Clinical domain	GOSK recommendations
Primary surgery and surgical staging	Surgical management is the recommended primary treatment for all patients with suspected early MOSCSTs. Open surgery is preferred, although a laparoscopic approach may be considered in selected patients. Surgical staging should include infracolic omentectomy, peritoneal washings for cytology, and biopsies of the diaphragmatic peritoneum, paracolic gutters, and pelvic peritoneum.
Fertility-sparing surgery	Fertility-sparing surgery (FSS) with preservation of the uterus and contralateral ovary may be considered in patients with apparent stage I disease desiring future fertility. Patients undergoing fertility preservation should be referred early to a reproductive endocrinologist and infertility (REI) specialist FSS is not recommended in: stage II–IV disease; small cell carcinoma of the ovary, hypercalcemic type (SCCOHT); and Sertoli-Leydig cell tumors with retiform pattern. Endometrial sampling should be performed in adult patients with granulosa cell tumors undergoing fertility-sparing surgery to exclude concomitant endometrial hyperplasia or carcinoma.
Management of gonadoblastoma	For patients with suspected gonadoblastomas, bilateral salpingo-oophorectomy (BSO) is the standard surgical management recommended once Y material + dysgenetic gonads are confirmed
Completion surgery	Recommend complete staging, including hysterectomy and salpingo-oophorectomy after childbearing, for those offered FSS.
Adjuvant therapy	Stage IA/IB disease may be managed with surveillance alone following adequate surgery. Adjuvant platinum-based chemotherapy should be considered for: stage IC disease, high-risk histology, poorly differentiated Sertoli-Leydig cell tumors (SLCT), and mesenchymal heterologous elements.
Chemotherapy regimens	The preferred chemotherapy regimen is bleomycin, etoposide, and cisplatin (BEP). Alternative regimens include carboplatin/paclitaxel, etoposide plus cisplatin (EP), or platinum monotherapy. For SLCT with mesenchymal elements: consider sarcoma-type regimens with Ifosfamide (PEI/VIP or alternating PEI/VAC)

Table 3: Summary of GOSK recommendations for management of local advanced (FIGO stage II-IV) and metastatic MOSCSTs

Clinical domain	**GOSK recommendations**
Cytoreductive surgery	Cytoreductive surgery remains the mainstay treatment for locally advanced and metastatic MOSCSTs.

Neoadjuvant chemotherapy	If primary cytoreductive surgery is not feasible, neoadjuvant chemotherapy followed by interval cytoreductive surgery is recommended.
Adjuvant chemotherapy	Platinum-based chemotherapy is recommended as adjuvant treatment for patients with advanced-stage disease.
Chemotherapy regimens	Recommended regimens include BEP for three cycles or carboplatin/paclitaxel for six cycles.

Table 4. Summary of GOSK recommendations for management of chemo-resistant MOSCSTs

Clinical domain	**GOSK recommendations**
Radiotherapy	Localized radiotherapy may be considered for symptom palliation, oligometastatic disease, or localized residual lesions
Second-line chemotherapy	Second-line chemotherapy with carboplatin/paclitaxel is recommended if BEP was used as first-line treatment. Alternative regimens include Vincristine, Actinomycin D, and Cyclophosphamide (VAC) or BEP if not previously administered
Clinical trials	Patients with chemoresistant disease should be considered for enrolment in clinical trials where available
Supportive and palliative care	Best supportive and palliative care should be integrated throughout management to optimize symptom control, psychosocial support, quality of life, and end-of-life care where appropriate

Table 5: Summary of GOSK recommendations for management of recurrent MOSCSTs

Clinical domain	GOSK recommendations
Secondary cytoreductive surgery	Consider secondary cytoreductive surgery if a complete resection is feasible.
Radiotherapy and systemic treatment	Localized radiotherapy may be considered for symptom palliation, oligometastatic disease, or localized residual lesions not amenable to surgery. Chemotherapy with carboplatin/paclitaxel is recommended for recurrent disease. The BEP regimen should not be repeated.
Hormonal therapy	Hormonal therapy may be considered in hormone receptor-positive tumors based on immunohistochemical profiling

Table 6. Summary of GOSK recommendations for post-treatment evaluation and survivorship in MOSCSTs

Clinical domain	**GOSK recommendations**
Long-term surveillance	Lifelong surveillance is recommended due to the risk of late recurrence
Tumor marker monitoring	Serum tumor markers, including Inhibin B, CA 125, Estrogen (E2), and Testosterone (T), should be monitored if initially elevated, as they may correlate with treatment response and disease recurrence.
Imaging during follow-up	CT scan of the abdomen and pelvis, chest imaging (where clinically indicated), and pelvic ultrasound are recommended for the assessment of treatment response and suspected recurrence.
Surveillance during fertility-sparing surgery	In patients who undergo FSS, pelvic ultrasound surveillance every 6 months is recommended.
Fertility counseling	Counsel patients who underwent FSS regarding conception timing, assisted reproductive technology options, and obstetric risks Delayed ovarian stimulation and oocyte cryopreservation after completion of chemotherapy may be considered in selected patients at risk of premature ovarian insufficiency.
Completion surgery after child-bearing	Following FSS, completion surgery should be considered after childbearing to reduce the long-term risk of recurrence, especially with adult-type granulosa cell tumor.
Hormone replacement therapy	Hormonal replacement therapy should generally be avoided in MOSCSTs because many tumors are hormonally responsive and may increase recurrence risks
Genetic counseling and surveillance	Genetic surveillance and family counseling for patients with suspected germline mutational syndromes associated with SCST is recommended
Psychosocial support	Screen for anxiety, depression, and fear of recurrence; refer for psycho-oncological support as appropriate
Bone health	Regularly evaluate bone health for patients with treatment-induced premature menopause or long-term GnRH antagonist use and manage osteopenia/osteoporosis with bisphosphonates, calcium, and vitamin D supplementation
Palliative care	Early integration of palliative care in MOSCSTs cancer care is recommended. Facilitate access to expertise in palliative therapeutics for patients with advanced and /or recurrent disease.

1.0 Introduction

1.1 Background

Ovarian cancer is the second most common gynecological cancer in Kenya after cervical cancer, accounting for approximately 4% of all female cancer cases. The estimated incidence is 3.8 cases per 100,000 women per year, corresponding to approximately 1,245 new cases and 895 deaths annually (1-2). Ovarian cancers are classified into three major histological groups: epithelial tumours, germ cell tumours, and sex cord-stromal tumors. These groups differ in their clinical presentation, management, and prognosis.

Malignant ovarian sex cord-stromal tumors (MOSCSTs) are a heterogeneous group of neoplasms arising from gonadal sex cord cells, including granulosa and Sertoli cells; specialized gonadal stromal cells, including theca and Leydig cells; and fibroblasts (3). These tumors may exhibit variable biological behavior, ranging from relatively indolent disease to aggressive malignancy. Many are hormonally active and may present with endocrine manifestations, whereas others are detected during the evaluation of an adnexal mass.

The diagnosis and management of MOSCSTs require consideration of histological subtype, disease stage, hormonal activity, and the patient's reproductive goals. Serum tumor markers, including inhibin and anti-Müllerian hormone (AMH), may support diagnosis and disease surveillance in selected patients (8). Surgical treatment is the primary management approach, with adjuvant or systemic treatment considered according to disease stage, tumor characteristics, and recurrence risk (9-10). Because recurrence may occur many years after initial treatment, long-term follow-up is an important component of care (11).

1.2 Epidemiology

MOSCSTs account for approximately 3% to 5% of ovarian malignancies (4). The average age at diagnosis is approximately 50 years, although the age distribution varies by histological subtype. Adult-type granulosa cell tumors are the most common subtype, accounting for approximately 70% of malignant MOSCSTs, with peak incidence between 50 and 55 years. Sertoli-Leydig cell tumors account for approximately 12% of MOSCSTs and occur more frequently in younger women, particularly those younger than 30 years (5).

Data from the United States Surveillance, Epidemiology, and End Results (SEER) program indicate a higher incidence of MOSCSTs among Black patients than among White patients, at 0.44 and 0.18 cases per 100,000, respectively (5). These estimates reflect the population studied and should not be assumed to represent incidence patterns in African populations. In a retrospective study, an age of 40 years or older at last birth and an interval of less than 10 years since last birth were associated with a lower risk of MOSCSTs (6). This association should be interpreted in the context of the study design and the limitations of observational evidence.

Some MOSCST subtypes are associated with genetic alterations or syndromic conditions. These include sex cord tumors with annular tubules associated with Peutz-Jeghers syndrome and STK11, Sertoli-Leydig cell tumors associated with DICER1, and adult-type granulosa cell tumors characterized by alterations involving FOXL2. Associations have also been reported between selected tumor subtypes and Ollier disease and Maffucci syndrome (7). These associations are relevant to diagnostic assessment and may inform consideration of genetic evaluation in appropriate patients.

Despite the recognized clinical significance of MOSCSTs, epidemiological data remain limited in Africa and Kenya. This scarcity of population-specific evidence constrains the assessment of their local incidence, distribution, and outcomes.

1.3 Ovarian sex cord-stromal tumors in Kenya

Available national estimates describe the burden of ovarian cancer overall rather than that of MOSCSTs specifically. The estimated incidence of ovarian cancer in Kenya is 3.8 cases per 100,000 women per year, with approximately 1,245 new cases and 895 deaths annually (1-2). These figures provide context for the broader burden of ovarian cancer but should not be interpreted as estimates of the incidence or mortality of MOSCSTs.

Kenya-specific epidemiological data on MOSCSTs are scarce. Consequently, the extent to which international estimates of incidence, demographic distribution, risk factors, and clinical outcomes reflect the Kenyan population remains uncertain. The rarity of these tumors and the limited availability of local evidence underscore the importance of consistent diagnostic assessment, histopathological characterization, staging, treatment planning, and follow-up.

The absence of dedicated, standardized national guidance for MOSCSTs has created a need for recommendations that support consistent clinical decision-making while accounting for Kenya's healthcare infrastructure and available resources. A nationally adapted protocol can provide a common framework for multidisciplinary care and help reduce unwarranted variation in clinical practice.

1.4 Rationale for the GOSK protocol

MOSCSTs are rare tumors, and the limited availability of high-quality evidence presents challenges for standardizing clinical management. The Kenya National Cancer Treatment Protocols (2019) do not provide specific guidance for MOSCSTs, leaving a need for recommendations that address the diagnostic and therapeutic requirements of this patient population. The Gynaecologic Oncology Society of Kenya (GOSK) developed this protocol by adapting selected international clinical practice guidelines to the Kenyan healthcare context. The adaptation approach aims to align clinical recommendations with available evidence while considering local service capacity and resource constraints.

The protocol provides guidance on the clinical evaluation and diagnostic work-up of suspected MOSCSTs; surgical management, including fertility-sparing approaches for

appropriately selected patients; management of advanced, metastatic, recurrent, and treatment-resistant disease; and post-treatment surveillance and survivorship care. It is intended to support multidisciplinary decision-making, promote consistency in clinical practice, and facilitate appropriate use of available resources across Kenya. By establishing a standardized framework for the management of MOSCSTs, this protocol seeks to reduce unwarranted variation in care and support evidence-informed clinical decisions. Its recommendations should be applied alongside individual clinical judgement, taking into account tumor characteristics, disease stage, patient preferences, reproductive goals, and the resources available.

2.0 Risk factors, Clinical features, Histology, and Staging

2.1 Risk Factors

Compared with epithelial ovarian cancer, relatively few risk factors for malignant ovarian sex cord-stromal tumors (MOSCSTs) have been established. Available evidence identifies several demographic, reproductive, genetic, and syndromic associations; however, the strength of evidence varies, and some reported associations remain uncertain.

Table 7. Risk factors and reported association with MOSCSTs

Risk Factor	Known association
Demographic and reproductive factors	**Age at diagnosis**: The peak incidence age of MOSCSTs varies by subtype. Adult granulosa cell tumors often occur in women aged 45–60, while juvenile granulosa cell tumors are seen in young girls, and Sertoli-Leydig cell tumors are more common in women under 30
	Race/Ethnicity: United States SEER data show a higher incidence in black patients (0.44 per 100,000) compared with white patients.
	Sex hormones: High levels of androgen and estrogen contribute to tumor development or progression.
	Infertility/ovulation induction: Some studies suggest a possible increased risk for granulosa cell tumors with infertility, but evidence is inconsistent
Genetic conditions and predispositions	**DICER1 syndrome**: Pathogenic variants in the *DICER1* gene are a risk factor for malignant Sertoli-Leydig cell tumors.
	Peutz-Jeghers syndrome: caused by mutations in the *STK11* gene, is linked to an increased risk of MOSCSTs, specifically Sex Cord Tumors with Annular Tubules (SCTAT).
	Family history: A family history of ovarian or breast cancer is a possible risk factor, especially for the adult granulosa cell tumor subtype. The rare gonadoblastoma is associated with gonadal dysgenesis and disorders of sexual development.
	***FOXL2* gene mutation**: A specific mutation in the *FOXL2* gene is pathognomonic of adult granulosa cell tumors.
	Ollier disease (enchondromatosis) and Maffucci syndrome: Linked to juvenile granulosa cell tumors.
Other health- related factors	**Preterm birth**: Children born before 37 weeks of gestation have an increased risk of MOSCSTs later in life.
Protective factors	**Oral contraceptives**: Using oral contraceptives appears to decrease the risk of MOSCSTs.
	Higher age at last birth: Women with a last birth at age ≥40 years had approximately half the risk of MOSCSTs compared with those whose last birth was before age 25 years
	Higher parity: While some studies show no association, others suggest that higher parity may reduce the risk of MOSCSTs.
BRCA – Breast Cancer gene; DICER – Dicer Endoribonuclease; FOXL2 - Forkhead box protein L2; MOSCSTs – Malignant Ovarian Sex Cord Stromal Tumors; SCTAT - Sex Cord Tumors with Annular Tubules; SEER – Surveillance, Epidemiology and End Results; SLCT – Sertoli Leydig Cell tumor; STK11 – Serine Threonine Kinase gene 11;	

2.2 Clinical Features

MOSCSTs have varied clinical presentations, reflecting differences in histological subtype, tumor size, hormonal activity, and disease stage. Hormone production may lead to endocrine manifestations that prompt early clinical evaluation. Other patients present with an adnexal mass or symptoms related to abdominal or pelvic pressure. Because some tumours may recur many years after initial treatment, clinical assessment and subsequent follow-up should account for the possibility of late recurrence.

Table 8. Clinical features associated with MOSCSTs

Clinical feature	Description
Abdominal or pelvic mass and mass effect	An abdominal or pelvic mass, with or without abdominal distension. The mass may be asymptomatic or cause pressure symptoms, including urinary frequency, constipation, bloating, and pain. MOSCSTs are almost always unilateral.
Acute abdominal presentation	Acute abdominal pain may occur with tumour torsion or rupture, with haemoperitoneum reported in 5%–15% of granulosa cell tumours.

Clinical feature	Description
Estrogenic manifestations	Excess estrogen production may cause abnormal uterine bleeding, postmenopausal bleeding, breast tenderness, and menstrual irregularities ranging from amenorrhea to menorrhagia in women of reproductive age. Endometrial hyperplasia or endometrial cancer occurs in approximately 10%–15% of estrogenic tumors.
Precocious puberty	Juvenile granulosa cell tumors may present with precocious pseudopuberty, including breast development and vaginal bleeding.
Androgenic manifestations (virilization)	Virilization may occur with androgen-producing tumors, particularly Sertoli-Leydig cell tumors, steroid cell tumors, and some sclerosing stromal tumors. Features include hirsutism, acne, amenorrhea, voice deepening, clitoromegaly, male-pattern baldness, infertility, and loss of female-pattern fat distribution.
Mixed hormonal manifestations	A combination of estrogenic and androgenic features may occur.
Incidental or asymptomatic presentation	MOSCSTs may be asymptomatic and detected incidentally as an adnexal mass.

2.3 Histological classification of MOSCSTs

Ovarian sex cord-stromal tumors (SCSTs) are a heterogeneous group of neoplasms classified according to their histological differentiation. They arise from gonadal sex cord cells, specialized gonadal stromal cells, or both. In the World Health Organization (WHO) classification of tumors of the female reproductive tract, these neoplasms are grouped into three main categories: pure stromal tumors, pure sex cord tumors, and mixed sex cord-stromal tumors (3) (Figure 1). The principal histological groups described in the source protocol include granulosa cell tumors, Sertoli-stromal tumors, and tumors of the thecafibroma group, including mixed or unclassified SCSTs. Histological classification is important for diagnosis and management because tumor subtype and specific histological features can influence treatment decisions. A distinct variant is the Sertoli-Leydig cell tumor with a retiform pattern, which may resemble an epithelial ovarian neoplasm. This variant has been described in young girls and is associated with an aggressive clinical course and poor prognosis. The source protocol therefore identifies it as a histological feature that should be considered when determining eligibility for conservative, fertility-sparing surgery (3,12).

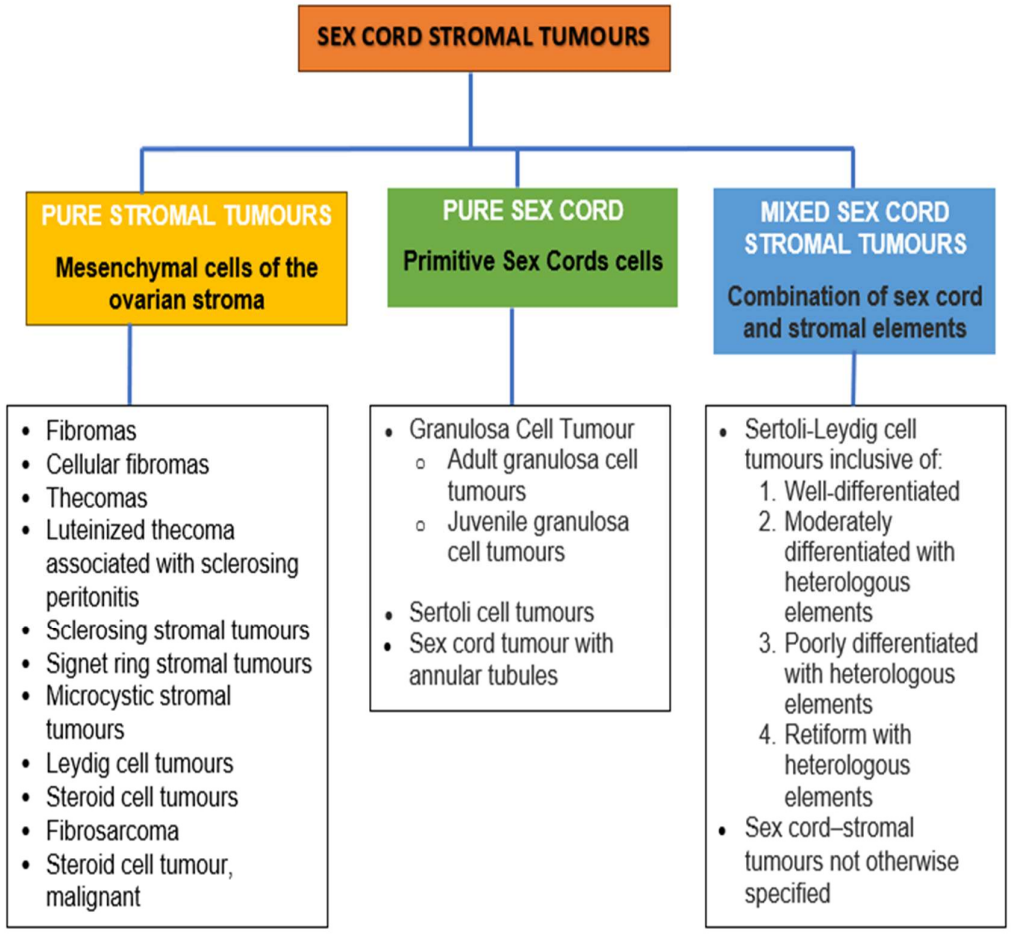


Figure 1. WHO classification of ovarian sex-cord stromal tumors

2.4 FIGO staging of MOSCSTS s

The International Federation of Gynecology and Obstetrics (FIGO) 2014 staging system for ovarian, fallopian tube, and primary peritoneal cancer is based on surgical findings and histopathological assessment. It is used to determine the extent of disease and guide treatment planning, prognostication, and post-treatment surveillance for malignant ovarian sex cord-stromal tumors (MOSCSTs) (4).

Table 9. FIGO (2014) staging of cancer of the ovary, fallopian tube, and peritoneum

Stage	Substage	Description
Stage I		Tumor limited to the ovaries or fallopian tubes
	IA	Tumor limited to one ovary (capsule intact) or fallopian tube. No tumor on the external surface of the ovary or fallopian tube. No malignant cells in ascites or peritoneal washings
	IB	Tumor limited to both ovaries (capsules intact) or fallopian tubes. No tumor on the external surface of the ovaries or fallopian tubes. No malignant cells in ascites or peritoneal washings
	IC	Tumor limited to one or both ovaries or fallopian tubes, with any of the following: IC1: Surgical spill; IC2: Capsule ruptured before surgery, or tumor on the ovarian or fallopian tube surface; IC3: Malignant cells in the ascites or peritoneal washings.
Stage II		Tumor involves one or both ovaries or fallopian tubes, with pelvic extension (below pelvic brim) or primary peritoneal cancer
	IIA	Extension and/or implants on the uterus and/or ovaries and/or fallopian tubes
	IIB	Extension to other pelvic intraperitoneal tissues
Stage III		Tumor involves one or both ovaries or fallopian tubes, or primary peritoneal cancer, with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes
	IIIA1	Positive (cytologically or histologically proven) retroperitoneal lymph nodes: IIIA1(i): Metastasis up to 10 mm in greatest dimension; IIIA1(ii): Metastasis more than 10 mm in greatest dimension
	IIIA2	Microscopic extra-pelvic (above the pelvic brim) peritoneal involvement with or without positive retroperitoneal lymph nodes
	IIIB	Macroscopic peritoneal metastasis beyond the pelvis up to 2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes
	IIIC	Macroscopic peritoneal metastasis beyond the pelvis, more than 2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes. Stage IIIC includes extension of the tumor to the capsule of the liver and spleen without parenchymal involvement of either organ
Stage IV		Distant metastasis, excluding peritoneal metastases
	IVA	Pleural effusion with positive cytology
	IVB	Parenchymal metastases and metastases to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of the abdominal cavity)

3.0 Objectives

3.1 Overall Objective

To establish a standardized, evidence-based approach to the management of malignant ovarian sex cord-stromal tumors (MOSCSTs) in Kenya.

3.2 Specific Objectives

This management protocol provides recommendations and guidance on:

1. Clinical evaluation and diagnostic workup of suspected MOSCSTs.
2. Fertility-sparing management of early-stage MOSCSTs in patients who desire future fertility.
3. Management of early-stage MOSCSTs in patients who do not desire fertility preservation or for whom fertility-sparing surgery is not indicated.
4. Multidisciplinary management of locally advanced and metastatic MOSCSTs.
5. Management of recurrent and treatment-resistant MOSCSTs.
6. Post-treatment surveillance, survivorship care, and long-term follow-up for patients with MOSCSTs.

4.0 Clinician responsibility

This protocol represents the evidence-based consensus of the multidisciplinary development group under GOSK for the management of patients with malignant ovarian sex cord stromal tumors. They are intended to guide clinicians; however, application of these recommendations should always be informed by independent clinical judgment, considering each patient's individual circumstances.

5.0 Methods

5.1 Guideline adaptation approach

This protocol was developed using an adaptation approach, drawing on existing international clinical practice guidelines and contextualizing their recommendations to Kenya's health care system and available resources. The process involved systematic appraisal of published guidelines and protocols and adaptation of recommendations to local clinical practice and resource constraints. The aim was to align the protocol with internationally accepted standards while addressing the needs of the Kenyan health care setting.

5.2 Development panel

A multidisciplinary protocol development panel was convened, comprising gynecologic oncologists, pathologists, radiologists, gynecologic oncology nurses, oncology pharmacists, radiation oncologists, public health specialists, and patient representatives. The panel received technical orientation from experts at the University of Nairobi and Kenyatta National Hospital on evidence-based guideline adaptation. The training covered standardized appraisal tools, systematic evaluation of published guidelines and protocols, and approaches for contextualizing recommendations to local needs.

5.3 Search strategy

A comprehensive literature search was conducted in PubMed and Google Scholar to identify relevant evidence-based guidelines, systematic reviews, and best-practice statements on the management of MOSCSTs. The search terms included: "ovarian sex-cord stromal tumor," "clinical guideline," "gynecologic oncology," "protocols," and "guidelines."

5.4 Source guideline identification

The protocol reports that seven primary reference guidelines were identified, of which four were selected as source documents for adaptation. These are summarized in the source protocol's table of retrieved guidelines (**Table 10**).

Table 10. Summary of source guidelines for protocol adaptation

No.	Guideline title	Type of document	Publisher or Organization	Year of last update
1	Clinical Practice Guidelines in Oncology: Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer	Clinical guideline	National Cancer Comprehensive Network (NCCN)	2025
2	Non-epithelial ovarian cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up (13)	Clinical guideline	European Society of Medical Oncology (ESMO)	2017
3	Guidelines for the treatment of ovarian cancer, fallopian tube cancer, and primary peritoneal cancer (14)	Clinical guideline	Japan Society of Gynaecologic Oncology (JSGO)	2020
4	Ovarian, tubal and primary peritoneal cancer guidelines: Recommendations for practice update 2024 (15)	Clinical guideline	British Gynaecological Cancer Society (BGCS)	2024
5	Consensus Review for Ovarian Sex Cord Stromal Tumors (16)	Update review	Gynaecologic Cancer InterGroup (GCIG)- Discover Oncology	2024
6	Definition Guideline for Ovarian Cancer	Benefit definition guideline	Council for Medical Schemes (CMS) - South Africa	2021
7	Guidelines for the management of non-epithelial ovarian cancers in adolescents and young adults	Clinical guideline	European Society of Gynaecological Oncology (ESGO)	2024

5.5 AGREE II appraisal

All retrieved guidelines were independently appraised by two trained panelists using the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument. The instrument assesses 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 domain was scored using a 7-point Likert scale, ranging from 1 (strongly disagree) to 7 (strongly agree). Domain scores were standardized as percentages using the following formula:

Standardized domain score (%) = ((Obtained score) – (Minimum possible score) / ((Maximum possible score) – (Minimum possible score)) x 100

Where the two reviewers did not reach consensus, a facilitator served as a tiebreaker. Overall quality ratings and recommendations regarding the suitability of the guidelines for adaptation in Kenya were then recorded. The AGREE II domain scores and the overall decisions on the suitability of the identified guidelines for adaptation are summarized in Table 12.

Table 11. Summary of AGREE II domain scores

No.	Title	Domain % score	Overall Decision

		Domain 1	Domain 2	Domain 3	Domain 4	Domain 5	Domain 6	
1	NCCN - Clinical Practice Guidelines in Oncology: Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer	86	75	88	97	60	88	Included
2	Non-epithelial ovarian cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up	81	72	96	94	44	83	Included
3	JSGO - Guidelines for the treatment of ovarian cancer, fallopian tube cancer, and primary peritoneal cancer	81	69	84	94	48	92	Included
4	BGCS - Ovarian, tubal and primary peritoneal cancer guidelines: Recommendations for practice update 2024	72	53	81	72	56	88	Excluded
5	GCIG - Consensus Review for Ovarian Sex Cord Stromal Tumors	58	58	55	64	31	33	Excluded
6	CMS Definition Guideline for Ovarian Cancer	92	58	56	47	85	38	Excluded
7	ESGO - Guidelines for the management of non-epithelial ovarian cancers in adolescents and young adults	92	86	82	94	67	46	Included
	BGCS - British Gynaecological Cancer Society, CMS - Council for Medical Schemes, GCIG - Gynaecologic Cancer InterGroup, ESGO - European Society of Gynaecological Oncology, ESMO - European Society of Medical Oncology, JSGO - Japan Society of Gynaecologic Oncology, NCCN - National Comprehensive Cancer Network							

6.0 Review of evidence synthesis

Table 12. Comparison of guideline recommendations for clinical presentation and investigations for MOSCSTs

Clinical domain	NCCN	ESMO	JSGO	ESGO
History	Bloating, pelvis/abdomen pain, difficulty eating or feeling full quickly, urinary symptoms [urgency or frequency	Unilateral solid ovarian tumor Young age,	No data	Symptoms of hormonal excess – early secondary sexual characteristics, symptoms of androgen excess – deepening of voice, excess facial and body hair (hirsutism), acne, male-pattern baldness, deepening of the voice, increased muscle mass, a decreased breast size, and clitoromegaly, menstrual irregularities
Examination	Suspicious/ palpable pelvic mass on abdomen/ pelvis exam and/or ascites, abdominal distention		No data	Features of isosexual precocious puberty – early breast development, pubic and axillary hair growth, body odour, and menstruation (menarche) Features of virilization
Imaging	Pelvic Ultrasound	Pelvic Ultrasound	No data	Pelvic Ultrasound
	Abdominal - Pelvic CT scan	Computed tomography (CT) scan	No data	Abdomino-Pelvic computed tomography (CT) scan
	Chest CT scan	chest X-ray	No data	Chest X-ray
	PET/CT, MRI, or PET/MRI may be indicated for indeterminate lesions OR metastatic disease	PET Scan	No data	Positron emission tomography (PET) scan in selected cases
Tumor markers	CA 125, BHCG, AFP, LDH, other tumor markers as clinically indicated	Quantitative hCG, AFP, LDH, and cancer antigen	No data	Serum AFP, β-HCG, CA-125, inhibin, AMH, calcium, and LDH are required

Clinical domain	NCCN	ESMO	JSGO	ESGO
		125 (CA 125) should be measured preoperatively		
Other tumor markers	CEA, CA 19-9, and HE4	No data	No data	Estrogen, dehydroepiandrosterone, testosterone, luteinizing hormone, and follicle-stimulating hormone are also required with signs of hormonal production.
Other tests	No data	Karyotype if gonadoblastoma is suspected	No data	SLCT or gonadoblastoma, screened for other disorders associated with DICER1 syndrome, especially thyroid disease
Histology	Surgical histopathological diagnosis is required	Histopathology by gynaecological pathologists A two-tiered grading (low and high grades) system	No data	Histology Grade (well, moderate, poorly differentiated) and the presence of specific histologic features such as retiform pattern or presence of heterologous elements (mucinous glandular, skeletal muscle, or cartilage).
IHC		immunopanel of inhibin A, calretinin, and FOXL2 to confirm adult granulosa cell tumor SMARCA4 for the diagnosis of SCCOHT	No data	Calretinin, CD56, melan A, CD99, steroidogenic factor-1 (SF-1), FOXL2, and WT1
CT Scan – Computed Tomography Scan, DICER1 - Double-stranded RNA-specific endoribonuclease (Dicer 1, ribonuclease III), FOXL2 – Forkhead Box L2, EMA – Epithelial Membrane Antigen, ESMO – European Society for Medical Oncology, IHC – Immunohistochemistry, JSGO – Japanese Society for Gynaecologic Oncology, ESGO – European Society for Gynaecologic Oncology, MRI – Magnetic Resonance Imaging, NCCN – National Comprehensive Cancer Network, PET-CT – Positron Emission Tomography Computed Tomography, SCCOHT – Small Cell Carcinoma of the Ovary -Hypercalcemic type, SLCT – Sertoli Leydig Cell Tumor, SMARCA4 - SWI/SNF (Switch/Sucrose Non-Fermentable)-Related, Matrix-Associated, Actin-Dependent Regulator of Chromatin, Subfamily A, Member 4, WT1 – Wilms Tumor Protein 1,				

Table 13. Comparison of guideline recommendations for primary treatment of early-stage (FIGO Stage I) MOSCSTs with desired fertility preservation

FIGO stage	NCCN	ESMO	JSGO	ESGO
Stage I **IA** **IB** **IC**	Unilateral salpingo-oophorectomy (USO) + Comprehensive surgical staging after completing childbearing	Fertility Sparing Surgery and staging, Fertility not desired - comprehensive staging Retroperitoneal evaluation is not mandatory	USO (affected side) + OMT + peritoneal cytology + biopsies from sites in the abdominal cavity	Unilateral Salpingo-oophorectomy; comprehensive staging FSS – USO or BSO with uterus sparing; Cystectomy not recommended
ESGO – European Society for Gynaecologic Oncology, ESMO – European Society for Medical Oncology, JSGO – Japanese Society for Gynaecologic Oncology, NCCN – National Comprehensive Cancer Network, OMT – Omentectomy, USO – Unilateral Salpingo-oophrectomy, *∞ 47% of patients with granulosa cell tumors have atypical hyperplasia or endometrial carcinoma (13)*				

Table 14. Comparison of guideline recommendations for primary treatment of MOSCSTs with do desired fertility or fertility-sparing not indicated

FIGO Stage	NCCN	ESMO	JSGO	ESGO
Stage I **IA** **IB** **IC**	Comprehensive staging and surgery - TAH+ BSO+ Omentectomy	Comprehensive staging and surgery – TAH+ BSO+ Omentectomy biopsy of the diaphragmatic peritoneum, paracolic gutters, pelvic peritoneum, and peritoneal washings in macroscopic stage I disease	Comprehensive staging and surgery - TAH+ BSO+ Omentectomy	Comprehensive staging and surgery - TAH+ BSO+ Omentectomy
Stage II to IV	Hysterectomy+BSO + Comprehensive staging as needed -	Debulking surgery and staging	Hysterectomy+BSO + Comprehensive staging as needed - Neoadjuvant	MDT decision; primary cytoreductive

FIGO Stage	NCCN	ESMO	JSGO	ESGO
	Neoadjuvant chemotherapy for poor surgical candidates or low likelihood of optimal cytoreduction		chemotherapy for poor surgical candidates or low likelihood of optimal cytoreduction Omit lymph node dissection	surgery (TAH+ BSO+ Infracolic omentectomy) + comprehensive surgical staging
BSO – Bilateral Salpingo-oophorectomy, ESGO – European Society for Gynaecologic Oncology, ESMO – European Society for Medical Oncology, GOSK – Gynaecologic Oncology Society of Kenya, JSGO – Japanese Society for Gynaecologic Oncology, NCCN – National Comprehensive Cancer Network, MDT – Multi-Disciplinary Team, TAH – Total Abdominal Hysterectomy,				

Table 15. Comparison of guideline recommendations for post-treatment surveillance for MOSCSTs

	FIGO stage	Clinical examination	Tumor markers	Imaging		Pro-screening
				Abdominopelvic ultrasound	Abdominopelvic MRI	
ESGO	Stage I IA & IB	Every 4 months for 2 years, then annually	Every 4 months for 2 years, then annually	Every 4 months for 2 years, then annually	Not Indicated	Beginning of treatment, 2 to 5 years follow-up
	IC	Every 4 months for 2 years; then every 6/12 for 5 years, then annually.	Every 4 months for 2 years, then every 6/12 months for 5 years, then annually	Every 4 months for 2 years, then every 6/12 for 5 years, then annually	Every 6 months for 2 years	
	Stage II & III	Every 2-4 months for 2 years, then 6-monthly for 5 years, then annually	Every 2-4 months for 2 years, then 6-monthly for 5 years, then annually	If FSS, every 4 months for 2 years; then every 6 months for 5 years, then annually	Every 6 months for 6 years	
	Stage IV	As clinically indicated	As clinically indicated	As clinically indicated	As clinically indicated	No data
NCCN	Time 0-2 Years	6–12 months if early-stage, low-risk disease. 4–6 months if high-risk disease	Testing as clinically indicated, if applicable •If done, frequency based on stage (i.e., 6–12 months if early-stage, low-risk disease; 4–6 months if high-risk disease)	Reserved for patients with symptoms, elevated biomarkers, or suspicious findings on physical exam. Imaging - Chest x-ray, C/A/P CT, MRI, PET/CT, or PET (with contrast unless contraindicated)		No data

	FIGO stage	Clinical examination	Tumor markers	Imaging		Pro-screening
				Abdominopelvic ultrasound	Abdominopelvic MRI	
ESGO	Stage I IA & IB	Every 4 months for 2 years, then annually	Every 4 months for 2 years, then annually	Every 4 months for 2 years, then annually	Not Indicated	Beginning of treatment, 2 to 5 years follow-up
	IC	Every 4 months for 2 years; then every 6/12 for 5 years, then annually.	Every 4 months for 2 years, then every 6/12 months for 5 years, then annually	Every 4 months for 2 years, then every 6/12 for 5 years, then annually	Every 6 months for 2 years	
	Stage II & III	Every 2-4 months for 2 years, then 6-monthly for 5 years, then annually	Every 2-4 months for 2 years, then 6-monthly for 5 years, then annually	If FSS, every 4 months for 2 years; then every 6 months for 5 years, then annually	Every 6 months for 6 years	
	Stage IV	As clinically indicated	As clinically indicated	As clinically indicated	As clinically indicated	No data
	After 2 years	As clinically indicated based on stage (that is 6–12 months if early-stage, low-risk disease; 4–6 months if high-risk disease)	•Testing as clinically indicated, if applicable • If done, frequency based on stage (ie, 6–12 months if early-stage, low-risk disease; 4–6 months if high-risk disease)	Reserved for patients with symptoms, elevated biomarkers, or suspicious findings on physical exam Imaging - Chest x-ray, C/A/P CT, MRI, PET/CT, or PET (with contrast unless contraindicated)		
Notes on surveillance - ESGO						
	Imaging - Reserved for patients with symptoms, elevated tumor markers, or suspicious findings on clinical examination					
	PRO - Should use a standardized age-appropriate questionnaire to screen for psychological (late) effects					
	Abdominal-Pelvic US - for patients with residual ovary or limited access to MRI					
	Clinical examination - include monitoring for potential toxicities (organ, endocrine, hearing)					
CT Scan – Computed Tomography Scan C/A/P = Chest/Abdomen/Pelvis, ESGO – European Society for Gynaecologic Oncology, ESMO – European Society for Medical Oncology, FSS = Fertility Sparing Surgery, IHC – Immunohistochemistry, NCCN – National Comprehensive Cancer Network, MRI – Magnetic Resonance Imaging, PET-CT – Positron Emission Tomography Computed Tomography, PRO - Patient Reported Outcomes						

Table 16. Comparison of guideline recommendations for management of recurrent MOSCSTs

FIGO stage	NCCN	ESMO	JSGO	ESGO
Stage I IA IB IC Stage II IIA IIB Stage III IIIA1 IIIA2	Consider secondary Cytoreductive surgery. or Recurrence therapy: Localized RT to palliate symptoms or oligometastatic disease Chemotherapy - Carboplatin/Paclitaxel preferred. Other regimen: • EP, if not previously used • Paclitaxel/Ifosfamide • Docetaxel • Paclitaxel Supportive care only	BEP regimen for three cycles or Six cycles of carboplatin/paclitaxel are recommended for postoperative (secondary CRS) chemotherapy and patients with recurrent MOSCSTs	Surgery or radiation therapy (palliative) is suggested for patients with localized residual lesions Drug therapy is recommended for patients who are not eligible for surgery	There is no standard treatment. Clinical trials with new drugs tailored to the biology of the tumor are strongly recommended.

FIGO stage	NCCN	ESMO	JSGO	ESGO
IIIB	Targeted therapy: Bevacizumab (single agent) Aromatase inhibitors (ie, anastrozole, letrozole) • Leuprolide acetate or goserelin acetate (for granulosa cell tumors) • Tamoxifen • BEP (if not used before) • VAC Option of a clinical trial			
IIIC				
Stage IV				
IVA				
IVB				

BEP – Bleomycin Etoposide Cisplatin, EP – Etoposide Paclitaxel, ESGO – European Society for Gynaecologic Oncology ESMO – European Society for Medical Oncology, JSGO – Japanese Society for Gynaecologic Oncology MOSCSTs - Sex Cord Stroma Tumors, NCCN – National Comprehensive Cancer Network, RT - Radiotherapy, VAC - Vincristine Doxorubicin (Adriamycin) Cyclophosphamide,

Table 17 Comparison of guideline recommendations for chemotherapy treatment regimens for MOSCSTs

Regimen/Agent	Dosage	Guideline
BEP – Bleomycin + Etoposide + Cisplatin	Three (early disease) or four cycles (locally advanced and recurrent disease) Weekly Bleomycin 30,000 IU Day 1 – 5: • Cisplatin 20mg/m^2 IV infusion, • Etoposide 100 mg/m^2 IV infusion Repeated every 21 days	NCCN, ESMO, ESGO,
VIP – Vepeside (Etoposide) + Ifosfamide + Cisplatin	Every 21 days, 4 cycles equivalent to BEP 4 cycles Etoposide 75 mg/m² IV days 1–5; Ifosfamide 1,200 mg/m² IV days 1–5; Cisplatin 20 mg/m² IV days 1–5	NCCN, ESMO, ESGO,
VAC – Cyclophosphamide+ Dactinomycin-Vincristine	Four cycles Day 1: Mesna 500mg/m^2 Intravenous infusion in 100ml sodium chloride 0.9% over 15minutes. Cyclophosphamide 1500mg/m^2 + Mesna 1500/m^2 Intravenous infusion in 1000ml sodium chloride 0.9% over 3 hours. Mesna 600mg/m^2 Oral. Take 0, 2, and 6 hours post-cyclophosphamide infusion (in take-home medicines) Vincristine 1.5mg/m^2 (max 2mg) 1 Intravenous bolus in 50ml sodium chloride 0.9% over 10minutes Actinomycin D 750mcg/m^2 (max 1500mcg) Day 2: Actinomycin D 750mcg/m^2 (max 1500mcg) Every 21 days,	NCCN
EP – Etoposide + Cisplatin	Four cycles Etoposide 100 mg/m^2 and Cisplatin 20 mg/m^2 on days 1 to 5 Every 21 days	NCCN, ESGO
PEI – Ifosfamide + Cisplatin + Etoposide	Three or four cycles Ifosfamide at 2.5 g/m^2 on days 1 and 2 (with intravenous Mesna protection at 600 mg/m^2 every 6 hours on days 1 and 2), followed by Cisplatin at 33 mg/m^2 and etoposide at 100 mg/m^2, both on days 3–5. Every 21 days	NCCN, JSGO, ESMO
TC – Taxane (Paclitaxel or Docetaxel) + Carboplatin	Six Cycles IV infusion Docetaxel 75mg/m^2 or Paclitaxel 175mg/m² and Carboplatin AUC 5 or 6* (6 cycles or neoadjuvant treatment, 3 cycles before surgery, and then 3 cycles post-surgery Every 21 days Carboplatin dose calculated using the Calvert equation: Carboplatin dose (mg) = AUC (CrCl +25).	NCCN, ESGO, ESMO
Bevacizumab	Every 21 days 15mg/kg as an infusion given over 90 minutes for the initial dose; if tolerated, the next infusion can be given over 60 minutes; thereafter, it can be given over 30 minutes. It can be given in 100ml Sodium Chloride, provided the final solution stays within the range of 1.4-16.5 mg/ml	NCCN, JSGO, ESGO

Regimen/Agent	Dosage	Guideline
Paclitaxel Monotherapy	Metastatic Disease (failure of initial chemotherapy or relapse within 6 months following adjuvant chemotherapy): 175 mg/m² IV over 3 hours every 3Weeks	NCCN, ESGO, ESMO
Docetaxel monotherapy	Metastatic Disease (failure of initial chemotherapy or relapse within 6 months following adjuvant chemotherapy): 60-100 mg/m² IV over 1 hr every 3 Weeks	NCCN, ESMO
Tamoxifen	20 mg orally daily for 5 years	NCCN
Leuprolide	3.75mg every 4 weeks or 11.25mg every 12 weeks, administered as a single subcutaneous or intramuscular injection until disease progression or unacceptable toxicity develops	NCCN
Letrozole	2.5mg daily orally as indicated until disease progression or unacceptable toxicity	NCCN
Anastrozole	1mg daily orally as indicated until disease progression or unacceptable toxicity. Supplementation with calcium and vitamin D, along with regular weight-bearing exercise, is recommended. A bisphosphonate should be considered if clinically indicated	NCCN
GNRH agonist	Subcutaneous Goserelin 3.6mg every 4 weeks or 12.8mg every 12 weeks	NCCN, ESMO
AUC – Area under the curve, CrCl – creatinine clearance, ESGO – European Society for Gynaecologic Oncology, ESMO – European Society for Medical Oncology, JSGO – Japanese Society for Gynaecologic Oncology, MOSCSTs - Sex Cord Stroma Tumors, NCCN – National Comprehensive Cancer Network,		

7.0 GOSK recommendations

TABLE 18. GOSK recommendations for clinical evaluation and investigations for MOSCSTs

Clinical domain	GOSK recommendations
History	A comprehensive history and physical examination should assess features of pelvic mass effect, including abdominal pain, bloating, abdominal distension, early satiety, and urinary symptoms such as urgency or frequency, as well as manifestations of hormonal activity including menstrual irregularities, postmenopausal bleeding, precocious puberty, and signs of virilization or defeminization such as hirsutism, acne, male-pattern baldness, voice deepening, clitoromegaly, increased muscle mass, and decreased breast size. Detailed family history and consideration of genetic evaluation should be undertaken in patients with suspected Double-Stranded RNA-Specific Endoribonuclease 1 (DICER1)-associated disease.
Examination	A comprehensive abdominal and pelvic examination should be performed to assess for a suspicious or palpable pelvic mass, ascites, abdominal distension, and other signs suggestive of advanced disease, as well as features of isosexual precocious puberty including early breast development, pubic and axillary hair growth, body odour, and menstruation (menarche), and signs of virilization such as hirsutism, deepening of the voice, and clitoromegaly.
Imaging	First-line imaging evaluation should include pelvic ultrasound (transvaginal or transabdominal) to characterize the adnexal mass and assess for associated endometrial pathology. Further imaging work-up should include an abdominopelvic CT scan or MRI for staging, assessment of tumor extent, peritoneal spread, and lymph node involvement. Chest imaging with chest X-ray or CT scan should be performed to evaluate thoracic metastases. PET-CT may be considered in selected patients with recurrent, metastatic, or advanced disease.
Tumor markers	Recommended tumor markers for diagnostic work-up include Inhibin A and B, CA 125, and Anti-Müllerian Hormone (AMH) to support diagnosis AFP, hCG, and LDH are recommended to exclude other ovarian tumors, particularly germ cell tumors.
	Hormonal profiling, including estrogen, dehydroepiandrosterone, testosterone, luteinizing hormone, and follicle-stimulating hormone, should be guided by the presence of clinical features suggestive of hormonal activity.
Other tumor markers and tests	Carcinoembryonic antigen (CEA) should be considered where gastrointestinal tract malignancy is suspected in the differential diagnosis.
	Serum calcium levels should be assessed in patients with suspected Small Cell Carcinoma of the Ovary, Hypercalcemic Type (SCCOHT).
	Thyroid function tests should be performed in patients with suspected Sertoli-Leydig cell tumors (SLCTs) or gonadoblastomas because of their association with Double-Stranded RNA-Specific Endoribonuclease 1 (DICER1) syndrome.
	Karyotyping should be carried out if gonadoblastoma is suspected to rule out gonadal dysgenesis
Histology	Histopathological confirmation should be obtained before initiation of adjuvant therapy.
	Histopathology reports should include a two-tier grading system (low-grade or high-grade) where applicable

Clinical domain	GOSK recommendations
	Histopathology reports should document specific histologic features associated with prognosis and treatment planning, including retiform pattern and heterologous elements such as mucinous glandular, skeletal muscle, or cartilaginous differentiation.
	Endometrial sampling should be performed in adult patients with granulosa cell tumors to exclude concomitant endometrial hyperplasia or carcinoma.
	Endometrial sampling is not routinely recommended in adolescents and young adults; however, transvaginal ultrasound assessment of the endometrium should be performed where clinically indicated
Immuno-histochemistry	Immunohistochemistry should be performed in morphologically ambiguous cases or where histopathological diagnosis is equivocal. Also useful in identifying MOSCSTs at high risk of recurrence.
	Recommended immunohistochemical markers include inhibin-α, calretinin, Steroidogenic Factor-1 (SF-1), and FOXL2, particularly in suspected adult granulosa cell tumors.
	FOXL2 mutational analysis should be considered in suspected adult granulosa cell tumors where diagnostic uncertainty persists.
	Additional immunohistochemical markers, including WT1, CD56, CD99, and estrogen/progesterone receptors, may be used as adjunct markers depending on tumor morphology and differential diagnosis.
	SMARCA4 immunohistochemistry should be performed in cases suspicious for Small Cell Carcinoma of the Ovary, Hypercalcemic Type (SCCOHT).
	Estrogen/Progesterone Receptors are often positive in the granulosa/thecoma group and are useful in guiding hormonal therapy
AFP – Alpha-foetal protein, MH - Anti-Müllerian Hormone, CA 125 – Cancer Antigen 125, CEA – Carcinoembryonic antigen, CT – Computed Tomography, DICER – Dicer Endoribonuclease, FDG PET scan - Fluorodeoxyglucose Positron Emission Tomography, FOXL2 - Forkhead box protein L2 , hCG – Human chorionic gonadotropin, IHC – Immunohistochemistry, LDH – Lactate Dehydrogenase, SLCT – Sertoli Leydig Cell tumor, SCCOHT – Small cell carcinoma of the ovary hypercalcemic type, TAS - Transabdominal Scan, TVS – Transvaginal Scan	

Table 20. GOSK recommendations for fertility-sparing primary management of early-stage MOSCSTs

FIGO stage	GOSK recommendations
IA/IB/IC	Facilitate early referral and cross-consultation with a reproductive endocrinologist and infertility (REI) specialist for patients undergoing fertility preservation.
	Fertility-sparing unilateral salpingo-oophorectomy of the affected ovary, with omentectomy, peritoneal washings for cytology, and peritoneal biopsies from the diaphragmatic peritoneum, paracolic gutters, and pelvic peritoneum, should be performed.
	Bilateral salpingo-oophorectomy with uterine preservation may be considered in selected patients with suspected bilateral disease.
	Routine retroperitoneal lymphadenectomy is not mandatory unless lymph nodes are clinically or radiologically suspicious.
	Routine biopsy of the contralateral ovary is not recommended if grossly normal, as bilaterality is exceedingly rare
	Endometrial assessment and endometrial sampling should be performed in patients with adult granulosa cell tumors.
	Intensive and prolonged surveillance is recommended: physical examination, tumor markers, and pelvic ultrasound every 6 months for at least 3 years, then annually indefinitely
	Completion surgery should be recommended after completion of childbearing.
	Fertility-sparing surgery is not recommended in high-risk histologies, including Small Cell Carcinoma of the Ovary Hypercalcemic Type (SCCOHT) and Sertoli-Leydig Cell Tumor with retiform or sarcomatous pattern.
	Ovarian cystectomy alone is not recommended for suspected or confirmed malignant disease because of the risk of residual disease and recurrence.

Table 21 GOSK recommendations for adjuvant management of early-stage MOSCSTs following fertility-sparing surgery

FIGO stage	GOSK recommendations
IA & IB	Active surveillance is recommended following complete surgical staging in low-risk disease.
IC	Adjuvant chemotherapy should be considered in the presence of high-risk histopathologic features, including high-grade tumors, mesenchymal heterologous elements, or retiform pattern. Sarcoma-type regimens to be considered include Carboplatin / Paclitaxel, Cisplatin/Etoposide/Ifosfamide, and Vincristine/Dactinomycin/Cyclophosphamide
	Recommended regimens include Bleomycin, Etoposide, and Cisplatin (BEP) for 3 cycles

	Alternative regimens include etoposide and cisplatin (EP), carboplatin/paclitaxel, or platinum monotherapy in selected patients, e.g., patients unable to tolerate combination chemotherapy or those with severe comorbidities.
	Fertility preservation counselling and cross consultation with a reproductive endocrinology and infertility (REI) specialist should be undertaken before initiation of therapy.

Table 22. GOSK recommendations for early-stage MOSCSTs where fertility preservations is not desired nor indicated

FIGO stage	GOSK recommendations
I-II	Comprehensive surgical staging and cytoreductive surgery is the recommended first-line management A midline vertical abdominal incision is recommended for adequate exposure and evaluation of the whole abdomen Minimally invasive surgical techniques (laparoscopy or robotic surgery) may be performed to accomplish surgical staging for selected patients based on preoperative imaging, such as computed tomography (CT), magnetic resonance imaging, or positron emission tomography/CT Before systemic exploration, free peritoneal fluid should be aspirated for cytology. Peritoneal washing with at least 50 to 100 mL of saline should be obtained in case of no free fluid in the peritoneal cavity Inspection and palpation of all peritoneal surfaces, including diaphragms, serosa, and mesentery of the entire gastrointestinal tract, should be performed Multiple intraperitoneal biopsies from the cul-de-sac, vesical peritoneum, both pelvic sidewalls, and both paracolic gutters should be conducted in case of no evidence of disease
III - IV	Multidisciplinary team (MDT) management involving gynaecologic oncology, medical oncology, pathology, and radiology specialists is recommended.
	Upfront cytoreductive surgery is recommended as the primary treatment. It should be performed where a complete or optimal gross resection is considered feasible. Stage III or IV disease does not require cytologic assessment The ovarian tumor should be removed intact, and a frozen biopsy is strongly recommended during the operation if possible. Hysterectomy with bilateral salpingo-oophorectomy should be carried out Tumors throughout the abdomen should be removed as much as possible. All visible and palpable tumor volume should be resected as much as possible with debulking operations, such as visceral and parietal peritonectomy Omentectomy (infracolic or infragastric) should be fulfilled during surgical staging Retroperitoneal inspection should be carried out to check for metastasis to pelvic and para-aortic lymph nodes. Enlarged nodes should be resected.
	Neoadjuvant chemotherapy followed by interval cytoreductive surgery should be considered in patients who are poor surgical candidates or where optimal cytoreduction is unlikely to be achieved with primary surgery. Pathologic diagnosis should be obtained before neoadjuvant chemotherapy (NACT). The methods for pathologic diagnosis of MOSCSTs are as follows: laparoscopic biopsy, image-guided core biopsy or aspiration, or cell block from ascitic fluid aspiration.
	Routine pelvic and para-aortic lymphadenectomy is not recommended unless lymph nodes are clinically or radiologically suspicious
	For SCCOHT (any stage): Management should include comprehensive surgical staging with total abdominal hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, pelvic and para-aortic lymphadenectomy, and platinum-based chemotherapy.

Table 23. GOSK recommendations for adjuvant treatment of MOSCSTs with no desired fertility nor indication

FIGO stage	GOSK recommendations
IA/IB/IC1	Active surveillance is recommended following primary cytoreductive surgery and complete surgical staging in low-risk disease.
	For poorly differentiated or mesenchymal heterologous elements or retiform pattern, and Sertoli-Leydig cell tumors (SLCT), adjuvant chemotherapy should be considered The preferred chemotherapy regimen is Bleomycin, Etoposide, and Cisplatin (BEP). Alternative regimens include carboplatin/paclitaxel, Etoposide plus Cisplatin (EP), or platinum monotherapy. For SLCT with mesenchymal elements: consider sarcoma-type regimens with Ifosfamide (PEI/VIP or PEI/VAC)
IC2/IC3/II	Adjuvant chemotherapy with BEP 3-4 cycles is recommended for patients below 40 years. Patients with high-grade MOSCSTs should receive 4 cycles of BEP. For patients above 40 years or with chronic pulmonary disease, EP or TC 6 cycles is the preferred regimen
III - IV	Adjuvant Chemotherapy with BEP 4 cycles is recommended for patients below 40 years. The preferred regimen for patients > 40 yrs or with chronic pulmonary disease is Carboplatin/Paclitaxel or EP. Radiotherapy may be used for localized residual lesions after primary/interval cytoreductive surgery and adjuvant chemotherapy

Table 94. GOSK recommendations for management of chemoresistant MOSCSTs

FIGO stage	GOSK recommendations
All FIGO stages	A multidisciplinary team (MDT) decision is recommended for individualized care. The MDT team should include a gynaecological oncologist, a radiologist, a pathologist, a medical oncologist, and a palliative care expert.
	Localized radiotherapy is recommended for palliation of symptoms, or oligometastatic disease, or localized residual lesion
	Chemotherapy with Carboplatin/Paclitaxel if BEP was the primary chemotherapy, or VAC or BEP if not used before, is recommended.
	Regimens including Etoposide/Cisplatin, Paclitaxel/Ifosfamide, and Taxane monotherapy may be considered if the second-line regimen is not tolerated or cross-resistance is suspected
	Targeted therapy with Bevacizumab (single agent or combination with chemotherapy) is recommended
	Hormonal therapy for ER and PR positive tumors with aromatase inhibitors (letrozole or anastrozole), or Tamoxifen is recommended. Gonadotropin-releasing hormone (GnRH) agonists (leuprolide or goserelin) are recommended for chemoresistant granulosa cell tumors
	Recommend enrolment in clinical trials for novel treatments if accessible.
	Facilitate early palliative care referral and provide the best available supportive care throughout the patient care journey.
BEP- Bleomycin, Etoposide, Cisplatin; ER – Estrogen Receptor, MDT – Multidisciplinary Team, PR- Progesterone Receptor, VAC – Vincristine, ActinomycinD, Cyclophosphamide	

Table 25. GOSK recommendations for management of recurrent MOSCSTs

FIGO stage	GOSK recommendations
IA-IVB	Individualized care by an MDT is recommended. The MDT should include a gynecological oncologist, a radiologist, a pathologist, a medical oncologist, and a palliative care expert.
	Secondary cytoreductive surgery is the preferred treatment if complete gross resection of the recurrent tumor is feasible. Surgery may also be carried out to palliate symptoms like bowel obstruction.
	Secondary cytoreductive surgery should be followed by any of the recurrence therapy modalities or targeted therapy, taking into consideration previous treatments and toxicities, disease-free interval, performance status, and comorbidities
	Systemic platinum-based chemotherapy with Carboplatin/Paclitaxel is recommended after secondary cytoreductive surgery or in patients with multiple or unresectable recurrences. Alternative regimens include EP, Paclitaxel/Ifosfamide/Cisplatin (TIP), or BEP if not used before, and no preexisting lung disease
	Targeted therapy with Bevacizumab as a single agent or in combination with chemotherapy is recommended
	Hormonal therapy for ER and PR positive tumors with aromatase inhibitors (letrozole or anastrozole), or Tamoxifen is recommended. Gonadotropin-releasing hormone (GnRH) agonists (leuprolide or goserelin) are recommended for recurrent granulosa cell tumors
	Localized radiotherapy may be used to palliate symptoms or for oligometastatic disease, inoperable disease, or residual disease Where accessible modern techniques like stereotactic body radiotherapy (SBRT) are recommended, as they can achieve high local control with limited toxicity
	Recommend enrolment in clinical trials for novel treatments if accessible.
	Facilitate early palliative care referral and provide the best available supportive care throughout the patient care journey.
BEP- Bleomycin, Etoposide, Cisplatin, EP – Etoposide, Cisplatin, ER – Estrogen Receptor, MDT – Multidisciplinary Team, PR- Progesterone Receptor, VAC – Vincristine, Actinomycin D, Cyclophosphamide	

Table 26. GOSK recommendations for managements of MOSCSTs in special circumstances

Circumstance	GOSK recommendations
Unstaged disease – incidental following ovarian cystectomy	If fertility preservation is desired, completion surgery with unilateral salpingo-oophorectomy of the affected ovary and staging with omentectomy, peritoneal washings for cytology, and peritoneal biopsies from the diaphragmatic peritoneum, paracolic gutters, and pelvic peritoneum should be performed. Routine random biopsies of a normal-appearing contralateral ovary are not recommended If fertility preservation is not desired or indicated due to suspected advanced-stage disease, comprehensive surgical staging and cytoreductive surgery is the recommended first-line management
Incomplete staging	Secondary surgical staging is recommended. Radiological staging with contrast-enhanced computed tomography (CECT) scans of the abdomen, pelvis, and chest, and/or Positron Emission Tomography (PET) scan is an acceptable alternative.

	Fertility-sparing surgery for early-stage disease may be considered if fertility preservation is desired.
Suspected MOSCSTs, but the patient is unfit for staging surgery	Image-guided core biopsy for histopathological diagnosis and CECT of the chest, abdomen, and pelvis for staging are recommended. Fluorodeoxyglucose (FDG) PET/CT scan may be used in cases with elevated tumor markers but inconclusive CT findings
Suspected advanced MOSCSTs not amenable to primary cytoreductive surgery	Image-guided core biopsy for histopathological diagnosis is recommended. CECT scan of the abdomen, pelvis, and chest for metastatic workup and staging is recommended. Neoadjuvant chemotherapy (NACT) with BEP 3 cycles or Carboplatin/Paclitaxel 3 cycles is recommended Assess for interval cytoreductive surgery after NACT
Ovarian MOSCSTs in pregnancy	Facilitate urgent referral to a tertiary hospital with a specialist MDT involving gynecologic oncology, maternal-fetal medicine, radiology, neonatology, anesthesia, and pathology. Individualized care is recommended, taking into consideration gestational age, tumor histology and stage, symptoms (acute vs. incidental finding), and the patient's fertility desires. Initial assessment with ultrasound (and MRI if needed) to determine size, complexity, and radiological staging is recommended Perform inhibin B levels for suspected granulosa cell tumors and Testosterone levels for SLCT – The two tumor markers are typically not affected by normal pregnancy Definitive surgical management: defer to optimal gestation for delivery if asymptomatic; consider caesarean section with concurrent staging and cytoreductive surgery. The recommended extent of surgery is similar to that of a nonpregnant individual. Emergency fertility-sparing unilateral oophorectomy is recommended if torsion or rupture with haemorrhage occurs; a laparoscopic approach may be used for pregnancy less than 20 weeks. Patients with large tumor size should undergo surgical intervention, preferably scheduled in the second trimester (14-20 weeks), to minimize pregnancy risks. NACT and adjuvant chemotherapy in pregnancy are only recommended for advanced-stage (III-IV) or aggressive subtypes (e.g., poorly differentiated Sertoli-Leydig cell tumors, juvenile granulosa cell tumors) Where chemotherapy is indicated during pregnancy, carboplatin/paclitaxel is preferred over BEP due to bleomycin toxicity (foetal leukaemia and pulmonary toxicity) Adjuvant chemotherapy, similar to that of a nonpregnant individual, should be deferred until 4-6 weeks postpartum.
BEP- Bleomycin, Etoposide, Cisplatin, MDT – Multidisciplinary Team, SLCT – Sertoli Leydig Cell Tumor, MRI - Magnetic Resonance Imaging	

Table 27. GOSK recommendations for chemotherapy treatment regimens, dosage, and scheduling for MOSCSTs

Regimen/Agent	**Dosage and scheduling**
BEP – Bleomycin + Etoposide + Cisplatin	**Either of the two protocols is recommended:** **Protocol – 1** Administered every 21 days Three (nonmetastatic disease) or four cycles (metastatic and recurrent disease) - Weekly Bleomycin 30,000 IU (lifetime total cumulative dose not to exceed 360,000 IU in the elderly and 400,000 IU in other patients) - Day 1 – 5: • Cisplatin 20mg/m^2 IV infusion and • Etoposide 100 mg/m^2 IV infusion **Protocol – 2 >** Administered every 21 days, three cycles, for patients aged <40 - Bleomycin 30,000 IU on days 2, 8, and 15. - Etoposide 165mg/m^2 on days 1, 2, and 3. - Cisplatin 50mg/m^2 days 1 and 2
EP – Etoposide + Cisplatin	Every 21 days, four cycles Etoposide 100 mg/m^2 Cisplatin 20 mg/m^2 on days 1 - 5
VIP – Vepeside (Etoposide) + Ifosfamide + Cisplatin	Every 21 days, 4 cycles equivalent to BEP 4 cycles Etoposide 75 mg/m² IV days 1–5; Ifosfamide 1,200 mg/m² IV days 1–5; Cisplatin 20 mg/m² IV days 1–5
VAC – Vincristine+ Dactinomycin+ Cyclophosphamide	Every 21 days Day 1: - Mesna 500mg/m^2 Intravenous infusion in 100ml sodium chloride 0.9% over 15minutes. - Cyclophosphamide 1500mg/m2 + Mesna 1500/m^2 Intravenous infusion in 1000ml sodium chloride 0.9% over 3 hours. - Mesna 600mg/m^2 Oral. Take 0-, 2-, and 6-hours post-cyclophosphamide infusion (in take-home medicines) - Vincristine 1.5mg/m^2 (max 2mg) 1 Intravenous bolus in 50ml sodium chloride 0.9% over 10minutes

Regimen/Agent	Dosage and scheduling
	- Actinomycin D 750mcg/m^2 (max 1500mcg) Day 2: - Actinomycin D 750mcg/m^2 (max 1500mcg)
PEI – Ifosfamide + Cisplatin + Etoposide	Every 21 days, three or four cycles Ifosfamide at 2.5 g/m^2 on days 1 and 2 (with intravenous Mesna protection at 600 mg/m^2 every 6 hours on days 1,2) Cisplatin at 33 mg/m^2 and Etoposide at 100 mg/m^2, both on days 3–5.
TC – Taxane (Paclitaxel or Docetaxel) + Carboplatin	Every 21 days, Six Cycles Docetaxel 75mg/m^2. IV infusion or Paclitaxel 175mg/m² and Carboplatin AUC 5 or 6* (6 cycles for neoadjuvant treatment given 3 cycles before surgery and then 3 cycles post-surgery) Carboplatin dose calculated using the Calvert equation: Carboplatin dose (mg) = AUC (CrCl +25).
Bevacizumab	Every 21 days 15mg/kg as an infusion given over 90 minutes for the initial dose; if tolerated, the next infusion can be given over 60 minutes; thereafter, it can be given over 30 minutes. It can be given in 100ml sodium chloride, provided the final solution stays within the range of 1.4-16.5 mg/ml
Paclitaxel Monotherapy	Every 3 Weeks Metastatic disease (failure of initial chemotherapy or relapse within 6 months following adjuvant chemotherapy): 175 mg/m² IV over 3 hours
Docetaxel monotherapy	Every 3 Weeks Metastatic Disease (failure of initial chemotherapy or relapse within 6 months following adjuvant chemotherapy): 60-100 mg/m² IV over 1 hour.
Tamoxifen	20 mg orally daily for 5 years
Leuprolide	3.75 mg once every 4 weeks or 11.25mg once every 12 weeks, subcutaneous or intramuscular injection until disease progression or unacceptable toxicity develops
Goserelin	3.6 mg subcutaneously every 4 weeks or 10.8 mg subcutaneously every 12 weeks.
Letrozole	2.5mg daily orally as indicated until disease progression or unacceptable toxicity
Anastrozole	1mg daily as indicated until disease progression or unacceptable toxicity.

Table 28. GOSK recommendations for post-treatment surveillance of MOSCSTs

Period	Disease stage	Clinical examination	Tumor markers	Imaging
0-2 years	Early-stage, low-risk disease	4–6 months	Every 6-12 months if initially elevated or with clinical features suggestive of recurrence	Reserved for patients with symptoms, elevated biomarkers, or suspicious findings on physical examination. May include chest X-ray, CT, MRI, FDG PET/CT, or PET, with contrast unless contraindicated
	High-risk disease	2–4 months	4–6 months if initially elevated or with clinical features suspicious of recurrence	
After 2 years	Early-stage, low-risk disease	6–12 months	6–12 months if initially elevated or with clinical features suggestive of recurrence	
	High-risk disease	4–6 months	4–6 months if initially elevated or with clinical features suggestive of recurrence	
Low Risk Disease • Stages I (Stage IA or IB) • Complete surgical resection • Favourable histology/differentiation, e.g., most adult granulosa cell tumors (AGCTs) and Sertoli-Leydig Cell Tumors (SLCTs) • Small tumors – less than 5 - 7 cm in diameter **High Risk Disease** • Advanced or metastatic stage disease, i.e., Stage II – IV • In complete surgical staging • Poorly differentiated histology, e.g., SCCOH histology, SLCT with heterologous elements • Recurrent disease • Large size tumor >10cm				
CT – Computed Tomography, FDG PET scan - Fluorodeoxyglucose Positron Emission Tomography, PET – Positron Emission Tomography, SCCOH – Small Cell Carcinoma of the Ovary Hypercalcaemic Type.				

Table 29. GOSK recommendations for post-treatment quality of life and survivorship for MOSCSTs

Domain	GOSK recommendations

Psychosocial support	Screen for anxiety, depression, and fear of recurrence; timely referral to psycho-oncology services as appropriate Recommend and refer to cancer support and survivor groups
Sexual health	Assess for dyspareunia, vaginal atrophy, and libido changes; offer lubricants, local estrogen, or specialist referral
Hormonal replacement therapy and surgical menopause	Because malignant ovarian sex cord stromal tumors (like granulosa cell tumors) are often hormonally active and hormone-sensitive, hormone replacement therapy (HRT) is generally not recommended. Estrogen can, in theory, promote the growth of any remaining microscopic cancer cells. If symptoms of surgical menopause are severe, review the cancer risk posed by HRT against the risks of premature osteoporosis and cardiovascular disease. Low-dose antidepressants: Medications such as Selective serotonin reuptake inhibitors (SSRIs), e.g., paroxetine, or serotonin and norepinephrine reuptake inhibitors (SNRIs), e.g., venlafaxine, are highly effective at reducing hot flashes.
Bone health	Routinely evaluate bone mineral density for patients with premature menopause or long-term gonadotropin-releasing hormone (GnRH) antagonist use; bisphosphonates, calcium, and vitamin D supplementation are recommended for patients with significant bone density loss.
Cardiovascular health	Risk factor modification; heightened awareness, as HRT is often contraindicated, or if the patient has declined
Return to work/education	Occupational therapy referral; flexible return-to-work planning; assist with school resumption
Lifestyle counselling	Link to smoking cessation, weight management, physical activity, and nutrition support programmes
Transition of care	**Adolescent to adult care** – Provide a structured transition for patients diagnosed in paediatric/adolescent settings; ensure continuity of surveillance **Palliative care integration** – Offer early referral for supportive care in recurrent or advanced disease; focus on symptom control and quality of life

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