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 germ cell tumors in Kenya - 2026

Steven M. Ibua[1,2], Innocent O. Maranga[1,2,3], Gonzaga Ngonyani[1,2], Anwar Z. Mohamed[1,2], Naomi N. Sitati[1,2], Stella N. Njenga[1,2], Gideon M. Mutua[1,2], Simon M. Gitau[1,2], Diana Marion[1,2], Bruce O. Semo[1,2,4], Isaac M. Maingi[1,2], Francis O. Abinya[1,2], Margaret Kilonzo[1,2], Eunice Cheserem[1,2], Alfred Mokomba[1,2], Wycliffe Musalia[1,2], Millicent Masinde[1,2], Benjamin E. Odongo[4], Jacqueline Chesang'[5], Victor T. Otieno[1,2], Rose J. Kosgei[1,2]

[1]Department of Obstetrics and Gynecology, University of Nairobi, Nairobi, Kenya
[2]Department of Obstetrics and Gynecology, Kenyatta National Hospital, Nairobi, Kenya
[3]School of Medical Sciences, Amref International University, Nairobi, Kenya
[4]Department of Obstetrics and Gynecology, Kenyatta University, Nairobi, Kenya
[5]Department of Public and Global Health, University of Nairobi, Nairobi, Kenya

***Correspondence:** smrefu@yahoo.com

DOI: 10.59692/fhn9g641

Copyright © 2026, The authors. Published by JOGECA. This is an open access article under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted reuse, distribution, and reproduction in any medium provided the original author(s) and the source are properly cited.

Abstract

Objective: To develop a standardized, evidence-based national clinical management protocol for malignant ovarian germ cell tumors in Kenya, under the auspices of the Gynaecologic Oncology Society of Kenya (GOSK). The protocol addresses diagnosis and diagnostic workup, stage-specific surgical and adjuvant management, follow-up and surveillance, management of recurrent and chemoresistant disease, and supportive and palliative care.

Methods: A guideline-adaptation methodology was used. A multidisciplinary panel convened by GOSK conducted a systematic search of PubMed and Google Scholar to identify existing international guidelines on MOGCT management. Six candidate guidelines were retrieved and independently appraised by 2 trained panelists using the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument across 6 quality domains. A tiebreaker mechanism was used to resolve disagreements. Guidelines that did not meet the prespecified thresholds for rigor of development and clarity of presentation were excluded. Recommendations from the retained guidelines were synthesized and contextualized to the Kenyan health care system and available resources.

Results: Of the 6 guidelines appraised, the following were evaluated: the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology; the American Society of Clinical Oncology (ASCO) guidelines; the British Gynaecological Cancer Society (BGCS) guidelines; the European Society of Gynaecological Oncology (ESGO) guidelines; the European Society for Medical Oncology (ESMO) guidelines; and the guidelines of the Council for Medical Schemes (CMS/PBS). Four guidelines (NCCN, ASCO, BGCS, and ESGO) met the prespecified quality thresholds and were retained for adaptation. The resulting protocol provides recommendations on clinical presentation and imaging; tumor marker and histopathological evaluation; fertility-sparing surgery and comprehensive surgical staging for early-stage disease; bleomycin, etoposide, and cisplatin (BEP)-based adjuvant and first-line chemotherapy for advanced disease; structured follow-up over a minimum 5-year surveillance period; management of recurrent and chemoresistant disease according to platinum sensitivity; and early integration of psychosocial and palliative support.

Recommendations: This protocol represents the first standardized, adapted, evidence-based national guideline for the management of malignant ovarian germ cell tumors in Kenya. Its adoption is anticipated to harmonize clinical practice, improve diagnostic accuracy and treatment outcomes, support the efficient use of limited resources, and reduce disparities in the quality of care delivered to this young and vulnerable patient population.

Keywords: Kenya, Ovarian germ cell tumors; Teratoma

List of abbreviations

AFP	Alpha-fetoprotein
AGREE II	Appraisal of Guidelines for Research and Evaluation II
ASCO	American Society of Clinical Oncology
BEP	Bleomycin, etoposide, and cisplatin
BGCS	British Gynaecological Cancer Society
β-hCG	Beta-human chorionic gonadotropin
CBC	Complete blood count
CrCl	Creatinine clearance
CT	Computed tomography
EP	Etoposide and cisplatin
ESGO	European Society of Gynaecological Oncology
FIGO	International Federation of Gynecology and Obstetrics
G-CSF	Granulocyte colony-stimulating factor
GCT	Germ cell tumor
GOSK	Gynaecologic Oncology Society of Kenya
HDCT	High-dose chemotherapy
hCG	Human chorionic gonadotropin
IHC	Immunohistochemistry
IV	Intravenous
JEB	Carboplatin, etoposide, and bleomycin
LDH	Lactate dehydrogenase
MDT	Multidisciplinary team
MOGCT	Malignant ovarian germ cell tumor
MRI	Magnetic resonance imaging
NCCN	National Comprehensive Cancer Network
OCT3/4	Octamer-binding transcription factor 3/4
OGCT	Ovarian germ cell tumor
PET/CT	Positron emission tomography/computed tomography
PFT	Pulmonary function test
PLAP	Placental alkaline phosphatase
QoL	Quality of life
R0	Complete resection with no residual tumor
SALL4	Spalt-like transcription factor 4
TAH	Total abdominal hysterectomy
TAH-BSO	Total abdominal hysterectomy with bilateral salpingo-oophorectomy
TIP	Paclitaxel, ifosfamide, and cisplatin
US	Ultrasound
USO	Unilateral salpingo-oophorectomy
VeIP	Vinblastine, ifosfamide, and cisplatin
VIP	Etoposide, ifosfamide, and cisplatin
WHO	World Health Organization

Summary of recommendations

Table 1. Summary of GOSK recommendations for diagnosis and initial workup of malignant ovarian germ cell tumors

Clinical domain	GOSK recommendations
Clinical presentation	Ovarian germ cell tumors should be considered in adolescents and young females presenting with a pelvic mass, pelvic pain, abdominal bloating, acute abdomen, or rare hormonal manifestations such as precocious puberty or virilization.
Imaging	• Transvaginal or transabdominal ultrasound is recommended as the initial imaging modality. • CT of the abdomen and pelvis, with or without the chest, should be performed for staging. • MRI is indicated for complex cases or when fertility-sparing surgery is planned. • PET/CT is reserved for suspected recurrence, metastasis, and post-treatment surveillance.
Tumor markers	• AFP, β-hCG, and LDH: indicated for diagnosis, histological subtyping, and treatment monitoring. • CA-125: recommended to exclude epithelial ovarian malignancy. • Inhibin: recommended to exclude sex cord-stromal tumors.
Pathology	Histopathological examination with immunohistochemistry (IHC) is required. An IHC panel including SALL4, PLAP, AFP, hCG, and OCT3/4 should be employed for accurate subtype classification.
Additional considerations	• Multidisciplinary team (MDT) review is mandatory for all cases. • Fertility assessment (AMH measurement and antral follicle count) should be performed prior to treatment. • Psychosocial support should be offered to all patients at diagnosis.

Table 2. Summary of GOSK recommendations for the surgical management of malignant ovarian germ cell tumors by FIGO stage

Clinical scenario	GOSK recommendations
Early-stage (FIGO stage I), fertility desired	• Fertility-sparing unilateral salpingo-oophorectomy (USO) with wedge biopsy of the contralateral ovary (Stage IA). • Bilateral salpingo-oophorectomy (BSO) with uterine preservation (Stage IB). • Comprehensive surgical staging (omentectomy, peritoneal washings, peritoneal biopsies, and lymph node assessment if enlarged or clinically suspicious) in all cases.
Early-stage (FIGO stage I), fertility not desired	Total abdominal hysterectomy (TAH) with bilateral salpingo-oophorectomy (BSO), combined with comprehensive surgical staging (omentectomy, peritoneal washings, peritoneal biopsies, and lymph node assessment).
Advanced disease (FIGO stages II–IV)	Maximal cytoreductive surgery is recommended, with the surgical goal of no residual disease. Procedures include TAH-BSO, omentectomy, and comprehensive staging.
Recurrent disease	Secondary cytoreductive surgery is recommended for patients with resectable recurrent disease.

Table 3. Summary of GOSK recommendations for adjuvant chemotherapy by FIGO stage and histology in malignant ovarian germ cell tumors

Category	GOSK recommendations
Stage IA/IB dysgerminoma or grade 1 immature teratoma	Observation (active surveillance) is recommended; adjuvant chemotherapy is not indicated.
High-risk Stage I (yolk sac tumor, embryonal carcinoma, mixed histology) or stage IC–II	Three cycles of BEP chemotherapy are recommended.
Advanced disease (stages III–IV)	Four cycles of BEP chemotherapy are recommended. In patients for whom bleomycin is contraindicated, the EP regimen should be substituted.
Chemoresistant disease	• Surgical resection for localized disease. • Salvage chemotherapy regimens (TIP or VeIP). • Enrolment in clinical trials is strongly encouraged.

Table 4. Summary of GOSK recommendations for chemotherapy regimens and treatment monitoring in malignant ovarian germ cell tumors

Category	GOSK recommendations
Standard BEP regimen (Option 1)	• Bleomycin 30 units IV (Days 1, 8, and 15). • Etoposide 100 mg/m² IV (Days 1–5). • Cisplatin 20 mg/m² IV (Days 1–5).
Standard BEP regimen (Option 2)	• Bleomycin 30 units IV (Days 1, 8, and 15).

Category	GOSK recommendations
	• Cisplatin 50 mg/m² IV (Days 1–2). • Etoposide 165 mg/m² IV (Days 1–3).
Alternative regimens	• EP (etoposide + cisplatin): indicated for low-risk disease. • VIP (etoposide + ifosfamide + cisplatin): indicated for poor-risk or recurrent disease. • JEB (carboplatin + etoposide + bleomycin): preferred regimen in pediatric patients.
Monitoring requirements	• Tumor marker assessment prior to each cycle. • Pulmonary function tests (PFTs) and/or chest imaging, due to bleomycin pulmonary toxicity. • Renal function tests and audiometry, due to cisplatin nephrotoxicity and ototoxicity. • G-CSF for the management of chemotherapy-induced neutropenia.
Special considerations	• Fertility counselling and oocyte or embryo cryopreservation should be offered prior to initiating chemotherapy. • Psychological support should be provided throughout the course of treatment.

Table 5. Summary of GOSK recommendations for follow-up and surveillance after treatment for malignant ovarian germ cell tumors

Category	GOSK recommendations
Surveillance schedule	• Every 3 months during Years 1–2. • Every 6 months during Years 3–5. • Annually thereafter; a minimum total surveillance duration of 5 years is required given the risk of late recurrence.
Surveillance components	• Physical examination. • Tumor markers: AFP, β-hCG, and LDH. • Pelvic ultrasound. • CT or MRI, if tumor markers are elevated or clinical symptoms develop.
Long-term monitoring	• Monitoring for gonadal dysfunction, including infertility and hormonal deficits. • Monitoring for secondary malignancies, including therapy-related leukemia and solid tumors.

Table 6. Summary of GOSK recommendations for the management of recurrent malignant ovarian germ cell tumors

Category	GOSK recommendations
Secondary surgical cytoreduction	• Recommended for patients with resectable recurrent disease. • The surgical goal is complete gross resection (R0 resection). • The decision to proceed should be determined through MDT review.
Platinum-sensitive recurrence	Platinum-based chemotherapy is recommended: BEP (3–4 cycles), TIP (3–4 cycles), or EP as an alternative regimen.
Platinum-resistant recurrence	Non-platinum-based chemotherapy is recommended, such as paclitaxel combined with gemcitabine.
Radiation therapy	Reserved for localized recurrent dysgerminoma when surgical resection and/or chemotherapy are insufficient or not clinically feasible.

Table 7. Summary of GOSK recommendations for supportive and palliative care in patients with malignant ovarian germ cell tumors

Category	GOSK recommendations
Definition	Supportive and palliative care encompasses holistic, patient-centered care that integrates symptom management, quality-of-life (QoL) optimization, and psychosocial support. It is delivered by specialized palliative care teams in conjunction with oncological treatment.
Goals of care	• Optimize quality of life throughout the disease trajectory. • Minimize symptom burden. • Support patients in making informed treatment decisions. • Provide comprehensive psychosocial and caregiver support.
Specific recommendations (advanced or recurrent disease)	• Early integration of palliative care to facilitate proactive management of disease-related symptoms and chemotherapy-induced toxicities. • Psychosocial support addressing fertility loss, body image concerns, and psychological distress, which are particularly prevalent in young patients. • Advance care planning and hospice referral initiated at an appropriate stage for patients requiring end-of-life care.

1.0 Introduction

1.1 Background

Ovarian cancers are classified into three principal histological categories: epithelial, germ cell, and sex cord–stromal tumors. Each arises from a distinct cellular compartment of the ovary or adnexa and requires different management strategies. Epithelial ovarian cancers constitute the most common category. Although they were historically attributed to the ovarian surface epithelium, current evidence indicates that most epithelial ovarian cancers, particularly high-grade serous carcinoma, the predominant and most lethal subtype originate from the secretory epithelial cells of the fallopian tube, with the ovarian surface epithelium now regarded as a less common site of origin (1). Other histological subtypes have distinct origins: endometrioid and clear cell carcinomas are associated with endometriosis, whereas the cell of origin of mucinous carcinoma remains less well defined (2).

Germ cell tumors arise from primordial germ cells of the embryonic gonad within the ovarian cortex and, as the focus of this protocol, warrant further classification. They comprise a heterogeneous group of tumors, including dysgerminoma, yolk sac tumor (endodermal sinus tumor), embryonal carcinoma, non-gestational choriocarcinoma, immature teratoma, and mixed germ cell tumors. The broader category of ovarian germ cell tumors also includes benign mature (cystic) teratomas and rare monodermal and somatic-type teratomas (2-3). Dysgerminoma is the most common malignant ovarian germ cell tumor subtype (3).

Sex cord–stromal tumors originate from the hormonally active sex cord and stromal cells within the ovarian cortex. The substantial differences in tumor biology, natural history, and treatment responsiveness among these three histological categories necessitate subtype-specific diagnostic and therapeutic approaches.

1.2 Epidemiology

Non-epithelial ovarian tumors account for approximately 10% of all ovarian cancers. Malignant ovarian germ cell tumors (MOGCTs) constitute approximately 2%–5% of ovarian cancers in the general population but account for approximately 70%–80% of malignant ovarian tumors in preadolescent and adolescent females, underscoring their disproportionate burden in younger age groups (4). MOGCTs predominantly affect adolescents and young women. The age-specific incidence follows a unimodal distribution, with the highest rates observed during the second decade of life. The median age at diagnosis ranges from 16 to 20 years, although cases have been reported across a wider age range, from 6 to 60 years. Peak incidence occurs among females aged 15–19 years (5-7).

The incidence of MOGCTs varies across geographical regions and population groups. The source literature reports the highest incidence among females younger than 30 years in Eastern Asia and among females older than 30 years in Central America (5). In the United States, population-based registries have reported higher incidence rates among Asian and Hispanic populations than among non-Hispanic White and Black populations. International comparisons suggest approximately twofold to threefold variation in age-standardized incidence across geographical regions (5). These differences should be interpreted cautiously because variations in cancer registration and histopathological classification may influence reported estimates.

Reliable estimates of the incidence and burden of MOGCTs are constrained by limitations in cancer registration and histopathological classification. Many national cancer registries do not disaggregate ovarian cancers by histological subtype, potentially resulting in under-ascertainment of germ cell tumors. Misclassification may further compromise estimates, particularly in settings where immunohistochemical characterization is not readily available (5). In sub-Saharan Africa, including Kenya, incomplete population-based cancer registration limits the availability of reliable, histology-specific incidence estimates. Consequently, the true burden of MOGCTs may be underestimated (10).

1.3 Malignant ovarian germ cell in Kenya

Reliable, histology-specific data on the incidence and burden of malignant ovarian germ cell tumors (MOGCTs) in Kenya remain limited. Incomplete population-based cancer registration and potential misclassification of ovarian tumors may constrain accurate estimation of the national burden of these malignancies. These limitations make it difficult to characterize their distribution across age groups and geographical regions and to assess national patterns in stage at diagnosis, treatment, and clinical outcomes (10).

The management of MOGCTs in Kenya has historically been heterogeneous across institutions, contributing to potential disparities in the care delivered to affected patients. The management of these tumors requires coordinated diagnostic evaluation, accurate histopathological classification and staging, timely access to appropriate surgery and chemotherapy, and structured follow-up. These requirements are particularly important given the young age of many affected patients and the need to consider fertility preservation alongside oncological outcomes.

In this context, a standardized national clinical management protocol is needed to support consistent, evidence-based care across institutions. The Gynaecologic Oncology Society of Kenya (GOSK) has therefore adapted recommendations from high-quality international guidelines to the Kenyan health care context, with the aim of harmonizing clinical practice, improving diagnostic accuracy and treatment outcomes, promoting efficient use of available resources, and reducing disparities in the quality of care.

1.4 Rationale for the GOSK protocol

The management of malignant ovarian germ cell tumors (MOGCTs) requires coordinated diagnostic evaluation, accurate histopathological classification and staging, appropriate surgical and systemic treatment, and structured follow-up. Although international clinical practice guidelines provide recommendations for these components of care, their implementation must account for the health care infrastructure, diagnostic capacity, treatment availability, and resource constraints of individual settings.

In Kenya, the management of MOGCTs has been heterogeneous across institutions, potentially contributing to disparities in care delivery. The limited availability of reliable, histology-specific epidemiological data further highlights the need to strengthen standardized approaches to diagnosis, treatment, and outcome monitoring. In response to this need, the Gynaecologic Oncology Society of Kenya (GOSK) developed this clinical management protocol by adapting high-quality international guidelines to the Kenyan health care context. The adaptation process was intended to provide a consistent framework for clinical decision-making while considering available resources and the organization of cancer care in Kenya.

The overarching objectives of the GOSK protocol are to harmonize clinical practice, improve diagnostic accuracy, support appropriate and timely treatment, optimize clinical outcomes, promote efficient use of available resources, and reduce disparities in the quality of care delivered to patients with MOGCTs across the country. The protocol addresses diagnostic evaluation, stage-specific surgical and adjuvant management, follow-up and surveillance, management of recurrent and chemoresistant disease, and supportive and palliative care.

2.0 Risk factors, Clinical presentation, Histology and staging

2.1 Risk factors

Risk assessment in malignant ovarian germ cell tumors (MOGCTs) may help identify patients who require further clinical evaluation. However, established risk factors for these tumors are less well characterized than those for epithelial ovarian cancers. The factors discussed below include demographic characteristics, genetic and gonadal conditions, and possible epidemiological associations. Health care access and socioeconomic circumstances may also influence the timeliness of diagnosis and the stage at presentation, although these should be distinguished from biological risk factors for developing the tumors.

Table 8: Risk factors and associated characteristics of malignant ovarian germ cell tumors

Risk factor or domain	Description
Age	Peak incidence occurs in adolescents and young adults aged 15 - 30 years. MOGCTs are the predominant ovarian malignancy in this age group.
Genetic and gonadal conditions	Gonadal dysgenesis - including Turner syndrome (45,X) and Swyer syndrome (46,XY complete gonadal dysgenesis) - confers elevated risk for dysgerminoma. A positive family history represents a weak and insufficiently characterized association.
Race and ethnicity	Epidemiological data demonstrate higher incidence rates among Asian and Latina populations compared with other racial/ethnic groups; mechanisms remain under investigation.
Histological subtype	Dysgerminoma is the most common subtype (~50% of MOGCTs), followed by immature teratoma and yolk sac tumor (endodermal sinus tumor). Subtype influences prognosis, chemosensitivity, and surveillance strategy.
Stage at diagnosis	Advanced-stage disease (FIGO III - IV) is associated with delayed or missed diagnosis. Late presentation is disproportionately observed in low-resource settings where diagnostic capacity is limited.
Socioeconomic and access factors	Limited access to primary and secondary healthcare - including diagnostic imaging and specialist referral pathways - independently increases the probability of advanced-stage diagnosis and adversely affects outcomes.
FIGO: International Federation of Gynecology and Obstetrics; MOGCT = Malignant Ovarian Germ Cell Tumor	

2.2 Clinical presentation

Malignant ovarian germ cell tumors (MOGCTs) may present with symptoms and signs related to rapid tumor growth, hormonal activity, and mass effect on adjacent pelvic and abdominal structures. The clinical presentation is nonspecific and may mimic other gynecological or gastrointestinal conditions. Recognition of these features is important to support timely investigation and diagnosis.

Table 9. Signs and symptoms of malignant ovarian germ cell tumors

Symptom/sign	Clinical features and underlying mechanism
Abdominal distension	Results from rapid tumor enlargement and, in approximately 20% of cases, the concurrent development of ascites. The abdominal mass is often palpable and may cross the midline.
Abdominal or pelvic pain	May be acute (secondary to adnexal torsion or tumor rupture) or chronic (from progressive mass effect). Acute presentations warrant urgent surgical evaluation to exclude hemoperitoneum.

Symptom/sign	Clinical features and underlying mechanism
Precocious puberty	Observed predominantly in pre-pubertal patients. Results from ectopic hormone secretion — including estrogen or human chorionic gonadotrophin (hCG) — by the tumor, leading to premature secondary sexual development.
Symptoms mimicking pregnancy	Nausea, breast tenderness, and amenorrhea may occur in association with hCG-secreting subtypes (notably choriocarcinoma and some mixed GCTs). Urine pregnancy tests may return false-positive results, delaying diagnosis.
Abnormal uterine bleeding	Irregular or abnormal vaginal bleeding may occur secondary to hormonally active tumors disrupting normal endocrine signaling of the hypothalamic–pituitary–ovarian axis.
Hyperthyroidism	A rare but recognized paraneoplastic feature, attributed to TSH-like activity of hCG in highly secretory tumors. Clinical features include tachycardia, tremor, and weight loss. Thyroid function tests should be requested when hCG levels are markedly elevated.
GCT: Germ cell tumor; hCG: human chorionic gonadotrophin; MOGCT: malignant ovarian germ cell tumor; TSH: thyroid-stimulating hormone	

2.3 Histology and WHO classificaton

The histopathological classification of ovarian germ cell tumors is fundamental to diagnosis, prognostication, and treatment planning. These tumors arise from primordial germ cells and encompass a biologically diverse spectrum, ranging from benign lesions to highly aggressive malignancies. Mature teratomas account for the majority of benign ovarian germ cell tumors. Malignant ovarian germ cell tumors (MOGCTs) comprise tumors derived from primitive germ cell types that recapitulate the cellular architecture of embryonic or extraembryonic structures, as well as tumors containing malignant components arising within pre-existing teratomas. Accurate histological classification is essential because tumor subtype influences the tumor-marker profile, chemosensitivity, surgical approach, and surveillance strategy.

Table 10. WHO histological classification of ovarian germ cell tumors

WHO Group / Category	Histological entity	Behavior
Group I: Primitive germ cell tumors	Dysgerminoma	Malignant
	Yolk sac tumor (endodermal sinus tumor)	Malignant
	Embryonal carcinoma	Malignant
	Polyembryoma	Malignant
	Non-gestational choriocarcinoma	Malignant
	Mixed germ cell tumor (2 or more primitive germ cell tumor components)	Malignant
Group II: Biphasic or triphasic teratomas	Immature teratoma, grades 1–3 (Norris grading)	Malignant
Mature teratoma subtypes	Mature solid teratoma	Benign
	Mature cystic teratoma (dermoid cyst)	Benign
	Fetiform teratoma (homunculus)	Benign
Group III: Monodermal teratomas and somatic-type tumors associated with Group II	Struma ovarii (thyroid-type)	Variable
	Carcinoid tumor	Variable
	Neuroectodermal tumor	Variable
	Carcinoma (somatic-type)	Malignant
	Melanocytic tumor	Variable
	Sarcoma *(somatic-type)*	Malignant
	Sebaceous tumor	Variable
	Pituitary-type tumor	Variable
	Other monodermal teratomas	Variable
Behavior: malignant, confirmed malignant potential; Benign, no malignant potential in typical form; Variable, behavior depends on subtype, grade, or associated malignant component. Abbreviations: GCT: germ cell tumor; MOGCT: malignant ovarian germ cell tumor; WHO: World Health Organization.		

2.4 Staging classification

Accurate staging is essential for determining disease extent, assessing prognosis, guiding treatment decisions, and facilitating standardized reporting across clinical studies and cancer registries. The staging classification presented in this section applies to ovarian, fallopian tube, and primary peritoneal malignancies, including malignant ovarian germ cell tumors (MOGCTs). Staging is primarily surgical and pathological. When surgery is contraindicated and staging cannot be established surgically, the basis for clinical staging should be clearly documented. The assigned stage and substage should be recorded in the operative and pathology reports, where applicable, and communicated to the multidisciplinary tumor board (MDTB) to support treatment planning.

Table 11. FIGO 2013 staging classification for ovarian cancer, fallopian tube cancer, and primary peritoneal cancer

Stage / substage	Description	Key diagnostic features
Stage I: Tumor confined to the ovaries or fallopian tubes		
IA	Tumor limited to one ovary (capsule intact) or one fallopian tube; no tumor on ovarian or tubal surface	No capsule rupture; No malignant cells in peritoneal washings or ascites
IB	Tumor limited to both ovaries (capsules intact) or both fallopian tubes; no tumor on ovarian or tubal surface	
IC	Tumor limited to one or both ovaries or fallopian tubes, with any of the following:	
IC1	Surgical spill during operative procedure	Intraoperative capsule rupture only
IC2	Capsule ruptured prior to surgery, or tumor on ovarian or tubal surface	Pre-operative capsule rupture or surface tumor involvement
IC3	Malignant cells detected in peritoneal washings or ascitic fluid	Positive peritoneal cytology
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 to the uterus and/or fallopian tubes and/or ovaries	Involvement of uterus or adnexal structures
IIB	Extension to other pelvic intraperitoneal tissues	Involvement of bladder, rectum, sigmoid colon, or pelvic peritoneum
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 retroperitoneal lymph nodes only (cytologically or histologically confirmed)	—
IIIA1(i)	Nodal metastasis ≤10 mm in greatest dimension	Lymph node metastasis ≤10 mm
IIIA1(ii)	Nodal metastasis >10 mm in greatest dimension	Lymph node metastasis >10 mm
IIIA2	Microscopic extra pelvic peritoneal involvement with or without positive retroperitoneal lymph nodes	Microscopic peritoneal deposits beyond pelvis
IIIB	Macroscopic peritoneal metastasis beyond the pelvis ≤2 cm in greatest dimension, with or without positive retroperitoneal lymph nodes	Peritoneal deposits ≤2 cm
IIIC	Macroscopic peritoneal metastasis beyond the pelvis >2 cm in greatest dimension, with or without positive retroperitoneal lymph nodes	Peritoneal deposits >2 cm; may include extension to capsule of liver or spleen without parenchymal involvement
Stage IV: Distant metastasis excluding peritoneal metastasis		
IVA	Pleural effusion with positive cytological examination	Malignant pleural effusion confirmed by cytology
IVB	Parenchymal metastases and metastases to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside the abdominal cavity)	Hepatic or splenic parenchymal metastases; pulmonary metastases; extra-abdominal lymph node involvement (including inguinal nodes)
Source: Adapted from: Prat J, FIGO Committee on Gynecologic Oncology, 2014.		

3.0 Protocol objectives

3.1 Broad objective

To establish a standardized, evidence-based approach to the management of malignant ovarian germ cell tumors (MOGCTs) in Kenya.

3.2 Specific objectives

To provide evidence-based recommendations for the management of MOGCTs in the following areas:

1. Diagnosis and clinical workup.
2. Management according to disease stage.
3. Histology-specific management considerations.
4. Post-treatment surveillance.

5. Management of recurrent disease.
6. Supportive and palliative care.

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 malignant ovarian germ cell tumors (MOGCTs). The recommendations are intended to guide clinical practice. Their application should be informed by independent clinical judgment and tailored to each patient's individual circumstances, including clinical presentation, disease characteristics, available resources, and patient 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 care system and available resources. The process involved systematic identification and appraisal of published guidelines, followed by the synthesis 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 by the Gynaecologic Oncology Society of Kenya (GOSK). The panel comprised 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 the principles of evidence-based guideline adaptation. The orientation covered standardized appraisal tools, systematic evaluation of published guidelines and protocols, and approaches for contextualizing recommendations to local clinical needs and available resources.

5.3 Search strategy

A literature search was conducted in PubMed and Google Scholar to identify relevant evidence-based clinical practice guidelines, systematic reviews, and best-practice statements on the management of malignant ovarian germ cell tumors (MOGCTs). The search terms included "malignant ovarian germ cell tumors," "clinical guideline," "gynecologic oncology," "protocols," and "guidelines." Six candidate source guidelines were identified for appraisal.

5.4 Source guideline identification

Six candidate guidelines were identified and considered for adaptation. These included guidance from the National Comprehensive Cancer Network (NCCN), the American Society of Clinical Oncology (ASCO), the British Gynaecological Cancer Society (BGCS), the European Society of Gynaecological Oncology (ESGO), the European Society for Medical Oncology (ESMO), and the Council for Medical Schemes of South Africa (CMS/PBS). The retrieved documents varied in type, scope, and publication or update year. Their characteristics are summarized in Table 12. The identification of a guideline as a candidate source did not automatically qualify it for inclusion; each guideline was appraised before the final selection for adaptation.

5.5 Guideline quality appraisal

The six candidate guidelines were independently appraised by two trained panelists using the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument. AGREE II 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.

Where the two appraisers did not reach agreement, a designated facilitator acted as a tiebreaker to support a final decision. The appraisal process was used to assess the methodological quality and suitability of each candidate guideline for adaptation.

5.6 Guideline selection

Guideline selection was informed by the AGREE II appraisal results. Particular consideration was given to the domains of rigor of development and clarity of presentation. Guidelines that did not meet the prespecified thresholds for these domains were excluded from adaptation. Overall AGREE II scores were used to characterize guideline quality but were not, in themselves, an exclusion criterion. Following appraisal, four guidelines were retained for adaptation: those from NCCN, ASCO, BGCS, and ESGO. The appraisal results and final inclusion decisions are presented in Table 13.

5.7 Synthesis and contextualization of recommendations

Recommendations from the retained guidelines were synthesized and adapted to the Kenyan health care context, taking into account local clinical needs, available diagnostic and treatment services, and resource constraints. The resulting recommendations address the diagnostic evaluation and histopathological classification of MOGCTs; stage-specific surgical and systemic treatment; fertility preservation; post-treatment surveillance; management of recurrent and chemoresistant disease; and supportive and palliative care.

The adapted recommendations provide a standardized framework to guide clinical decision-making across institutions in Kenya. Their application should remain responsive to individual patient circumstances and informed by multidisciplinary review and independent clinical judgment.

Table 12. Summary of retrieved guidelines

	Title	Type	Publisher	Year of last update
1	Clinical Practice Guidelines in Oncology: Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer	Clinical Guideline	National Comprehensive Cancer Network (NCCN)	2025
2	Non-epithelial ovarian cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up	Clinical Guideline	European Society of Medical Oncology (ESMO)	2017
3	Ovarian, tubal and primary peritoneal cancer guidelines: Recommendations for practice update 2024	Clinical Guideline	British Gynecological Cancer Society (BGCS)	2024
4	Updates in the Management of Ovarian Germ Cell Tumors	Update Review	American Society of Clinical Oncology (ASCO)	2013
5	Definition Guideline for Ovarian Cancer	Benefit Definition Guideline	Council for Medical Schemes - South Africa CMS/PBS	2021
6	Guidelines for the management of non-epithelial ovarian cancers in adolescents and young adults	Clinical Guideline	European Society of Gynecological Oncology (ESGO)	2024

Table 13. Summary of AGREE II domain scores

	Title	Domain 1	Domain 2	Domain 3	Domain 4	Domain 5	Domain 6	Overall Decision
1	Clinical Practice Guidelines in Oncology: Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer NCCN	78%	83%	81%	83%	79%	71%	Included
2	Updates in the Management of Ovarian Germ Cell Tumors ASCO	72%	72%	81%	83%	58%	8%	Included
3	Ovarian, tubal and primary peritoneal cancer guidelines: Recommendations for practice update 2024 BGCS	78%	83%	81%	83%	80%	71%	Included
4	Non-epithelial ovarian cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up	58%	58%	55%	64%	31%	33%	Excluded
5	CMS PBS Definition Guideline for Ovarian Cancer	92%	58%	56%	47%	85%	38%	Excluded
6	Guidelines for the management of non-epithelial ovarian cancers in adolescents and young adults ESGO	92%	86%	81%	83%	80%	71%	Included

6.0 Review of evidence

Recommendations from the four selected source guidelines were systematically compared and analyzed against the predefined objectives of this adapted national protocol for the management of malignant ovarian germ cell tumors (MOGCTs). The comparison focused on areas relevant to clinical decision-making, including diagnostic evaluation, surgical management, adjuvant chemotherapy, treatment of advanced disease, management of chemoresistant or recurrent disease, follow-up and surveillance, and supportive and palliative care.

The comparative findings informed the development of recommendations by the Gynaecologic Oncology Society of Kenya (GOSK), taking into account the Kenyan health care context and available resources. The recommendations from the individual source guidelines are presented in Tables 9–18, while the corresponding GOSK recommendations are presented in the subsequent section.

Table 14. Comparative evidence from source guidelines for diagnosis and workup of malignant ovarian germ cell tumor

Clinical domain	NCCN	ASCO	BGCS	ESGO
Clinical presentation	Presents in adolescents/young adults with pelvic pain, abdominal distension, or palpable mass. Acute abdomen possible due to tumor rupture or torsion. Precocious puberty or virilization in rare cases.	Young patients with pelvic mass, pain, or bloating. Rare endocrine symptoms (e.g., hCG-related amenorrhea).	Pelvic mass in young females, often with pain or acute symptoms. Hormonal symptoms (e.g., precocious puberty) noted in some subtypes.	Pelvic mass, pain, or acute abdomen in young patients.
Imaging	Primary: Transvaginal or transabdominal ultrasound (US). Staging: CT or MRI of abdomen/pelvis for metastasis evaluation. Chest X-ray or CT for pulmonary metastases. PET/CT optional for specific cases (e.g., suspected recurrence).	Initial: US (transvaginal preferred) for mass characterization. Staging: CT abdomen/pelvis; chest CT if markers elevated or metastasis suspected. MRI for complex cases or fertility preservation planning.	First-line: US to evaluate mass (size, heterogeneity). Staging: CT/MRI abdomen/pelvis; chest imaging (X-ray or CT) for metastasis. MRI emphasized for fertility-sparing surgery planning.	Initial: US for adnexal mass evaluation. Staging: CT abdomen/pelvis; chest imaging if clinically indicated. MRI for surgical planning in fertility preservation cases.
Tumor markers	Essential: AFP, hCG, LDH for diagnosis and monitoring. CA-125 may be elevated but less specific. Markers guide subtype (e.g., AFP in yolk sac tumors, hCG in choriocarcinoma).	AFP, hCG, LDH mandatory for suspected OGCTs. CA-125 not routinely recommended due to low specificity. Serial marker levels for treatment response and surveillance.	AFP, hCG, LDH critical for diagnosis, subtype classification, and follow-up. Optional CA-125, less relevant for OGCTs. Marker elevation guides chemotherapy decisions.	AFP, hCG, LDH recommended for diagnosis and monitoring. CA-125 not prioritized for OGCTs. Emphasis on correlating markers with imaging and pathology.
Pathology	Surgical pathology (biopsy or resection) confirms diagnosis. Subtypes: dysgerminoma, yolk sac tumor, embryonal carcinoma, choriocarcinoma, teratoma (immature/mature). IHC: SALL4, PLAP, AFP, hCG for subtype confirmation.	Histopathology via surgical specimen required. Subtype identification is critical for treatment planning. IHC (e.g., SALL4, OCT3/4) recommended to differentiate OGCTs from other tumors.	Histological confirmation via surgery or biopsy. Detailed IHC (SALL4, PLAP, AFP, hCG) to confirm subtype and rule out mimics. Central pathology review encouraged for rare tumors.	Pathology via surgical resection or biopsy. Subtype classification using IHC (SALL4, PLAP, OCT3/4).
Multidisciplinary evaluation	MDT consultation: gynecologic oncologist, medical oncologist, pathologist, radiologist. Fertility preservation counseling is critical due to young patient age. Genetic counseling if hereditary syndromes suspected (e.g., gonadal dysgenesis).	MDT approach mandatory, including gynecologic oncologist, pathologist, and fertility specialists. Fertility preservation discussion pre-treatment. Psychological support integrated for young patients.	MDT evaluation with gynecologic oncologist, pathologist, radiologist, and fertility experts. Psychosexual and fertility counseling emphasized. Genetic testing for rare syndromes (e.g., Swyer syndrome).	MDT consultation recommended, involving oncology, pathology, and fertility specialists. Fertility preservation counseling pre-treatment. Psychosocial support for young patients facing diagnosis.
Baseline investigations	Complete blood count, liver/renal function tests. Fertility assessment (e.g., AMH levels) if preservation planned. Bone scan or brain MRI if symptoms suggest metastases. Pregnancy test to rule out pregnancy (hCG elevation).	Blood tests: CBC, liver/renal function, electrolytes. Fertility assessment pre-surgery/chemotherapy. Pregnancy test mandatory. MRI brain if neurological symptoms present.	Routine blood work (CBC, liver/renal function). Fertility evaluation (AMH, antral follicle count). Pregnancy test to exclude pregnancy-related hCG elevation. Brain imaging for suspected metastases.	Standard blood work (CBC, liver/renal function). Fertility counseling and assessment pre-treatment. Pregnancy test required. Targeted imaging (e.g., brain MRI) for metastatic symptoms.

NCCN: National Comprehensive Cancer Network; ASCO: American Society of Clinical Oncology; BGCS: British Gynaecological Cancer Society; ESGO: European Society of Gynaecological Oncology; OGCT: ovarian germ cell tumor; US: ultrasound; CT: computed tomography; MRI: magnetic resonance imaging; PET/CT: positron emission tomography/computed tomography; AFP: alpha-fetoprotein; hCG: human chorionic gonadotropin; LDH: lactate dehydrogenase; CA-125: cancer antigen 125; IHC: immunohistochemistry; SALL4: sal-like protein 4; PLAP: placental alkaline phosphatase; OCT3/4: octamer-binding transcription factor 3/4; MDT: multidisciplinary team; AMH: anti-Müllerian hormone; CBC: complete blood count

Table 15. Comparative evidence from source guidelines for surgical management for early-stage (FIGO I) malignant ovarian germ cell tumors

Surgical aspect	NCCN	ASCO	BGCS	ESGO
Fertility preservation desired				
Fertility-sparing surgery	Unilateral salpingo-oophorectomy (USO) for Stage I–II in women desiring fertility.	Supports USO for stage I–II with a normal contralateral ovary and uterus.	Advocates USO for young patients with stage I–II disease.	Strongly recommends USO for Stage I–II, preserving the uterus and contralateral ovary.
Comprehensive staging	Includes omentectomy, peritoneal biopsies, and lymph node sampling.	Required, including staging procedures.	Includes peritoneal washings and biopsies.	Advised; includes staging procedures.
Lymphadenectomy	Required as part of staging.	May be omitted in early-stage disease if there is no clinical suspicion of spread.	May not impact survival in early-stage MOGCTs.	Optional unless enlarged nodes are detected.
No fertility preservation desired				
Recommended surgical management	Comprehensive surgical staging including total abdominal hysterectomy (TAH), bilateral salpingo-oophorectomy (BSO), infracolic omentectomy, peritoneal washings, multiple peritoneal biopsies, and pelvic and para-aortic lymph node sampling.	Comprehensive surgical staging similar to NCCN: TAH + BSO with full staging (omentectomy, washings, biopsies, lymphadenectomy). Fertility-sparing USO only if desired; otherwise, radical surgery to optimize outcomes.	Adequate non-fertility-sparing primary surgery: peritoneal washings/ascitic sampling, TAH, BSO, infracolic omentectomy, multiple random peritoneal biopsies, and bilateral pelvic and para-aortic lymph node sampling. Emphasizes joint management of young adults (18–24) via a gynae MDT and a teenage/young adult MDT.	Comprehensive surgical staging with TAH + BSO, omentectomy, peritoneal washings, biopsies, and lymph node assessment. Routine completion surgery after fertility-sparing initial surgery is not recommended for germ cell tumors (conservative approach even post-initial treatment).

USO: unilateral salpingo-oophorectomy; TAH: total abdominal hysterectomy; BSO: bilateral salpingo-oophorectomy; MOGCT: malignant ovarian germ cell tumor; MDT: multidisciplinary team

Table 16. Comparative evidence from source guidelines for adjuvant therapy for stage I malignant ovarian germ cell tumors

	NCCN	ASCO	BGCS	ESGO
Adjuvant chemotherapy	Recommended for stage IC–II or high-risk stage I (e.g., yolk sac tumor, embryonal carcinoma)	Supported for stage IC–II or high-risk stage I (e.g., yolk sac tumor, mixed GCTs)	Advised for stage IC–II or stage I with high-risk features (e.g., yolk sac tumor, embryonal carcinoma)	Recommended for stage IC–II or high-risk Stage I MOGCTs
Chemotherapy regimen and cycles	BEP × 3 cycles	BEP × 3 cycles	BEP × 3 cycles	BEP × 3 cycles
Observation *(No adjuvant therapy)*	Sufficient for stage IA/IB dysgerminoma or stage IA grade 1 immature teratoma	Recommended for low-risk stage IA/IB cases	Standard for stage IA dysgerminoma or grade 1 immature teratoma	Advised for stage IA dysgerminoma or grade 1 immature teratoma

NCCN: National Comprehensive Cancer Network; ASCO: American Society of Clinical Oncology; BGCS: British Gynaecological Cancer Society; ESGO: European Society of Gynaecological Oncology; MOGCT: malignant ovarian germ cell tumor; GCT: germ cell tumor; BEP: bleomycin, etoposide, and cisplatin

Note: Stage designations (IA, IB, IC, II) follow FIGO staging.

Table 17. Comparative evidence from source guidelines for management of advanced malignant germ cell tumors (stage II–IV)

	NCCN	ESGO	ASCO	BGCS
Surgical approach	Maximal cytoreduction (debulking) to achieve no residual disease; includes unilateral salpingo-oophorectomy (USO), omentectomy, peritoneal biopsies, and	Cytoreductive surgery aims for complete resection of all macroscopic disease. Comprehensive staging advised, including staging procedures; lymphadenectomy	Aggressive debulking to minimize residual disease. Comprehensive staging required, including staging procedures; lymphadenectomy may be omitted in early-stage	Optimal debulking surgery to remove macroscopic disease; staging includes peritoneal washings and biopsies; lymphadenectomy may

	NCCN	ESGO	ASCO	BGCS
	lymphadenectomy if indicated.	optional unless enlarged nodes detected.	disease if no clinical suspicion of spread.	not impact survival in early-stage MOGCTs.
Chemotherapy	Bleomycin, Etoposide, Cisplatin (BEP), 4 cycles for stage III–IV. For dysgerminoma specifically, Etoposide, Cisplatin (EP) × 4 cycles if bleomycin is contraindicated.	BEP, 4 cycles for stage III–IV; etoposide/cisplatin × 4 for patients unable to receive bleomycin.	BEP, 4 cycles for stage III–IV; etoposide/cisplatin × 4 for patients unable to receive bleomycin.	BEP, 3–4 cycles for stage III–IV; carboplatin-based regimens for dysgerminomas to avoid pulmonary toxicity.

NCCN: National Comprehensive Cancer Network; ESGO: European Society of Gynaecological Oncology; ASCO: American Society of Clinical Oncology; BGCS: British Gynaecological Cancer Society; MOGCT: malignant ovarian germ cell tumor; USO: unilateral salpingo-oophorectomy; BEP: bleomycin, etoposide, and cisplatin; EP: etoposide and cisplatin

Table 18. Comparative evidence from source guidelines for management of chemoresistant malignant ovarian germ cell tumors

	NCCN	ESGO	ASCO	BGCS
Management of chemoresistant / refractory disease	For chemoresistant or refractory cases, second-line chemotherapy regimens such as TIP (paclitaxel/ifosfamide/cisplatin), VeIP (vinblastine/ifosfamide/cisplatin), or VIP (etoposide/ifosfamide/cisplatin). High-dose chemotherapy (HDCT) with autologous stem cell transplant (ASCT) as an option, though its role is not well-established. Cytoreductive surgery for resectable residual disease aiming for complete resection. Enrollment in clinical trials encouraged.	Surgery for localized recurrences if resectable. Salvage chemotherapy with TIP or VeIP for disseminated disease. HDCT with ASCT recommended for platinum-sensitive recurrences; for platinum-resistant disease, consider clinical trials or palliative approaches. Multidisciplinary management is essential.	Confirm refractory status unequivocally. Cytoreductive surgery for resectable disease. Second-line chemotherapy (e.g., TIP, VeIP, VIP). HDCT with ASCT for poor-prognosis or refractory cases. Clinical trials recommended for novel therapies.	—

NCCN: National Comprehensive Cancer Network; ESGO: European Society of Gynaecological Oncology; ASCO: American Society of Clinical Oncology; BGCS: British Gynaecological Cancer Society; TIP: paclitaxel, ifosfamide, and cisplatin; VeIP: vinblastine, ifosfamide, and cisplatin; VIP: etoposide, ifosfamide, and cisplatin; HDCT: high-dose chemotherapy; ASCT: autologous stem cell transplant

Note: — indicates that no BGCS-specific recommendation was provided in the source.

Table 19. Comparative evidence from source guidelines for follow-up and surveillance of malignant ovarian germ cell tumors

	NCCN	ASCO	BGCS	ESGO
Follow-up schedule	Every 2–4 months for 2 years, then every 6 months for years 3–5	Every 3 months for 2 years, then every 6 months	Every 3 months for 2 years, then every 6 months up to 5 years	Every 3 months for 2 years, then every 6 months for 5 years
Components	Physical exams, tumor markers (AFP, β-hCG), imaging (CT/MRI)	Tumor marker monitoring, physical exams	Tumor markers, clinical evaluation	Tumor markers, physical exams, ultrasound
Imaging	CT/MRI every 2–4 months initially, then as needed	As clinically indicated	CT/MRI reserved for abnormal markers or symptoms	CT/MRI if markers rise or recurrence suspected
Long-term follow-up	Advised due to late recurrence risk	Not explicitly emphasized	Not explicitly emphasized	Emphasized for late relapses
Patient empowerment and shared decision-making	High – patient versions empower discussion with clinicians; survivorship planning	Strong focus on shared decision-making in follow-up choices and care plans	Patient-initiated follow-up options; key worker contact for rapid access	Encourages patient involvement in follow-up planning and QoL assessment

NCCN: National Comprehensive Cancer Network; ASCO: American Society of Clinical Oncology; BGCS: British Gynaecological Cancer Society; ESGO: European Society of Gynaecological Oncology; AFP: alpha-fetoprotein; β-hCG: beta-human chorionic gonadotropin; CT: computed tomography; MRI: magnetic resonance imaging; QoL: quality of life

Table 20. Comparative evidence from source guidelines for management of recurrent ovarian germ cell tumors

	NCCN	ESGO	ASCO	BGCS
Secondary surgery	Recommended for resectable disease if complete gross resection feasible; secondary	Debulking surgery cornerstone for resectable recurrent GCT [III, A]; aim for optimal resection.	Secondary cytoreductive surgery for selected patients aiming for complete	Surgery for resectable disease, especially if localized; aim for complete resection; MDT decision.

	NCCN	ESGO	ASCO	BGCS
	cytoreduction for selected patients.		resection; MDT review critical.	
Platinum-sensitive recurrence	Platinum-based chemotherapy (e.g., BEP × 3–4 cycles or EP); surgery if response.	Conventional-dose platinum-based chemotherapy (e.g., BEP or TIP); surgery post-response if feasible [III, A].	Platinum re-challenge (e.g., BEP); high salvage rates (>90% OS for sensitive cases).	Platinum-based regimens (e.g., BEP, TIP); surgery post-chemotherapy if residual disease.
Platinum-resistant recurrence	Non-platinum regimens (e.g., paclitaxel + gemcitabine); high-dose chemotherapy (HDCT) with autologous stem cell transplant (ASCT) for poor-risk.	Alternative chemotherapy (e.g., paclitaxel-based); HDCT + ASCT for refractory/recurrent post-platinum [III, B].	Alternative agents (e.g., paclitaxel, gemcitabine); HDCT + ASCT standard for refractory; cure unlikely but aim for control.	Non-platinum options; HDCT + ASCT for refractory cases; clinical trial enrollment encouraged.
Radiation therapy	Limited to localized recurrent dysgerminoma (sensitive histology); not routine.	For localized recurrent dysgerminoma if surgery/chemo insufficient [III, C].	Rarely used; consider for dysgerminoma recurrences in select cases.	Rarely indicated; may consider for localized dysgerminoma recurrences.

NCCN: National Comprehensive Cancer Network; ESGO: European Society of Gynaecological Oncology; ASCO: American Society of Clinical Oncology; BGCS: British Gynaecological Cancer Society; GCT: germ cell tumor; MDT: multidisciplinary team; BEP: bleomycin, etoposide, and cisplatin; EP: etoposide and cisplatin; TIP: paclitaxel, ifosfamide, and cisplatin; HDCT: high-dose chemotherapy; ASCT: autologous stem cell transplant; OS: overall survival

Table 21. Comparative evidence from source guidelines for chemotherapy schedule for malignant ovarian germ cell tumors

	NCCN	BGCS	ESGO	ASCO
Standard regimen	• BEP (bleomycin, etoposide, cisplatin): primary regimen for most OGCTs (e.g., dysgerminoma, yolk sac tumor, embryonal carcinoma). • Alternative: EP (etoposide, cisplatin) for stage IA/IB dysgerminoma or immature teratoma (fertility preservation). • VIP (etoposide, ifosfamide, cisplatin) for poor-risk or recurrent cases.	• BEP: preferred regimen for non-dysgerminomatous and advanced dysgerminoma. • EP: considered for early-stage dysgerminoma or fertility-sparing cases. • JEB (carboplatin, etoposide, bleomycin) for pediatric patients or to reduce toxicity.	• BEP: standard for most OGCTs, including non-dysgerminomatous and advanced dysgerminoma. • EP: option for stage I dysgerminoma or select cases. • VIP: for high-risk or relapsed disease.	• BEP: primary regimen for OGCTs, aligned with NCCN/ESGO. • EP: for early-stage disease or fertility preservation. • Limited specific guidance; defers to NCCN for detailed protocols.
Dosing schedule (BEP)	• Bleomycin: 30 units IV weekly (days 1, 8, 15 or days 2, 9, 16). • Etoposide: 100 mg/m² IV daily, days 1–5. • Cisplatin: 20 mg/m² IV daily, days 1–5. • Cycle: every 21 days.	• Bleomycin: 30,000 IU IV weekly (days 1, 8, 15). • Etoposide: 100 mg/m² IV daily, days 1–5. • Cisplatin: 20 mg/m² IV daily, days 1–5. • Cycle: every 21 days, with G-CSF support if needed.	• Bleomycin: 30 units IV weekly (days 1, 8, 15). • Etoposide: 100 mg/m² IV daily, days 1–5. • Cisplatin: 20 mg/m² IV daily, days 1–5. • Cycle: every 21 days, with monitoring for toxicity.	• Bleomycin: 30 units IV weekly (days 1, 8, 15). • Etoposide: 100 mg/m² IV daily, days 1–5. • Cisplatin: 20 mg/m² IV daily, days 1–5. • Cycle: every 21 days (defers to NCCN for specifics).
Number of cycles	• Stage I (grade 2/3 immature teratoma, stage IB/IC dysgerminoma): 3–4 cycles BEP or EP. • Stage II–IV: 3–4 cycles BEP (4 cycles for suboptimal response). • High-risk/recurrent: 4 cycles VIP or high-dose chemotherapy.	• Stage I (high-risk): 3 cycles BEP or JEB. • Stage II–IV: 4 cycles BEP, extended if marker decline incomplete. • Recurrent: 4 cycles VIP or salvage therapy.	• Stage IA/IB dysgerminoma: surveillance or 3 cycles EP/BEP. • Stage IC–IV: 3–4 cycles BEP. • High-risk/recurrent: 4 cycles VIP or clinical trial.	• Early-stage: 3 cycles BEP or EP. • Advanced-stage: 4 cycles BEP. • Recurrent: defers to NCCN for VIP or salvage regimens.

	NCCN	BGCS	ESGO	ASCO
Monitoring and adjustments	• Monitor tumor markers (AFP, hCG, LDH) before each cycle. • Pulmonary function tests (PFTs) for bleomycin toxicity. • Renal function (creatinine clearance) for cisplatin. • G-CSF for neutropenia. • Dose reduction or omission of bleomycin if pulmonary toxicity.	• Serial tumor markers (AFP, hCG, LDH) to assess response. • PFTs pre-bleomycin; omit if toxicity detected. • Renal and ototoxicity monitoring for cisplatin. • G-CSF support for prolonged neutropenia.	• Tumor markers (AFP, hCG, LDH) pre-cycle guide therapy. • PFTs and chest imaging for bleomycin-related risks. • Renal function and audiometry for cisplatin. • Dose adjustments for toxicities per protocol.	• Tumor markers monitored per NCCN guidelines. • PFTs and renal function tests recommended. • G-CSF and dose modifications for toxicities (defers to NCCN).
Special considerations	• Fertility preservation: counsel pre-chemotherapy; avoid alkylating agents if possible. • Bleomycin pulmonary toxicity: high risk in young patients; monitor PFTs closely. • Second-line therapy: TIP (paclitaxel, ifosfamide, cisplatin) or high-dose chemotherapy for relapse.	• Fertility counseling mandatory due to young patient age. • JEB considered for pediatric patients to reduce cisplatin toxicity. • Psychological support integrated for treatment burden.	• Fertility preservation emphasized; oocyte cryopreservation pre-treatment. • Bleomycin toxicity monitoring critical (PFTs, imaging). • Clinical trials encouraged for refractory disease.	• Fertility preservation counseling pre-treatment. • Limited OGCT-specific guidance; emphasizes toxicity monitoring (bleomycin, cisplatin). • Refers to NCCN for second-line regimens.

NCCN: National Comprehensive Cancer Network; BGCS: British Gynaecological Cancer Society; ESGO: European Society of Gynaecological Oncology; ASCO: American Society of Clinical Oncology; OGCT: ovarian germ cell tumor; BEP: bleomycin, etoposide, and cisplatin; EP: etoposide and cisplatin; VIP: etoposide, ifosfamide and cisplatin; JEB: carboplatin, etoposide and bleomycin; TIP: paclitaxel, ifosfamide and cisplatin; AFP: alpha-fetoprotein; hCG: human chorionic gonadotropin; LDH: lactate dehydrogenase; IV: intravenous; IU: international units; PFT: pulmonary function test; G-CSF: granulocyte colony-stimulating factor

Table 22. Comparative evidence from source guidelines for role of targeted therapy and immunotherapy in the management of malignant ovarian germ cell tumors

	NCCN	ESGO	ASCO	BGCS
Role of targeted therapy	Not standard in initial management. For recurrent/residual disease, consider targeted therapies if specific biomarkers are present (e.g., NTRK gene fusion), though not explicitly detailed for germ cell tumors in patient guidelines.	No specific recommendations; considered investigational.	No dedicated guidelines for MOGCT. Targeted therapies are investigational, with limited data.	No specific recommendations.
Role of immunotherapy	Not standard in initial management. For recurrent/residual disease with biomarkers such as microsatellite instability-high (MSI-H), mismatch repair deficient (dMMR), or tumor mutational burden-high (TMB-H), checkpoint inhibitors (e.g., pembrolizumab) may be an option.	No specific recommendations; considered investigational.	No dedicated guidelines. Immunotherapy is investigational; limited efficacy data (e.g., no responses in small trials for germ cell tumors). Considered for refractory cases, but not standard.	No specific recommendations.

NCCN: National Comprehensive Cancer Network; ESGO: European Society of Gynaecological Oncology; ASCO: American Society of Clinical Oncology; BGCS: British Gynaecological Cancer Society; MOGCT: malignant ovarian germ cell tumor; NTRK: neurotrophic tyrosine receptor kinase; MSI-H: microsatellite instability-high; dMMR: mismatch repair deficient; TMB-H: tumor mutational burden-high

Table 23. Comparative evidence from source guidelines for supportive and palliative care in malignant ovarian germ cell tumors

	NCCN	BGCS	ESGO	ASCO
Definition	Comprehensive care for patients with advanced disease, focusing on quality of life (QoL), symptom management, and end-of-life care,	Part of a continuum with supportive care, emphasizing symptom relief and QoL for patients with advanced or incurable disease, integrated within	Early integration to improve QoL, manage symptoms, and support patients and families throughout the disease trajectory,	Early integration with oncology care for advanced cancers, emphasizing QoL, symptom control, and caregiver support,

	NCCN	BGCS	ESGO	ASCO
	involving specialist palliative care teams.	multidisciplinary teams (MDTs).	with a holistic approach.	delivered alongside active treatment.
Goals	Relieve suffering, improve QoL, and facilitate informed decision-making for patients with limited prognosis. Includes pain management, psychosocial support, and end-of-life planning.	Alleviate symptoms (e.g., pain, ascites), provide psychological and social support, and ensure dignity in advanced disease.	Enhance QoL, reduce symptom burden, and support patients and families through advanced care planning and end-of-life care.	Improve QoL, reduce hospitalizations, manage symptoms, and support caregivers, with a focus on patient-centered care.
Symptom management	Symptom relief for pain, ascites, and chemotherapy-related toxicities (e.g., bleomycin pulmonary toxicity).	MDT-led symptom management (e.g., pain, nausea).	Early palliative care to manage symptoms like pain and fatigue.	Symptom management for chemotherapy-related toxicities and disease progression.
Psychosocial support	Psychosocial support addressing fertility loss and body image concerns in young patients.	Psychological support for young patients facing terminal illness.	Psychosocial support for patients and families.	Caregiver support and QoL-focused interventions.
End-of-life care	Hospice referral for end-of-life care.	Advance care planning emphasized.	Advance care planning to address end-of-life preferences.	Early integration with oncology care for holistic management.

NCCN: National Comprehensive Cancer Network; BGCS: British Gynaecological Cancer Society; ESGO: European Society of Gynaecological Oncology; ASCO: American Society of Clinical Oncology; QoL: quality of life; MDT: multidisciplinary team

7.0 GOSK recommendations

7.1 Diagnostic evaluation

Table 24. GOSK recommendations for diagnostic evaluation of malignant ovarian germ cell tumors

Diagnostic aspect	GOSK recommendations
Clinical presentation	Malignant ovarian germ cell tumors (MOGCTs) should be suspected in adolescents and young women presenting with a rapidly enlarging pelvic or abdominal mass, abdominal pain, abdominal distension, or acute abdomen. Rare endocrine manifestations should raise clinical suspicion for a hormonally active germ cell tumor. These include β-hCG–mediated effects such as isosexual precocious puberty (in prepubertal patients), menstrual irregularity or abnormal uterine bleeding, a positive pregnancy test in the absence of pregnancy, and — at markedly elevated hCG levels — secondary hyperthyroidism through cross-reactivity with the TSH receptor. Androgen-mediated virilization may occur less commonly.
Imaging	**First-line:** • Pelvic ultrasound (transabdominal and/or transvaginal where appropriate) should be performed as the first-line imaging modality to characterize the mass and exclude pregnancy, with a high index of suspicion maintained for solid masses. **Staging and advanced evaluation:** • Contrast-enhanced CT scan of the abdomen and pelvis should be undertaken for staging where malignancy is suspected. • Chest imaging (radiograph or CT) should be performed when metastatic disease or elevated tumor markers are present. • MRI should be reserved for indeterminate masses or fertility-preserving surgical planning. • PET/CT is not routinely recommended and should be limited to selected cases of suspected recurrence, metastasis, and post-treatment surveillance where available.
Tumor markers	Serum AFP, β-hCG, and LDH should be evaluated in all patients with suspected MOGCTs prior to any surgical intervention. Tumor markers serve the following roles: • Diagnosis and histological subtype classification • Monitoring of treatment response during chemotherapy • Surveillance and detection of disease recurrence CA-125 and inhibin testing should be considered where the differential diagnosis includes epithelial ovarian cancer or sex cord–stromal tumor, respectively.
Baseline investigations	The following baseline investigations should be completed prior to initiation of definitive treatment: • Complete blood count (CBC) • Renal function tests (urea, creatinine, eGFR) • Liver function tests • Serum electrolytes • Pregnancy test (urine or serum β-hCG) • HIV status in accordance with the national testing policy • ECOG performance status assessment

Diagnostic aspect	GOSK recommendations
Histopathology	Histopathological confirmation is mandatory before initiation of definitive treatment where clinically feasible. Immunohistochemistry (IHC) should be performed where available to support subtype classification. The recommended IHC panel includes: • **SALL4:** sensitive marker for germ cell tumors; positive in dysgerminoma, yolk sac tumor, and embryonal carcinoma • **PLAP:** placental alkaline phosphatase; supports dysgerminoma diagnosis • **AFP:** supports yolk sac tumor; correlates with serum AFP • **OCT3/4:** supports dysgerminoma and embryonal carcinoma Limited access to IHC must not delay urgent surgical or oncological management in clinically unstable patients.
Multidisciplinary team (MDT) evaluation	Management decisions should be reviewed by a multidisciplinary team (MDT) prior to initiation of definitive treatment. The recommended MDT composition includes: • Gynaecological oncologist • Medical oncologist • Pediatric oncologist • Pathologist • Radiologist • Oncology nurse coordinator • Fertility specialist • Palliative care provider Pre-treatment fertility preservation counselling and psychosocial support should be integrated into the MDT process, given the young age profile of this patient population.
Referral pathway	Patients with suspected MOGCTs should undergo prompt clinical evaluation and early specialist referral. The following referral principles apply: • Patients should be referred to a gynecological oncologist or designated cancer treatment center (Level 5–6 health facility) without undue delay. • Timely referral is important to minimize the risk of advanced-stage presentation and associated morbidity. • Where specialist services are not immediately accessible, initial stabilization and baseline workup should be completed at the referring facility prior to transfer.
Fertility preservation	Pre-treatment fertility counselling, including a discussion of its limitations within our local setting, should be offered to all patients of reproductive age who desire fertility preservation, prior to the initiation of chemotherapy or definitive surgery. Fertility preservation options should be discussed and, where available and oncologically appropriate, offered to eligible patients. Options include: • Oocyte cryopreservation • Embryo cryopreservation (where applicable) • Conservative (fertility-sparing) surgical management Documentation of fertility counselling and the patient's decision should be recorded in the clinical case file.
Psychosocial and supportive care	Psychological support, social assessment, and patient counselling should be integrated from the point of initial diagnosis, given the young age profile of MOGCT patients, the fertility implications of treatment, and the significant psychosocial burden associated with cancer diagnosis in adolescents and young adults. Psychosocial screening should be performed at baseline and at key clinical transitions throughout the treatment pathway.

AFP: alpha-fetoprotein; β-hCG: beta-human chorionic gonadotrophin; LDH: lactate dehydrogenase; CT: computed tomography; MRI: magnetic resonance imaging; IHC: immunohistochemistry; MDT: multidisciplinary team; AMH: anti-Müllerian hormone

7.2 Management of early stage (FIGO 1) disease

Table 25. GOSK recommendations for management of early stage (FIGO 1) malignant ovarian germ cell cancer

Phase	Management component	GOSK recommendations
Surgical management	**Guiding principles**	Surgical management should aim to achieve: • Complete tumor excision with accurate intraoperative and pathological staging • Preservation of fertility where oncologically appropriate and desired by the patient • Minimization of treatment-related surgical morbidity All procedures should be undertaken by, or in close consultation with, a gynecological oncologist wherever feasible.
	Fertility-sparing surgery for unilateral ovarian disease	Fertility-sparing surgery is recommended for appropriately selected patients with FIGO Stage I disease who desire future fertility and in whom the contralateral ovary and uterus appear macroscopically normal. **Recommended procedure:** • Unilateral salpingo-oophorectomy (USO) with preservation of the uterus and contralateral ovary

Phase	Management component	GOSK recommendations
		Contralateral ovary: • Routine biopsy of a macroscopically normal contralateral ovary is not recommended. It has limited diagnostic yield and potential impact on ovarian reserve. • Biopsy reserved for suspicious intraoperative findings or where malignancy cannot be excluded on inspection. A small (1cm) wedge biopsy using cold knife can be taken for frozen section.
	Fertility sparing surgery for bilateral ovarian disease	Bilateral salpingo-oophorectomy (BSO) with uterine preservation may be considered in patients with bilateral ovarian involvement (including selected Stage IB disease) to retain future reproductive options via assisted reproductive technology where available. Each case should be reviewed by the MDT with explicit documentation of the fertility preservation discussion and the patient's informed decision.
	Non-fertility-sparing surgery	Indicated in patients who have completed childbearing, do not desire future fertility, present with bilateral disease, or where oncologic considerations contraindicate conservative surgery. **Procedure includes:** • Total abdominal hysterectomy (TAH) + bilateral salpingo-oophorectomy (BSO) • Omentectomy • Peritoneal washings for cytological assessment • Biopsy of all suspicious peritoneal lesions
	Comprehensive surgical staging	Mandatory in all patients. Minimum required components: • Collection of peritoneal washings prior to any operative manipulation • Systematic inspection of the entire peritoneal cavity including diaphragmatic surfaces and paracolic gutters • Infracolic omentectomy • Biopsy of all suspicious peritoneal deposits or adhesions • Random peritoneal biopsies should be taken when accurate staging alters management Incomplete staging may necessitate re-staging surgery and should be avoided.
	Lymph node assessment	Routine systematic pelvic and para-aortic lymphadenectomy is not recommended in clinically early-stage disease in the absence of lymphadenopathy. Enlarged or clinically suspicious lymph nodes identified intraoperatively or on pre-operative imaging should be sampled or excised and submitted for histological assessment.
	Intraoperative frozen section	Intraoperative frozen section analysis should be requested where available to guide the extent of surgical resection, particularly when a pre-operative diagnosis of malignancy has not been established. The possibility of conversion to a more extensive operation should be discussed with the patient prior to the procedure.
Adjuvant management	**Observation only**	Active surveillance without adjuvant chemotherapy is recommended following complete surgical staging for: • Stage IA and IB dysgerminoma • Stage IA, Grade 1 immature teratoma Surveillance should include clinical assessment, serial tumor markers (AFP, β-hCG, LDH), and interval cross-sectional imaging per the surveillance schedule. Active surveillance is only appropriate following confirmed comprehensive surgical staging.
	Indications for adjuvant chemotherapy	Adjuvant chemotherapy is indicated in patients with high-risk Stage I disease, including: • Stage IC disease (IC1, IC2, or IC3) • Yolk sac tumor (endodermal sinus tumor), any Stage I substage • Embryonal carcinoma • Mixed malignant germ cell tumor containing high-risk components • Grade 2 or Grade 3 immature teratoma The MDT should review all adjuvant chemotherapy decisions prior to commencement.
	First-line regimen: BEP	Bleomycin, etoposide, cisplatin (BEP) is the recommended first-line adjuvant chemotherapy regimen. Standard BEP dosing per cycle: Option 1 • Bleomycin: 30 units IV, Days 1, 8, and 15

Phase	Management component	GOSK recommendations
		• Etoposide: 100 mg/m² IV, Days 1–5 • Cisplatin: 20 mg/m² IV, Days 1–5 Option 2 • Bleomycin: 30 units IV (Days 1, 8, 15) • Etoposide: 165 mg/m² IV (Days 1–3) • Cisplatin: 50 mg/m² IV (Days 1–2) Three (3) cycles of BEP are recommended for high-risk Stage I disease.
	Alternative regimen: EP	Etoposide, cisplatin (EP) is the recommended alternative where bleomycin is contraindicated, including patients with pre-existing pulmonary compromise, impaired pulmonary function, or bleomycin hypersensitivity. The number of EP cycles and any regimen modifications should be determined by MDT review and documented in the patient case file.
	Treatment response monitoring	Before each cycle: • Serum AFP, β-hCG, LDH • CBC with differential • Renal function (urea, creatinine, eGFR) — mandatory before cisplatin • Liver function tests and serum electrolytes (including magnesium) Toxicity surveillance: • Pulmonary function assessment as clinically indicated (bleomycin) • Audiology assessment if ototoxicity suspected (cisplatin) • Peripheral neuropathy assessment at each clinical visit Post-treatment CT abdomen/pelvis to assess response and establish a surveillance baseline.
	Dose modification criteria	The following thresholds apply: • Do not initiate chemotherapy if ANC <1.0 × 10⁹/L or platelets <100 × 10⁹/L • Cisplatin dose reduction or substitution if CrCl <50 mL/min • Discontinue bleomycin and substitute EP if cumulative pulmonary toxicity is suspected • Consider G-CSF prophylaxis in patients at high risk of febrile neutropenia All dose modifications must be approved by the treating oncologist and documented.
	MDT oversight of adjuvant tsreatment	The decision to initiate adjuvant chemotherapy, the choice of regimen, and the number of cycles must be reviewed and endorsed by the MDT prior to treatment commencement. Treatment summaries — including regimen, cycle completion, dose modifications, and toxicities — should be communicated to all relevant MDT members and retained in the patient case file.

AFP: alpha-fetoprotein; ANC: absolute neutrophil count; BEP: bleomycin, etoposide, cisplatin; BSO: bilateral salpingo-oophorectomy; β-hCG: beta-human chorionic gonadotrophin; CBC: complete blood count; CrCl: creatinine clearance; CT: computed tomography; EP: etoposide, cisplatin; eGFR: estimated glomerular filtration rate; G-CSF: granulocyte colony-stimulating factor; LDH: lactate dehydrogenase; MDT: multidisciplinary team; TAH: total abdominal hysterectomy; USO: unilateral salpingo-oophorectomy.

7.3 Management of advanced malignant germ cell tumors (FIGO stage II–IV)

Table 26. GOSK recommendations for management of advanced malignant germ cell tumors (FIGO stage II–IV)

Phase	Management component	GOSK recommendations
Surgical management	**Guiding principles of surgical management**	Surgical management of advanced MOGCT should be directed towards: • Achievement of complete cytoreduction (R0) where surgically feasible and oncologically appropriate • Maximum effort cytoreduction where complete resection cannot be achieved • Accurate comprehensive surgical staging • Minimization of treatment-related surgical morbidity The extent of surgery should be individualized according to disease burden, patient age, performance status, and multidisciplinary team (MDT) assessment. All procedures should be undertaken by, or in close consultation with, a gynecological oncologist wherever feasible.
	Multidisciplinary review	Treatment decisions for advanced MOGCT should be guided through multidisciplinary discussion prior to surgical intervention and prior to initiation of systemic therapy. The recommended MDT composition includes: • Gynaecological oncologist • Medical oncologist

<table>
<tr><th>Phase</th><th>Management component</th><th>GOSK recommendations</th></tr>
<tr><td></td><td></td><td>• Pediatric oncologist
• Pathologist
• Radiologist
• Fertility specialist
• Supportive and palliative care provider
• Oncology nurse coordinator</td></tr>
<tr><td></td><td>Surgical procedure</td><td>The standard surgical procedure for advanced MOGCT may include:
• Total abdominal hysterectomy (TAH) with bilateral salpingo-oophorectomy (BSO)
• Omentectomy (infracolic, minimum; infragastric where feasible)
• Peritoneal washings for cytological assessment
• Biopsy or resection of all macroscopically visible peritoneal disease
• Resection of involved adjacent structures where required to achieve cytoreduction
• Lymph node sampling reserved for enlarged or clinically suspicious nodes
The goal of surgery should be complete gross resection (R0). Where R0 is not achievable, optimal cytoreduction (residual disease ≤1 cm) should be the surgical objective.</td></tr>
<tr><td></td><td>Comprehensive surgical staging</td><td>Comprehensive surgical staging should be performed in all patients where feasible and includes:
• Collection of peritoneal washings prior to any operative manipulation
• Systematic inspection of all peritoneal surfaces including diaphragm, paracolic gutters, and bowel mesentery
• Infracolic omentectomy
• Biopsy of all suspicious peritoneal deposits, adhesions, and nodules
• Assessment and documentation of lymph node status
Documentation of the extent of disease, residual tumor volume, and completeness of cytoreduction is mandatory and should be recorded in the operative report.</td></tr>
<tr><td></td><td>Fertility preservation in advanced disease</td><td>Fertility-sparing surgery is generally not recommended in advanced-stage (FIGO II–IV) MOGCT.
For highly selected patients with FIGO Stage II disease, fertility-sparing surgery may be considered following MDT discussion and only where:
• Disease is limited to one ovary with no involvement of the uterus
• The contralateral ovary appears macroscopically normal
• The oncologic outcome is unlikely to be compromised by fertility preservation

Pre-operative fertility counselling, including discussion of oocyte or embryo cryopreservation, should be offered to all reproductive-age patients irrespective of whether fertility-sparing surgery is undertaken.</td></tr>
<tr><td>Adjuvant management</td><td>First-line chemotherapy: BEP</td><td>Bleomycin, Etoposide, Cisplatin (BEP) is the recommended first-line chemotherapy regimen for FIGO Stage II–IV MOGCT.
Number of cycles:
Four (4) cycles of BEP are recommended for advanced-stage disease.
Standard BEP dosing (per 21-day cycle):
<table><tr><th>Drug</th><th>Dose</th><th>Schedule</th></tr><tr><td>Bleomycin</td><td>30 units</td><td>IV, Days 1, 8, and 15 of each 21-day cycle</td></tr><tr><td>Etoposide</td><td>100 mg/m²</td><td>IV infusion, Days 1–5 of each cycle</td></tr><tr><td>Cisplatin</td><td>20 mg/m²</td><td>IV infusion, Days 1–5 of each cycle</td></tr></table>Adequate hydration, antiemetic prophylaxis, and renal function assessment are mandatory prior to each cisplatin-containing cycle.</td></tr>
<tr><td></td><td>Alternative regimen: EP</td><td>Etoposide, cisplatin (EP) is the recommended alternative regimen where bleomycin is contraindicated or poorly tolerated, including patients with pre-existing pulmonary disease, impaired pulmonary function tests, or bleomycin hypersensitivity.
Standard EP dosing (per 21-day cycle):
<table><tr><th>Drug</th><th>Dose</th><th>Schedule</th></tr><tr><td>Etoposide</td><td>100 mg/m²</td><td>IV infusion, Days 1–5 of each cycle</td></tr></table></td></tr>
</table>

Phase	Management component	GOSK recommendations
		Cisplatin 20 mg/m² IV infusion, Days 1–5 of each cycle The number of EP cycles and any further regimen modifications should be determined by MDT review and documented in the patient case file.
	Neoadjuvant chemotherapy	Neoadjuvant chemotherapy (NACT) followed by interval cytoreductive surgery may be considered in selected patients with: • Unresectable advanced disease at initial presentation • Poor performance status precluding upfront surgical resection • Significant comorbidities that increase perioperative risk BEP (as above) is the preferred NACT regimen. The decision to proceed with NACT should be made following MDT review with documented rationale. Interval cytoreductive surgery should be considered following 2–3 cycles of NACT in patients demonstrating an adequate tumor marker and radiological response.
	Treatment response assessment	Treatment response should be evaluated at regular intervals during and following chemotherapy using: Clinical assessment: the performance status and clinical improvement should be evaluated. Biochemical assessment (before each cycle and at completion): • Serum AFP • Serum β-hCG • Serum LDH Radiological assessment: • CT abdomen and pelvis following completion of chemotherapy to assess residual disease and establish a post-treatment surveillance baseline • Interim imaging should be considered after cycle 2 in patients with bulky disease or where clinical response is uncertain Persistent or rising tumor markers following two cycles of chemotherapy should prompt reassessment for refractory or progressive disease and MDT review for salvage options.
	Monitoring during treatment	Clinical and laboratory monitoring should be performed before each chemotherapy cycle and includes: Hematological: • Complete blood count (CBC) with differential — do not administer if ANC <1.0 × 10⁹/L or platelets <100 × 10⁹/L Biochemical: • Renal function tests (urea, creatinine, eGFR) — mandatory before each cisplatin cycle • Liver function tests • Serum electrolytes including magnesium Toxicity monitoring: • Pulmonary function assessment as clinically indicated in patients receiving bleomycin • Audiology where ototoxicity is suspected (cisplatin) • Peripheral neuropathy assessment at each clinical visit
	Dose modification criteria	The following dose modification principles apply: • Delay chemotherapy if ANC <1.0 × 10⁹/L or platelet count <100 × 10⁹/L • Reduce or substitute cisplatin if CrCl falls below 50 mL/min • Discontinue bleomycin and substitute EP if cumulative pulmonary toxicity develops • Consider G-CSF prophylaxis in patients at high risk of febrile neutropenia • Dose reductions should follow validated toxicity grading criteria (CTCAE) and be reviewed by the treating oncologist All dose modifications must be documented and the rationale recorded in the patient case file.
	Supportive care	Comprehensive supportive and palliative care should be integrated from the point of diagnosis and provided throughout the treatment pathway. This includes: • Psychosocial support and counselling for the patient and family • Symptom management including pain, nausea, and fatigue • Pre-treatment fertility counselling and preservation planning for all reproductive-age patients • Nutritional assessment and support • Early referral to palliative care services for patients with advanced or refractory disease

Phase	Management component	GOSK recommendations
		• Psychosocial screening at baseline and at key treatment transitions

AFP: alpha-fetoprotein; ANC: absolute neutrophil count; BEP: bleomycin, etoposide, cisplatin; BSO: bilateral salpingo-oophorectomy; β-hCG: beta-human chorionic gonadotrophin; CBC: complete blood count; CrCl: creatinine clearance; CTCAE: Common Terminology Criteria for Adverse Events; CT: computed tomography; EP: etoposide, cisplatin; eGFR: estimated glomerular filtration rate; FIGO: International Federation of Gynecology and Obstetrics; G-CSF: granulocyte colony-stimulating factor; LDH: lactate dehydrogenase; MDT: multidisciplinary team; NACT: neoadjuvant chemotherapy; R0: complete gross resection; TAH: total abdominal hysterectomy

7.4 Management of chemoresistant and recurrent malignant ovarian germ cell tumors

Table 27. GOSK recommendations for management of chemoresistant and recurrent malignant ovarian germ cell tumors

Phase	Management component	GOSK recommendations
Assessment and multidisciplinary team review	**Confirmation of recurrence or refractory disease**	Suspected recurrent or refractory MOGCT should be confirmed through a structured clinical assessment comprising: • Comprehensive clinical history and physical examination • Serial tumor marker measurement: serum AFP, β-hCG, and LDH • Appropriate cross-sectional imaging: CT abdomen/pelvis ± chest; consider PET/CT in selected cases Histopathological confirmation of recurrence should be sought, if possible, where the diagnosis is uncertain, where the histological subtype may have evolved, or where results would materially alter management. The following clinical scenarios should prompt evaluation for platinum-resistant or refractory disease and MDT reassessment: • Persistent or rising tumor markers during first-line platinum-based chemotherapy • Progressive disease on imaging despite ongoing treatment • Disease recurrence within six months of completing platinum-based chemotherapy • Failure to achieve complete tumor marker normalization following completion of first-line therapy
	Multidisciplinary team (MDT) review	All patients with recurrent or refractory MOGCT must undergo MDT review before any further treatment is initiated. MDT discussion should address: • Platinum sensitivity status based on response to and interval from prior platinum-based therapy • Prior treatment history including cumulative drug doses and documented toxicities • Resectability of recurrent disease • Patient performance status and comorbidities • Fertility considerations and psychosocial status • Availability of clinical trials Documentation of MDT review, including the decision rationale, must be recorded in the patient case file.
Surgical management	**Secondary cytoreductive surgery**	Secondary cytoreductive surgery should be considered in patients with recurrent MOGCT where: • Disease is anatomically localized and complete gross resection (R0) is assessed to be surgically achievable • The patient has adequate performance status to tolerate re-operative surgery Surgical decisions should be individualized through MDT review, considering disease burden, prior treatment exposure, available chemotherapy options, and patient goals of care. Palliative surgery for symptom relief (obstruction, hemorrhage, or pain) may be appropriate in selected patients with advanced refractory disease following MDT review.
Systemic treatment	**Platinum-sensitive recurrence**	Platinum-based rechallenge is recommended for patients with platinum-sensitive recurrence (defined as disease recurrence occurring ≥6 months following completion of prior platinum-based therapy). Preferred regimens include: Option 1 — BEP: Drug — Dose — Schedule Bleomycin — 30 units — IV, Days 1, 8, and 15 per 21-day cycle Etoposide — 100 mg/m² — IV infusion, Days 1–5 per cycle Cisplatin — 20 mg/m² — IV infusion, Days 1–5 per cycle

Phase	Management component	GOSK recommendations
		Option 2 — TIP: Drug / Dose / Schedule Paclitaxel / 175 mg/m² / IV infusion over 3 hours, Day 1 Ifosfamide / 1,200 mg/m² / IV infusion, Days 1–5 with Mesna 300mg/m² over 15 minutes, three times daily (one dose before ifosfamide, then at 4 and 8 hours from the start of each ifosfamide dose) on days 1-5 for uroprotection Cisplatin / 20 mg/m² / IV infusion, Days 1–5 per 21-day cycle Option 3 — EP: Drug / Dose / Schedule Etoposide / 100 mg/m² / IV infusion, Days 1–5 per cycle Cisplatin / 20 mg/m² / IV infusion, Days 1–5 per 21-day cycle Three to four cycles are generally recommended; the precise number should be determined by MDT review based on response, tolerability, and prior cumulative drug exposure. Mesna uroprotection is mandatory with all ifosfamide-containing regimens.
	Platinum-resistant or refractory disease	Patients with platinum-resistant disease (recurrence within <6 months of prior platinum) or refractory disease (progression during or immediately after platinum-based treatment) should be considered for non-platinum or alternative platinum-containing salvage chemotherapy regimens. Recommended salvage regimens: Option 1 — TIP (preferred salvage): Drug / Dose / Schedule Paclitaxel / 175 mg/m² / IV infusion over 3 hours, Day 1 Ifosfamide / 1,200 mg/m² / IV infusion, Days 1–5 with Mesna 300mg/m² over 15 minutes, three times daily (one dose before ifosfamide, then at 4 and 8 hours from the start of each ifosfamide dose) on days 1-5 for uroprotection Cisplatin / 20 mg/m² / IV infusion, Days 1–5 per 21-day cycle Option 2 — VeIP: Drug / Dose / Schedule Vinblastine / 0.11 mg/kg / IV bolus, Days 1 and 2 Ifosfamide / 1,200 mg/m² / IV infusion, Days 1–5 with Mesna 300mg/m² over 15 minutes, three times daily (one dose before ifosfamide, then at 4 and 8 hours from the start of each ifosfamide dose) on days 1-5 for uroprotection Cisplatin / 20 mg/m² / IV infusion, Days 1–5 per 21-day cycle Option 3 — VIP:

<table>
<tr><th>Phase</th><th>Management component</th><th>GOSK recommendations</th></tr>
<tr><td></td><td></td><td>
<table>
<tr><th>Drug</th><th>Dose</th><th>Schedule</th></tr>
<tr><td>Etoposide</td><td>75 mg/m²</td><td>IV infusion, Days 1–5</td></tr>
<tr><td>Ifosfamide</td><td>1,200 mg/m²</td><td>IV infusion, Days 1–5 with Mesna 300mg/m² over 15 minutes, three times daily (one dose before ifosfamide, then at 4 and 8 hours from the start of each ifosfamide dose) on days 1-5 for uroprotection</td></tr>
<tr><td>Cisplatin</td><td>20 mg/m²</td><td>IV infusion, Days 1–5 per 21-day cycle</td></tr>
</table>
Regimen selection should be guided by prior treatment exposure, cumulative toxicity profile, and available institutional expertise.
Enrollment into a clinical trial is strongly encouraged where available.
Mesna uroprotection is mandatory with all ifosfamide-containing regimens.
</td></tr>
<tr><td></td><td>Radiation therapy</td><td>Radiation therapy is not recommended as a routine component of management for recurrent or refractory MOGCT.
Radiation may be considered in the following limited clinical scenarios:
• Localized recurrent dysgerminoma where surgery is not feasible and the patient has failed, declined, or is unable to tolerate further chemotherapy
• Palliative radiation for symptomatic localized disease (bone metastases, CNS involvement) where systemic options are exhausted
The decision to use radiation therapy should be made through MDT review with explicit documentation of the indication and treatment intent (curative versus palliative).</td></tr>
<tr><td></td><td>Targeted therapy</td><td>There is currently insufficient evidence to support the routine use of targeted therapies in recurrent or refractory MOGCT outside of a clinical trial setting.
Targeted agents may be considered in highly selected patients with recurrent or refractory disease where:
• Conventional chemotherapy options have been exhausted
• Molecular profiling has identified a potentially actionable genomic target
• The patient is being managed at a specialist center with access to molecular diagnostics and novel therapeutics
Patients considered for targeted therapy should be referred to a specialist gynecological or medical oncology center. Participation in a clinical trial is preferred over off-label use of targeted agents.</td></tr>
<tr><td></td><td>Immunotherapy</td><td>Immunotherapy, including immune checkpoint inhibitors (e.g., pembrolizumab, nivolumab), is not recommended as routine treatment for recurrent or refractory MOGCT.
Consideration of immune checkpoint inhibitors may be appropriate in the following exceptional circumstances:
• Confirmed microsatellite instability-high (MSI-H) or mismatch repair-deficient (dMMR) tumor
• Exhaustion of standard chemotherapy options with no viable alternative
• Management within a clinical trial or under specialist multidisciplinary review with access to immune-oncology expertise
Immunotherapy for MOGCT should not be commenced outside of a clinical trial or formal MDT-endorsed compassionate use framework.</td></tr>
<tr><td></td><td>Clinical trial enrollment</td><td>Enrollment into appropriately designed clinical trials is strongly encouraged for all patients with recurrent or refractory MOGCT, particularly in the following clinical settings:
• Platinum-resistant or refractory disease
• Exhaustion of conventional salvage chemotherapy options
• Assessment of novel therapeutic strategies including targeted agents, immunotherapy, and high-dose chemotherapy protocols
The treating MDT should actively assess clinical trial eligibility at each point of disease recurrence or treatment failure and facilitate referral to trial sites where participation is appropriate.
Where clinical trials are not locally available, referral to a national or regional specialist oncology center should be considered.</td></tr>
</table>

AFP: alpha-fetoprotein; ASCT: autologous stem cell transplantation; β-hCG: beta-human chorionic gonadotrophin; BEP: bleomycin, etoposide, cisplatin; dMMR: mismatch repair-deficient; EP: etoposide, cisplatin; HDCT: high-dose chemotherapy; LDH: lactate dehydrogenase; MDT: multidisciplinary team; Mesna: sodium 2-mercaptoethane sulphonate; MSI-H: microsatellite instability-high; MOGCT: malignant ovarian germ cell tumor; PET/CT: positron emission tomography / computed tomography; R0: complete gross resection; TIP: paclitaxel, ifosfamide, cisplatin; VeIP: vinblastine, ifosfamide, cisplatin; VIP: etoposide, ifosfamide, cisplatin.

7.5 Follow up, surveillance and supportive care of malignant ovarian germ cell tumors

Table 28. GOSK recommendations for follow-up, surveillance and supportive care of malignant ovarian germ cell tumors

Phase	Management component	GOSK recommendations
Follow-up and surveillance	**Follow-Up Schedule**	Following completion of primary treatment, all patients with MOGCT should be enrolled into a structured surveillance program according to the following schedule: Time period — Assessment frequency Years 1–2 — Every 3 months Years 3–5 — Every 6 months Beyond 5 years — Annual assessment The follow-up interval may be extended or modified based on individual patient risk profile, histological subtype, and clinical response to treatment. Any adjustment should be documented with MDT rationale.
	Components of each follow-up assessment	Each scheduled follow-up assessment should include the following minimum components: Clinical assessment: • Comprehensive history including any new symptoms, treatment-related late effects, and psychosocial concerns • Full physical examination including pelvic examination • Performance status evaluation Biochemical assessment: • Serum AFP • Serum β-hCG • Serum LDH Imaging: • Pelvic ultrasound as the primary imaging modality for routine follow-up assessment • CT abdomen/pelvis or MRI reserved for patients with elevated tumor markers, clinical signs or symptoms suggestive of recurrence, or ambiguous ultrasound findings • PET/CT may be considered in selected cases where conventional imaging is equivocal and clinical suspicion of recurrence is high
	Long-term surveillance	Long-term surveillance for a minimum of five years is strongly recommended for all patients with MOGCT, given the documented risk of late relapse, particularly in dysgerminoma and mixed germ cell tumors. Following completion of the five-year structured surveillance period, annual clinical assessment should continue indefinitely and should address the following long-term sequelae: • Late relapse — rare but reported beyond five years; patients should be counselled to report any new symptoms promptly • Treatment-related late effects — bleomycin-associated pulmonary fibrosis, cisplatin-related nephrotoxicity, ototoxicity, and peripheral neuropathy, and etoposide-associated secondary malignancy risk • Ovarian function and fertility — assessment of ovarian reserve, menstrual cycle regularity, and reproductive outcomes in patients who underwent fertility-sparing surgery • Cardiovascular and metabolic health — monitoring for chemotherapy-related long-term cardiovascular and metabolic sequelae • Psychosocial wellbeing — ongoing assessment of psychological adjustment, body image, and quality of life
	Criteria for unscheduled reassessment	Patients should be assessed outside the routine surveillance schedule if any of the following are present: • New or worsening abdominal pain, pelvic pain, or abdominal distension • Rising or persistently elevated tumor markers on serial assessment • New palpable abdominal or pelvic mass on examination • Unexplained constitutional symptoms — weight loss, fatigue, or night sweats • Respiratory symptoms in patients with prior bleomycin exposure

Phase	Management component	GOSK recommendations
		Patients should be provided with clear written information detailing symptoms warranting urgent reassessment and an accessible point of contact within the treating oncology service.
Postoperative workup timeline	**Post-operative assessment timeline**	The following timeline outlines the minimum required clinical assessments and actions in the post-operative period following primary surgical management. The schedule may be adapted based on individual patient clinical status, surgical complications, or institutional protocols; any deviation should be documented with clinical rationale. **Time point** — **Required assessments and actions** **0–72 hours (inpatient)** • Assessment for immediate post-operative complications (hemorrhage, wound dehiscence, ileus, urinary retention) • Monitoring of urinary output and fluid balance • Vital signs monitoring and daily clinical review • Venous thromboembolism (VTE) prophylaxis per institutional protocol • Pain management optimization • – Discharge planning — patient suitable for discharge when hemodynamically stable, tolerating oral intake, and adequate analgesia achieved **2 weeks** • Wound assessment and early post-operative complication review • Confirmation of histopathological results where available; discussion with patient and family • Preliminary planning for adjuvant therapy where indicated — commence MDT scheduling • Tumor marker reassessment (AFP, β-hCG, LDH) to establish post-operative baseline • Fertility preservation counselling where applicable and not yet completed pre-operatively **1 Month** • Comprehensive review of post-operative recovery and wound healing • Confirmation and formal discussion of all histopathological results • Finalization and documentation of adjuvant therapy plan through MDT review • Referral to medical oncology or gynecological oncology for chemotherapy planning where indicated • Psychosocial assessment and referral to supportive care services as needed **3 Months** • First formal post-treatment surveillance assessment • FDG-PET/CT or contrast-enhanced CT abdomen/pelvis to establish post-treatment radiological baseline, where indicated • Tumor markers (AFP, β-hCG, LDH) • Full clinical assessment as per surveillance protocol • Commencement of structured follow-up schedule (refer follow-up schedule component) The timeline above represents the minimum standard of post-operative assessment. The treating gynecological oncologist and MDT should determine the appropriate intervals and content of assessments based on individual clinical circumstances.
Supportive and palliative care	**Definition and scope**	Supportive and palliative care encompasses the holistic, patient-centered care delivered alongside and integrated with active oncological treatment. It is not restricted to end-of-life care and should be initiated at the point of diagnosis. The scope of supportive and palliative care in MOGCT management includes:

Phase	Management component	GOSK recommendations
		• Systematic symptom assessment and evidence-based management of treatment-related and disease-related symptoms • Optimization of health-related quality of life throughout diagnosis, treatment, and survivorship • Psychosocial and psychological support for the patient, family, and caregivers • Facilitation of informed decision-making and communication regarding treatment goals • Coordination of specialist referrals to palliative care, social work, psychology, nutrition, and allied health services
	Goals of supportive care	The overarching goals of supportive and palliative care in the management of MOGCT are to: • Optimize health-related quality of life across all phases of the disease trajectory • Minimize symptom burden attributable to disease and treatment • Support the patient's informed decision-making throughout the clinical course • Provide comprehensive psychological, social, and spiritual support to the patient and caregivers • Facilitate timely and dignified end-of-life care for patients with advanced or refractory disease Supportive care goals should be reviewed and documented at each clinical encounter and adapted as the patient's clinical status and treatment intent evolve.
	Symptom management	Systematic symptom assessment should be performed at each clinical contact using a validated assessment tool. Management should address: • Chemotherapy-related toxicities: Nausea and vomiting, mucositis, fatigue, peripheral neuropathy, alopecia, and hematological toxicities • Disease-related symptoms: Pelvic or abdominal pain, bowel or urinary dysfunction, ascites, and dyspnea • Late treatment effects: Pulmonary fibrosis (bleomycin), nephrotoxicity and ototoxicity (cisplatin), peripheral neuropathy, and risk of secondary malignancy (etoposide) • Hormonal and reproductive sequelae: Premature ovarian insufficiency, menopausal symptoms, and infertility following bilateral oophorectomy Symptom management protocols should follow evidence-based guidelines and be adapted to available resources within the Kenyan healthcare setting.
	Psychosocial support	Psychosocial support is particularly important in MOGCT, given the young age at diagnosis, fertility implications, and the significant psychological impact of a cancer diagnosis in adolescence and early adulthood. Support should address: • Psychological adjustment to diagnosis, treatment, and survivorship • Body image concerns, particularly in relation to surgical scarring, alopecia, and premature menopause • Grief related to fertility loss or reduced reproductive potential • Relationship and sexuality concerns • Return to education and employment • Caregiver and family support needs Formal psychological or psychiatric referral should be offered where clinically indicated. Peer support programs and community-based resources should be integrated where available. Psychosocial screening should be performed at diagnosis, at treatment transitions, at completion of therapy, and at any point of disease recurrence.
	Fertility counselling and preservation in survivorship	Fertility counselling should continue throughout the survivorship phase for patients who received fertility-sparing surgery or wish to pursue future pregnancy. This should include: • Assessment of ovarian reserve (AMH, antral follicle count) and menstrual function at defined surveillance intervals • Discussion of time to safe conception following completion of chemotherapy — generally a minimum of 12 months following completion of chemotherapy is advised, subject to specialist review • Referral to reproductive medicine or fertility services where conception is desired and additional specialist support is required • Monitoring and management of premature ovarian insufficiency in patients who underwent bilateral oophorectomy
	End-of-life and advance care planning	Advance care planning should be initiated for all patients with progressive or refractory disease and should address:

Phase	Management component	GOSK recommendations
		• Patient values, preferences, and goals of care in the context of advanced or terminal illness • Resuscitation status and preferred place of care and death • Formal documentation of advance care decisions in the patient case file • Referral to specialist palliative care and hospice services, where indicated • Bereavement support planning for family members and caregivers Advance care planning discussions should be conducted sensitively and in a culturally appropriate manner, with access to interpreter services or pastoral support as needed. These discussions should be initiated proactively, not deferred until clinical deterioration is imminent.

AFP: alpha-fetoprotein; AMH: anti-Müllerian hormone; β-hCG: beta-human chorionic gonadotrophin; CT: computed tomography; FDG-PET: fluorodeoxyglucose positron emission tomography; LDH: lactate dehydrogenase; MDT: multidisciplinary team; MOGCT: malignant ovarian germ cell tumor; MRI: magnetic resonance imaging; QoL: quality of life; VTE: venous thromboembolism.

References

1. Mei J, Tian H, Huang HS, et al. Cellular models of development of ovarian high-grade serous carcinoma: a review of cell of origin and mechanisms of carcinogenesis. Cell Prolif 2021; 54: e13029.

2. WHO Classification of Tumors Editorial Board. Female genital tumors. 5th ed. Lyon: International Agency for Research on Cancer; 2020.

3. Dantkale KS, Agrawal M. A comprehensive review of current trends in the diagnosis and treatment of ovarian germ cell tumors. Cureus 2024; 16: e52650.

4. Gatta G, van der Zwan JM, Casali PG et al. Rare cancers are not so rare: the rare cancer burden in Europe. Eur J Cancer 2011; 47: 2493–2511.

5. Hubbard AK, Poynter JN. Global incidence comparisons and trends in ovarian germ cell tumors by geographic region in girls, adolescents and young women: 1988-2012. Gynecol Oncol 2019; 154: 608.

6. Gershenson DM, Del Junco G, Copeland LJ, et al. Mixed germ cell tumors of the ovary. Obstet Gynecol. 1984; 64: 200–206.

7. Bryant CS, Kumar S, Shah JP, et al. Racial disparities in survival among patients with germ cell tumors of the ovary in United States. Gynecol Oncol. 2009; 114: 437–443.

8. Poynter JN, Radzom AH, Spector LG, et al. Family history of cancer and malignant germ cell tumors in children: a report from the Children's Oncology Group. Cancer Causes Control. 2010; 21: 181–189.

9. Walker AH, Ross RK, Haile RW, Henderson BE. Hormonal factors and risk of ovarian germ cell cancer in young women. Br J Cancer 1988; 57: 418–422.

10. Omonisi AE, Liu B, Parkin DM. Population-based cancer registration in sub-Saharan Africa: its role in research and cancer control. JCO Glob Oncol 2020; 6: 1721–1728.