# Endometrial Cancer





**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[1]
- 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[2]

## 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 with IV contrast and vaginal gel to rule out myometrial invasion
  - Referral to Oncofertility
- No → Hysterectomy[4], BSO, and SLN mapping

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

- Yes → Progesterone therapy (oral or progestin-containing IUD)
  - Re-sample at every 3-6 month interval

Does the patient have progression or persistence of disease > 12 months?

- Yes → Hysterectomy
- No → Progesterone therapy (oral or progestin-containing IUD)

- No → Hysterectomy[4], BSO, and SLN mapping

Is patient suitable for surgery?

- Yes → Disease confined to uterus[3]
- No → Primary radiation or progesterone therapy (oral or progestin-containing IUD if low grade and non-invasive) → See surveillance on Page 6

Hysterectomy[4], BSO, and SLN mapping

- Bilateral SLN identified → Conclude procedure
- Unable to identify or map bilateral SLN → Intraoperative frozen section

Intraoperative frozen section

- 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)

Conclude procedure with/without lymph node dissection → See Pages 3-4 for endometroid cell type and Page 5 for serous cell type

Side specific staging with pelvic and para-aortic node sampling (omental biopsy for non-endometrioid cell type) → See Pages 3-4 for endometroid cell type and Page 5 for serous cell type

- Stage II with gross cervical involvement
- Disease not confirmed to uterus

→ See Page 2

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

[1] See MD Anderson Approved Biomarkers

[2] See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice

[3] MRI with vaginal contrast (gel preferred) is recommended to assess for myometrial and cervical invasion. PET/CT may help with lymph node involvement. PET/MR if available. If none of these modalities are available, ultrasound can be performed

[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

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



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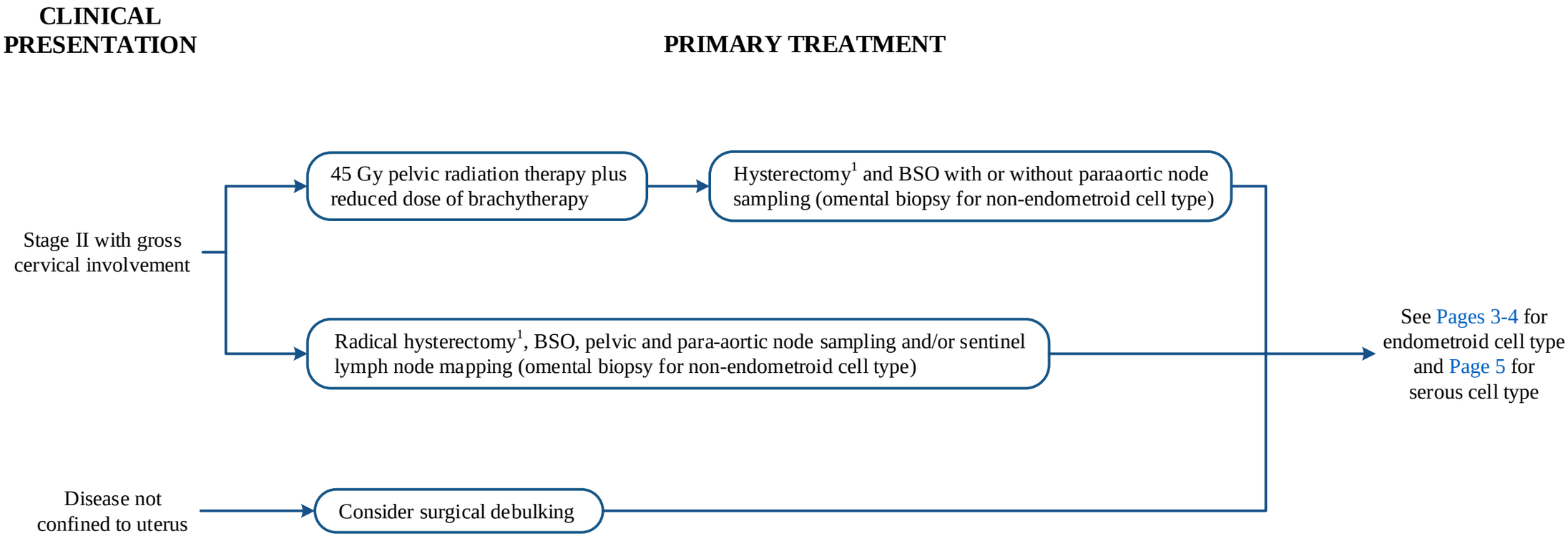


Please refer to American College of Obstetricians and Gynecologists (ACOG) Guidelines for referral.

[1] Hysterectomy may be performed through open or minimally invasive techniques based on surgeon/patient discretion

# Endometrial Cancer (Endometroid Cell Type)





**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.

| Risk Group[1] | ADJUVANT THERAPY |
|---|---|
| **Low Risk:**<br>Grade 1 or 2<br>< 50% myometrial invasion<br>No LVSI (or focal LVSI) | Observation |
| **Low intermediate risk:**<br>Grade 1 or 2<br>≥ 50% myometrial invasion<br>No LVSI (or focal LVSI) | • Observation **or**<br>• Vaginal cuff brachytherapy |
| **High intermediate risk:**<br>• Grade 1 or 2, any invasion positive LVSI (not focal) **or**<br>• Grade 3, < 50% myometrial invasion | Vaginal cuff brachytherapy |
| **High risk:**<br>Grade 3<br>≥ 50% myometrial invasion | • Pelvic radiation therapy **or**<br>• Vaginal cuff brachytherapy **and/or**<br>• 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)





**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.

| STAGE[1] | ADJUVANT THERAPY |
|---|---|
| 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]and vaginal brachytherapy with or without concurrent chemotherapy, followed by with or without adjuvant chemotherapy[4] **or**<br>• Adjuvant chemotherapy alone |
| Stage IIIC2 | • Adjuvant chemotherapy[2] **or**<br>• Extended-field radiation therapy **and** vaginal brachytherapy with or without concurrent chemotherapy, followed by with or without adjuvant chemotherapy[2] |
| Stage IV | 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



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





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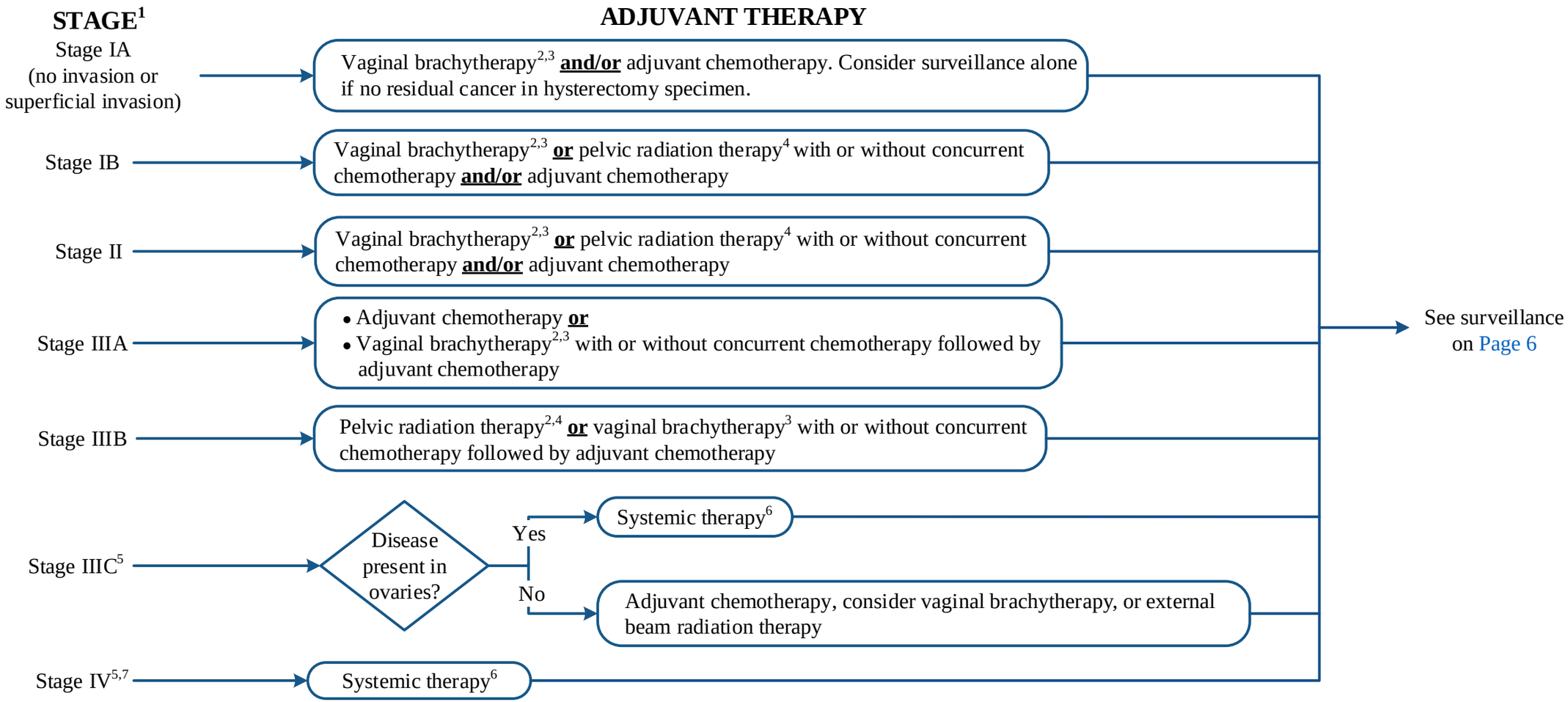


[1] See Appendix A for International Federation of Gynecology and Obstetrics (FIGO) Staging
[2] Preferred
[3] Stage IA/IB/II/IIIA/IIIB vaginal brachytherapy: Consider MRI with contrast and vaginal gel to asses response
[4] Consider concurrent paclitaxel for disease confined to the pelvis
[5] Stage IIIC 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





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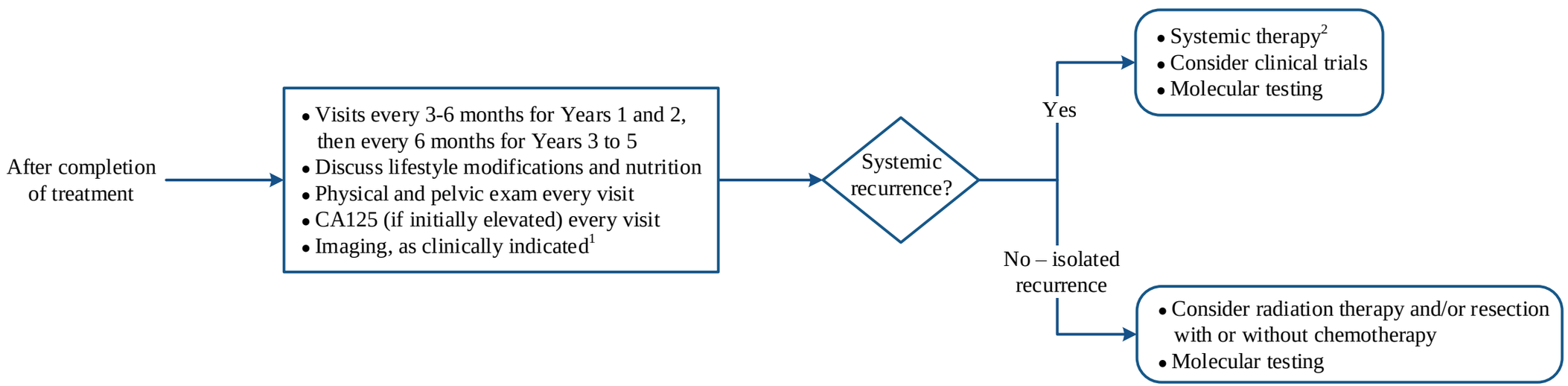
## SURVEILLANCE




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

[1] Consider imaging with development of new symptoms, for patents 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

| Stage | Description |
|---|---|
| I[1] | Tumor confined to the corpus uteri<br>IA: No or less than half myometrial invasion<br>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<br>IIIA: Tumor invades the serosa of the corpus uteri and/or adnexae[3]<br>IIIB: Vaginal and/or parametrial invovlement[3]<br>IIIC: Metastases to pelvic and/or para-aortic lymph nodes[3]<br>IIIC1: Positive pelvic nodes<br>IIIC2: 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<br>IVA: Tumor invasion of bladder and/or bowel mucosa<br>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

| Multi-agent Chemotherapy | Single-agent IV Therapy | | Hormonal Therapy |
|---|---|---|---|
| • Paclitaxel and carboplatin<br>• Paclitaxel, carboplatin, and trastuzumab (stage III/IV or recurrent HER2-positive uterine serous carcinoma)<br>• Docetaxel and carboplatin<br>• Ifosfamide and paclitaxel[1]<br>• Cisplatin and ifosfamide[1]<br>• Cisplatin and gemcitabine<br>• Lenvatinib/pembrolizumab (MSS) | • Cisplatin<br>• Carboplatin<br>• Doxorubicin<br>• Liposomal doxorubicin<br>• Paclitaxel<br>• Nab-paclitaxel<br>• Topotecan<br>• Bevacizumab | • Temsirolmus<br>• Docetaxel<br>• Ifosfamide (carcinosarcoma)<br>• Pembrolizumab (for MSI-H and MMR-D tumors) | • Everolimus and letrozole (for endometrioid histology)<br>• Alternating megestrol acetate and tamoxifen<br>• Megestrol acetate<br>• Medroxyprogesterone acetate<br>• Letrozole |

[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

Creutzberg, C., van Putten, W., Koper, P., Lybeert, M., Jobsen, J., Wárlám-Rodenhuis, C., . . . van Lent, M. (2000). Surgery and postoperative radiotherapy versus surgery alone for patients with stage-1 endometrial carcinoma: Multicentre randomised trial. *The Lancet, 355*(9213), 1404-1411. https://doi.org/10.1016/S0140-6736(00)02139-5

Eifel, P. & Klopp, A. (2017). Uterine Cancer. *Gynecologic radiation oncology: A practical guide*. (pp. 224-254). Wolters Kluwer.

Homesley, H., Filiaci, V., Gibbons, S., Long, H., Cella, D., Spirtos, N., . . . Montag, A. (2009). A randomized phase III trial in advanced endometrial carcinoma of surgery and volume directed radiation followed by cisplatin and doxorubicin with or without paclitaxel: A gynecologic oncology group study. *Gynecologic Oncology, 112*(3), 543-552. https://doi.org/10.1016/j.ygyno.2008.11.014

Jhingran, A., Ramondetta, L., Bodurka, D., Slomovitz, B., Brown, J., Levy, L., . . . Burke, T. (2013). A prospective phase II study of chemoradiation followed by adjuvant chemotherapy for FIGO stage I-IIIA (1988) uterine papillary serous carcinoma of the endometrium. *Gynecologic Oncology, 129*(2), 304-309. https://doi.org/10.1016/j.ygyno.2013.01.025

Keys, H., Roberts, J., Brunetto, V., Zaino, R., Spirtos, N., Bloss, J., . . . Bell, J. (2004). A phase III trial of surgery with or without adjunctive external pelvic radiation therapy in intermediate risk endometrial adenocarcinoma: A gynecologic oncology group study. *Gynecologic Oncology, 92*(3), 744-751. https://doi.org/10.1016/j.ygyno.2003.11.048

National Comprehensive Cancer Network. (2021). *Uterine Neoplasms* (NCCN Guideline Version 1.2021). Retrieved from https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf

Nout, R., Smit, V., Putter, H., Jürgenliemk-Schulz, I., Jobsen, J., Lutgens, L., . . . Creutzberg, C. (2010). Vaginal brachytherapy versus pelvic external beam radiotherapy for patients with endometrial cancer of high-intermediate risk (PORTEC-2): An open-label, non-inferiority, randomised trial. *The Lancet*, 375(9717), 816-823. https://doi.org/10.1016/S0140-6736(09)62163-2

Pecorelli, S. (2009). Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. *International Journal of Gynaecology and Obstetrics, 105*(2), 103-104. https://doi.org/10.1016/j.ijgo.2009.02.012

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