Endometrial Cancer

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.

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.

INITIAL EVALUATION

- History and physical
- Chest x-ray
- Pathology review
- Nutrition consult
- Labs
- Consider CA125 and pre-operative imaging of abdomen and pelvis
- Screen for Lynch Syndrome by family history or molecular testing
- Lifestyle risk assessment

CLINICAL PRESENTATION

Does the patient desire fertility?

- Yes
  - Dilation and curettage to confirm low-grade disease if initial diagnosis was from endometrial biopsy
  - Pelvic MRI to rule out myometrial invasion

- No
  - Hysterectomy
  - Bilateral SLN identified, BSO, and SLN mapping

PRIMARY TREATMENT

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

- Yes
  - Conclude procedure

- No
  - Hysterectomy

Grade 1-2, less than or equal to 50% invasion and tumor diameter less than or equal to 2 cm

- Conclude procedure with/without lymph node dissection

Grade 1-2, greater than 50% invasion or tumor diameter greater than 2 cm with any invasion

- Side specific staging with pelvic and para-aortic node sampling (omentum biopsy for non-endometroid cell type)

Grade 3 and non-endometroid cell type (papillary serous, clear cell, carcinosarcoma)

Stage II with gross cervical involvement

Disease not confirmed to uterus

- Hysterectomy
- See Page 2

SLN = sentinel lymph nodes
BSO = bilateral salpingo-oophorectomy

1 See MD Anderson Approved Biomarkers (Click here)
2 See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice
3 Hysterectomy may be performed through open or minimally invasive techniques based on surgeon/patient discretion

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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

PRIMARY TREATMENT

Hysterectomy\(^1\) and BSO with para-aortic node sampling (omental biopsy for non-endometroid cell type)

See Pages 3-4 for Endometroid Cell Type and Page 5 for Serous Cell Type

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

BSO = bilateral salpingo-oophorectomy

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

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.
Endometrial Cancer (Endometroid Cell Type)

STAGE 1

Stage 1A (less than 50%) myometrial invasion

Adverse risk-factors² present?

Yes

Adverse risk-factors² present?

No

Stage 1B (greater than or equal to 50%) myometrial invasion

Grade 1

- Vaginal brachytherapy

Grade 2

- Observe or vaginal brachytherapy³ and/or pelvic radiation therapy

Grade 3

- Vaginal brachytherapy³ and/or pelvic radiation therapy

Grade 1/Grade 2

- Observe

Grade 3

- Observe or

- Vaginal brachytherapy

Grade 1/Grade 2

- Vaginal brachytherapy³ and/or pelvic radiation therapy

Grade 3

- Pelvic radiation therapy with or without chemotherapy³ or vaginal brachytherapy with or without chemotherapy

Grade 1

- Observe or vaginal brachytherapy³

Grade 2

- Vaginal brachytherapy

Grade 3

- Vaginal brachytherapy and/or pelvic radiation therapy³

Grade 1

- Vaginal brachytherapy and/or pelvic radiation therapy

Grade 2

- Pelvic radiation therapy with or without chemotherapy

Grade 3

- Pelvic radiation therapy with vaginal brachytherapy and/or with or without chemotherapy

Grade 1

- Observe or vaginal brachytherapy

Grade 2

- Vaginal brachytherapy

Grade 3

- Vaginal brachytherapy and pelvic radiation therapy

Grade 1

- Vaginal brachytherapy

Grade 2

- Pelvic radiation therapy with or without chemotherapy

Grade 3

- Pelvic radiation therapy with vaginal brachytherapy with or without chemotherapy

1 See Appendix A for FIGO Staging
2 Potential adverse risk factors include the following: age, positive lymphovascular invasion, tumor size, and lower uterine (cervical/glandular) involvement
3 Preferred
4 Depends on depth of invasion in uterus and cervical stroma plus other risk factors
5 This does not influence the choice of adjuvant treatment

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STAGE I

Stage IIIA with serosal involvement

- 45 Gy pelvic radiation therapy and vaginal brachytherapy with or without concurrent chemotherapy and/or adjuvant chemotherapy

Stage IIIA with adnexal involvement

- Adjuvant chemotherapy, consider vaginal brachytherapy, or external beam radiation therapy

Stage IIIB, Stage IIIC1

- 45 Gy pelvic radiation therapy and vaginal brachytherapy with or without concurrent chemotherapy, followed by adjuvant chemotherapy
- Higher dose than 45 Gy needs to be given for sites of ECE and for any other residual suspicious nodes seen on post-op CT

Stage IIIC2

- Extended-field radiation therapy and vaginal brachytherapy with or without concurrent chemotherapy, followed by adjuvant chemotherapy

Stage IV

- Chemotherapy

ADJUVANT THERAPY

See Surveillance on Page 6

ECE = extra-capsular (nodal) extension

1 See Appendix A for FIGO Staging

2 See Appendix B for Systemic Therapy
## Stage I

<table>
<thead>
<tr>
<th>Stage</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage IA (no invasion or superficial invasion)</td>
<td>Vaginal brachytherapy(^2) followed by adjuvant chemotherapy. (^3) Consider surveillance alone if no residual cancer in hysterectomy specimen.</td>
</tr>
<tr>
<td>Stage IB</td>
<td>Vaginal brachytherapy(^2) or pelvic radiation therapy(^4) with or without concurrent chemotherapy followed by adjuvant chemotherapy(^3)</td>
</tr>
<tr>
<td>Stage II</td>
<td>Pelvic radiation therapy(^2,4) or vaginal brachytherapy with or without concurrent chemotherapy followed by adjuvant chemotherapy(^3)</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>Vaginal brachytherapy(^2) or pelvic radiation therapy with or without concurrent chemotherapy followed by adjuvant chemotherapy(^3)</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>Pelvic radiation therapy(^2,4) or vaginal brachytherapy with or without concurrent chemotherapy followed by adjuvant chemotherapy(^3)</td>
</tr>
</tbody>
</table>

### Stage IIIC

- **Disease present in ovaries?**
  - Yes → Chemotherapy\(^3\)
  - No → Pelvic radiation therapy\(^2,4\) or vaginal brachytherapy with or without concurrent chemotherapy followed by adjuvant chemotherapy\(^3\)

### Stage VI

Chemotherapy\(^3\)

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\(^1\) See Appendix A for FIGO Staging  
\(^2\) Preferred  
\(^3\) See Appendix B for Systemic Therapy  
\(^4\) Consider concurrent paclitaxel for disease confined to the pelvis
Endometrial Cancer

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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

After completion of treatment

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

Systemic recurrence?

Yes

Chemotherapy

No – isolated recurrence

Consider radiation therapy and/or resection with or without chemotherapy

1 See Appendix B for Systemic Therapy

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

APPENDIX A: International Federation of Gynecology and Obstetrics (FIGO) Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
</table>
| I¹    | 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 |
| II¹   | Tumor invades cervical stroma, but does not extend beyond the uterus² |
| III¹  | Local and/or regional spread of the tumor  
IIIA: Tumor invades the serosa of the corpus uteri and/or adnexae³  
IIIB: Vaginal and/or parametrial involvement³  
IIIC: Metastases to pelvic and/or para-aortic lymph nodes³  
IIIC1: Positive pelvic nodes  
IIIC2: Positive para-aortic lymph nodes with or without positive pelvic lymph nodes |
| IV¹   | 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 |

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 Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paclitaxel and carboplatin</td>
<td>Cisplatin</td>
</tr>
<tr>
<td>Docetaxel and carboplatin</td>
<td>Carboblatin</td>
</tr>
<tr>
<td>Ifosfamide and paclitaxel (carcinosarcoma)</td>
<td>Doxorubicin</td>
</tr>
<tr>
<td>Cisplatin and ifosfamide (carcinosarcoma)</td>
<td>Liposomal doxorubicin</td>
</tr>
<tr>
<td>Cisplatin and gemcitabine</td>
<td>Paclitaxel</td>
</tr>
<tr>
<td>Everolimus and letrozole</td>
<td>Hormonal agents</td>
</tr>
<tr>
<td>Topotecan</td>
<td></td>
</tr>
<tr>
<td>Bevacizumab</td>
<td></td>
</tr>
<tr>
<td>Temsirolimus</td>
<td></td>
</tr>
<tr>
<td>Docetaxel</td>
<td></td>
</tr>
<tr>
<td>Ifosfamide (carcinosarcoma)</td>
<td></td>
</tr>
<tr>
<td>Pembrolizumab (for MSI-H and MMR-D tumors)</td>
<td></td>
</tr>
</tbody>
</table>
SUGGESTED READINGS


This practice consensus algorithm is based on majority expert opinion of the Endometrial cancer faculty at the University of Texas MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following medical, radiation and surgical oncologists.

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