

Ovarian Cancer

Common Epithelial Mullerian Tumors

Can arise from ovarian or fallopian tube epithelium

1. Serous	High Grade (predominantly)	<ul style="list-style-type: none"> • Most common ovarian cancer (70%) • p53 mutations (95%) • Associated w/ BRCA1/2 (20%) • Associated with HRD mutations (50%) • Can be HER2+ • Chemo-sensitive
	Low Grade (rare)	<ul style="list-style-type: none"> • Distinct profile from high grade serous • Less chemo-sensitive • Somatic KRAS mutations 30% • BRAF/MEK activation --> sensitive to MEK inhibitors
2. Endometrioid	Low Grade (predominantly)	<ul style="list-style-type: none"> • Associated w/ endometriosis (20%) • Associated w/ Lynch Syndrome • Often found at earlier stage, lower grade • Chemo-sensitive
3. Clear Cell	High Grade	<ul style="list-style-type: none"> • Associated w/ endometriosis (20%) • Chemo-resistant
4. Mucinous	High Grade	<ul style="list-style-type: none"> • Rare • Often lower CA-125 • Rule out GI primary (EGD/Colonoscopy) • Chemo-resistant

Ovarian Cancer: Histology

Rare Ovarian Tumors

Carcinosarcoma

Mixed epithelial/mesenchymal

Undifferentiated Carcinoma

Germ Cell Ovarian

Sex Cord Stromal

Borderline Epithelial Ovarian Tumors of Low Malignant Potential

Not malignant

Ovarian Cancer: Diagnosis & Staging

Work Up:

Imaging

CT Torso (even for stage I)

Biopsy

Often omental biopsy

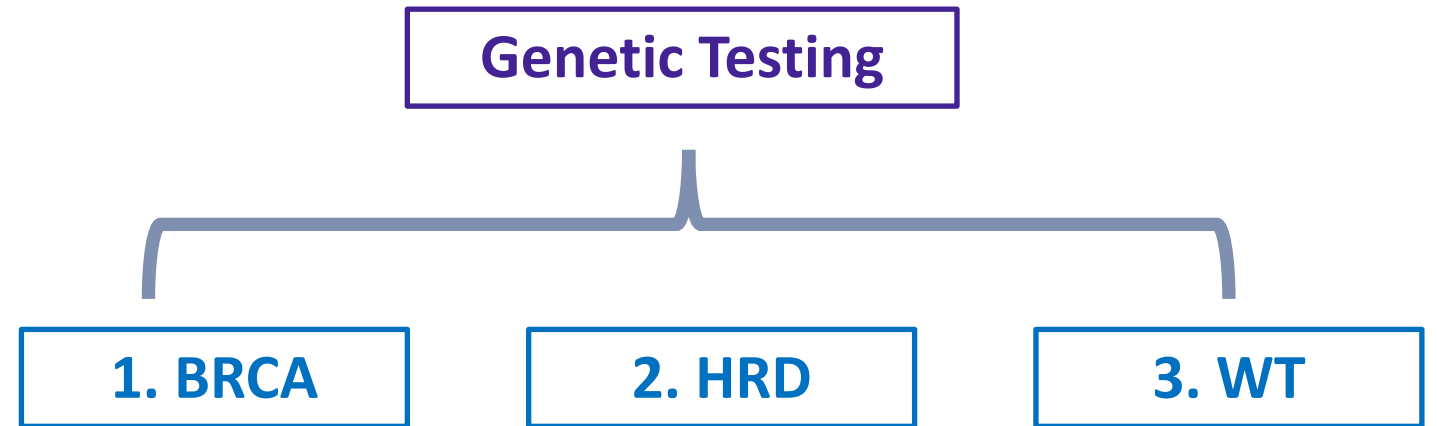
CK7+/CK20-

PAX8+, WT1+

Labs

CA-125 (pre-op)

- * Can be falsely elevated iso ascites
- * Not specific for ovarian cancer
- * Elevated in most cases of advanced disease, but only 50% of early-stage disease



BRCA or HRD = difficulty repairing dsDNA breaks

- 1. BRCA** = mutation in BRCA1/2. 5-15% of Ovarian Cancers
BRCA1 risk of ovarian cancer is 30-40% (mid-late 30s)
BRCA2 risk of ovarian cancer is 10% (mid-late 40s)

- 2. HRD** = Homologous Recombination Deficiency ("BRCA-Like")
HRD status is assessed by a score evaluating several genomic abnormalities

- 3. Wild Type** = no mutation in BRCA or HRD

Ovarian Cancer: Diagnosis & Staging

Staging:

Stage 1: Ovary or Fallopian Tube

1A: Single ovary, capsule intact or fallopian tube

1B: Both ovaries, capsule intact or fallopian tubes

1C: Capsule rupture, surgical spill, +peritoneal washings

Stage 2: Pelvic Extension

Uterus or fallopian tubes

Pelvic organs (bladder, rectum, vagina)

Stage 3: Abdominal Extension

Retroperitoneal LN (pelvic, para-aortic)

Peritoneal carcinomatosis

Serosa of liver/spleen

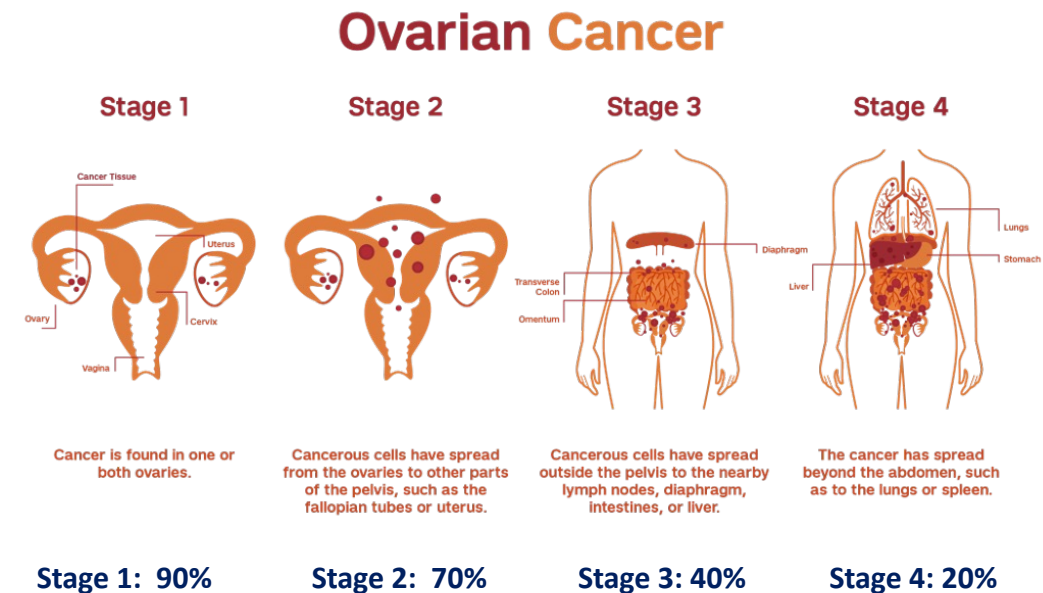
Stage 4: Distant Metastases

Inguinal LN

Parenchymal mets liver, spleen, lung, transmural bowel

Extra-abdominal extension (pleural effusion)

Prognosis: 5Y OS Rates



Ovarian Cancer: Treatment

Stage IA-IB: single or bilateral ovaries or fallopian tubes, no capsule rupture

TAH/BSO + Surgical Staging **+/- Adjuvant Chemotherapy**

Stage IC-II: capsule rupture, +peritoneal washings, local pelvic spread

TAH/BSO + Surgical Staging **+ Adjuvant Chemotherapy**

Stage III-IV: peritoneal, abdominal or extrapelvic mets

TAH/BSO + Surgical Staging **+ Neo or Adjuvant Chemotherapy**
+ Maintenance Therapy

Early Stage (Stage I-II)

Surveillance: CA-125, no routine imaging

TAH/BSO + Surgical Staging

Consider USO/BSO only
if fertility preservation desired

surgical staging includes evaluation of:

- Pelvic peritoneum, para-colic gutters
- Serosal surface of liver, spleen, diaphragm
- Ascitic fluid
- Retroperitoneal LN
- Omentum

Stage IA/IB Grade 1-2:

ex: low-grade serous, endometrioid

Observation

- **Stage IA/IB Grade 2-3**
ex: high-grade serous, clear cell
- **Stage IC-II**
ex: capsule rupture, pelvic extension

Adjuvant Chemotherapy

Early Stage (Stage I-II)

Surveillance: CA-125, no routine imaging

TAH/BSO + Surgical Staging + Adjuvant Chemotherapy

Adjuvant Chemotherapy

Carboplatin/Paclitaxel

3 vs. 6 cycles

3 cycles: if poor ECOG, Stage 1 or low-grade tumors

6 cycles: if high-grade serous

Important Side Effects:

Carboplatin → cytopenias, neuropathy, nephropathy, ototoxicity

Paclitaxel → neuropathy, hair loss, hypersensitivity reaction, skin/nail changes

Stage III-IV: Abdominal or Distant Mets

Surveillance: CA-125, no routine imaging

TAH/BSO + Surgical Staging

Stage IV disease is curable (15-20%):

** usually not candidates for up-front surgery, would require neoadjuvant tx*

Neo or Adjuvant Chemotherapy

Carboplatin/Paclitaxel x6 cycles total

** Intraperitoneal chemo also an option after maximal debulking*

Maintenance Therapy

if High Grade Serous or Endometrioid

Stage III-IV: Maintenance Therapy

Maintenance Therapy

only for:
High Grade Serous
Endometrioid

PARP inhibitors:

Olaparib (BRCA, HRD required) x2Y
Niraparib (BRCA, HRD preferred) x3Y

VEGF Inhibitors:

Bevacizumab x 15M

Endocrine therapy:

Aromatase Inhibitor (low-grade endometrioid)

Important Side Effects:

PARP → GI toxicity, cytopenias, 1% risk MDS
Bevacizumab → proteinuria, HTN, bleeding
(contraindicated if h/o TIA/strokes, bowel obstruction/perforation)

Genetic Testing

Tx Options:

1. BRCA

1. Olaparib +/- Bev
2. Niraparib

2. HRD

1. Olaparib +/- Bev
2. Niraparib

3. WT

1. Bevacizumab
2. AI low grade endometrial
3. Consider Niraparib small PFS benefit in WT
4. Surveillance

Stage III-IV: Abdominal or Distant Mets

Upfront Surgical Candidate



Not Surgical Candidate



Recurrent Disease

Recurrence > 6 months:
Platinum Sensitive

Consider

Secondary Cytoreduction

In selected patients:

Isolated focus, no ascites, good PS

Platinum Chemotherapy

Carboplatin Doublet +/- Bevacizumab x6 cycles

Carbo/Taxol

Carbo/Gem

Carbo/Doxil

Maintenance Therapy

1. PARP (if BRCA+)

Olaparib

Niraparib

Rucaparib

2. Bevacizumab

Recurrent Disease

**Recurrence < 2 months
Never Remission:
Platinum Refractory**

**Recurrence < 6 months:
Platinum Resistant**

Refractory/Resistant Treatment Options:

Clinical Trial

Chemotherapy

Doxil, Paclitaxel, Docetaxel, Gemcitabine, Topotecan
+/- Bevacizumab

Mirvetuximab (*Elahere*)

ADC: Folate receptor antibody + microtubule inhibitor

Only if Folate Receptor (FOLR) positive > 75%

AEs: Ocular toxicity (requires frequent ophtho visits + eye drops)

Recurrent Low Grade Serous

Endocrine therapy (ER+)

MEK Inhibitors: Trametinib +/- Dabrafenib (BRAF+)

Chemotherapy

Ovarian Cancer

Rare Pathologies

Carcinosarcoma

Malignant epithelial + Mesenchymal components

Treatment Stage I-IV: Surgery + Carbo/Taxol

* *OR other Carbo doublet: Docetaxel, Doxil, Ifosphamide*

* *NOT candidates for fertility sparing surgery*

Mucinous

Very rare: need to rule out GI primary cancer with metastases to ovaries (EGD, Colonoscopy)

Treatment Stage IA-IB:

Observation or Surgery

Treatment Stage IC:

Observation or Surgery +/- adjuvant therapy

Treatment Stage II-IV:

Carbo/Taxol +/- Bev

FOLOX or CAPOX +/- Bev

Ovarian Cancer

Rare Pathologies

Germ Cell Tumors

Benign or Malignant



Dysgerminoma

Non-Dysgerminoma

Embryonal

Choriocarcinoma

Endodermal Sinus/Yolk Sac

Teratoma

Dysgerminoma & Teratoma	Stage I	Observation
	Stage II-IV	BEP x3-4
Non-Dysgerminoma	Stage I-IV	BEP x3-4

Sex Cord Stromal Tumors

Benign or Malignant

Types: Stromal or Sex Cord

Stromal: Fibromas, Thecomas, Leydig

Sex Cord: Granulosa, Sertoli

Mixed: Sertoli-Leydig

Symptoms: Produce hormones

Estrogen: Granulosa, Thecoma

Androgen: Sertoli-Leydig

Meig's Syndrome:

Benign ovarian tumors can cause ascites, effusions

Removal of tumor → resolution of ascites, effusions

Treatment

Stage I → observe or chemotherapy

Stage II-IV → chemo (carbo/taxol) or RT (limited disease)

Ovarian Cancer Reference Handout

Ovarian Histology

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3. Clear Cell	High Grade	<ul style="list-style-type: none">• Associated w/ endometriosis• Chemoresistant
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Work Up:

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Often omental biopsy

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Genetic Testing

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2. HRD

3. WT

Ovarian Cancer Staging

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Stage 4: Distant Metastases

Inguinal LN

Parenchymal mets liver, spleen, lung, transmural bowel

Extra-abdominal extension (pleural effusion)

Prognosis: 5Y OS Rates

Stage 1: 90%

Stage 2: 70%

Stage 3: 40%

Stage 4: 20%

Ovarian Cancer Initial Treatment

Surveillance: CA-125, no routine imaging

Stage IA-IB: Ovary or Fallopian Tubes

TAH/BSO + 

- Grade 1:**
Observation
- Grade 2:**
Adjuvant chemo if high-risk
- Grade 3:**
Adjuvant chemo

Adjuvant Chemotherapy:

Carboplatin/Paclitaxel
3-6 cycles (usually 6 cycles)

Important Side Effects:

Carboplatin → cytopenias
Paclitaxel → neuropathy, hair loss,
hypersensitivity reaction, skin/nail changes

Stage IC-II: Capsule Rupture, Pelvic Extension

TAH/BSO + 

Adjuvant Chemotherapy
Carboplatin/Paclitaxel x 6 cycles

Stage III-IV: Abdominal Extension or Distant Mets

TAH/BSO + 

Stage IV disease is curable (15-20%):
usually not candidates for up-front surgery

Important Side Effects:

PARP → GI toxicity, cytopenias, 1% risk MDS
Bevacizumab → proteinuria, HTN, bleeding
(contraindicated if h/o TIA/strokes, bowel obstruction)

Neo or Adjuvant Chemotherapy
Carboplatin/Paclitaxel +/- Bevacizumab x 6 cycles

Maintenance Therapy

- PARP inhibitors:**
Olaparib (BRCA/HRD required) x 2Y
Niraparib (BRCA/HRD preferred) x3Y
- Bevacizumab** x 15M (no contraindication)
- AI** (low-grade endometrioid)

Recurrent Disease Treatment

Recurrence > 6 months: Platinum Sensitive

Secondary Cytoreduction
if isolated focus, no ascites, good PS

Carboplatin Doublet +/- Bevacizumab x6
Carbo/Taxol, Carbo/Doxil, Carbo/Gem

Maintenance

- PARP** Olaparib, Niraparib, Rucaparib (BRCA)
- Bevacizumab**

Recurrence < 6 months: Platinum Resistant

Clinical Trial

Chemotherapy

Doxil, Paclitaxel, Docetaxel, Topotecan, Gemcitabine
+/- Bevacizumab

Mirvetuximab Elahere (FOLR+)

Recurrent Low Grade Serous

Endocrine therapy (ER+)
Trametinib +/- Dabrafenib (BRAF+)