Endometrial Cancer

**Initial Evaluation**
- History and physical
- Chest x-ray
- Pathology review
- Nutrition consult
- Labs
- Consider CA125
- Consider pre-operative imaging in patients with high risk histology
- Screen for Lynch Syndrome by family history or molecular testing
- Lifestyle risk assessment

**Clinical Presentation**
- Does the patient desire fertility?
  - Yes
  - No
- Disease confined to uterus
  - Yes
  - No
- Is patient suitable for surgery?
  - Yes
  - No
- Hysterectomy, BSO, and SLN mapping
  - Primary radiation or progesterone therapy (oral or progesterone-containing IUD if low grade and non-invasive)
  - See surveillance on Page 6
- Stage II with gross cervical involvement
  - Disease not confirmed to uterus
    - See Page 2

**Primary Treatment**
- Does the patient have low-grade disease and no myometrial invasion?
  - Yes
  - No
- Pelvic MRI with IV contrast and vaginal gel to rule out myometrial invasion
- Referral to Oncofertility

- Does the patient have low-grade disease if initial diagnosis was from endometrial biopsy?
  - Yes
  - No
- Progesterone therapy (oral or progesterone-containing IUD)
  - Re-sample at every 3-6 month interval

**Note:** If available, Clinical Trials should be considered as preferred treatment options for eligible patients (www.mdanderson.org/gynonctrials). Other co-morbidities are taken into consideration prior to treatment selection.

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson’s specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient’s care. This algorithm should not be used to treat pregnant women.

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BSO = bilateral salpingo-oophorectomy
SLN = sentinel lymph nodes
IUD = intrauterine device

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4 Hysterectomy may be performed through open or minimally invasive techniques based on surgeon/patient discretion. Minimal invasive surgery is the preferred method of surgery.
Endometrial Cancer

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CLINICAL PRESENTATION

- Stage II with gross cervical involvement
  - 45 Gy pelvic radiation therapy plus reduced dose of brachytherapy
  - Radical hysterectomy\(^1\), BSO, pelvic and para-aortic node sampling and/or sentinel lymph node mapping (omental biopsy for non-endometroid cell type)

- Disease not confined to uterus
  - Consider surgical debulking
  - Hysterectomy\(^2\) and BSO with or without paraaortic node sampling (omental biopsy for non-endometroid cell type)

PRIMARY TREATMENT

See Pages 3-4 for endometroid cell type and Page 5 for serous cell type

Please refer to American College of Obstetricians and Gynecologists (ACOG) Guidelines for referral.

\(^1\) Hysterectomy may be performed through open or minimally invasive techniques based on surgeon/patient discretion
Risk Group 1

**Low Risk:**
- Grade 1 or 2
- < 50% myometrial invasion
- No LVSI (or focal LVSI)

**Low intermediate risk:**
- Grade 1 or 2
- ≥ 50% myometrial invasion
- No LVSI (or focal LVSI)

**High intermediate risk:**
- Grade 1 or 2, any invasion positive LVSI (not focal) or
- Grade 3, < 50% myometrial invasion

**High risk:**
- Grade 3
- ≥ 50% myometrial invasion

**ADJUVANT THERAPY**

- Observation
- Observation or Vaginal cuff brachytherapy
- Vaginal cuff brachytherapy
- Pelvic radiation therapy or Vaginal cuff brachytherapy and/or Chemotherapy

LVSI = lymphovascular space invasion

1 Imaging Considerations:
- CT of the abdomen and pelvis with IV, oral and rectal contrast. If high chance of recurrence, consider pelvic MRI with IV contrast and vaginal gel.
- For recurrence localization, consider PET/CT.
- For distant disease, PET/CT may be useful. MRI will be helpful to assess the extent of locally recurrent disease.
Endometrial Cancer (Endometroid Cell Type)

STAGE

Stage IIIA with serosal involvement

Stage IIIA with adnexal involvement

Stage IIIB, Stage IIIC1

Stage IIIC2

Stage IV

ADJUVANT THERAPY

Adjuvant chemotherapy\(^2\), consider vaginal brachytherapy, or external beam radiation therapy

Adjuvant chemotherapy\(^2\), consider vaginal brachytherapy, or external beam radiation therapy

- 45 Gy pelvic radiation therapy\(^3\) and vaginal brachytherapy with or without concurrent chemotherapy, followed by with or without adjuvant chemotherapy\(^4\) or
- Adjuvant chemotherapy alone

• Adjuvant chemotherapy\(^2\) or
• Extended-field radiation therapy and vaginal brachytherapy with or without concurrent chemotherapy, followed by with or without adjuvant chemotherapy\(^2\)

Chemotherapy\(^2\)

See surveillance on Page 6

1 See Appendix A for International Federation of Gynecology and Obstetrics (FIGO) Staging
2 See Appendix B for Systemic Therapy
3 Consider radiation alone in grade 1,2 patients
4 Higher dose than 45 Gy needs to be given for sites of ECE (extra-capsular nodal extension) and for any other residual suspicious nodes
Endometrial Cancer (Serous Carcinoma, Clear Cell Carcinoma and Carcinosarcoma)

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### STAGE 1
- **Stage IA** (no invasion or superficial invasion)
  - Vaginal brachytherapy\(^2,3\) and/or adjuvant chemotherapy. Consider surveillance alone if no residual cancer in hysterectomy specimen.

- **Stage IB**
  - Vaginal brachytherapy\(^2,3\) or pelvic radiation therapy\(^4\) with or without concurrent chemotherapy and/or adjuvant chemotherapy.

- **Stage II**
  - Vaginal brachytherapy\(^2,3\) or pelvic radiation therapy\(^4\) with or without concurrent chemotherapy and/or adjuvant chemotherapy.
  - **• Adjuvant chemotherapy or**
  - **• Vaginal brachytherapy\(^2,3\)** with or without concurrent chemotherapy followed by adjuvant chemotherapy.

- **Stage IIIA**
  - Pelvic radiation therapy\(^2,4\) or vaginal brachytherapy\(^3\) with or without concurrent chemotherapy followed by adjuvant chemotherapy.

- **Stage IIIB**
  - Pelvic radiation therapy\(^2,4\) or vaginal brachytherapy\(^3\) with or without concurrent chemotherapy followed by adjuvant chemotherapy.

- **Stage IIIC**
  - Disease present in ovaries?
    - Yes
      - Systemic therapy\(^6\)
    - No
      - Adjuvant chemotherapy, consider vaginal brachytherapy, or external beam radiation therapy

- **Stage IV**
  - Systemic therapy\(^6\)

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\(^1\) See Appendix A for International Federation of Gynecology and Obstetrics (FIGO) Staging
\(^2\) Preferred
\(^3\) Stage IA/IB/IIA/IIIA: vaginal brachytherapy: Consider MRI with contrast and vaginal gel to assess response
\(^4\) Consider concurrent paclitaxel for disease confined to the pelvis
\(^5\) Stage IIIC and IV: Consider PET/CT or contrast enhanced CT with oral and rectal contrast or PET/MR if available
\(^6\) See Appendix B for Systemic Therapy. For stage III/IV or recurrent HER2-positive uterine serous carcinoma, consider paclitaxel, carboplatin, and trastuzumab
\(^7\) For stage IV with only bladder or rectal involvement without distant disease: Consider MRI with vaginal gel to assess response

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Endometrial Cancer

SURVEILLANCE

After completion of treatment

- Visits every 3-6 months for Years 1 and 2, then every 6 months for Years 3 to 5
- Discuss lifestyle modifications and nutrition
- Physical and pelvic exam every visit
- CA125 (if initially elevated) every visit
- Imaging, as clinically indicated

Systemic recurrence?

Yes

- Systemic therapy
- Consider clinical trials
- Molecular testing

No – isolated recurrence

- Consider radiation therapy and/or resection with or without chemotherapy
- Molecular testing

Note: If available, Clinical Trials should be considered as preferred treatment options for eligible patients (www.mdanderson.org/gynonc_trials). Other co-morbidities are taken into consideration prior to treatment selection.

1 Consider imaging with development of new symptoms, for patients with high risk for recurrence (e.g. positive pelvic nodes who received pelvic RT only)

2 See Appendix B for Systemic Therapy
# APPENDIX A: International Federation of Gynecology and Obstetrics (FIGO) Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
</table>
| I\(^1\) | Tumor confined to the corpus uteri  
   IA: No or less than half myometrial invasion  
   IB: Invasion equal to or more than half of the myometrium |
| II\(^1\) | Tumor invades cervical stroma, but does not extend beyond the uterus\(^2\) |
| III\(^1\) | Local and/or regional spread of the tumor  
   IIA: Tumor invades the serosa of the corpus uteri and/or adnexae\(^3\)  
   IIB: Vaginal and/or parametrial involvement\(^3\)  
   IIC: Metastases to pelvic and/or para-aortic lymph nodes\(^3\)  
   IIC1: Positive pelvic nodes  
   IIC2: Positive para-aortic lymph nodes with or without positive pelvic lymph nodes |
| IV\(^1\) | Tumor invades bladder and/or bowel mucosa, and/or distant metastases  
   IVA: Tumor invasion of bladder and/or bowel mucosa  
   IVB: Distant metastases, including intra-abdominal metastases and/or inguinal lymph nodes |

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\(^1\) Either G1, G2, or G3  
\(^2\) Endocervical glandular involvement only should be considered as Stage I and no longer as Stage II  
\(^3\) Positive cytology has to be reported separately without changing the stage
APPENDIX B: Systemic Therapy

<table>
<thead>
<tr>
<th>Multi-agent Chemotherapy</th>
<th>Single-agent IV Therapy</th>
<th>Hormonal Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paclitaxel and carboplatin</td>
<td>Cisplatin</td>
<td>Everolimus and letrozole (for endometrioid histology)</td>
</tr>
<tr>
<td>Paclitaxel, carboplatin, and trastuzumab (stage III/IV or</td>
<td>Carboplatin</td>
<td>Alternating megestrol acetate and tamoxifen</td>
</tr>
<tr>
<td>recurrent HER2-positive uterine serous carcinoma)</td>
<td>Doxorubicin</td>
<td>Megestrol acetate</td>
</tr>
<tr>
<td>Docetaxel and carboplatin</td>
<td>Liposomal doxorubicin</td>
<td>Medroxyprogesterone acetate</td>
</tr>
<tr>
<td>Ifosfamide and paclitaxel</td>
<td>Paclitaxel</td>
<td>Letrozole</td>
</tr>
<tr>
<td>Cisplatin and ifosfamide</td>
<td>Nab-paclitaxel</td>
<td></td>
</tr>
<tr>
<td>Cisplatin and gemcitabine</td>
<td>Topotecan</td>
<td></td>
</tr>
<tr>
<td>Lenvatinib/pembrolizumab (MSS)</td>
<td>Bevacizumab</td>
<td></td>
</tr>
</tbody>
</table>

1 For carcinosarcoma, consider ifosfamide/paclitaxel or cisplatin/ifosfamide

HER2 = human epidermal growth factor receptor 2
MSI-H = high levels of microsatellite instability
MMR-D = mismatch repair deficient
MSS = microsatellite stable
SUGGESTED READINGS


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