Endometrial Cancer

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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
- Discuss Goal Concordant Care (GCC) with patient or if clinically indicated, with Patient Representative

CLINICAL PRESENTATION

Disease confined to uterus

Is patient suitable for surgery?

Yes ➔ See Page 3

No ➔ Primary radiation or progesterone therapy (oral or progestin-containing IUD if low grade and non-invasive) ➔ See surveillance on Page 8

Stage II with gross cervical involvement

Disease not confined to uterus ➔ See Page 4

PRIMARY TREATMENT

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

IUD = intrauterine device

Note: Please reference the American College of Obstetricians and Gynecologists (ACOG) Guidelines

1 See MD Anderson Approved Biomarkers
2 See Physical Activity, Nutrition, and Tobacco Cessation Treatment algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice

GCC should be initiated by the Primary Oncologist. If Primary Oncologist is unavailable, Primary Team/Attending Physician to initiate GCC discussion and notify Primary Oncologist. Patients, or if clinically indicated, the Patient Representative should be informed of therapeutic and/or palliative options. GCC discussion should be consistent, timely, and re-evaluated as clinically indicated. The Advance Care Planning (ACP) note should be used to document GCC discussion. Refer to GCC home page (for internal use only).

MRI with vaginal contrast (gel preferred) is recommended to assess for myometrial, cervical invasion and assessment of extrauterine disease. PET/CT may help with lymph node involvement. PET/MR if available, may help in T staging, evaluation of lymph nodes, and distant metastasis. If none of these modalities are available, ultrasound can be performed.

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Endometrial Cancer

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INITIAL EVALUATION

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**Disease confined to uterus and patient eligible for surgery**

- Does the patient desire fertility?
  - Yes → **Hysterectomy**, BSO, and SLN mapping (see Box A on this page)
  - No → **Bilateral SLN identified**

A. **Bilateral SLN identified**

- Conclude procedure

---

**Grade 1-2, ≤ 50% invasion and tumor diameter ≤ 2 cm**

- **Conclude procedure with/without lymph node dissection**

---

**Grade 1-2, > 50% invasion or Tumor diameter > 2 cm with any invasion or Grade 3 and non-endometroid cell type (papillary serous, clear cell, carcinosarcoma)**

- **Side specific staging with pelvic and para-aortic node sampling (omental biopsy for non-endometrioid cell type)**

---

**Does the patient have low-grade disease and no myometrial invasion?**

- Yes → **Does the patient have progression or persistence of disease > 12 months?**
  - Yes → **Hysterectomy**, BSO, and SLN mapping (see Box A on this page)
  - No → **Intraoperative frozen section**

---

**Conclude procedure**

---

**Does the patient have grade 1-2, ≤ 50% invasion and tumor diameter ≤ 2 cm?**

- Yes
- No → **Grade 1-2, > 50% invasion or Tumor diameter > 2 cm with any invasion or Grade 3 and non-endometroid cell type (papillary serous, clear cell, carcinosarcoma)**

---

**BSO = bilateral salpingo-oophorectomy**

**SLN = sentinel lymph nodes**

**IUD = intrauterine device**

1 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**

**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

**PRIMARY TREATMENT**

- Hysterectomy\(^1\) and BSO with or without paraaortic node sampling (omental biopsy for non-endometroid cell type)

---

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

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**Note:** Please reference the American College of Obstetricians and Gynecologists (ACOG) Guidelines

---

**BSO = bilateral salpingo-oophorectomy**

---

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**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.
Endometrial Cancer (Endometroid Cell Type Stage I-II)

MOLECULAR TESTING

Risk Group 1

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

Observation

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

Observation or Vaginal cuff brachytherapy

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

Vaginal cuff brachytherapy

High risk:
Grade 3
≥ 50% myometrial invasion

Pelvic radiation therapy or Vaginal cuff brachytherapy and/or Chemotherapy

ADJUVANT THERAPY

Pathology testing for MSI testing, p53, and consider POLE

LVSI = lymphovascular space invasion

1 Imaging Considerations:
• CT abdomen and pelvis with IV, oral and rectal contrast. If high chance of recurrence, consider MRI pelvis 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.

2 See Appendix A for Systemic Therapy

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Notes:
- 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.

See surveillance on Page 8

Page 5 of 11
Endometrial Cancer (Endometroid Cell Type Stage III-IV)

2 See Appendix A 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

MOLECULAR TESTING

Stage IIIA with serosal involvement
- Adjuvant chemotherapy\(^2\), consider vaginal brachytherapy, or external beam radiation therapy

Stage IIIA with adnexal involvement
- Adjuvant chemotherapy\(^2\), consider vaginal brachytherapy, or external beam radiation therapy

Stage IIIB, Stage IIIC1
- 45 Gy pelvic radiation therapy\(^3,4\) and vaginal brachytherapy with or without concurrent chemotherapy, followed by with or without adjuvant chemotherapy\(^2\) or
- Adjuvant chemotherapy\(^2\) with or without radiation therapy for local control

Stage IIIC2
- Adjuvant chemotherapy\(^2\) with or without radiation therapy for local control or
- Extended-field radiation therapy and vaginal brachytherapy with or without concurrent chemotherapy, followed by with or without adjuvant chemotherapy\(^2\)

Stage IV
- Chemotherapy\(^2\)

ADJUVANT THERAPY

Pathology testing for MSI testing, p53, and consider POLE

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.

See surveillance on Page 8

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Endometrial Cancer (Serous Carcinoma, Clear Cell Carcinoma and Carcinosarcoma)  

**Stage I**
- (no invasion or superficial invasion)
  - Vaginal brachytherapy\(^3\)\(^4\) **and/or** adjuvant chemotherapy
  - Consider surveillance alone if no residual cancer in hysterectomy specimen

**Stage II**
- Vaginal brachytherapy\(^3\)\(^4\) **or** pelvic radiation therapy\(^5\) with or without concurrent chemotherapy **and/or** adjuvant chemotherapy

**Stage II A, IB, II B**
- Vaginal brachytherapy\(^3\)\(^4\) **or** pelvic radiation therapy\(^5\) with or without concurrent chemotherapy **and/or** adjuvant chemotherapy

**Stage II C**
- Adjuvant chemotherapy\(^6\) **or**
- Vaginal brachytherapy\(^3\)\(^4\) with or without concurrent chemotherapy followed by adjuvant chemotherapy

**Stage III A**
- Pelvic radiation therapy\(^3\)\(^5\) **or** vaginal brachytherapy\(^4\) with or without concurrent chemotherapy followed by adjuvant chemotherapy

**Stage III B**
- **Yes**
  - Systemic therapy\(^6\)\(^8\)
- **No**
  - Adjuvant chemotherapy\(^6\), consider vaginal brachytherapy, or external beam radiation therapy

**Stage IV**
- Systemic therapy\(^6\)\(^8\)

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1. For serous carcinoma, consider human epidermal growth factor receptor 2 (HER2) testing
3. Preferred
4. Stage IA/IB/IIA:IIB vaginal brachytherapy: Consider MRI with contrast and vaginal gel to assess response
5. Consider concurrent paclitaxel for disease confined to the pelvis
6. For serous carcinoma, adjuvant systemic therapy with trastuzumab for HER2 positive tumors
7. Stage IIIC and IV: Consider PET/CT or contrast enhanced CT with oral and rectal contrast or PET/MR if available
8. See Appendix A for Systemic Therapy. For stage III/IV or recurrent HER2-positive uterine serous carcinoma, consider paclitaxel, carboplatin, and trastuzumab.
9. For stage IV with only bladder or rectal involvement without distant disease: Consider MRI with vaginal gel to assess response

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.
**SURVEILLANCE**

- 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\(^1\)

**Systemic recurrence?**

- Yes
  - Systemic therapy\(^2\)
  - Consider clinical trials
  - Molecular testing

- No (isolated recurrence)
  - Consider radiation therapy and/or resection with or without chemotherapy\(^2\)
  - Molecular testing

---

Note: Please reference the American College of Obstetricians and Gynecologists (ACOG) Guidelines

\(^1\) 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 A for Systemic Therapy
APPENDIX A: Systemic Therapy

<table>
<thead>
<tr>
<th>Multi-agent Chemotherapy</th>
<th>Single-agent IV Therapy</th>
<th>Hormonal Therapy</th>
<th>Maintenance Therapy</th>
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<tbody>
<tr>
<td>Paclitaxel and carboplatin</td>
<td>Cisplatin</td>
<td>Everolimus and letrozole</td>
<td>Trastuzumab</td>
</tr>
<tr>
<td>Paclitaxel, carboplatin, and trastuzumab (stage III/IV or recurrent HER2-positive uterine serous carcinoma)</td>
<td>Carboplatin</td>
<td>Alternating megestrol acetate and tamoxifen</td>
<td>Pembrolizumab</td>
</tr>
<tr>
<td>Paclitaxel, carboplatin, and pembrolizumab</td>
<td>Doxorubicin</td>
<td>Megestrol acetate</td>
<td>Dostarlimab</td>
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<tr>
<td>Paclitaxel, carboplatin, and dostarlimab-gxly</td>
<td>Liposomal doxorubicin</td>
<td>Medroxyprogesterone acetate</td>
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<td>Docetaxel and carboplatin</td>
<td>Paclitaxel</td>
<td>Letrozole</td>
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<td>Ifosfamide and paclitaxel¹</td>
<td>Nab-paclitaxel</td>
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<td>Cisplatin and ifosfamide¹</td>
<td>Topotecan</td>
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<td>Cisplatin and gemcitabine</td>
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<td></td>
<td>Docetaxel</td>
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<tr>
<td></td>
<td>Ifosfamide (carcinosarcoma)</td>
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<tr>
<td></td>
<td>Pembrolizumab (for MSI-H/dMMR tumors)</td>
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</tbody>
</table>

dMMR = deficient mismatch repair  
MSI-H = high levels of microsatellite instability  
pMMR = proficient mismatch repair  
MSS = microsatellite stable  

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


MD Anderson Institutional Policy #CLN1202 - Advance Care Planning Policy. Advance Care Planning (ACP) Conversation Workflow (ATT1925).


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DEVELOPMENT CREDITS

This practice algorithm is based on majority expert opinion of the Endometrial Cancer providers at the University of Texas MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following:

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