

Bölüm 87

ENDOMETRİUM KANSERİ

Ayşe Büşra ÖNDER¹

GİRİŞ

Endometrium kanseri, gelişmiş ülkelerde en sık görülen jinekolojik malignitedir ve gelişmekte olan ülkelerde serviks kanserinden sonra en sık görülen ikinci jinekolojik malignitedir. Endometrial karsinom ve uterus maligniteleri içerisinde en sık görülen histolojik tip endometrioid karsinomdur. Endometrioid tümörler iyi prognoza sahip olma eğilimindedir ve tipik olarak erken evrede anomal uterin kanamayla klinik semptom verir. Diğer histolojik endometrial karsinom tipleri (seröz, berrak hücre gibi) ve diğer uterus kanseri tipleri kötü prognoz ile ilişkilidir.

Progesterinlerle yeterli karşılanmamış endojen veya eksojen estrogen maruziyeti fazlalığı (örneğin progestinsiz postmenozal hormon replasman tedavisi), tamoksifen kullanımı, obezite, nulliparite ve Lynch sendromu Endometrioid endometrial karsinom için ana risk faktörleri arasında yer alır.

EPİDEMİYOLOJİ

Gelişmiş ülkelerde, 74 yaşına kadar olan kadınlarda uterus kanser insidansı 100.000'de 14,7 ve ölüm oranı 100.000'de 2,3'tür (1). Gelişmekte olan ülkelerde ise 74 yaşına kadar olan kadınlarda insidans 100.000'de 5,5 ve mortalite oranı 100.000'de 1,5'tir.

Endometrium kanserinin Amerika Birleşik Devletleri'nde (ABD) görülme sıklığı diğer gelişmiş ülkelerdeki görülme sıklığından fazladır. Bu durum, ABD popülasyonundaki artmış obezite

veya diğer risk faktörleriyle ilişkilendirilebilir. Her yıl 60.000'in üzerinde vaka ve 10.000'den fazla ölüm vakası vardır (2). ABD Ulusal Kanser Veri Tabanı verilerine göre 2009-2013 yılları arasında endometrium kanseri insidansı 100.000 kadın başına 25,4 idi. İnsidans oranları beyaz kadınlarda (100.000'de 26,0) siyahı (100.000'de 24,6), İspanyol (100.000'de 21,4) veya Asyalı/Pasifik Adalı kadınlardan (100.000'de 20,3) daha yükseldi.

ABD'de uterus kanseri tanısının yaş ortalaması 62'dir (3). 2005'ten 2009'a kadar tanı alan uterus kanser vakalarının yaş dağılımı şöyle bildirilmiştir:

- 20 yaşın altında %0
- 20-34 yaş arası %1,6
- 35-44 yaş arası %5,4
- 45-54 yaş arası %17,2
- 55-64 yaş arası %34,5
- 65-74 yaş arası %25
- 75-84 yaş arası %11,9
- 85 yaş ve üstünde %4,3

ABD'deki kadınların yaşam boyu uterus kanseri riski yüzde 2,8 olarak bildirilmiştir (3). Uterin kanserli kadınların çoğunluğu erken bir aşamada teşhis edilir. Tanı konulduğunda hastaların yüzde 67'sinde hastalık birincil bölgeyle sınırlı, yüzde 21'inde bölgesel organlara ve lenf bezlerine yayılmış göstermiş ve yüzde 8'inde uzak metastazlar gelişmiş olur (3).

İnsidans ve prevalansla ilgili verilerin çoğu, yalnızca endometrial karsinom için değil, genel

¹ Operatör Doktor, Bakırköy Dr. Sadi Konuk Eğitim ve Araştırma Hastanesi, Kadın Hastalıkları ve Doğum ABD, Jinekolojik Onkoloji Cerahisi Bölümü, aysebusraonder@hotmail.com

Kaynaklar

1. Torre LA, Bray F, Siegel RL, et al. Global cancer statistics, 2012. *CA Cancer J Clin* 2015; 65:87.
2. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. *CA Cancer J Clin*. 2019 Jan;69(1):7-34.
3. <http://seer.cancer.gov/statfacts/html/corp.html> (Accessed on June 06, 2016).
4. Bokhman JV. Two pathogenetic types of endometrial carcinoma. *Gynecol Oncol* 1983; 15:10.
5. Felix AS, Weissfeld JL, Stone RA, et al. Factors associated with Type I and Type II endometrial cancer. *Cancer Causes Control* 2010; 21:1851.
6. Brinton LA, Berman ML, Mortel R, et al. Reproductive, menstrual, and medical risk factors for endometrial cancer: results from a case-control study. *Am J Obstet Gynecol* 1992; 167:1317.
7. Barakat RR, Park RC, Grigsby PW, et al. Corpus: Epithelial Tumors. In: Principles and Practice of Gynecologic Oncology, 2nd, Hoskins WH, Perez CA, Young RC (Eds), Lippincott-Raven Publishers, Philadelphia 1997. p.859.
8. American College of Obstetricians and Gynecologists Committee on Gynecologic Practice: Tamoxifen and endometrial Cancer. Committee opinion 232. ACOG 2000; Washington, DC.
9. Iqbal J, Ginsburg OM, Wijeratne TD, et al. Endometrial cancer and venous thromboembolism in women under age 50 who take tamoxifen for prevention of breast cancer: a systematic review. *Cancer Treat Rev* 2012; 38:318.
10. Early Breast Cancer Trialists' Collaborative Group (EBCTCG), Davies C, Godwin J, et al. Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials. *Lancet* 2011; 378:771.
11. Zeleniuch-Jacquotte A, Akhmedkhanov A, Kato I, et al. Postmenopausal endogenous oestrogens and risk of endometrial cancer: results of a prospective study. *Br J Cancer* 2001; 84:975.
12. Lukanova A, Lundin E, Micheli A, et al. Circulating levels of sex steroid hormones and risk of endometrial cancer in postmenopausal women. *Int J Cancer* 2004; 108:425.
13. Potschman N, Hoover RN, Brinton LA, et al. Case-control study of endogenous steroid hormones and endometrial cancer. *J Natl Cancer Inst* 1996; 88:1127.
14. Yin W, Falconer H, Yin L, et al. Association Between Polycystic Ovary Syndrome and Cancer Risk. *JAMA Oncol* 2019; 5:106.
15. Renehan AG, Tyson M, Egger M, et al. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. *Lancet* 2008; 371:569.
16. Setiawan VW, Pike MC, Kolonel LN, et al. Racial/ethnic differences in endometrial cancer risk: the multiethnic cohort study. *Am J Epidemiol* 2007; 165:262.
17. Salazar-Martínez E, Lazcano-Ponce EC, Lira-Lira GG, et al. Case-control study of diabetes, obesity, physical activity and risk of endometrial cancer among Mexican women. *Cancer Causes Control* 2000; 11:707.
18. Ko EM, Walter P, Clark L, et al. The complex triad of obesity, diabetes and race in Type I and II endometrial cancers: prevalence and prognostic significance. *Gynecol Oncol* 2014; 133:28.
19. Setiawan VW, Yang HP, Pike MC, et al. Type I and II endometrial cancers: have they different risk factors? *J Clin Oncol* 2013; 31:2607.
20. McPherson CP, Sellers TA, Potter JD, et al. Reproductive factors and risk of endometrial cancer. The Iowa Women's Health Study. *Am J Epidemiol* 1996; 143:1195.
21. Xu WH, Xiang YB, Ruan ZX, et al. Menstrual and reproductive factors and endometrial cancer risk: Results from a population-based case-control study in urban Shanghai. *Int J Cancer* 2004; 108:613.
22. Berek JS, Hacker NF. Berek & Hacker's Gynecologic Oncology, 6th edition, Wolters Kluwer, Philadelphia 2015.
23. Schumer ST, Cannistra SA. Granulosa cell tumor of the ovary. *J Clin Oncol* 2003; 21:1180.
24. Ollikainen M, Abdel-Rahman WM, Moisio AL, et al. Molecular analysis of familial endometrial carcinoma: a manifestation of hereditary nonpolyposis colorectal cancer or a separate syndrome? *J Clin Oncol* 2005; 23:4609.
25. Lucenteforte E, Talamini R, Montella M, et al. Family history of cancer and the risk of endometrial cancer. *Eur J Cancer Prev* 2009; 18:95.
26. Sandles LG, Shulman LP, Elias S, et al. Endometrial adenocarcinoma: genetic analysis suggesting heritable site-specific uterine cancer. *Gynecol Oncol* 1992; 47:167.
27. Win AK, Reece JC, Ryan S. Family history and risk of endometrial cancer: a systematic review and meta-analysis. *Obstet Gynecol* 2015; 125:89.
28. Lancaster JM, Powell CB, Kauff ND, et al. Society of Gynecologic Oncologists Education Committee statement on risk assessment for inherited gynecologic cancer predispositions. *Gynecol Oncol* 2007; 107:159.
29. Kwon JS, Scott JL, Gilks CB, et al. Testing women with endometrial cancer to detect Lynch syndrome. *J Clin Oncol* 2011; 29:2247.
30. Thompson D, Easton DF, Breast Cancer Linkage Consortium. Cancer Incidence in BRCA1 mutation carriers. *J Natl Cancer Inst* 2002; 94:1358.
31. Beiner ME, Finch A, Rosen B, et al. The risk of endometrial cancer in women with BRCA1 and BRCA2 mutations. A prospective study. *Gynecol Oncol* 2007; 104:7.
32. Heald B, Mester J, Rybicki L, et al. Frequent gastrointestinal polyps and colorectal adenocarcinomas in a prospective series of PTEN mutation carriers. *Gastroenterology* 2010; 139:1927.
33. Riegert-Johnson DL, Gleeson FC, Roberts M, et al. Cancer and Lhermitte-Duclos disease are common in Cowden syndrome patients. *Hered Cancer Clin Pract* 2010; 8:6.
34. Committee opinion no. 634: Hereditary cancer syndromes and risk assessment. *Obstet Gynecol* 2015; 125:1538.
35. Bandera EV, Kushi LH, Moore DF, et al. Consumption of animal foods and endometrial cancer risk: a systematic literature review and meta-analysis. *Cancer Causes Control* 2007; 18:967.
36. Yang TO, Crowe F, Cairns BJ, et al. Tea and coffee and risk of endometrial cancer: cohort study and meta-analysis. *Am J Clin Nutr* 2015; 101:570.
37. Mulholland HG, Murray LJ, Cardwell CR, Cantwell MM. Dietary glycaemic index, glycaemic load and en-

- dometrial and ovarian cancer risk: a systematic review and meta-analysis. *Br J Cancer* 2008; 99:434.
38. Loerbroks A, Schouten LJ, Goldbohm RA, van den Brandt PA. Alcohol consumption, cigarette smoking, and endometrial cancer risk: results from the Netherlands Cohort Study. *Cancer Causes Control* 2007; 18:551.
 39. Setiawan VW, Monroe KR, Goodman MT, et al. Alcohol consumption and endometrial cancer risk: the multiethnic cohort. *Int J Cancer* 2008; 122:634.
 40. Parazzini F, Negri E, La Vecchia C, et al. Role of reproductive factors on the risk of endometrial cancer. *Int J Cancer* 1998; 76:784.
 41. Parazzini F, Pelucchi C, Talamini R, et al. Use of fertility drugs and risk of endometrial cancer in an Italian case-control study. *Eur J Cancer Prev* 2010; 19:428.
 42. Lerner-Geva L, Rabinovici J, Lunenfeld B. Ovarian stimulation: is there a long-term risk for ovarian, breast and endometrial cancer? *Womens Health (Lond)* 2010; 6:831.
 43. Furberg AS, Thune I. Metabolic abnormalities (hypertension, hyperglycemia and overweight), lifestyle (high energy intake and physical inactivity) and endometrial cancer risk in a Norwegian cohort. *Int J Cancer* 2003; 104:669.
 44. Noto H, Osame K, Sasazuki T, Noda M. Substantially increased risk of cancer in patients with diabetes mellitus: a systematic review and meta-analysis of epidemiologic evidence in Japan. *J Diabetes Complications* 2010; 24:345.
 45. Shoff SM, Newcomb PA. Diabetes, body size, and risk of endometrial cancer. *Am J Epidemiol* 1998; 148:234.
 46. Soliman PT, Wu D, Tortolero-Luna G, et al. Association between adiponectin, insulin resistance, and endometrial cancer. *Cancer* 2006; 106:2376.
 47. Friberg E, Mantzoros CS, Wolk A. Diabetes and risk of endometrial cancer: a population-based prospective cohort study. *Cancer Epidemiol Biomarkers Prev* 2007; 16:276.
 48. Zhang Y, Liu Z, Yu X, et al. The association between metabolic abnormality and endometrial cancer: a large case-control study in China. *Gynecol Oncol* 2010; 117:41.
 49. Hale GE, Hughes CL, Cline JM. Endometrial cancer: hormonal factors, the perimenopausal "window of risk," and isoflavones. *J Clin Endocrinol Metab* 2002; 87:3.
 50. Gehrig PA, Bae-Jump VL, Boggess JF, et al. Association between uterine serous carcinoma and breast cancer. *Gynecol Oncol* 2004; 94:208.
 51. Liang SX, Pearl M, Liang S, et al. Personal history of breast cancer as a significant risk factor for endometrial serous carcinoma in women aged 55 years old or younger. *Int J Cancer* 2011; 128:763.
 52. Winer I, Lehman A, Wactawski-Wende J, et al. Tubal Ligation and Risk of Endometrial Cancer: Findings From the Women's Health Initiative. *Int J Gynecol Cancer* 2016; 26:464.
 53. Felix AS, Brinton LA, McMeekin DS, et al. Relationships of Tubal Ligation to Endometrial Carcinoma Stage and Mortality in the NRG Oncology/ Gynecologic Oncology Group 210 Trial. *J Natl Cancer Inst* 2015; 107.
 54. Parslov M, Lidegaard O, Klintorp S, et al. Risk factors among young women with endometrial cancer: a Danish case-control study. *Am J Obstet Gynecol* 2000; 182:23.
 55. Tao MH, Xu WH, Zheng W, et al. Oral contraceptive and IUD use and endometrial cancer: a population-based case-control study in Shanghai, China. *Int J Cancer* 2006; 119:2142.
 56. Vessey M, Painter R. Oral contraceptive use and cancer. Findings in a large cohort study, 1968-2004. *Br J Cancer* 2006; 95:385.
 57. Mueck AO, Seeger H, Rabe T. Hormonal contraception and risk of endometrial cancer: a systematic review. *Endocr Relat Cancer* 2010; 17:R263.
 58. Collaborative Group on Epidemiological Studies on Endometrial Cancer. Endometrial cancer and oral contraceptives: an individual participant meta-analysis of 27 276 women with endometrial cancer from 36 epidemiological studies. *Lancet Oncol* 2015; 16:1061.
 59. Iversen L, Sivasubramaniam S, Lee AJ, et al. Lifetime cancer risk and combined oral contraceptives: the Royal College of General Practitioners' Oral Contraception Study. *Am J Obstet Gynecol* 2017; 216:580.e1.
 60. Cullins VE. Noncontraceptive benefits and therapeutic uses of depot medroxyprogesterone acetate. *J Reprod Med* 1996; 41:428.
 61. Montz FJ, Bristow RE, Bovicelli A, et al. Intrauterine progesterone treatment of early endometrial cancer. *Am J Obstet Gynecol* 2002; 186:651.
 62. Setiawan VW, Pike MC, Karageorgi S, et al. Age at last birth in relation to risk of endometrial cancer: pooled analysis in the epidemiology of endometrial cancer consortium. *Am J Epidemiol* 2012; 176:269.
 63. Jordan SJ, Na R, Johnatty SE, et al. Breastfeeding and Endometrial Cancer Risk: An Analysis From the Epidemiology of Endometrial Cancer Consortium. *Obstet Gynecol* 2017; 129:1059.
 64. Zhou B, Yang L, Sun Q, et al. Cigarette smoking and the risk of endometrial cancer: a meta-analysis. *Am J Med* 2008; 121:501.
 65. Schmid D, Behrens G, Keimling M, et al. A systematic review and meta-analysis of physical activity and endometrial cancer risk. *Eur J Epidemiol* 2015; 30:397.
 66. Moore SC, Gierach GL, Schatzkin A, Matthews CE. Physical activity, sedentary behaviours, and the prevention of endometrial cancer. *Br J Cancer* 2010; 103:933.
 67. Bravi F, Scotti L, Bosetti C, et al. Coffee drinking and endometrial cancer risk: a metaanalysis of observational studies. *Am J Obstet Gynecol* 2009; 200:130.
 68. Butler LM, Wu AH. Green and black tea in relation to gynecologic cancers. *Mol Nutr Food Res* 2011; 55:931.
 69. McCullough ML, Bandera EV, Moore DF, Kush LH. Vitamin D and calcium intake in relation to risk of endometrial cancer: a systematic review of the literature. *Prev Med* 2008; 46:298.
 70. Neill AS, Nagle CM, Protani MM, et al. Aspirin, nonsteroidal anti-inflammatory drugs, paracetamol and risk of endometrial cancer: a case-control study, systematic review and meta-analysis. *Int J Cancer* 2013; 132:1146.
 71. Vargas R, Rauh-Hain JA, Clemmer J, et al. Tumor size, depth of invasion, and histologic grade as prognostic factors of lymph node involvement in endometrial cancer: a SEER analysis. *Gynecol Oncol* 2014; 133:216.
 72. Stephan JM, Hansen J, Samuelson M, et al. Intra-operative frozen section results reliably predict final pathology in endometrial cancer. *Gynecol Oncol* 2014; 133:499.

73. Alcazar JL, Dominguez-Piriz J, Juez L, et al. Intraoperative Gross Examination and Intraoperative Frozen Section in Patients With Endometrial Cancer for Detecting Deep Myometrial Invasion: A Systematic Review and Meta-analysis. *Int J Gynecol Cancer* 2016; 26:407.
74. Kurman RJ, Carcangiu ML, Herrington CS, et al. WHO Classification of tumours of the female reproductive organs, Fourth Edition. World Health Organization, 2014. p.126, 150.
75. Conlon N, Leitao MM Jr, Abu-Rustum NR, Soslow RA. Grading uterine endometrioid carcinoma: a proposal that binary is best. *Am J Surg Pathol* 2014; 38:1583.
76. Robert A. Soslow, Carmen Tornos, Kay J. Park, et all. Endometrial Carcinoma Diagnosis: Use of FIGO Grading and Genomic Subcategories in Clinical Practice: Recommendations of the International Society of Gynecological Pathologists. *Int J Gynecol Pathol.* 2019 Jan; 38(Iss 1 Suppl 1): S64-S74.
77. Huang CY, Tang YH, Chiang YC, et al. Impact of management on the prognosis of pure uterine papillary serous cancer- a Taiwanese Gynecologic Oncology Group (TGOOG) study. *Gynecol Oncol* 2014; 133:221.
78. Quddus MR, Sung CJ, Zhang C, Lawrence WD. Minor serous and clear cell components adversely affect prognosis in "mixed-type" endometrial carcinomas: a clinicopathologic study of 36 stage-I cases. *Reprod Sci* 2010; 17:673.
79. McCluggage WG. Malignant biphasic uterine tumours: carcinosarcomas or metaplastic carcinomas? *J Clin Pathol* 2002; 55:321.
80. Lopez-Garcia MA, Palacios J. Pathologic and molecular features of uterine carcinosarcomas. *Semin Diagn Pathol* 2010; 27:274.
81. Berton-Rigaud D, Devouassoux-Shisheboran M, Ledermann JA, et al. Gynecologic Cancer InterGroup (GCIG) consensus review for uterine and ovarian carcinosarcoma. *Int J Gynecol Cancer* 2014; 24:S55.
82. Broaddus RR, Lynch HT, Chen LM, et al. Pathologic features of endometrial carcinoma associated with HNPCC: a comparison with sporadic endometrial carcinoma. *Cancer* 2006; 106:87.
83. Mutter GL, Lin MC, Fitzgerald JT, et al. Altered PTEN expression as a diagnostic marker for the earliest endometrial precancers. *J Natl Cancer Inst* 2000; 92:924.
84. Kandoth C, Schultz N, et al. Cancer Genome Atlas Research Network, Integrated genomic characterization of endometrial carcinoma. *Nature* 2013; 497:67.
85. Brinton LA, Felix AS, McMeekin DS, et al. Etiologic heterogeneity in endometrial cancer: evidence from a Gynecologic Oncology Group trial. *Gynecol Oncol* 2013; 129:277.
86. Ambros RA, Sherman ME, Zahn CM, et al. Endometrial intraepithelial carcinoma: a distinctive lesion specifically associated with tumors displaying serous differentiation. *Hum Pathol* 1995; 26:1260.
87. Fadare O, Liang SX, Ulukus EC, et al. Precursors of endometrial clear cell carcinoma. *Am J Surg Pathol* 2006; 30:1519.
88. Fadare O, Zheng W, Crispens MA, et al. Morphologic and other clinicopathologic features of endometrial clear cell carcinoma: a comprehensive analysis of 50 rigorously classified cases. *Am J Cancer Res* 2013; 3:70.
89. Hoang LN, McConechy MK, Meng B, et al. Targeted mutation analysis of endometrial clear cell carcinoma. *Histopathology* 2015; 66:664.
90. Pothuri B, Ramondetta L, Eifel P, et al. Radiation-associated endometrial cancers are prognostically unfavorable tumors: a clinicopathologic comparison with 527 sporadic endometrial cancers. *Gynecol Oncol* 2006; 103:948.
91. Taylor NP, Zighelboim I, Huettner PC, et al. DNA mismatch repair and TP53 defects are early events in uterine carcinosarcoma tumorigenesis. *Mod Pathol* 2006; 19:1333.
92. McConechy MK, Ding J, Cheang MC, et al. Use of mutation profiles to refine the classification of endometrial carcinomas. *J Pathol* 2012; 228:20.
93. Le Gallo M, Bell DW. The emerging genomic landscape of endometrial cancer. *Clin Chem* 2014; 60:98.
94. Billingsley CC, Cohn DE, Mutch DG, et al. Polymerase (POLE) mutations in endometrial cancer: clinical outcomes and implications for Lynch syndrome testing. *Cancer* 2015; 121:386.
95. Diaz-Padilla I, Romero N, Amir E, et al. Mismatch repair status and clinical outcome in endometrial cancer: a systematic review and meta-analysis. *Crit Rev Oncol Hematol* 2013; 88:154.
96. Alkushi A, Köbel M, Kaloger SE, Gilks CB. High-grade endometrial carcinoma: serous and grade 3 endometrioid carcinomas have different immunophenotypes and outcomes. *Int J Gynecol Pathol* 2010; 29:343.
97. Voss MA, Ganesan R, Ludeman L, et al. Should grade 3 endometrioid endometrial carcinoma be considered a type 2 cancer-a clinical and pathological evaluation. *Gynecol Oncol* 2012; 124:15.
98. Alvarez T, Miller E, Duska L, Oliva E. Molecular profile of grade 3 endometrioid endometrial carcinoma: is it a type I or type II endometrial carcinoma? *Am J Surg Pathol* 2012; 36:753.
99. Lancaster JM, Powell CB, Kauff ND, et al. Society of Gynecologic Oncologists Education Committee statement on risk assessment for inherited gynecologic cancer predispositions. *Gynecol Oncol* 2007; 107:159.
100. Committee opinion no. 634: Hereditary cancer syndromes and risk assessment. *Obstet Gynecol* 2015; 125:1538.
101. Garg K, Leitao MM Jr, Kauff ND, et al. Selection of endometrial carcinomas for DNA mismatch repair protein immunohistochemistry using patient age and tumor morphology enhances detection of mismatch repair abnormalities. *Am J Surg Pathol* 2009; 33:925.
102. American College of Obstetricians and Gynecologists. ACOG practice bulletin, clinical management guidelines for obstetrician-gynecologists, number 65, August 2005: management of endometrial cancer. *Obstet Gynecol* 2005; 106:413.
103. Kimura T, Kamiura S, Yamamoto T, et al. Abnormal uterine bleeding and prognosis of endometrial cancer. *Int J Gynaecol Obstet* 2004; 85:145.
104. Seebacher V, Schmid M, Polterauer S, et al. The presence of postmenopausal bleeding as prognostic parameter in patients with endometrial cancer: a retrospective multi-center study. *BMC Cancer* 2009; 9:460.
105. Espindola D, Kennedy KA, Fischer EG. Management of abnormal uterine bleeding and the pathology of en-

- dometrial hyperplasia. *Obstet Gynecol Clin North Am* 2007; 34:717.
106. Ronghe R, Gaudoin M. Women with recurrent postmenopausal bleeding should be re-investigated but are not more likely to have endometrial cancer. *Menopause Int* 2010; 16:9.
 107. Reed SD, Newton KM, Clinton WL, et al. Incidence of endometrial hyperplasia. *Am J Obstet Gynecol* 2009; 200:678.e1.
 108. Committee on Practice Bulletins—Gynecology. Practice bulletin no. 128: diagnosis of abnormal uterine bleeding in reproductive-aged women. *Obstet Gynecol* 2012; 120:197. Reaffirmed 2016.
 109. Wright TC Jr, Massad LS, Dunton CJ, et al. 2006 consensus guidelines for the management of women with abnormal cervical screening tests. *J Low Genit Tract Dis* 2007; 11:201.
 110. Vernooy F, Heintz P, Witteveen E, van der Graaf Y. The outcomes of ovarian cancer treatment are better when provided by gynecologic oncologists and in specialized hospitals: a systematic review. *Gynecol Oncol* 2007; 105:801.
 111. McKenney, J.K. and T.A. Longacre, Low-grade endometrial adenocarcinoma: a diagnostic algorithm for distinguishing atypical endometrial hyperplasia and other benign (and malignant) mimics. *Adv Anat Pathol*, 2009. 16(1): p. 1-22.
 112. Leitao, M.M., Jr., et al., Comparison of D&C and office endometrial biopsy accuracy in patients with FIGO grade 1 endometrial adenocarcinoma. *Gynecol Oncol*, 2009. 113(1): p. 105-8.
 113. Torres ML, Weaver AL, Kumar S, et al. Risk factors for developing endometrial cancer after benign endometrial sampling. *Obstet Gynecol* 2012; 120:998.
 114. Twu NF, Chen SS. Five-year follow-up of patients with recurrent postmenopausal bleeding. *Zhonghua Yi Xue Za Zhi (Taipei)* 2000; 63:628.
 115. Larson DM, Johnson KK, Broste SK, et al. Comparison of D&C and office endometrial biopsy in predicting final histopathologic grade in endometrial cancer. *Obstet Gynecol* 1995; 86:38.
 116. Frumovitz M, Singh DK, Meyer L, et al. Predictors of final histology in patients with endometrial cancer. *Gynecol Oncol* 2004; 95:463.
 117. Randall LM, Pothuri B, Swisher EM, et al. Multi-disciplinary summit on genetics services for women with gynecologic cancers: A Society of Gynecologic Oncology White Paper. *Gynecol Oncol* 2017; 146:217.
 118. Lancaster JM, Powell CB, Chen LM, et al. Society of Gynecologic Oncology statement on risk assessment for inherited gynecologic cancer predispositions. *Gynecol Oncol* 2015; 136:3.
 119. Committee on Practice Bulletins-Gynecology, Society of Gynecologic Oncology. ACOG Practice Bulletin No. 147: Lynch syndrome. *Obstet Gynecol* 2014; 124:1042. Reaffirmed 2019.
 120. https://www.nccn.org/professionals/physician_gls/default.aspx#genetics_colon (Accessed on January 17, 2018).
 121. Umar A, Boland CR, Terdiman JP, et al. Revised Bethesda guidelines for hereditary nonpolyposis colorectal cancer (Lynch syndrome) and microsatellite instability. *J Natl Cancer Inst* 2004; 96: 261–268.
 122. Heald B, Mester J, Rybicki L, et al. Frequent gastrointestinal polyps and colorectal adenocarcinomas in a prospective series of PTEN mutation carriers. *Gastroenterology* 2010; 139:1927.
 123. Riegert-Johnson DL, Gleeson FC, Roberts M, et al. Cancer and Lhermitte-Duclos disease are common in Cowden syndrome patients. *Hered Cancer Clin Pract* 2010; 8:6.
 124. Pilarski R, Stephens JA, Noss R, et al. Predicting PTEN mutations: an evaluation of Cowden syndrome and Bannayan-Riley-Ruvalcaba syndrome clinical features. *J Med Genet* 2011; 48:505.
 125. Tan MH, Mester JL, Ngeow J, et al. Lifetime cancer risks in individuals with germline PTEN mutations. *Clin Cancer Res* 2012; 18:400.
 126. http://www.nccn.org/professionals/physician_gls/pdf/genetics_screening.pdf (Accessed on January 18, 2012).
 127. Colombo, N., et al., ESMO-ESGO-ESTRO Consensus Conference on Endometrial Cancer: Diagnosis, Treatment and Follow-up. *Int J Gynecol Cancer*, 2016. 26(1): p. 2-30.
 128. Kinkel K, Kaji Y, Yu KK, et al. Radiologic staging in patients with endometrial cancer: a meta-analysis. *Radiology* 1999; 212:711.
 129. Beddy P, Moyle P, Kataoka M, et al. Evaluation of depth of myometrial invasion and overall staging in endometrial cancer: comparison of diffusion-weighted and dynamic contrast-enhanced MR imaging. *Radiology* 2012; 262:530.
 130. Selman TJ, Mann CH, Zamora J, Khan KS. A systematic review of tests for lymph node status in primary endometrial cancer. *BMC Womens Health* 2008; 8:8.
 131. Park JY, Kim EN, Kim DY, et al. Comparison of the validity of magnetic resonance imaging and positron emission tomography/computed tomography in the preoperative evaluation of patients with uterine corpus cancer. *Gynecol Oncol* 2008; 108:486.
 132. Horowitz NS, Dehdashti F, Herzog TJ, et al. Prospective evaluation of FDG-PET for detecting pelvic and para-aortic lymph node metastasis in uterine corpus cancer. *Gynecol Oncol* 2004; 95:546.
 133. Kitajima K, Murakami K, Yamasaki E, et al. Accuracy of integrated FDG-PET/contrast-enhanced CT in detecting pelvic and paraaortic lymph node metastasis in patients with uterine cancer. *Eur Radiol* 2009; 19:1529.
 134. Dotters DJ. Preoperative CA 125 in endometrial cancer: is it useful? *Am J Obstet Gynecol* 2000; 182:1328.
 135. Todo Y, Sakuragi N, Nishida R, et al. Combined use of magnetic resonance imaging, CA 125 assay, histologic type, and histologic grade in the prediction of lymph node metastasis in endometrial carcinoma. *Am J Obstet Gynecol* 2003; 188:1265.
 136. Powell JL, Hill KA, Shiro BC, et al. Preoperative serum CA-125 levels in treating endometrial cancer. *J Reprod Med* 2005; 50:585.
 137. Chung HH, Kim JW, Park NH, et al. Use of preoperative serum CA-125 levels for prediction of lymph node metastasis and prognosis in endometrial cancer. *Acta Obstet Gynecol Scand* 2006; 85:1501.

138. Kim HS, Park CY, Lee JM, et al. Evaluation of serum CA-125 levels for preoperative counseling in endometrioid endometrial cancer: a multi-center study. *Gynecol Oncol* 2010; 118:283.
139. Kalogera E, Scholler N, Powless C, et al. Correlation of serum HE4 with tumor size and myometrial invasion in endometrial cancer. *Gynecol Oncol* 2012; 124:270.
140. Pecorelli S. Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. *Int J Gynaecol Obstet.* 2009 May;105(2):103-4.
141. Mutch DN. The new FIGO staging system for cancers of the vulva, cervix, endometrium and sarcomas. *Gynecol Oncol.* 2009;115:325–328.
142. Seagle BL, Alexander AL, Lantsman T, Shahabi S. Prognosis and treatment of positive peritoneal cytology in early endometrial cancer: matched cohort analyses from the National Cancer Database. *Am J Obstet Gynecol* 2018; 218:329.e1.
143. Wethington, S.L., et al., Prognostic significance and treatment implications of positive peritoneal cytology in endometrial adenocarcinoma: Unraveling a mystery. *Gynecol Oncol*, 2009. 115(1): p. 18-25.
144. Takeshima, N., et al., Positive peritoneal cytology in endometrial cancer: enhancement of other prognostic indicators. *Gynecol Oncol*, 2001. 82(3): p. 470-3.
145. DeNardis SA, Holloway RW, Bigsby GE 4th, et al. Robotically assisted laparoscopic hysterectomy versus total abdominal hysterectomy and lymphadenectomy for endometrial cancer. *Gynecol Oncol* 2008; 111:412.
146. Mäenpää MM, Nieminen K, Tomás EI, et al. Robotic-assisted vs traditional laparoscopic surgery for endometrial cancer: a randomized controlled trial. *Am J Obstet Gynecol* 2016; 215:588.e1.
147. Walker JL, Piedmonte MR, Spirtos NM, et al. Recurrence and survival after random assignment to laparoscopy versus laparotomy for comprehensive surgical staging of uterine cancer: Gynecologic Oncology Group LAP2 Study. *J Clin Oncol* 2012; 30:695.
148. Kornblith AB, Huang HQ, Walker JL, et al. Quality of life of patients with endometrial cancer undergoing laparoscopic international federation of gynecology and obstetrics staging compared with laparotomy: a Gynecologic Oncology Group study. *J Clin Oncol* 2009; 27:5337.
149. Janda M, Gebski V, Davies LC, et al. Effect of Total Laparoscopic Hysterectomy vs Total Abdominal Hysterectomy on Disease-Free Survival Among Women With Stage I Endometrial Cancer: A Randomized Clinical Trial. *JAMA* 2017; 317:1224.
150. Galaal K, Bryant A, Fisher AD, et al. Laparoscopy versus laparotomy for the management of early stage endometrial cancer. *Cochrane Database Syst Rev* 2012; :CD006655.
151. Janda M, Gebski V, Brand A, et al. Quality of life after total laparoscopic hysterectomy versus total abdominal hysterectomy for stage I endometrial cancer (LACE): a randomised trial. *Lancet Oncol* 2010; 11:772.
152. Gehrig PA, Cantrell LA, Shafer A, et al. What is the optimal minimally invasive surgical procedure for endometrial cancer staging in the obese and morbidly obese woman? *Gynecol Oncol* 2008; 111:41.
153. Wright JD, Burke WM, Wilde ET, et al. Comparative effectiveness of robotic versus laparoscopic hysterectomy for endometrial cancer. *J Clin Oncol* 2012; 30:783.
154. Walker JL, Piedmonte MR, Spirtos NM, et al. Laparoscopy compared with laparotomy for comprehensive surgical staging of uterine cancer: Gynecologic Oncology Group Study LAP2. *J Clin Oncol* 2009; 27:5331.
155. Aarts JW, Nieboer TE, Johnson N, et al. Surgical approach to hysterectomy for benign gynaecological disease. *Cochrane Database Syst Rev* 2015; :CD003677.
156. Beck TL, Morse CB, Gray HJ, et al. Route of hysterectomy and surgical outcomes from a statewide gynecologic oncology population: is there a role for vaginal hysterectomy? *Am J Obstet Gynecol* 2016; 214:348.e1.
157. Cohn DE, Huh WK, Fowler JM, Straughn JM Jr. Cost-effectiveness analysis of strategies for the surgical management of grade 1 endometrial adenocarcinoma. *Obstet Gynecol* 2007; 109:1388.
158. Rossi, E.C., et al., A comparison of sentinel lymph node biopsy to lymphadenectomy for endometrial cancer staging (FIRES trial): a multicentre, prospective, cohort study. *Lancet Oncol*, 2017. 18(3): p. 384-392.
159. Ballester M, Dubernard G, Lécuru F, et al. Detection rate and diagnostic accuracy of sentinel-node biopsy in early stage endometrial cancer: a prospective multicentre study (SENTI-ENDO). *Lancet Oncol* 2011; 12:469.
160. Holloway RW, Abu-Rustum NR, Backes FJ, et al. Sentinel lymph node mapping and staging in endometrial cancer: A Society of Gynecologic Oncology literature review with consensus recommendations. *Gynecol Oncol* 2017; 146:405.
161. Matsuo K, Machida H, Takiuchi T, et al. Prognosis of women with apparent stage I endometrial cancer who had supracervical hysterectomy. *Gynecol Oncol* 2017; 145:41.
162. Todo Y, Yamamoto R, Minobe S, et al. Risk factors for postoperative lower-extremity lymphedema in endometrial cancer survivors who had treatment including lymphadenectomy. *Gynecol Oncol* 2010; 119:60.
163. Abu-Rustum NR, Alektiar K, Iasonos A, et al. The incidence of symptomatic lower-extremity lymphedema following treatment of uterine corpus malignancies: a 12-year experience at Memorial Sloan-Kettering Cancer Center. *Gynecol Oncol* 2006; 103:714.
164. Carlson JW, Kauderer J, Hutson A, et al. GOG 244, the lymphedema and gynecologic cancer (LEG) study: Incidence and risk factors in newly diagnosed patients. Abstract, Society of Gynecologic Oncology, New Orleans, LA, March 2018. Abstract #11.
165. Yost KJ, Cheville AL, Al-Hilli MM, et al. Lymphedema after surgery for endometrial cancer: prevalence, risk factors, and quality of life. *Obstet Gynecol* 2014; 124:307.
166. Mahdi H, Kumar S, Al-Wahab Z, et al. Prognostic impact of lymphadenectomy in uterine serous cancer. *BJOG* 2013; 120:384.
167. Kumar S, Podratz KC, Bakkum-Gamez JN, et al. Prospective assessment of the prevalence of pelvic, paraaortic and high paraaortic lymph node metastasis in endometrial cancer. *Gynecol Oncol* 2014; 132:38.
168. Koh WJ, Abu-Rustum NR, Bean S, et al. Uterine Neoplasms, Version 1.2018, NCCN Clinical Practice Gu-

- idelines in Oncology. *J Natl Compr Canc Netw.* 2018 Feb;16(2):170-199.
169. Benedetti Panici P, Basile S, Maneschi F, et al. Systematic pelvic lymphadenectomy vs. no lymphadenectomy in early-stage endometrial carcinoma: randomized clinical trial. *J Natl Cancer Inst* 2008; 100:1707.
170. ASTEC study group, Kitchener H, Swart AM, et al. Efficacy of systematic pelvic lymphadenectomy in endometrial cancer (MRC ASTEC trial): a randomised study. *Lancet* 2009; 373:125.
171. Mariani A, Dowdy SC, Cliby WA, et al. Prospective assessment of lymphatic dissemination in endometrial cancer: a paradigm shift in surgical staging. *Gynecol Oncol* 2008; 109:11.
172. Mariani A, Webb MJ, Keeney GL, et al. Low-risk corpus cancer: is lymphadenectomy or radiotherapy necessary? *Am J Obstet Gynecol* 2000; 182:1506.
173. Todo Y, Kato H, Kaneuchi M, et al. Survival effect of para-aortic lymphadenectomy in endometrial cancer (SE-PAL study): a retrospective cohort analysis. *Lancet* 2010; 375:1165.
174. Barlin JN, Puri I, Bristow RE. Cytoreductive surgery for advanced or recurrent endometrial cancer: a meta-analysis. *Gynecol Oncol* 2010; 118:14.
175. Landrum LM, Moore KN, Myers TK, et al. Stage IVB endometrial cancer: does applying an ovarian cancer treatment paradigm result in similar outcomes? A case-control analysis. *Gynecol Oncol* 2009; 112:337.
176. Wilkinson-Ryan I, Frolova AI, Liu J, et al. Neoadjuvant chemotherapy versus primary cytoreductive surgery for stage IV uterine serous carcinoma. *Int J Gynecol Cancer* 2015; 25:63.
177. Lewin SN, Herzog TJ, Barrena Medel NI, et al. Comparative performance of the 2009 international Federation of gynecology and obstetrics' staging system for uterine corpus cancer. *Obstet Gynecol* 2010; 116:1141.
178. Creasman WT, Odicino F, Maisonneuve P, et al. Carcinoma of the corpus uteri. FIGO 26th Annual Report on the Results of Treatment in Gynecological Cancer. *Int J Gynaecol Obstet* 2006; 95 Suppl 1:S105-43.
179. Matsuo K, Machida H, Shoupe D, et al. Ovarian Conservation and Overall Survival in Young Women With Early-Stage Low-Grade Endometrial Cancer. *Obstet Gynecol* 2016; 128:761.
180. Society of Gynecologic Oncology (SGO). SGO Clinical Practice Statement: Screening for Lynch Syndrome in Endometrial Cancer. <https://www.sgo.org/clinical-practice/guidelines/screening-for-lynch-syndrome-in-endometrial-cancer/> (Accessed on June 03, 2019).
181. In memoriam William Henry Daines Trubshaw 1908-1971. *S Afr J Surg* 1971; 9:172.
182. Zaino R, Whitney C, Brady MF, et al. Simultaneously detected endometrial and ovarian carcinomas--a prospective clinicopathologic study of 74 cases: a gynecologic oncology group study. *Gynecol Oncol* 2001; 83:355.
183. Soliman PT, Slomovitz BM, Broaddus RR, et al. Synchronous primary cancers of the endometrium and ovary: a single institution review of 84 cases. *Gynecol Oncol* 2004; 94:456.
184. Walsh C, Holschneider C, Hoang Y, et al. Coexisting ovarian malignancy in young women with endometrial cancer. *Obstet Gynecol* 2005; 106:693.
185. Ulbright TM, Roth LM. Metastatic and independent cancers of the endometrium and ovary: a clinicopathologic study of 34 cases. *Hum Pathol* 1985; 16:28.
186. Morrow CP, Bundy BN, Kurman RJ, et al. Relationship between surgical-pathological risk factors and outcome in clinical stage I and II carcinoma of the endometrium: a Gynecologic Oncology Group study. *Gynecol Oncol* 1991; 40:55.
187. Eifel PJ, Ross J, Hendrickson M, et al. Adenocarcinoma of the endometrium. Analysis of 256 cases with disease limited to the uterine corpus: treatment comparisons. *Cancer* 1983; 52:1026.
188. Orr JW Jr, Holimon JL, Orr PF. Stage I corpus cancer: is teletherapy necessary? *Am J Obstet Gynecol* 1997; 176:777.
189. Straughn JM Jr, Huh WK, Kelly FJ, et al. Conservative management of stage I endometrial carcinoma after surgical staging. *Gynecol Oncol* 2002; 84:194.
190. ASTEC/EN.5 Study Group, Blake P, Swart AM, et al. Adjuvant external beam radiotherapy in the treatment of endometrial cancer (MRC ASTEC and NCIC CTG EN.5 randomised trials): pooled trial results, systematic review, and meta-analysis. *Lancet* 2009; 373:137.
191. Creutzberg, C.L., et al., Surgery and postoperative radiotherapy versus surgery alone for patients with stage-1 endometrial carcinoma: multicentre randomised trial. PORTEC Study Group. Post Operative Radiation Therapy in Endometrial Carcinoma. *Lancet*, 2000. 355(9213): p. 1404-11.
192. Kong, A., et al., Adjuvant radiotherapy for stage I endometrial cancer: an updated Cochrane systematic review and meta-analysis. *J Natl Cancer Inst*, 2012. 104(21): p. 1625-34.
193. Madom LM, Brown AK, Lui F, et al. Lower uterine segment involvement as a predictor for lymph node spread in endometrial carcinoma. *Gynecol Oncol* 2007; 107:75.
194. Kizer NT, Gao F, Guntupalli S, et al. Lower uterine segment involvement is associated with poor outcomes in early-stage endometrioid endometrial carcinoma. *Ann Surg Oncol* 2011; 18:1419.
195. Brown AK, Madom L, Moore R, et al. The prognostic significance of lower uterine segment involvement in surgically staged endometrial cancer patients with negative nodes. *Gynecol Oncol* 2007; 105:55.
196. Keys HM, Roberts JA, Brunetto VL, et al. A phase III trial of surgery with or without adjunctive external pelvic radiation therapy in intermediate risk endometrial adenocarcinoma: a Gynecologic Oncology Group study. *Gynecol Oncol* 2004; 92:744.
197. Creutzberg CL, van Putten WL, Koper PC, et al. Surgery and postoperative radiotherapy versus surgery alone for patients with stage-1 endometrial carcinoma: multicentre randomised trial. PORTEC Study Group. Post Operative Radiation Therapy in Endometrial Carcinoma. *Lancet* 2000; 355:1404.
198. Nout RA, Smit VT, Putter H, et al. 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. *Lancet* 2010; 375:816.

199. Creutzberg CL, van Putten WL, Koper PC, et al. The morbidity of treatment for patients with Stage I endometrial cancer: results from a randomized trial. *Int J Radiat Oncol Biol Phys* 2001; 51:1246.
200. Creutzberg CL, Nout RA, Lybeert ML, et al. Fifteen-year radiotherapy outcomes of the randomized PORTEC-1 trial for endometrial carcinoma. *Int J Radiat Oncol Biol Phys* 2011; 81:e631.
201. Kong A, Johnson N, Kitchener HC, Lawrie TA. Adjuvant radiotherapy for stage I endometrial cancer. *Cochrane Database Syst Rev* 2012; :CD003916.
202. Alektiar KM, Venkatraman E, Chi DS, Barakat RR. Intravaginal brachytherapy alone for intermediate-risk endometrial cancer. *Int J Radiat Oncol Biol Phys* 2005; 62:111.
203. Jolly S, Vargas C, Kumar T, et al. Vaginal brachytherapy alone: an alternative to adjuvant whole pelvis radiation for early stage endometrial cancer. *Gynecol Oncol* 2005; 97:887.
204. Soljhjem MC, Petersen IA, Haddock MG. Vaginal brachytherapy alone is sufficient adjuvant treatment of surgical stage I endometrial cancer. *Int J Radiat Oncol Biol Phys* 2005; 62:1379.
205. McCloskey SA, Tchabo NE, Malhotra HK, et al. Adjuvant vaginal brachytherapy alone for high risk localized endometrial cancer as defined by the three major randomized trials of adjuvant pelvic radiation. *Gynecol Oncol* 2010; 116:404.
206. Klopp AH, Jhingran A, Ramondetta L, et al. Node-positive adenocarcinoma of the endometrium: outcome and patterns of recurrence with and without external beam irradiation. *Gynecol Oncol* 2009; 115:6.
207. Alvarez Secord A, Havrilesky LJ, Bae-Jump V, et al. The role of multi-modality adjuvant chemotherapy and radiation in women with advanced stage endometrial cancer. *Gynecol Oncol* 2007; 107:285.
208. Frigerio L, Mangili G, Aletti G, et al. Concomitant radiotherapy and paclitaxel for high-risk endometrial cancer: first feasibility study. *Gynecol Oncol* 2001; 81:53.
209. Greven K, Winter K, Underhill K, et al. Final analysis of RTOG 9708: adjuvant postoperative irradiation combined with cisplatin/paclitaxel chemotherapy following surgery for patients with high-risk endometrial cancer. *Gynecol Oncol* 2006; 103:155.
210. Lupe K, D'Souza DP, Kwon JS, et al. Adjuvant carboplatin and paclitaxel chemotherapy interposed with involved field radiation for advanced endometrial cancer. *Gynecol Oncol* 2009; 114:94.
211. Onda T, Yoshikawa H, Mizutani K, et al. Treatment of node-positive endometrial cancer with complete node dissection, chemotherapy and radiation therapy. *Br J Cancer* 1997; 75:1836.
212. Lupe K, Kwon J, D'Souza D, et al. Adjuvant paclitaxel and carboplatin chemotherapy with involved field radiation in advanced endometrial cancer: a sequential approach. *Int J Radiat Oncol Biol Phys* 2007; 67:110.
213. Hogberg T, Rosenberg P, Kristensen G, et al. A randomized phase III study on adjuvant treatment with radiation (RT) ± chemotherapy (CT) in early stage high-risk endometrial cancer (NSGO-EC-9501/EORTC 55991) (abstract). *J Clin Oncol* 2007; 25:274s.
214. Scholten AN, van Putten WL, Beerman H, et al. Postoperative radiotherapy for Stage 1 endometrial carcinoma: long-term outcome of the randomized PORTEC trial with central pathology review. *Int J Radiat Oncol Biol Phys* 2005; 63:834.
215. Liang LW, Perez AR, Cangemi NA, et al. An Assessment of Prognostic Factors, Adjuvant Treatment, and Outcomes of Stage IA Polyp-Limited Versus Endometrium-Limited Type II Endometrial Carcinoma. *Int J Gynecol Cancer* 2016; 26:497.
216. McMeekin DS, Filiaci VL, Aghajanian C, et al. Randomized phase III trial of pelvic radiation therapy (PXRT) versus vaginal cuff brachytherapy followed by paclitaxel/carboplatin chemotherapy (VCB/C) in patients with high risk (HR), early stage endometrial cancer (EC): a Gynecologic Oncology Group trial. *Gynecol Oncol* 2014; 134S:438.
217. Randall ME, Filiaci V, McMeekin DS, et al. Phase III Trial: Adjuvant Pelvic Radiation Therapy Versus Vaginal Brachytherapy Plus Paclitaxel/Carboplatin in High-Intermediate and High-Risk Early Stage Endometrial Cancer. *J Clin Oncol* 2019; 37:1810.
218. Bernardini MQ, Gien LT, Lau S, et al. Treatment related outcomes in high-risk endometrial carcinoma: Canadian high risk endometrial cancer consortium (CHREC). *Gynecol Oncol* 2016; 141:148.
219. de Boer SM, Powell ME, Mileskein L, et al. Adjuvant chemoradiotherapy versus radiotherapy alone for women with high-risk endometrial cancer (PORTEC-3): final results of an international, open-label, multicentre, randomised, phase 3 trial. *Lancet Oncol* 2018; 19:295.
220. de Boer SM, Powell ME, Mileskein L, et al. Toxicity and quality of life after adjuvant chemoradiotherapy versus radiotherapy alone for women with high-risk endometrial cancer (PORTEC-3): an open-label, multicentre, randomised, phase 3 trial. *Lancet Oncol* 2016; 17:1114.
221. Matei D, Filiaci V, Randall ME, et al. Adjuvant Chemotherapy plus Radiation for Locally Advanced Endometrial Cancer. *N Engl J Med* 2019; 380:2317.
222. Shih KK, Yun E, Gardner GJ, et al. Surgical cytoreduction in stage IV endometrioid endometrial carcinoma. *Gynecol Oncol* 2011; 122:608.
223. Patsavas K, Woessner J, Giedla B, et al. Optimal surgical debulking in uterine papillary serous carcinoma affects survival. *Gynecol Oncol* 2011; 121:581.
224. Rauh-Hain JA, Growdon WB, Schorge JO, et al. Prognostic determinants in patients with stage IIIC and IV uterine papillary serous carcinoma. *Gynecol Oncol* 2010; 119:299.
225. Bristow RE, Zerbe MJ, Rosenshein NB, et al. Stage IVB endometrial carcinoma: the role of cytoreductive surgery and determinants of survival. *Gynecol Oncol* 2000; 78:85.
226. Martin-Hirsch PP, Bryant A, Keep SL, et al. Adjuvant progestagens for endometrial cancer. *Cochrane Database Syst Rev* 2011; :CD001040.
227. Miller D, Filiaci V, Fleming G, et al. Late-Breaking Abstract 1: Randomized phase III noninferiority trial of first line chemotherapy for metastatic or recurrent endometrial carcinoma: A Gynecologic Oncology Group study. *Gynecol Oncol* 2012; 125S:771.

228. Del Carmen MG, Boruta DM 2nd, Schorge JO. Recurrent endometrial cancer. *Clin Obstet Gynecol* 2011; 54:266.
229. Khouri-Collado F, Einstein MH, Bochner BH, et al. Pelvic exenteration with curative intent for recurrent uterine malignancies. *Gynecol Oncol* 2012; 124:42.
230. Vale CL, Tierney J, Bull SJ, Symonds PR. Chemotherapy for advanced, recurrent or metastatic endometrial carcinoma. *Cochrane Database Syst Rev* 2012; :CD003915.
231. Decruze SB, Green JA. Hormone therapy in advanced and recurrent endometrial cancer: a systematic review. *Int J Gynecol Cancer* 2007; 17:964.
232. Fiorica JV, Brunetto VL, Hanjani P, et al. Phase II trial of alternating courses of megestrol acetate and tamoxifen in advanced endometrial carcinoma: a Gynecologic Oncology Group study. *Gynecol Oncol* 2004; 92:10.
233. Howitt BE, Shukla SA, Sholl LM, et al. Association of Polymerase e-Mutated and Microsatellite-Instable Endometrial Cancers With Neoantigen Load, Number of Tumor-Infiltrating Lymphocytes, and Expression of PD-1 and PD-L1. *JAMA Oncol* 2015; 1:1319.
234. Ott PA, Bang YJ, Berton-Rigaud D, et al. Safety and Antitumor Activity of Pembrolizumab in Advanced Programmed Death Ligand 1-Positive Endometrial Cancer: Results From the KEYNOTE-028 Study. *J Clin Oncol* 2017; 35:2535.
235. Ueda Y, Miyake T, Egawa-Takata T, et al. Second-line chemotherapy for advanced or recurrent endometrial carcinoma previously treated with paclitaxel and carboplatin, with or without epirubicin. *Cancer Chemother Pharmacol* 2011; 67:829.
236. Moore KN, Tian C, McMeekin DS, et al. Does the progression-free interval after primary chemotherapy predict survival after salvage chemotherapy in advanced and recurrent endometrial cancer?: a Gynecologic Oncology Group ancillary data analysis. *Cancer* 2010; 116:5407.
237. Aghajanian CA, Filaci VL, Dizon DS, et al. A randomized phase II study of paclitaxel/carboplatin/bevacizumab, paclitaxel/carboplatin/temsirolimus and ixabepilone/carboplatin/bevacizumab as initial therapy for measurable stage III or IVA, stage IVB or recurrent endometrial cancer, GOG-86P. *J Clin Oncol* 2015; 33S: abstract 5500.