Outline

• Female Cancer Statistics
• Uterine Cancer
• Adnexal Cancer
• Cervical Cancer
• Vulvar Cancer
Estimated New Cancer Cases* in the US in 2016

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>841,390</td>
<td>843,820</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>21%</td>
<td>29%</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>14%</td>
<td>13%</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>8%</td>
<td>8%</td>
</tr>
<tr>
<td>Melanoma of skin</td>
<td>7%</td>
<td>7%</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>6%</td>
<td>6%</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>5%</td>
<td>4%</td>
</tr>
<tr>
<td>Oral cavity &amp; pharynx</td>
<td>5%</td>
<td>3%</td>
</tr>
<tr>
<td>Leukemia</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>All other sites</td>
<td>22%</td>
<td>21%</td>
</tr>
</tbody>
</table>

*Excludes basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.
The Lifetime Probability of Developing Cancer for Females, 2010-2012

<table>
<thead>
<tr>
<th>Site</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>All sites*</td>
<td>1 in 3</td>
</tr>
<tr>
<td>Breast</td>
<td>1 in 8</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>1 in 17</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>1 in 23</td>
</tr>
<tr>
<td>Uterine corpus</td>
<td>1 in 36</td>
</tr>
<tr>
<td>Melanoma of the skin†</td>
<td>1 in 52</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>1 in 53</td>
</tr>
<tr>
<td>Thyroid</td>
<td>1 in 58</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1 in 67</td>
</tr>
<tr>
<td>Ovary</td>
<td>1 in 77</td>
</tr>
<tr>
<td>Leukemia</td>
<td>1 in 82</td>
</tr>
</tbody>
</table>

*All sites exclude basal cell and squamous cell skin cancers and in situ cancers except urinary bladder. †Statistic for white females.
## Estimated Cancer Deaths in the US in 2016

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Males 314,290</th>
<th>Females 281,400</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung &amp; bronchus</td>
<td>27%</td>
<td>26%</td>
</tr>
<tr>
<td>Prostate</td>
<td>8%</td>
<td>14%</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>8%</td>
<td>8%</td>
</tr>
<tr>
<td>Pancreas</td>
<td>7%</td>
<td>7%</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>6%</td>
<td>5%</td>
</tr>
<tr>
<td>Leukemia</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Esophagus</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Brain &amp; other nervous system</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>All other sites</td>
<td>24%</td>
<td>24%</td>
</tr>
</tbody>
</table>

- Lung & bronchus accounted for 27% of male deaths and 26% of female deaths.
- Breast cancer was the second most common cause of female cancer deaths at 14%.
- Colon & rectum was the second most common cause of male cancer deaths at 8%.
- Pancreas accounted for 7% of male deaths and 7% of female deaths.
- Liver & intrahepatic bile duct accounted for 6% of male deaths and 5% of female deaths.
- Leukemia accounted for 4% of both male and female deaths.
- Esophagus accounted for 4% of both male and female deaths.
- Urinary bladder accounted for 4% of male deaths and 3% of female deaths.
- Non-Hodgkin lymphoma accounted for 4% of male deaths and 3% of female deaths.
- Brain & other nervous system accounted for 3% of male deaths and 2% of female deaths.
- All other sites accounted for 24% of male deaths and 24% of female deaths.
Uterine Cancer

Endometrial Cancer

Uterine Sarcoma
Endometrial Cancer

• Epidemiology and Risk Factors
• Histology
• Presentation
• Diagnosis
• Staging
• Therapy
  • Early
  • Locally Advanced
  • Metastatic
  • Recurrent
• Follow-Up
• Future Therapy
Epidemiology

- 60,500 cases expected in 2016
  - 25.3 per 100,000 women
- 10,470 deaths expected in 2016
Epidemiology

Increased Risk
• Age
• Unopposed Estrogens
  • Exogenous
  • Tamoxifen
  • Obesity
• Genetic Risk
  • Lynch Syndrome
  • Cowden Syndrome

Decreased Risk
• Progestational Agents
  • Oral Contraceptive Pills
  • Levonorgestrel IUS
• Physical Activity
• Pregnancy
• Breastfeeding
Histology

- **Type I**
  - Endometrioid, well differentiated
  - Less aggressive
  - Usually localized
  - Good Prognosis

- **Type II**
  - Clear cell, papillary serous, MMMT, poorly differentiated
  - More aggressive
  - Likely to spread
  - Worse Prognosis
Histology – Molecular Features

Type I
- Diploid
- K-ras overexpression
- PTEN mutations
- Microsatellite instability

Type II
- Aneuploid
- K-ras overexpression
- P53 overexpression
Clinical Presentation

• Abnormal Uterine Bleeding
• Postmenopausal Uterine Bleeding
• Abnormal Vaginal Discharge
• Endometrial cells on a pap smear
• Bloating/pelvic pressure/pain (if advanced disease)
Diagnosis

• Ultrasound
• Endometrial Biopsy
• Hysteroscopy
• Dilation and Curettage

• Hysterectomy +/- BSO +/- Lymph node sampling
Staging
Therapy – Early disease

Endometrial Carcinoma

CLINICAL FINDINGS

ADVERSE RISK FACTORS

HISTOLOGIC GRADE/ADJUVANT TREATMENT

G1
Observe

G2
Observe or Vaginal brachytherapy

G3
Observe or Vaginal brachytherapy

All staging in guideline is based on updated 2010 FIGO staging. (See ST-1)
Therapy – Locally advanced disease

Endometrial Carcinoma

All staging in guideline is based on updated 2010 FIGO staging. (See ST-1)

CLINICAL FINDINGS

HISTOLOGIC GRADE/ADJUVANT TREATMENT

<table>
<thead>
<tr>
<th>Histologic Grade</th>
<th>Treatment Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>Vaginal brachytherapy and/or EBRT</td>
</tr>
<tr>
<td>G2</td>
<td>Vaginal brachytherapy and/or EBRT</td>
</tr>
<tr>
<td>G3</td>
<td>EBRT ± vaginal brachytherapy ± chemotherapy (category 2B for chemotherapy)</td>
</tr>
</tbody>
</table>

Surgically staged:

Stage IIq,r

Stage IIIA

Chemotherapy ± RT or Tumor-directed RT ± chemotherapy or EBRT ± vaginal brachytherapy

Chemotherapy ± RT or Tumor-directed RT ± chemotherapy or EBRT ± vaginal brachytherapy

Chemotherapy ± RT or Tumor-directed RT ± chemotherapy or EBRT ± vaginal brachytherapy
Therapy – Metastatic disease

Endometrial Carcinoma

All staging in guideline is based on updated 2010 FIGO staging. (See ST-1)

CLINICAL FINDINGS

Stage IIIB

Stage IIIC1 → Pelvic node positive

Stage IIIC2 → Para-aortic node positive ± pelvic node positive

Stage IVA, IVB

ADJUVANT TREATMENT

Chemotherapy and/or tumor-directed RT

Chemotherapy and/or tumor-directed RT

Debunked1 and with no gross residual disease or microscopic abdominal disease

Chemotherapy ± RT
Therapy - Recurrence

- Re-excision
- Radiation
- Systemic Therapies:

<table>
<thead>
<tr>
<th>Hormone Therapy</th>
<th>Chemotherapy Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Megestrol/tamoxifen (alternating)</td>
<td>Multi-agent chemotherapy regimens preferred, if tolerated</td>
</tr>
</tbody>
</table>
| Progestational agents | Carboplatin/paclitaxel
| Aromatase inhibitors | Cisplatin/doxorubicin
| Tamoxifen | Cisplatin/doxorubicin/paclitaxel

- Single agents
  - Cisplatin
  - Carboplatin
  - Doxorubicin
  - Liposomal doxorubicin
  - Paclitaxel
  - Topotecan
  - Bevacizumab
  - Temsirolimus
  - Docetaxel (category 2B)
  - Ifosfamide (for carcinosarcoma)
Follow-up

- Regular pelvic examinations
- Symptom awareness
- No role for routine imaging/vaginal cytology
Emerging Therapies

• Sentinel Node Mapping
• Fertility Preservation
• Targeted Therapies
Uterine Sarcoma

• Epidemiology and Risk Factors
• Histology
• Presentation
• Diagnosis/Staging
• Therapy
• Follow-Up
• Future Therapy
Epidemiology

- Median age ranges is 40s to 50s based on histologic type
- Leiomyosarcomas are more common in black women than white women (age adjusted risk is 1.5 vs 0.9 per 100,000)
Risk Factors

• Prior radiation exposure
• Hormone exposure
  • ESS is the only true contraindication to hormone replacement after surgery for a gynecologic malignancy
• Tamoxifen Use
• Hereditary Predisposition
  • HNPCC/Lynch syndrome
Histology

• Leiomyosarcoma
  • Fleshy
  • Nuclear Atypia
  • Tumor Necrosis

• Endometrial stromal sarcoma
  • Low Grade
  • “Bland”
  • Single mass
  • ER/PR positive
Histology

- Undifferentiated Uterine Sarcoma
  - VERY atypical cells
Presentation

- Abnormal vaginal bleeding
- Abdominopelvic mass
- Incidental diagnosis at the time of hysterectomy
# Diagnosis/Staging

**Staging for uterine sarcomas (leiomyosarcomas, endometrial stromal sarcomas, adenosarcomas, and carcinosarcomas)**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Tumor limited to uterus</td>
</tr>
<tr>
<td>IA</td>
<td>&lt;5 cm</td>
</tr>
<tr>
<td>IB</td>
<td>&gt;5 cm</td>
</tr>
<tr>
<td>II</td>
<td>Tumor extends to the pelvis</td>
</tr>
<tr>
<td>IIA</td>
<td>Adnexal involvement</td>
</tr>
<tr>
<td>IIB</td>
<td>Tumor extends to extraterine pelvic tissue</td>
</tr>
<tr>
<td>III</td>
<td>Tumor invades abdominal tissues (not just protruding into the abdomen)</td>
</tr>
<tr>
<td>IIIA</td>
<td>One site</td>
</tr>
<tr>
<td>IIIB</td>
<td>&gt; one site</td>
</tr>
<tr>
<td>IIIC</td>
<td>Metastasis to pelvic and/or para-aortic lymph nodes</td>
</tr>
<tr>
<td>IV</td>
<td>Tumor invades bladder and/or rectum</td>
</tr>
<tr>
<td>IVA</td>
<td>Distant metastasis</td>
</tr>
</tbody>
</table>

**Endometrial stromal sarcomas (ESS) and adenosarcomas**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Tumor limited to uterus</td>
</tr>
<tr>
<td>IA</td>
<td>Tumor limited to endometrium/endocervix with no myometrial invasion</td>
</tr>
<tr>
<td>IB</td>
<td>Less than or equal to half myometrial invasion</td>
</tr>
<tr>
<td>IC</td>
<td>More than half myometrial invasion</td>
</tr>
<tr>
<td>II</td>
<td>Tumor extends to the pelvis</td>
</tr>
<tr>
<td>IIA</td>
<td>Adnexal involvement</td>
</tr>
<tr>
<td>IIB</td>
<td>Tumor extends to extraterine pelvic tissue</td>
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<td>III</td>
<td>Tumor invades abdominal tissues (not just protruding into the abdomen)</td>
</tr>
<tr>
<td>IIIA</td>
<td>One site</td>
</tr>
<tr>
<td>IIIB</td>
<td>&gt; one site</td>
</tr>
<tr>
<td>IIIC</td>
<td>Metastasis to pelvic and/or para-aortic lymph nodes</td>
</tr>
<tr>
<td>IV</td>
<td>Tumor invades bladder and/or rectum</td>
</tr>
<tr>
<td>IVA</td>
<td>Distant metastasis</td>
</tr>
</tbody>
</table>
Therapy

- Endometrial Stromal Sarcoma
  - Observation
  - Hormonal Therapy
  - Consider Radiotherapy

- LMS/UUS
  - Chemotherapy
  - Radiotherapy

- Lots of negative trials... disappointing results
- Most trials have slow accrual due to rarity of tumors
### Therapy


**Uterine Sarcoma**

**Systemic Therapy for Uterine Sarcoma**

*(Clinical trials strongly recommended)*

**Combination regimens:**
- Docetaxel/gemcitabine *(preferred for leiomyosarcoma)*
- Doxorubicin/ifosfamide
- Doxorubicin/dacarbazine
- Gemcitabine/dacarbazine
- Gemcitabine/vinorelbine

**Single-agent options:**
- Dacarbazine
- Doxorubicin
- Epirubicin
- Eribulin
- Gemcitabine
- Ifosfamide
- Liposomal doxorubicin
- Pazopanib
- Temozolomide
- Trabectedin
- Vinorelbine (category 2B)
- Docetaxel (category 3)

**Hormone Therapy** *(For Low-grade ESS or Hormone Receptor Positive (ER/PR) uLMS)*

- Medroxyprogesterone acetate *(category 2B for ER/PR positive uLMS)*
- Megestrol acetate *(category 2B for ER/PR positive uLMS)*
- Aromatase inhibitors
- GnRH analogs *(category 2B for low-grade ESS and ER/PR positive uLMS)*
Follow-Up

• Recurrence is common
• Routine exams
• Routine CT scans
• Patient symptom monitoring
Emerging Therapies

• Continued chemotherapy trials
• Biologic therapies
• Numerous genetic mutations in these tumors
  • Targeted therapies
    • Anti-VEGF
    • Multi-kinase inhibitors
    • mTOR inhibitors
Adnexal Cancers

Epithelial Tumors
Germ Cell Tumors
Stromal Tumors
Epithelial Cancers (OV/FT/PP)

• Epidemiology and Risk Factors
• Histology
• Presentation
• Diagnosis
• Staging
• Therapy
  • Primary Disease
  • Recurrent
• Follow-Up
• Future Therapy
Epidemiology

• 22,280 cases expected in 2016
  • 11.9 per 100,000 women
• 14,240 deaths expected in 2016
Epidemiology

Increased Risk
- Age
- Family History
  - BRCA
  - Lynch
- PID
- Endometriosis
- Smoking (mucinous)

Decreased Risk
- Oral Contraceptive Pills
- Tubal Interruption
- Hysterectomy
- Pregnancy
- Breastfeeding
- Low fat diet
Histology

- Serous
- Mucinous
- Endometrioid
- Clear Cell
- Transitional Cell
- Squamous
- Undifferentiated
- Carcinosarcoma

Table 24.10

<table>
<thead>
<tr>
<th>Cell Type</th>
<th>Benign (%)</th>
<th>Atypical proliferative/borderline (%)</th>
<th>Malignant (%)</th>
<th>Total (%)</th>
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<tbody>
<tr>
<td>Serous</td>
<td>48.6</td>
<td>1.8</td>
<td>17.8</td>
<td>68.2</td>
</tr>
<tr>
<td>Endometrioid</td>
<td>0.8</td>
<td>0.2</td>
<td>1.9</td>
<td>2.9</td>
</tr>
<tr>
<td>Clear cell</td>
<td>0</td>
<td>0.2</td>
<td>2.2</td>
<td>2.4</td>
</tr>
<tr>
<td>Mucinuous</td>
<td>7.6</td>
<td>1.0</td>
<td>0.8</td>
<td>9.4</td>
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<tr>
<td>Seromucinuous</td>
<td>1.8</td>
<td>0.3</td>
<td>0.2</td>
<td>2.3</td>
</tr>
<tr>
<td>Transitional</td>
<td>9.9</td>
<td>0.2</td>
<td>0.3</td>
<td>10.4</td>
</tr>
<tr>
<td>Mixed</td>
<td>0.6</td>
<td>0</td>
<td>0.7</td>
<td>1.3</td>
</tr>
<tr>
<td>Undifferentiated</td>
<td>–</td>
<td>–</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Carcinosarcoma</td>
<td>–</td>
<td>–</td>
<td>1.6</td>
<td>1.6</td>
</tr>
<tr>
<td>Squamous</td>
<td>1.3</td>
<td>–</td>
<td>0.1</td>
<td>1.4</td>
</tr>
<tr>
<td>Totals</td>
<td>70.6</td>
<td>3.7</td>
<td>25.7</td>
<td>100</td>
</tr>
</tbody>
</table>

Seidman, unpublished data.
<table>
<thead>
<tr>
<th>Category</th>
<th>Count</th>
<th>Proportion of patients with inherited mutation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ALL PATIENTS</strong></td>
<td></td>
<td>0.23</td>
</tr>
<tr>
<td>Age at diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 40</td>
<td>10</td>
<td>0.10</td>
</tr>
<tr>
<td>40 - 49</td>
<td>57</td>
<td>0.30</td>
</tr>
<tr>
<td>50 - 59</td>
<td>99</td>
<td>0.35</td>
</tr>
<tr>
<td>60 - 69</td>
<td>114</td>
<td>0.21</td>
</tr>
<tr>
<td>&gt; 70</td>
<td>80</td>
<td>0.06</td>
</tr>
<tr>
<td>Self, in addition to ovarian cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast cancer</td>
<td>31</td>
<td>0.71</td>
</tr>
<tr>
<td>No breast cancer</td>
<td>329</td>
<td>0.19</td>
</tr>
<tr>
<td>Family history</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast cancer</td>
<td>141</td>
<td>0.35</td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td>35</td>
<td>0.54</td>
</tr>
<tr>
<td>Pancreatic cancer</td>
<td>18</td>
<td>0.28</td>
</tr>
<tr>
<td>Uterine cancer</td>
<td>19</td>
<td>0.42</td>
</tr>
<tr>
<td>Colon cancer</td>
<td>60</td>
<td>0.15</td>
</tr>
<tr>
<td>Breast or ovarian cancer</td>
<td>157</td>
<td>0.36</td>
</tr>
<tr>
<td>Neither breast nor ovarian cancer</td>
<td>203</td>
<td>0.12</td>
</tr>
<tr>
<td>Disease site</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ovary</td>
<td>273</td>
<td>0.22</td>
</tr>
<tr>
<td>Peritoneum</td>
<td>48</td>
<td>0.27</td>
</tr>
<tr>
<td>Fallopian tube</td>
<td>31</td>
<td>0.39</td>
</tr>
<tr>
<td>Ovary/Endometrium</td>
<td>8</td>
<td>0.13</td>
</tr>
<tr>
<td>Histology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serous</td>
<td>242</td>
<td>0.24</td>
</tr>
<tr>
<td>Carcinoma, undifferentiated</td>
<td>64</td>
<td>0.20</td>
</tr>
<tr>
<td>Endometrioid</td>
<td>23</td>
<td>0.17</td>
</tr>
<tr>
<td>Clear cell</td>
<td>17</td>
<td>0.06</td>
</tr>
<tr>
<td>Carcinosarcoma, other</td>
<td>14</td>
<td>0.14</td>
</tr>
<tr>
<td>Grade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>19</td>
<td>0.11</td>
</tr>
<tr>
<td>2</td>
<td>13</td>
<td>0.15</td>
</tr>
<tr>
<td>3</td>
<td>328</td>
<td>0.24</td>
</tr>
<tr>
<td>Stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>22</td>
<td>0.18</td>
</tr>
<tr>
<td>II</td>
<td>26</td>
<td>0.23</td>
</tr>
<tr>
<td>III or IV</td>
<td>308</td>
<td>0.22</td>
</tr>
</tbody>
</table>

![Pie chart showing distribution of genetic mutations](chart.png)
Clinical Presentation

• Early disease is usually asymptomatic
• Symptoms are generally benign and non-specific
  • Anorexia
  • Fatigue
  • Early satiety
  • Loss of appetite
  • Bloating
  • Diffuse/dull/constant abdominal pain

“The cancer that whispers”
Diagnosis

• Ultrasound
• CA 125
• CT for extent of disease spread
• Paracentesis/thoracentesis

• Limited role for screening patients at population risk
• Surgical evaluation
Staging
Therapy – Primary disease

**NCCN Guidelines Version 2.2015**
Epithelial Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer

**Pathologic Staging**

<table>
<thead>
<tr>
<th>Stage IA or IB</th>
<th>Grade 1</th>
<th>Observe $^\text{O}$</th>
<th>Primary Chemotherapy/Primary Adjuvant Therapy $^\text{n}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 2</td>
<td>Observe or Intravenous (IV) taxane/carboplatin $^k$ for 3–6 cycles</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3 or clear cell</td>
<td>IV taxane/carboplatin $^k$ for 3–6 cycles</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Stage IC | Grade 1, 2, or 3 | IV taxane/carboplatin $^k$ for 3–6 cycles |

| Stage II | Stage III | Stage IV |

- Chemotherapy $^p$
  - Intraperitoneal (IP) chemotherapy $^{l,k}$ in <1 cm optimally debulked stage II and stage III patients (category 1 for stage III) or
  - IV taxane/carboplatin $^k$ for a total of 6–8 cycles (category 1)
- Completion surgery as indicated by tumor response and potential resectability in selected patients $^l$
Therapy – Recurrence

<table>
<thead>
<tr>
<th>Preferred Single Agents or Combinations</th>
<th>Cytotoxic Therapy (In alphabetical order)</th>
<th>Hormonal Therapy</th>
<th>Targeted Therapy</th>
<th>Radiation Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Platinum-Sensitive Disease</strong> b,c</td>
<td>Carboplatin b,d,e,17,18 Olaparib g,19,20</td>
<td>Bevacizumab</td>
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<tr>
<td></td>
<td>Carboplatin/docetaxel 2,3</td>
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<tr>
<td></td>
<td>Carboplatin/gemcitabine</td>
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<tr>
<td></td>
<td>Carboplatin/gemcitabine/bevacizumab d,e</td>
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<tr>
<td></td>
<td>(category 2B) 4</td>
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<tr>
<td></td>
<td>Carboplatin/liposomal doxorubicin 5</td>
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<tr>
<td></td>
<td>(category 1) 6</td>
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<tr>
<td></td>
<td>Carboplatin/paclitaxel (category 1) 6</td>
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<tr>
<td></td>
<td>Carboplatin/paclitaxel (weekly) 7</td>
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<tr>
<td></td>
<td>Cisplatin 8</td>
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<tr>
<td></td>
<td>Cisplatin/gemcitabine 8</td>
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</tr>
<tr>
<td><strong>Platinum-Resistant Disease</strong></td>
<td>Bevacizumab b,d,e,17,18 Olaparib g,19,20</td>
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<tr>
<td></td>
<td>Docetaxel 9</td>
<td></td>
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<tr>
<td></td>
<td>Etoposide, oral 10</td>
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<td></td>
<td>Gemcitabine 11,12</td>
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<tr>
<td></td>
<td>Liposomal doxorubicin 11,12</td>
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<td></td>
<td>Liposomal doxorubicin/bevacizumab d,e,13</td>
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<tr>
<td></td>
<td>Paclitaxel (weekly) 14</td>
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<tr>
<td></td>
<td>Paclitaxel (weekly)/bevacizumab d,e,13</td>
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<tr>
<td></td>
<td>Topotecan 15,16</td>
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<tr>
<td></td>
<td>Topotecan/bevacizumab d,e,13</td>
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<tr>
<td><strong>Other Potentially Active Agents</strong> f</td>
<td>Single Agents 21</td>
<td>Aromatase</td>
<td>Palipate localized radiation therapy</td>
<td></td>
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<tr>
<td></td>
<td>Altretamine</td>
<td>inhibitors</td>
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<tr>
<td></td>
<td>Capecitabine</td>
<td>Leuprolide acetate</td>
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<tr>
<td></td>
<td>Cyclophosphamide</td>
<td>Megestrol acetate</td>
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<tr>
<td></td>
<td>Doxorubicin</td>
<td>Tamoxifen</td>
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<td></td>
<td>Ifosfamide</td>
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<td></td>
<td>Irinotecan</td>
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<td></td>
<td>Melphalan</td>
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<td></td>
<td>Oxaliplatin</td>
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<tr>
<td></td>
<td>Paclitaxel</td>
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<tr>
<td></td>
<td>Paclitaxel, albumin bound (nab-paclitaxel)</td>
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<tr>
<td></td>
<td>Pemetrexed</td>
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<tr>
<td></td>
<td>Vinorelbine</td>
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</tbody>
</table>
Follow-up

• Regular pelvic examinations
• Monitor CA 125 - controversial
• Imaging for symptoms (or elevated CA 125)
• GENETIC COUNSELING/TESTING
• Cascade Testing for family members
• Clinical trials
Emerging Therapies

• Targeted therapies
• Cytotoxic agents
  • HIPEC
  • Alternate dosing schemes
• Vaccine therapies
• Revisiting radiotherapy
Germ Cell Tumors

- Epidemiology
- Histology
- Presentation
- Diagnosis
- Staging
- Therapy
  - Early
  - Locally Advanced
  - Metastatic
  - Recurrent
- Follow-Up
- Future Therapy
Epidemiology

• Approximately 5% of ovarian tumors
• “Juvenile Ovarian Cancer”
  • Median age 16-20 years depending on histology
• 10-year survival up to 88.6%
Histology

• Dysgerminoma
  • Most common malignant ovarian germ cell tumor
  • 5-10% associated with gonadoblastomas
  • 10% bilateral on gross exam and another 10% have microscopic involvement

• Yolk Sac Tumor (endodermal sinus tumor)
  • Tan-gray
  • Abundant hemorrhage and necrosis
  • AFP is elevated
Histology

• Choriocarcinoma
  • Rare as a primary tumor of the ovary
  • Syncytiotrophoblast/cytotrophoblast admixture
  • Spreads by vascular invasion

• Teratomas
  • Mature cystic teratomas (Benign, “dermoids”)
  • Immature (malignant) teratomas = 3% of teratomas
  • Most are unilateral
Presentation

• Abdominal pain associated with a palpable abdominopelvic mass (85% of patients)
• Acute abdominal pain (10%)
  • Due to rupture, hemorrhage, or torsion
• Abdominal distension (35%)
• Fever (10%)
• Vaginal bleeding (10%)
Diagnosis

• Large mass, generally found at the time of surgery
• Primary surgery is often required for diagnosis and therapy (resolution of symptoms)
• Fertility preservation:
  • removal of abnormal ovary and sampling of other pelvic tissues
  • preferable if possible (young patient ages)
Staging
Therapy – Primary Setting

• Observation for:
  • Stage I Grade 1 immature teratomas
  • Stage I dysgerminoma

• Systemic cytotoxic chemotherapy for everyone else
  • Bleomycin/Etoposide/Clisplatin (BEP)
    • 5 days of therapy every 3 weeks for 3-4 cycles
  • Etoposide/Carboplatin
    • 3 days of therapy every 3 weeks for 3 cycles
    • Selected patients only based on risk of toxicity and disease
Therapy – Recurrence

**Malignant Germ Cell Tumors**

- High-dose chemotherapy
- Cisplatin/etoposide
- Docetaxel
- Docetaxel/carboplatin
- Paclitaxel
- Paclitaxel/ifosfamide
- Paclitaxel/carboplatin
- Paclitaxel/gemcitabine
- VIP (etoposide, ifosfamide, cisplatin)
- VelP (vinblastine, ifosfamide, cisplatin)
- VAC (vincristine, dactinomycin, cyclophosphamide)
- TIP (paclitaxel, ifosfamide, cisplatin)
- Radiation therapy
- Supportive care only

Borrowed from testicular cancer studies
Follow-up

• Psychosocial Support
• Routine exams
• Serum biomarkers (if indicated)
Emerging Therapies

• Clinical trials
• Less extensive surgery
• Less cytotoxic treatment
• Targeted therapies
Stromal Tumors

- Epidemiology
- Histology
- Presentation
- Diagnosis
- Staging
- Therapy
  - Early
  - Locally Advanced
  - Metastatic
  - Recurrent
- Follow-Up
- Future Therapy
Epidemiology

• Account for 7% of malignant ovarian neoplasms
• Account for 90% of functional tumors
• Annual incidence between 0.5 and 1.7 cases per 100,000 women
Histology

• Granulosa Cell Tumors
  • Estrogen producing
  • Inhibin as a biomarker
    • B is better than A
  • Adult type
    • Low grade/indolent
    • Diagnosed later in life
• Juvenile type
  • 44% diagnosed before age 10
  • Isosexual precocious puberty
• Thecoma/Fibroma
  • Lipid-laden stromal cells
  • Occur later than other stromal tumors (most in 30s/40s)
  • Abnormal bleeding and/or a pelvic mass
Histology

• Stertoli-Leydig Tumors
  • Less than 0.2% of ovarian tumors
  • Androgen producing tumors leading to virilization
Presentation

- Abdominopelvic mass
- Abnormal bleeding
- Virilization (Sertoli-Leydig cell tumors)
Staging / Therapy / Follow-up

• Staging
  • Same as other ovarian tumors

• Therapy
  • Hybrid of germ cell and epithelial cancers

• Follow-up
  • Routine exams
  • Serum markers if appropriate
Cervical Cancer
Cervical Cancer

• Epidemiology and Risk Factors
• Histology
• Presentation
• Diagnosis
• Staging
• Therapy
  • Early
  • Locally Advanced
  • Metastatic
  • Recurrent
• Follow-Up
• Future Therapy
Epidemiology

- 12,990 cases expected in 2016
  - 7.7 per 100,000 women
- 4,120 deaths expected in 2016
Epidemiology

• HPV infection
• High parity
• Increased number of sexual partners
• Young age at time of first sexual intercourse
• Low socioeconomic status
• History of smoking
• Long-term use of oral contraceptives
• Physical inactivity
Histology

• Squamous
• Adenocarcinoma
• Rare histologies
  • Clear cell
  • Serous
  • Glassy Cell
  • Neuroendocrine
  • Mesenchymal tumors
Pathogenesis

- **Cytology**
  - LSIL (CIN 1)
  - HSIL (CIN 3)

- **Histology**
  - Normal
  - Very mild/mild dysplasia
  - Moderate dysplasia
  - Severe dysplasia
  - In situ carcinoma
  - Invasive carcinoma

**Pathogenesis:**
- HPV infection, virus production
- No virus production
- High E6 and E7
- Viral DNA integration
- Microinvasive carcinoma
Clinical Presentation

- Post-coital bleeding
- Abnormal uterine bleeding
- Abnormal Pap smear
- Pelvic pain
- Flank pain
- Uncontrolled leakage of urine/stool from vagina
Diagnosis

• Pelvic examination/biopsies
• Cone biopsy
• Chest x-ray
• IVP
• Cystoscopy
• Proctoscopy

Cervical Cancer Develop at the Transition Zone Between Squamous and Columnar Epithelium

High-grade Precursor  Invasive Cancer
Takes 10 years on average
Staging

- Clinically staged
- PET CT often used in western countries but not available in the highest prevalence regions of the world
Therapy

- Stage IA1 – Cone biopsy, hysterectomy
- Stage IA2 – modified radical hysterectomy
- Stage IB and IIA – radical hysterectomy OR pelvic RT
  - Add chemotherapy to RT in IB2 and IIA2
  - Can add to RT in IB1 and IIA1
- Stage IIB to IVA – pelvic RT with chemotherapy
- Stage IVB – systemic chemotherapy/clinical trials
Follow-up

- Psychosocial Support
- Routine exams
- Cytologic testing
Emerging Therapies

- Sentinel Node Mapping
- Fertility Preservation
- Targeted Therapies
Vulvar Cancer
Vulvar Cancer

• Epidemiology and Risk Factors
• Histology
• Presentation / Diagnosis
• Staging
• Therapy
  • Early
  • Locally Advanced
  • Metastatic
• Follow-Up
Epidemiology

- 5,950 cases expected in 2016
- 1,110 deaths expected in 2016
Epidemiology

- Condyloma
- History of squamous dysplasia
- HPV infection in basaloid or warty types
- Common risk factors with cervical cancer
  - Multiple sex partners
  - Early age at initiation of sexual intercourse
  - History of abnormal Pap smears
- HPV associated more common in women < 50 years
- Non-HPV is more common in older women
Histology
Presentation – Early disease

Persistent Irritation
Discoloration
Bleeding
Presentation – Late disease

Pain
Bleeding
Pressure from enlarged masses
Foul odor
Staging

# Staging

<table>
<thead>
<tr>
<th>FIGO</th>
<th>AJCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>T</td>
<td>N</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>I: Tumor confined to the vulva</td>
<td>Tis: No invasion past basement membrane (not in FIGO system)</td>
</tr>
<tr>
<td>IIA</td>
<td>T1a</td>
</tr>
<tr>
<td>IIB</td>
<td>T1b</td>
</tr>
<tr>
<td>IIC</td>
<td>T2</td>
</tr>
<tr>
<td>III</td>
<td>T1 or T2</td>
</tr>
<tr>
<td>IIIA</td>
<td>(i) 1–2 lymph node metastases (&lt; 5 mm), or (ii) 1 lymph node metastasis (≥ 5 mm)</td>
</tr>
<tr>
<td>IIIB</td>
<td>(i) 3 or more lymph node metastases (&lt; 5 mm) or (ii) 2 or more lymph node metastases (≥ 5 mm)</td>
</tr>
<tr>
<td>IIC</td>
<td>Positive nodes with extracapsular spread</td>
</tr>
<tr>
<td>IV</td>
<td>T3 = any size, involves upper urethra, bladder, rectum, bone</td>
</tr>
<tr>
<td>IVA</td>
<td>T3</td>
</tr>
<tr>
<td>IVB</td>
<td>Distant metastasis: includes pelvic nodes</td>
</tr>
</tbody>
</table>
Therapy – Early

- Local excision (simple or radical)
Therapy – Locally Advanced
Therapy – Metastatic

• Systemic cytotoxic therapy is disappointing
• Targeted therapies are under development
Follow-up

• Psychosocial Support
• Routine exams
Summary

• Risk can be reduced by modifying risk factors
• Most cancers are responsive to front-line therapy
• Management of recurrent disease varies by site of origin/histology but is often sub-optimal
• More discoveries are needed to overcome these diseases