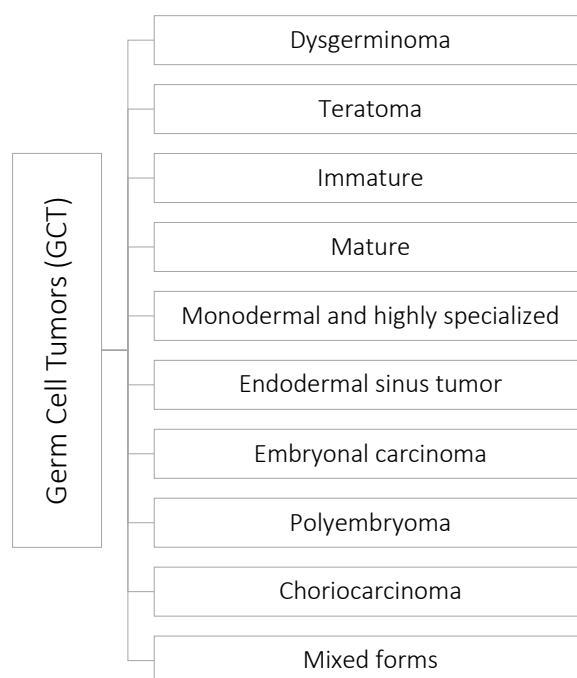
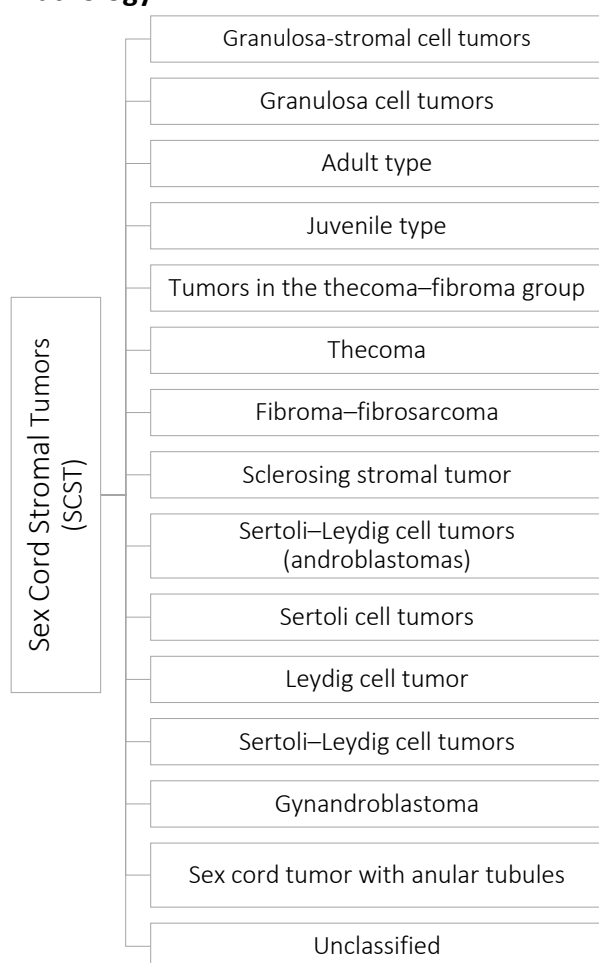


NON-EPITHELIAL OVARIAN CANCER

Initial Workup

- **Clinical:**
 - Performance status
- **Pathology review**
- **Laboratory Investigations:**
 - Complete blood count (CBC)
 - Chemistry profile
 - Human chorionic gonadotropin (β -HCG)
 - Alpha-fetoprotein (AFP)
 - Lactate Dehydrogenase (LDH)
- **Imaging:**
 - Chest X-ray
 - Pelvic ultrasound
 - Abdominopelvic CT scan
 - PET scan (if clinically indicated)
- **Pathology**



Staging and Risk Assessment

- The staging system for non-epithelial ovarian cancers is generally adopted from that used for epithelial ovarian cancer.
- The majority of germ cell tumors (GCTs) (60–70%) are diagnosed at an early stage.
- Stage I patients have an excellent prognosis (long-term disease-free status is 90%).

Surgical Approaches for Non-epithelial Ovarian Cancer

- Surgical Staging:
 - The staging procedure includes infra-colic omentectomy and biopsy of:
 - Diaphragmatic peritoneum,
 - Paracolic gutters,
 - Pelvic peritoneum and
 - Peritoneal washings.
 - Systematic lymphadenectomy is not required. Only in cases of evidence of nodal abnormality, lymph node dissection is required.
 - Surgical staging for endodermal sinus tumor is not indicated because all patients need chemotherapy.

Special Considerations:

1) Sex cord-stromal tumors (SCSTs):

- Conservative surgery seems like an appropriate approach in young patients with SCSTs at stage I disease.
- Retroperitoneal evaluation is not mandatory for SCSTs because of the very low incidence of retroperitoneal metastases in the early stage.

2) In patients with granulosa cell tumor:

- Endometrial curettage must be performed to rule out concomitant uterine cancers

3) In postmenopausal women, patients with advanced stage disease or with bilateral ovarian involvement:

- Abdominal hysterectomy and
- Bilateral salpingo-oophorectomy should be performed with careful surgical staging.

Treatment Algorithm

I. Germ Cell Tumors

Stage I – IIA:

Stage IA immature teratoma grade 1 or Stage I pure dysgerminoma	Surgery only
Stage IA immature teratoma grade 2 and 3 and IB – IC	Still controversial
All patients with stage I endodermal sinus (yolk sac tumor)	Adjuvant chemotherapy in the form of (BEP) for 3 cycles

BEP regimen:

Cisplatin 20 mg/m² D1-5

Etoposide 100 mg/m² D1-5

Bleomycin 30 mg D1, 8, 15

Stage IIb – IV Germ Cell Tumors:

Debulking surgery



Adjuvant chemotherapy:

Three cycles of BEP with the completely resected disease or

Four cycles for patients with macroscopic residual disease.



Post adjuvant chemotherapy



If a complete remission is achieved:

Patients will undergo surveillance



If Residual tumor with normal markers:

- If patients subjected to resection revealed necrotic tissue or mature teratoma; they will be opted for surveillance.
- If the residual tumor is present and/or having elevated markers will be candidates for second-line chemotherapy.

Salvage Chemotherapy**VIP (PEI)**

Ifosfamide: 1200 mg/m² IV infusion over 1 hour on days 1-5

Etoposide (VP-16): 75 mg/m² IV infusion over 1 hour on days 1-5

Cisplatin: 20 mg/m² IV infusion over 30 minutes on days 1-5

Every 3 weeks FOR 4 cycles with mesna cyto-protection

VeIP

Similar to VIP except giving Vinblastine 0.11 mg /kg iv days 1 and 2 instead of Etoposide.

TIP

Paclitaxel: 250 mg/m² IV infusion for 24 hours on day 1

Cisplatin: 25 mg/m² IV infusion over 30 minutes on days 2-5

Ifosfamide: 1500 mg/m² IV infusion over 1 hour on days 2-5

Every 3 weeks for 4 cycles with mesna and growth factor support

High dose chemotherapy with stem cell support

May play a role in selected relapsed cases.

II. Sex-cord Tumors

- The most common cases are the granulosa variant:
 - There is no standard chemotherapy for these patients.
 - Optimal surgical resection is the most important factor in potentially curing these cases.
- The majority of sex-cord tumors are mostly stage I at the time of diagnosis:
 - Stage I patients have an excellent prognosis (long-term disease-free status is 90%).

Stage I

- Surgery followed by observation.
- Platinum-based chemotherapy is the treatment of choice.
- Adjuvant chemotherapy is not standard but may be used in:
 - High-risk disease profile including:
 - Tumor rupture,
 - Stage IC,
 - Poorly differentiated tumor,
 - Size more than 10-15 cm.

Stage II-IV

- Surgery and complete surgical staging.
- Adjuvant treatment:
 - BEP regimen for 3–6 cycles is recommended.

Relapsed Cases

- Clinical trials enrolment.
- Chemotherapy:
 - Taxanes, oxaliplatin, gemcitabine or carboplatin.
- Second cytoreduction.

Follow-up

- The follow-up visit must include:
 - History,
 - Physical examination with pelvic examination and
 - Tumor markers every:
 - 3 months for the first 2 years then
 - 6 months during years 3–5 or until progression is documented.
- Pelvic ultrasound should be performed every 6 months in those patients who underwent fertility-sparing surgery.
- CT scans of the abdomen and pelvis is usually performed yearly.

References

- 1) Horn-Ross PL, et al. Collaborative Ovarian Cancer Group, 1992 characteristics relating to ovarian cancer risk. Collaborative analysis of 12 US case-control studies. VI. Nonepithelial cancers among adults. Collaborative Ovarian Cancer Group. *Epidemiology*. 1992;3(6):490-495.
- 2) Hildebrandt RH, et al. Value of inhibin in the identification of granulosa cell tumors of the ovary. *Hum Pathol*. 1997;28(12):1387-1395.
- 3) Homesley HD, et al. Bleomycin, etoposide, and cisplatin combination therapy of ovarian granulosa cell tumors and other stromal malignancies: a Gynecologic Oncology Group study. *Gynecol Oncol*. 1999;72(2):131-137.
- 4) Balasubramaniam S, et al. FDA Approval Summary: Rucaparib for the treatment of patients with deleterious BRCA mutation-associated advanced ovarian cancer. *Clin Cancer Res*. 2017;23(23):7165-7170.
- 5) Pujade-Lauraine E, et al. Olaparib tablets as maintenance therapy in patients with platinum-sensitive, relapsed ovarian cancer and a BRCA1/2 mutation (SOLO2/ENGOT-Ov21): a double-blind, randomized, placebo-controlled, phase 3 trial. *Lancet Oncol*. 2017;18(9):1274-1284.
- 6) Scott LJ. Niraparib: First global approval. *Drugs*. 2017;77(9):1029-1034.