Management of Recurrent Endometrial Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. *CA Cancer J Clin.* 2015;65(1):5-29.	Review/Other-Tx	N/A	To provide the expected numbers of new cancer cases and deaths in 2015 nationally and for each state, as well as a comprehensive overview of cancer incidence, mortality, and survival rates and trends using the most current population-based data. The article also estimates the total number of deaths averted nationally during the past 2 decades and by state in 2011 as a result of the continual decline in cancer death rates and present actual number of deaths reported in 2011 by age for the 10 leading causes of death and for the 5 leading causes of cancer death.	Cancer death rates have been continuously declining for the past 2 decades. Overall, the risk of dying from cancer decreased by 22% between 1991 and 2011. Regionally, progress has been most rapid for residents of the Northeast, among whom death rates have declined by 25% to 30%, and slowest in the South, where rates declined by about 15%. Further reductions in cancer death rates can be accelerated by applying existing cancer control knowledge across all segments of the population, with an emphasis on those in the lowest socioeconomic bracket and other disadvantaged populations.	4
2. 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(9213):1404-1411.	Experimental-Tx	714 patients	A multicenter prospective randomized trial to find whether postoperative pelvic RT improves locoregional control and survival for patients with stage-1 EC.	The median duration of follow-up was 52 months. 5-year actuarial LRR rates were 4% in the RT group and 14% in the control group (P<0.001). Actuarial 5-year OS rates were similar in the 2 groups: 81% (RT) and 85% (controls), P=0.31. Endometrial-cancer-related death rates were 9% in the RT group and 6% in the control group (P=0.37). Treatment-related complications occurred in 25% of RT patients, and in 6% of the controls (P<0.0001). Two-thirds of the complications were grade 1. Grade 3-4 complications were seen in 8 patients, of which 7 were in the RT group (2%). 2-year survival after vaginal recurrence was 79%, in contrast to 21% after pelvic recurrence or distant metastases. Survival after relapse was significantly (P=0.02) better for patients in the control group. Multivariate analysis showed that for LRR, RT and age <60 years were significant favorable prognostic factors.	1

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
3. 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(3):744-751.	Experimental-Tx	392 patients	To determine if adjunctive EBRT lowers the risk of recurrence and death in women with EC FIGO stages IB, IC, and II (occult disease).	392 women met all eligibility requirements (202 no additional therapy, 190 RT). Median follow-up was 69 months. In the entire study population, there were 44 recurrences and 66 deaths (32 disease or treatment-related deaths), and the estimated 2-year cumulative incidence of recurrence was 12% in the no additional therapy arm and 3% in the RT arm (relative hazard: 0.42; *P*=0.007). The treatment difference was particularly evident among the high intermediate risk subgroup (2-year cumulative incidence of recurrence in no additional therapy vs RT: 26% vs 6%; relative hazard = 0.42). Overall, radiation had a substantial impact on pelvic and vaginal recurrences (18 in no additional therapy and 3 in RT). The estimated 4-year survival was 86% in the no additional therapy arm and 92% for the RT arm, not significantly different (relative hazard: 0.86; *P*=0.557).	1
4. Klopp AH, Jhingran A, Ramondetta L, Lu K, Gershenson DM, Eifel PJ. Node-positive adenocarcinoma of the endometrium: outcome and patterns of recurrence with and without external beam irradiation. *Gynecol Oncol.* 2009;115(1):6-11.	Observational-Tx	71 patients	To evaluate treatment outcomes and patterns of recurrence in patients with node-positive FIGO stage IIIC adenocarcinoma of the uterus without serous or clear cell differentiation.	39% (28/71) of patients had involved para-aortic lymph nodes, while 61% (43/71) had only pelvic lymph nodes. 5- and 10-year DSS rates were 63% and 54%, respectively; corresponding OS rates were 60% and 47%. Grade was strongly associated with DSS (76% vs 46% at 5 years for low-grade vs high-grade tumors, *P*=0.004). Cervical or adnexal involvement was associated with decreased DSS, but lymph-vascular space invasion, age, race, body mass index, and number and location of positive nodes were not. 5-year pelvic-relapse-free survival (98% vs 61%, *P*=0.001), DSS (78% vs 39%, *P*=0.01), and OS (73% vs 40%, *P*=0.03) were significantly better for the regional RT group than the systemic therapy group. In patients treated without regional RT, the most common site of relapse was the pelvis. DSS was not significantly correlated with number of nodes removed in the regional RT group but was in patients treated without regional RT (*P*=0.001).	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
5. Randall ME, Filiaci VL, Muss H, et al. Randomized phase III trial of whole-abdominal irradiation versus doxorubicin and cisplatin chemotherapy in advanced endometrial carcinoma: a Gynecologic Oncology Group Study. *J Clin Oncol.* 2006;24(1):36-44.	Experimental-Tx	396 patients	To compare whole-abdominal irradiation and doxorubicin-cisplatin chemotherapy in women with stage III or IV EC having a maximum of 2 cm of postoperative residual disease.	Most patient and tumor characteristics were well balanced. The median patient age was 63 years; 50% had endometrioid tumors. Median follow-up time was 74 months. The stage for progression adjusted for stage was 0.71 favoring doxorubicin-cisplatin (95% CI, 0.55 to 0.91; $P<.01$). At 60 months, 50% of patients receiving doxorubicin-cisplatin were predicted to be alive and disease free when adjusting for stage compared with 38% of patients receiving whole-abdominal irradiation. The stage-adjusted death stage was 0.68 (95% CI, 0.52 to 0.89; $P<.01$) favoring doxorubicin-cisplatin. Moreover, at 60 months and adjusting for stage, 55% of doxorubicin-cisplatin patients were predicted to be alive compared with 42% of whole-abdominal irradiation patients. Greater acute toxicity was seen with doxorubicin-cisplatin. Treatment probably contributed to the deaths of 8 patients (4%) on the doxorubicin-cisplatin arm and 5 patients (2%) on the whole-abdominal irradiation arm.	1

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
6. Creutzberg CL, van Putten WL, Koper PC, et al. Survival after relapse in patients with endometrial cancer: results from a randomized trial. *Gynecol Oncol.* 2003;89(2):201-209.	Experimental-Tx	714 patients	To determine the rates of LC and survival after relapse in patients with stage I EC treated in the multicenter randomized Post-Operative Radiation Therapy in Endometrial Carcinoma (PORTEC) trial.	The analysis was done by intention-to-treat. A total of 714 patients were evaluated. At a median follow-up of 73 months, 8-year actuarial LRR rates were 4% in the RT group and 15% in the control group ($P<0.0001$). The 8-year actuarial OS rates were 71 (RT group) and 77% (control group, $P=0.18$). 8-year rates of distant metastases were 10% and 6% ($P=0.20$). The majority of the locoregional relapses were located in the vagina, mainly in the vaginal vault. Of the 39 patients with isolated vaginal relapse, 35 (87%) were treated with curative intent, usually with external RT and brachytherapy, and surgery in some. A complete remission was obtained in 31 of the 35 patients (89%), and 24 patients (77%) were still in complete remission after further follow-up. 5 patients subsequently developed distant metastases, and 2 had a second vaginal recurrence. The 3-year survival after first relapse was 51% for patients in the control group and 19% in the RT group ($P=0.004$). The 3-year survival after vaginal relapse was 73%, in contrast to 8% and 14% after pelvic and distant relapse ($P<0.001$). At 5 years, the survival after vaginal relapse was 65% in the control group compared to 43% in the RT group.	1

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
7. 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(4):e631-638.	Experimental-Tx	714 patients	To evaluate the very long-term results of the randomized PORTEC-1 trial for patients with Stage I EC, focusing on the role of prognostic factors for treatment selection and the long-term risk of second cancers.	426 patients were alive at the date of analysis. The median follow-up time was 13.3 years. The 15-year actuarial LRR rates were 6% for EBRT vs 15.5% for no additional treatment (P<0.0001). The 15-year OS was 52% vs 60% (P=0.14), and the failure-free survival was 50% vs 54% (P=0.94). For patients with high-intermediate risk criteria, the 15-year OS was 41% vs 48% (P=0.51), and the 15-year EC-related death was 14% vs 13%. Most LRR in the no additional treatment group were vaginal recurrences (11.0% of 15.5%). The 15-year rates of distant metastases were 9% vs 7% (P=0.25). Second primary cancers had been diagnosed over 15 years in 19% of all patients, 22% vs 16% for EBRT vs no additional treatment (P=0.10), with observed vs expected ratios of 1.6 (EBRT) and 1.2 (no additional treatment) compared with a matched population (P=NS). Multivariate analysis confirmed the prognostic significance of Grade 3 for LRR (HR 3.4, P=0.0003) and for EC death (HR 7.3, P<0.0001), of age >60 (HR 3.9, P=0.002 for LRR and 2.7, P=0.01 for EC death) and myometrial invasion >50% (HR 1.9, P=0.03 and HR 1.9, P=0.02).	1
8. Yechieli R, Robbins JR, Schultz D, Munkarah A, Elshaikh MA. Vaginal recurrence more than 17 years after hysterectomy and adjuvant treatment for uterine carcinoma with successful salvage brachytherapy: a case report. *Case Rep Oncol.* 2011;4(1):242-245.	Review/Other-Tx	1	To report herein a successful salvage vaginal brachytherapy in a patient with endometrioid uterine carcinoma which recurred more than 17 years after initial treatment.	The patient remained disease free until her death from unrelated causes 7 years later.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
9. Wylie J, Irwin C, Pintilie M, et al. Results of radical radiotherapy for recurrent endometrial cancer. *Gynecol Oncol.* 2000;77(1):66-72.	Observational-Tx	58 patients	To determine the OS and LC achieved in patients developing a LRR of EC and to define those prognostic factors that predict for improved LC and OS.	The median time to relapse from original diagnosis was 1.3 years (range 0.2–13.4 years). The actuarial 5- and 10-year OS was 53% and 41%, respectively. The respective results for LC were 65% and 62%. All end-points were measured from the time of relapse. The median total dose received was 81.5 Gy. Univariate analysis showed that favorable histological features at original diagnosis (<50% myometrial involvement, grade 1-2, *P*=0.007) and Perez modified staging (*P*=0.02) were significant predictors for OS. The Perez staging (*P*=0.02) and size of recurrence (<2 cm vs ≥2 cm, *P*=0.04) were predictors for LC.	2
10. Robbins JR, Yechieli R, Laser B, Mahan M, Rasool N, Elshaikh MA. Is time to recurrence after hysterectomy predictive of survival in patients with early stage endometrial carcinoma? *Gynecol Oncol.* 2012;127(1):38-42.	Observational-Tx	57 patients	To determine the prognostic significance of time to recurrence on OS and DSS following recurrence in patients with stage I-II uterine endometrioid carcinoma.	Median follow-up times were 54.8 months from hysterectomy and 19.8 months after recurrence. Median time to recurrence was 20.2 months. 28 (47%) patients had a recurrence <18 months after hysterectomy and 29 (53%) had a recurrence ≥18 months. Both groups were evenly matched regarding initial pathological features and adjuvant treatments. The median OS and DSS in patients with time to recurrence <18 months was shorter than those with time to recurrence ≥18 months, but not statistically significant (*P*=0.216). Time to recurrence did not impact outcomes after loco-regional recurrence, but for extrapelvic recurrence, a shorter time to recurrence resulted in worse OS and DSS (*P*=0.03). On multivariate analysis, isolated loco-regional recurrence (HR 0.28, *P*=0.001) and salvage RT (HR 0.47, *P*=0.045) were statistically significant independent predictors of longer OS following recurrence. Time to recurrence as a continuous variable or dichotomized was not predictive of OS or DSS.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
11. Boruta DM, 2nd, Gehrig PA, Fader AN, Olawaiye AB. Management of women with uterine papillary serous cancer: a Society of Gynecologic Oncology (SGO) review. *Gynecol Oncol.* 2009;115(1):142-153.	Review/Other-Tx	N/A	To summarize the available literature concerning uterine papillary serous carcinoma in an effort to provide the clinician with information pertinent to its management.	Uterine papillary serous carcinoma is morphologically and genetically different from endometrioid EC. Women often present with postmenopausal vaginal bleeding, but may also present with abnormal cervical cytology, ascites, or a pelvic mass. In some cases, the diagnosis may be made with endometrial biopsy, while in other cases it is not made until the time of definitive surgery. Metastatic disease is common and best identified via comprehensive surgical staging. Local and distant recurrences occur frequently, with extra-pelvic relapses reported most commonly. Optimal cytoreduction and adjuvant platinum/taxane-based chemotherapy appear to improve survival, while adjuvant RT may contribute to loco-regional disease control.	4
12. Olawaiye AB, Boruta DM, 2nd. Management of women with clear cell endometrial cancer: a Society of Gynecologic Oncology (SGO) review. *Gynecol Oncol.* 2009;113(2):277-283.	Review/Other-Tx	N/A	To explore the differences between clear cell and endometrioid EC. In addition, it uses available evidence to determine the best approach to management.	Clear cell histology is diagnosed in <6% of all ECs and its incidence increases with age. Diagnosis can be made using the same tests that are used in the diagnosis of other types of EC. Clear cell histology is morphologically and genetically different from the more prevalent endometrioid EC histology. It shares many similarities with clear cell neoplasms of the ovary and kidney. Comprehensive surgical staging is critical in order to plan appropriate postoperative management. Adjuvant pelvic and/or whole abdominal RT have not been shown to be clearly beneficial in women diagnosed with clear cell EC. Adjuvant chemotherapy with cisplatin, taxol and doxorubicin either in a doublet or triplet combination has demonstrated efficacy.	4
13. Del Carmen MG, Boruta DM, 2nd, Schorge JO. Recurrent endometrial cancer. *Clin Obstet Gynecol.* 2011;54(2):266-277.	Review/Other-Tx	N/A	To review the treatment options of surgery, radiation, hormonal therapy, cytotoxic chemotherapy, and biological agents for women with recurrent EC.	No results stated in the abstract.	4

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14. van Wijk FH, van der Burg ME, Burger CW, Vergote I, van Doorn HC. Management of recurrent endometrioid endometrial carcinoma: an overview. *Int J Gynecol Cancer.* 2009;19(3):314-320.	Review/Other-Tx	N/A	To present an overview of the literature on the management of recurrent EC, focusing on patients with histopathologic endometrioid type of tumors.	The different treatment modalities are described, and a management recommendation scheme is presented. Indications for surgical treatment depend on resectability, site and size of the tumor, and performance status of the patient. Indications for RT depend on the site of the recurrence and also on the initial therapy received. When considering systemic treatment for patients with recurrent EC, it is important to take into account the general health status and condition of the patient as well as which prior therapy the patient has received. The treatments of choice for patients with hormone-sensitive tumors (positive receptor levels, low-grade tumors, and long disease-free interval) are progestagens as first-line treatment and tamoxifen as second-line treatment. Patients with high-grade tumors, negative hormone receptor levels, and short treatment-free interval are best treated with chemotherapy. Paclitaxel, doxorubicin, and cisplatin are the most active combination therapy for these patients but with significant toxicity. In phase II studies, the combination therapy with paclitaxel and carboplatin seems to be as effective but less toxic and can be administered in outpatient clinic. The literature on the management of patients with recurrent EC is discussed in detail. The different sites of recurrent disease (ie, local, regional, and/or distant) are evaluated separately; management recommendations are proposed, and alternative approaches are given.	4

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15. Ozen A, Falchook AD, Varia MA, Gehrig P, Jones EL. Effect of race and histology on patterns of failure in women with early stage endometrial cancer treated with high dose rate brachytherapy. *Gynecol Oncol.* 2015;138(2):429-433.	Observational-Tx	208 patients	To examine patterns of failure for early stage EC patients treated with postoperative high dose rate brachytherapy.	Median follow-up was 46.4 (range, 6.2–137.3) months. 13 (6.3%) patients developed with locoregional recurrent disease and 15 (7.2%) patients developed distant metastasis. Freedom from recurrence at 5 years was 88.6% for white patients and 60.5% for black patients (P=0.0093). 5-year recurrence free survival for white vs black patients was 82.9% vs 48.9% (P=0.0007). 5-year OS was 86.8% for white patients and 59.5% for black patients (P=0.0023). Black patients with unfavorable histology treated with chemotherapy and vaginal brachytherapy had a 15% locoregional recurrence rate, more than double the rate of local recurrence compared to AA patients with endometrioid histology and white patients with any histology (6% locoregional recurrence rate).	2
16. Kitajima K, Murakami K, Yamasaki E, et al. Performance of FDG-PET/CT in the diagnosis of recurrent endometrial cancer. *Ann Nucl Med.* 2008;22(2):103-109.	Observational-Dx	30 patients; 2 reviewers	To evaluate the accuracy of integrated PET and CT using FDG compared with PET alone, in the diagnosis of suspected EC recurrence.	Patient-based analysis showed: Sensitivity, specificity, and accuracy of PET/CT were 93% (14/15), 93% (14/15), and 93% (28/30), respectively. Sensitivity, specificity, and accuracy of PET were 80% (12/15), 80% (12/15), and 80% (24/30), respectively (P=0.479, 0.479, and 0.134, respectively). Integrated FDG-PET/CT is a useful complementary modality for providing good anatomic and functional localization of sites of recurrence during follow-up of patients with EC.	2

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17. Sharma P, Kumar R, Singh H, et al. Carcinoma endometrium: role of 18-FDG PET/CT for detection of suspected recurrence. *Clin Nucl Med.* 2012;37(7):649-655.	Observational-Dx	101 patients	To evaluate the role of FDG-PET/CT in patients suspected to have recurrence of EC.	The mean age was 56.9+/-8.6 years. FDG-PET/CT was positive for recurrence in 51 (50.5%) patients and negative in 50 (49.5%). Locoregional disease was observed in 24 patients, metastatic disease was observed in 10, and 17 showed both locoregional and metastatic disease. The sensitivity, specificity, positive and negative predictive values, and accuracy of FDG-PET/CT were 88.9%, 93.6%, 94.1%, 88%, and 91%, respectively. FDG-PET/CT showed strong positive correlation with final diagnosis based on reference standard (kappa 0.823; *P*=0.0001). Compared to CI, FDG-PET/CT has much higher specificity (62% vs 96.4%), and accuracy (76.3% vs 92.1%), with comparable sensitivity (85.1% vs 89.5%).	3
18. Kadkhodayan S, Shahriari S, Treglia G, Yousefi Z, Sadeghi R. Accuracy of 18-F-FDG PET imaging in the follow up of endometrial cancer patients: systematic review and meta-analysis of the literature. *Gynecol Oncol.* 2013;128(2):397-404.	Meta-analysis	11 studies; 541 patients	To review the available literature on the accuracy of FDG-PET/CT imaging in the follow up of the EC patients and to present the results in systematic review and meta-analysis format.	11 studies (541 patients in total) were included in the analysis. Pooled diagnostic indices (patient basis) for detection of overall recurrence were as follows: sensitivity 95.8% [92.2–98.1], specificity 92.5% [89.3–94.9], positive likelihood ratio 9.53 [6.52–13.91], negative likelihood ratio 0.075 [0.044–0.128], and diagnostic odds ratio 204 [91.97–453.5]. FDG performance was better in studies conducted by PET/CT as compared to PET. The treatment plan changed in 22%–35% of the studied patients.	M
19. Lalwani N, Dubinsky T, Javitt MC, et al. ACR Appropriateness Criteria(R) pretreatment evaluation and follow-up of endometrial cancer. *Ultrasound Q.* 2014;30(1):21-28.	Review/Other-Tx	N/A	Evidence-based guidelines to assist referring physicians and other providers in making the most appropriate imaging or treatment decision for EC.	N/A	4

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20. Jhingran A, Burke TW, Eifel PJ. Definitive radiotherapy for patients with isolated vaginal recurrence of endometrial carcinoma after hysterectomy. *Int J Radiat Oncol Biol Phys.* 2003;56(5):1366-1372.	Observational-Tx	91 patients	To determine the outcome of patients after radical RT for isolated vaginal recurrence of EC and to determine the clinical and pathologic predictors of outcome.	The 2- and 5-year LC rate and OS rate was 82% and 75% and 69% and 43%, respectively. The median time from initial diagnosis of EC to death from disease was 38 months. On univariate analysis, a dose to the relapse site of ≥80 Gy and EBRT plus brachytherapy vs single-modality therapy were significant predictors of improved LC. On multivariate analysis, only the type of treatment correlated significantly with LC (P=0.03). On univariate analysis, Grade 1 or 2 vs Grade 3 tumor and EBRT plus brachytherapy vs single-modality therapy were significant predictors of improved OS.	2
21. Lin LL, Grigsby PW, Powell MA, Mutch DG. Definitive radiotherapy in the management of isolated vaginal recurrences of endometrial cancer. *Int J Radiat Oncol Biol Phys.* 2005;63(2):500-504.	Observational-Tx	50 patients	To assess prognostic factors and OS after salvage RT for patients who had EC and who experienced an isolated vaginal recurrence.	The 5-year and 10-year DFS and OS were 68% and 55%, and 53% and 40%, respectively. On multivariate analysis, age (P=0.0242), Grade 1 or 2 vs Grade 3 tumor (P=0.002), and size of recurrence (P<0.001) were significant predictors of OS. All patients who had Grade 3 disease were dead by 3.6 years from the time of recurrence. 5 patients experienced a Grade 3 or 4 complication.	3

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22. Nag S, Yacoub S, Copeland LJ, Fowler JM. Interstitial brachytherapy for salvage treatment of vaginal recurrences in previously unirradiated endometrial cancer patients. *Int J Radiat Oncol Biol Phys*. 2002;54(4):1153-1159.	Experimental-Tx	13 patients	To evaluate whether interstitial brachytherapy can effectively salvage vaginal recurrence from EC.	The patients had initially presented with FIGO stage I (n = 11) or III (n = 2) cancer. Vaginal recurrences were diagnosed at a mean interval of 27.5 months after hysterectomy (range 2–83). The patients were followed for a median of 60 months (range 15–105). 10 patients had recurrence at the vaginal apex and 3 had recurrence in the lower two-thirds of the vagina. The median time to recurrence was 22 months. The tumor size ranged from 1.5 to 6 cm (mean 2.2, median 2.5). 11/13 patients received 45–50 Gy pelvic EBRT, followed by a mean interstitial brachytherapy boost of 28.3 Gy (range 18–35). The 2 other patients received brachytherapy only of 40 Gy and 50 Gy, respectively. All tumors were locally controlled. 3 (23%) of 13 patients had a relapse at distant sites (2 in the para-aortic region and 1 in the liver). The overall 8-year actuarial DSS rate was 77%. Major (Grade 3 and 4) long-term morbidity occurred in 2 patients (15%) and included Grade 3 vaginal ulceration in 1 patient, and Grade 4 colovesical fistula requiring surgical intervention in 1 patient. Additional long-term morbidity included Grade 2 proctitis in 1 patient.	2
23. Huh WK, Straughn JM, Jr., Mariani A, et al. Salvage of isolated vaginal recurrences in women with surgical stage I endometrial cancer: a multiinstitutional experience. *Int J Gynecol Cancer*. 2007;17(4):886-889.	Observational-Tx	69 patients	To evaluate the treatment outcomes and risk factors of women with surgical stage I endometrial adenocarcinoma who were initially treated with surgery alone and subsequently developed isolated vaginal recurrences.	Of the 69 patients, 10 (15%) were diagnosed with stage IA disease, 43 (62%) were diagnosed with stage IB disease, and 16 (23%) were diagnosed with stage IC disease. Patients diagnosed with grade 1 disease were 22 (32%), grade 2 disease were 26 (38%), and grade 3 disease were 21 (30%). Among women, 81% with isolated vaginal recurrences were salvaged with RT. The mean time to recurrence was 24 months, and the mean follow-up was 63 months. Among women, 18% died from subsequent recurrent disease. The 5-year OS was 75%.	2

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24. Jereczek-Fossa B, Badzio A, Jassem J. Recurrent endometrial cancer after surgery alone: results of salvage radiotherapy. *Int J Radiat Oncol Biol Phys.* 2000;48(2):405-413.	Observational-Tx	73 patients	To assess the long-term results of salvage RT in previously nonirradiated EC patients who developed local recurrence, and to evaluate the impact of patient- and treatment-related factors on treatment efficacy.	3- and 5-year OS rates were 33% and 25%, respectively. In the univariate analysis, lower stage of recurrent disease (P<0.0005), combined EBRT and brachytherapy (P=0.027), higher total radiation dose (P=0.031), and higher normalized total dose (P=0.006) were significantly correlated with better survival. In the multivariate analysis, only stage of recurrent disease (P<0.005) and high total dose (P=0.047) were independently correlated with better survival. Lower FIGO stage of recurrence (P=0.023) and higher total dose (P=0.005) were also independently correlated with longer time to progression, whereas higher RT dose was the only factor correlated with better LC (P=0.029).	2
25. Lee LJ, Damato AL, Viswanathan AN. Clinical outcomes following 3D image-guided brachytherapy for vaginal recurrence of endometrial cancer. *Gynecol Oncol.* 2013;131(3):586-592.	Observational-Tx	44 patients	To evaluate clinical outcomes for women with recurrent EC treated with 3D image-guided brachytherapy.	Histologic subtypes were endometrioid (33), papillary serous/clear cell (5) and carcinosarcoma (6). The 2-year DFS/OS rates were 75%/89% for endometrioid and 11%/24% for papillary serous/clear cell/carcinosarcoma (both P<0.01). On multivariate analysis, high tumor grade was associated with recurrence (HR 3.2 for grade 2, 9.6 for grade 3, P<0.01). The local failure rate at 2 years was 4% for patients without vs 39% for those with prior RT (P=0.1). Patients who had prior RT received lower cumulative doses at recurrence (66.5 Gy vs 74.4 Gy, P<0.01). The 2-year DFS/OS rates with and without prior RT were 26%/55% and 72%/80% (both P=0.1). 4 patients (9%) experienced grade 3 late toxicity, including 3 of 13 (23%) in the re-irradiation setting and 1 of 31 (3%) with no prior RT.	2

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26. Lee LJ, Damato AL, Viswanathan AN. Clinical outcomes of high-dose-rate interstitial gynecologic brachytherapy using real-time CT guidance. *Brachytherapy.* 2013;12(4):303-310.	Observational-Tx	68 patients	To evaluate clinical outcomes of CT-guided HDR interstitial brachytherapy for primary and recurrent gynecologic cancer.	Primary disease sites were endometrial (34), cervical (17), vaginal (11), ovarian (3), and vulvar (3). Median age was 61.5 years, and tumor size at diagnosis was 3.4 cm. Median D90 and V100 were 73.6 Gy and 87.5%, respectively; median D2cc for bladder, rectum, and sigmoid were 67.1, 64.6, and 53.7 Gy, respectively. With a median follow-up of 17 months, actuarial rates of LC, PFS, and OS at 2 years for all patients were 86%, 60%, and 64%, respectively. There were 9 grade 3 late toxicities (6 gastrointestinal and 3 vulvovaginal).	2
27. Hasbini A, Haie-Meder C, Morice P, et al. Outcome after salvage radiotherapy (brachytherapy +/- external) in patients with a vaginal recurrence from endometrial carcinomas. *Radiother Oncol.* 2002;65(1):23-28.	Observational-Tx	25 patients	To evaluate the efficacy of vaginal brachytherapy combined or not with whole pelvic external RT for the treatment of patients with vaginal recurrences from EC.	LC was achieved in 23 patients (92%). With a follow-up ranging from 4 to 154 months, 13 patients have died (10 due to metastasis, 2 of intercurrent disease and 2 due to local tumor progression) and 10 patients are alive and disease free. The 3-year actuarial survival was 48%. Late radiation-related sequelae were observed in 9 patients (mucous necrosis in 1 patient, moderate sclerosis in 6 patients) in an interval varying between 8 and 45 months. The majority of recurrences occurred in patients who had not previously received irradiation, which emphasizes the role of systematic prophylactic postoperative vaginal brachytherapy. Extra-vaginal extension ($P<0.001$), the tumor size ($P<0.03$) and the stage of initial disease ($P<0.01$) appeared to have a significant impact on the prognosis.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
28. Sorbe B, Soderstrom K. Treatment of vaginal recurrences in endometrial carcinoma by high-dose-rate brachytherapy. *Anticancer Res.* 2013;33(1):241-247.	Observational-Tx	40 patients	To evaluate the efficacy and safety of HDR brachytherapy alone or in combination with external pelvic irradiation in treatment of vaginal recurrences in ECs. Predictive and prognostic factors were also evaluated.	The LC of vaginal recurrences treated with a combination of EBRT and brachytherapy was 92%. The LC rate was lower for EBRT-alone. In 11 patients (28%), a second recurrence occurred (5 vaginal and 6 distant metastases). The overall 5-year survival rate was 50%. Age, FIGO grade and time from diagnosis to recurrence were the only independent and significant prognostic factors. Upfront EBRT was associated with a worse OS rate. Site of recurrence was significant only in univariate analysis. Late gastrointestinal toxicity (grade 3-4) was recorded in 11% of irradiated patients.	2
29. Nag S, Martinez-Monge R, Copeland LJ, Vacarello L, Lewandowski GS. Perineal template interstitial brachytherapy salvage for recurrent endometrial adenocarcinoma metastatic to the vagina. *Gynecol Oncol.* 1997;66(1):16-19.	Observational-Tx	15 patients	To evaluate the use of interstitial brachytherapy salvage of recurrent endometrial adenocarcinoma metastatic to the vagina.	After a median follow-up of 47 months (range 14–81), the actuarial LC rate was 66.6%. The LC rate for patients treated with interstitial irradiation only was 64.3% and the LC rate for patients treated with interstitial irradiation + EBRT was 100%. Distant metastases occurred in 30.7% of the patients. Actuarial OS and DSS 5-year were 42.3% and 67.5%, respectively. Toxicity has been minimal, with 6 patients complaining of vaginal/rectal (RTOG) grade 1-3 complications (5 patients grade 1-2, 1 patient grade 3).	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
30. Randall ME, Evans L, Greven KM, McCunniff AJ, Doline RM. Interstitial reirradiation for recurrent gynecologic malignancies: results and analysis of prognostic factors. *Gynecol Oncol.* 1993;48(1):23-31.	Observational-Tx	13 patients	To evaluate the clinical utility of interstitial reirradiation in patients with recurrent or second primary gynecologic malignancies, all of whom had previous RT, and to assess patient selection and treatment factors which contribute efficacy.	13 patients with recurrent or new primary gynecologic malignancies after previous RT underwent interstitial reirradiation from July 1986 through December 1990. Mean and median ages were 63 and 70 years, respectively. Mean and median implanted volumes were 14.3 and 12 cc, respectively. Overall, 9/13 (69%) had complete responses to interstitial reirradiation and 6 (46%) continue to have no evidence of disease 24–71 months later (median follow-up, 59 months). Of 7 patients with recurrent cervical or new primary vaginal carcinoma, 5 (71%) remain free of disease 27–71 months (median, 58 months) after interstitial reirradiation. Of 6 patients with recurrent ECs, only 1 (16%) continues with no evidence of disease 24 months after interstitial reirradiation. Patients with no evidence of disease after interstitial reirradiation had a median disease-free interval prior to interstitial reirradiation of 100 months compared to 6 months in patients failing interstitial reirradiation.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
31. Mundt AJ, McBride R, Rotmensch J, Waggoner SE, Yamada SD, Connell PP. Significant pelvic recurrence in high-risk pathologic stage I--IV endometrial carcinoma patients after adjuvant chemotherapy alone: implications for adjuvant radiation therapy. *Int J Radiat Oncol Biol Phys.* 2001;50(5):1145-1153.	Observational-Tx	43 patients	To evaluate the risk of pelvic recurrence in high-risk pathologic stage I-IV EC patients after adjuvant chemotherapy alone.	29 women (67.4%) relapsed. 17 (39.5%) recurred in the pelvis and 23 (55.5%) in extrapelvic sites. The 3-year actuarial pelvic recurrence rate was 46.5%. The most significant factors correlated with pelvic recurrence were cervical involvement (P=0.01) and adnexal (P=0.05) involvement. Of the 17 women who developed a pelvic recurrence, 8 relapsed in the vagina, 3 in the nonvaginal pelvis, and 6 in both. The 3-year vaginal and nonvaginal pelvic recurrence rates were 37.8% and 26%, respectively. The most significant factor correlated with vaginal pelvic recurrence was cervical involvement (P=0.0007). Deep myometrial invasion (P=0.02) and lymph nodal involvement (P=0.03) were both correlated with nonvaginal pelvic recurrence. 9/29 relapsed patients (31%) developed pelvic recurrence as their only (6) or first site (3) of recurrence. Factors associated with a higher rate of pelvic recurrence (as the first or only site) were cervical involvement and stage I-II disease.	2
32. Poulsen MG, Roberts SJ. The salvage of recurrent endometrial carcinoma in the vagina and pelvis. *Int J Radiat Oncol Biol Phys.* 1988;15(4):809-813.	Observational-Tx	93 patients	To analyze only those patients with locally recurrent disease in the pelvis, vaginal vault or lower one-third vagina to see what proportion was salvageable with subsequent treatment.	There were 12 lower one-third vaginal recurrences, 24 vault recurrences and 57 pelvic recurrences from the 1,005 patients treated between 1960 and 1976. Median time to recurrence was 30 months. 26 patients had distant metastases also present at the time of recurrence in the sites mentioned above. 33% of lower one-third vaginal recurrences, 12.5% of vault recurrences, and 5.3% of pelvic recurrences were salvaged with further treatment. The 10-year actuarial survival rates of isolated lower one-third vaginal, vaginal vault, and pelvic recurrences were 50%, 45%, and 24%, respectively.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
33. Blecharz P, Brandys P, Urbanski K, Reinfuss M, Patla A. Vaginal and pelvic recurrences in stage I and II endometrial carcinoma--survival and prognostic factors. *Eur J Gynaecol Oncol.* 2011;32(4):403-407.	Observational-Tx	106 patients	To analyze prognostic factors and treatment outcomes in 106 patients with stage I and II EC treated between 1980 and 2005 in the Center of Oncology, Maria Sklodowska-Curie Memorial Institute, Krakow, Poland, who developed vaginal or pelvic recurrences.	The 5-year OS rate in the observed group was 17%. 5-year survival was 23.3% (14/60) for patients with KPS 60–70 vs 8.7% (4/46) with KPS 40-50, 25% (12/48) patients with stage I EC vs 10.3% (6/58) with stage II EC, and 34% (16/47) patients with vaginal recurrence vs 3.4% (2/59) with pelvic recurrences.	3
34. Kuten A, Grigsby PW, Perez CA, Fineberg B, Garcia DM, Simpson JR. Results of radiotherapy in recurrent endometrial carcinoma: a retrospective analysis of 51 patients. *Int J Radiat Oncol Biol Phys.* 1989;17(1):29-34.	Observational-Tx	51 patients	To analyze the Washington University experience in the treatment of LRRs of EC.	The 5- and 10-year overall actuarial survivals for all patients were 18% and 12.5%, respectively. The 5- and 10-year PFSs of patients with isolated vaginal recurrences were 40% and 29%, respectively; the 5-year PFS of patients with vaginal recurrence with pelvic extension was 20%. There were no survivors beyond 1.5 years among patients with pelvic recurrence (P=0.02). All patients with simultaneous locoregional and distant failure were dead by 3.5 years. Stage at original diagnosis, time to relapse from primary treatment, histologic pattern, and grade of malignancy were prognosticators of survival. 5 patients (10%) developed a total of 10 radiation-related sequelae.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
35. Homesley HD, Filiaci V, Gibbons SK, et al. 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. *Gynecol Oncol.* 2009;112(3):543-552.	Experimental-Tx	552 patients	Treatment was randomized to compare recurrence-free survival and toxicity between 2 chemotherapy regimens for the treatment of women with advanced stage EC.	Of 659 patients enrolled following surgery, 552 eligible patients were randomized to chemotherapy after irradiation. Accrual closed to stage IV patients in June, 2003. Approximately 80% completed 6 cycles of chemotherapy. 3 deaths resulted from bowel complications and 1 death was due to renal failure. Hematologic adverse events, sensory neuropathy and myalgia, were more frequent and severe in the paclitaxel arm ($P<0.01$) which was confirmed by Quality of Life assessments. Percentage of patients alive and recurrence-free at 36 months was 62% for cisplatin and doxorubicin vs 64% for cisplatin and doxorubicin with paclitaxel. The hazard of recurrence or death relative to the cisplatin and doxorubicin arm stratified by stage is 0.90 (95% CI, 0.69 to 1.17, $P=0.21$, one-tail). However, in subgroup analysis, cisplatin and doxorubicin with paclitaxel was associated with a 50% reduction in the risk of recurrence or death among patients with gross residual disease (95% CI, 0.26 to 0.92). Stage, residual disease, histology/grade, positive para-aortic node and cytology, pelvic metastases and age were significantly associated with recurrence-free survival.	1

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
36. 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;125(3):771.	Experimental-Tx	1,381 patients	To determine if the combination of carboplatin and paclitaxel chemotherapy is clinically inferior to the combination of doxorubicin, cisplatin, and paclitaxel chemotherapy with regard to survival, and to assess differences in toxicity profile, specifically neurotoxicity and infection between doxorubicin, cisplatin, and paclitaxel and carboplatin and paclitaxel.	Treatment was hematologically well tolerated, with only 7% of patients receiving doxorubicin, cisplatin, and paclitaxel and 6% on carboplatin and paclitaxel experiencing neutropenic fever. Neurologic toxicity for those receiving doxorubicin, cisplatin, and paclitaxel was 26% grade N1 sensory neuropathy compared with 19% in those receiving carboplatin and paclitaxel. Common grade N2 toxicities more often reported with doxorubicin, cisplatin, and paclitaxel included: Thrombocytopenia (23% vs 12%), other hematologic (30% vs 22%), vomiting (7% vs 4%), diarrhea (6% vs 2%), and metabolic (14% vs 8%); whereas neutropenia (52% vs 79%) was more often reported with carboplatin and paclitaxel. Study treatment was discontinued due to toxicity in 18% on doxorubicin, cisplatin, and paclitaxel and 12% on carboplatin and paclitaxel. The 7 planned cycles were completed in 62% of those on doxorubicin, cisplatin, and paclitaxel and 69% on carboplatin and paclitaxel (*P*=.01). The interim analysis adjusted 90% upper confidence limit for the death HR of carboplatin and paclitaxel relative to doxorubicin, cisplatin, and paclitaxel was 1.16 and excludes the inferiority region bounded at 1.2. PFS (median carboplatin and paclitaxel vs doxorubicin, cisplatin, and paclitaxel, 14 vs 14 months; HR=1.03) and OS (median carboplatin and paclitaxel vs doxorubicin, cisplatin, and paclitaxel, 32 vs 38 months; HR=1.01) results for carboplatin and paclitaxel were not inferior to doxorubicin, cisplatin, and paclitaxel. A homogeneity test suggests consistent treatment effects across strata defined by measurable/recurrent vs primary disease and pelvic irradiation history.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
37. Shirvani SM, Klopp AH, Likhacheva A, et al. Intensity modulated radiation therapy for definitive treatment of paraortic relapse in patients with endometrial cancer. *Pract Radiat Oncol.* 2013;3(1):e21-28.	Observational-Tx	27 patients	To review the outcomes of patients treated with intensity modulated RT for unresected or incompletely resected para-aortic recurrences of primary uterine cancer.	Of the 27 patients, 19 (70%) had LC of para-aortic disease after a median follow-up time of 25 months (range, 4–83 months). 2-year actuarial OS and PFS rates were 63% and 53%, respectively. 5 patients (19%) experienced severe late gastrointestinal toxic effects (grade 3-5).	3
38. Dowdy SC, Mariani A, Cliby WA, et al. Radical pelvic resection and intraoperative radiation therapy for recurrent endometrial cancer: technique and analysis of outcomes. *Gynecol Oncol.* 2006;101(2):280-286.	Observational-Tx	25 patients	To describe the technique and assess outcomes and morbidity following radical resection combined with IOERT in patients with recurrent EC.	Treatment prior to referral included radiation in 56% and either a secondary surgery or chemotherapy in 48%. EBRT was administered in addition to IOERT in 84%. Radical procedures performed at the time of IOERT included resection of the pelvic sidewall en bloc with the obturator nerve, external iliac vein, psoas, iliacus, or obturator internus muscles, ureter, or boney ileum. 7 patients required exenteration in combination with resection of the pelvic sidewall. The median IOERT dose was 1500 cGy (range 1000–2500 cGy). Overall 5-year survival was 47% vs 71% for those with a gross total resection but close margins. 2 patients with recurrences limited to the para-aortic area are alive without evidence of disease at 54 and 71 months. Proportional hazards modeling showed concurrent EBRT, tumor size after resection, grade, and age to be associated with improved survival. The most common complications were peripheral neuropathy, functional ureteral obstruction, and fistula formation.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
39. Choi CW, Cho CK, Yoo SY, et al. Image-guided stereotactic body radiation therapy in patients with isolated para-aortic lymph node metastases from uterine cervical and corpus cancer. *Int J Radiat Oncol Biol Phys.* 2009;74(1):147-153.	Observational-Tx	30 patients	To evaluate the role of SBRT as a local treatment for isolated para-aortic lymph node metastases originating from uterine cervical and corpus cancer.	The 4-year OS rate was 50.1%, and the median survival time was not reached. The OS rate among symptomatic patients was significantly lower than that among asymptomatic patients (P=0.002). The 4-year actuarial LC rate was 67.4%. Patients with a planning target volume of ≤17 ml had significantly higher LC rates (P=0.009). The 4-year disease progression-free survival rate was 45.0%, and the median time to disease progression was 32 months. Small planning target volume was a favorable prognostic factor (P=0.043). Grade 3 or 4 complications requiring hospitalization were reported in 1 patient at 20 months after SBRT.	2
40. 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(9717):816-823.	Experimental-Tx	427 patients	To compare outcomes and adverse effects after vaginal brachytherapy and EBRT, and to establish optimum adjuvant treatment for patients with EC of high-intermediate risk.	At median follow-up of 45 months (range 18–78), 3 vaginal recurrences had been diagnosed after vaginal brachytherapy and 4 after EBRT. Estimated 5-year rates of vaginal recurrence were 1.8% (95% CI, 0.6–5.9) for vaginal brachytherapy and 1.6% (0.5–4.9) for EBRT (stage [HR] 0.78, 95% CI, 0.17–3.49; P=0.74). 5-year rates of locoregional relapse (vaginal or pelvic recurrence, or both) were 5.1% (2.8–9.6) for vaginal brachytherapy and 2.1% (0.8–5.8) for EBRT (HR 2.08, 0.71–6.09; P=0.17). 1.5% (0.5–4.5) vs 0.5% (0.1–3.4) of patients presented with isolated pelvic recurrence (HR 3.10, 0.32–29.9; P=0.30), and rates of distant metastases were similar (8.3% [5.1–13.4] vs 5.7% [3.3–9.9]; HR 1.32, 0.63–2.74; P=0.46). We recorded no differences in OS (84.8% [95% CI, 79.3–90.3] vs 79.6% [71.2–88.0]; HR 1.17, 0.69–1.98; P=0.57) or DFS (82.7% [76.9–88.6] vs 78.1% [69.7–86.5]; HR 1.09, 0.66-1.78; P=0.74). Rates of acute grade 1-2 gastrointestinal toxicity were significantly lower in the vaginal brachytherapy group than in the EBRT group at completion of RT (12.6% [27/215] vs 53.8% [112/208]).	1

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
41. Bristow RE, Santillan A, Zahurak ML, Gardner GJ, Giuntoli RL, 2nd, Armstrong DK. Salvage cytoreductive surgery for recurrent endometrial cancer. *Gynecol Oncol.* 2006;103(1):281-287.	Observational-Tx	61 patients	To determine the survival impact of salvage cytoreductive surgery, and other prognostic variables, among patients with recurrent EC.	61 patients were identified with EC recurrence a median of 18.5 months after initial diagnosis. Median age at recurrence was 63 years, and the median post-recurrence follow-up time was 22.0 months. 35 patients underwent salvage cytoreductive surgery and had a median survival time of 28.0 months, compared to 13.0 months for patients treated nonsurgically (P<0.0001). Complete cytoreduction (no gross residual) was achieved in 23/35 surgical patients (65.7%). The median EBL was 350 cc and 28.6% of patients received blood products. There were no peri-operative deaths; however, 31.4% of patients experienced minor morbidity. Patients undergoing complete salvage cytoreduction had a median post-recurrence survival time of 39.0 months, compared to 13.5 months for those patients with gross residual disease (P=0.0005). On multivariate analysis, salvage surgery and residual disease status were significant and independent predictors of post-recurrence survival.	2
42. Campagnutta E, Giorda G, De Piero G, et al. Surgical treatment of recurrent endometrial carcinoma. *Cancer.* 2004;100(1):89-96.	Observational-Tx	75 patients	To present our standard surgical approach to abdominal and pelvic recurrences and demonstrate that, within well-defined limits, surgery can be feasible and efficient in the treatment of patients with recurrent EC.	56 patients (74.7%) underwent optimal debulking. Major surgical complications were observed in 23 patients (30.7%). Only 1 postoperative death was observed, although the mortality rate for surgical complications after the postoperative period was 8%. Patients who underwent optimal debulking had a significantly better cumulative survival rate compared with patients who had residual disease (36% vs 0% at 60 months; P<0.05). Residual disease, chemotherapy after rescue surgery, and central pelvis-vagina as the only site of recurrence were associated significantly with survival.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
43. Awtrey CS, Cadungog MG, Leitao MM, et al. Surgical resection of recurrent endometrial carcinoma. *Gynecol Oncol.* 2006;102(3):480-488.	Observational-Tx	27 patients	To determine the outcomes of nonexenterative secondary surgical resections in patients with recurrent EC.	15 patients (56%) had disease limited to the retroperitoneum, 10 patients (37%) had intraperitoneal disease, and 2 patients (7%) had both intra- and retroperitoneal disease. Cytoreduction to ≤2 cm of residual disease was achieved in 18 patients (67%), while 9 patients (33%) had cytoreduction to residual disease >2 cm. There were no major perioperative complications or mortalities. The median hospital stay was 7 days (range, 1–18 days). Additional therapies included IOERT therapy in 9 patients (33%), RT in 12 patients (44%), and chemotherapy in 10 patients (37%). The median follow-up for the entire cohort was 24 months (range, 5–84 months). The median PFS was 14 months (95% CI, 6–23), and the median DSS was 35 months (95% CI, 24-not reached). Size of residual disease was the only significant predictor for both PFS and DSS. Patients with residual disease ≤2 cm had a median DSS of 43 months (95% CI, 35-not reached) compared with 10 months (95% CI, 7–29) for those with >2 cm residual (P=0.01).	2
44. Scarabelli C, Campagnutta E, Giorda G, et al. Maximal cytoreductive surgery as a reasonable therapeutic alternative for recurrent endometrial carcinoma. *Gynecol Oncol.* 1998;70(1):90-93.	Observational-Tx	20	To determine if maximal cytoreductive surgery could carry any benefit in pelvic and abdominal recurrent EC.	Complete macroscopic resection of tumor was feasible in 13 women (65%). R0 group women had a significant both PFS (median reached at 9.1 months) and OS (median reached at 11.8 months) compared to R1 group women. There were 2 (10%) perioperative deaths. 8 women died of cancer, 5 in the R1 group and 3 in the R0 group. There were 4 intercurrent deaths in women still free from the disease. LC of neoplasia was achieved in 84.6% of R0 women and their survival was affected mostly by distant recurrences or intercurrent deaths. Residual tumor at the end of surgery was the only significant variable to affect both PFS and OS.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
45. Chi DS, Welshinger M, Venkatraman ES, Barakat RR. The role of surgical cytoreduction in Stage IV endometrial carcinoma. *Gynecol Oncol.* 1997;67(1):56-60.	Observational-Tx	55 patients	To evaluate the impact of surgical cytoreduction in patients with stage IV EC.	55 patients who underwent surgery as part of their primary treatment for stage IV EC were identified. They were divided into 3 groups: Group I consisted of 24 patients (44%) who underwent optimal surgical cytoreduction (diameter of largest residual tumor nodule ≤2 cm); Group II contained 21 patients (38%) who underwent suboptimal surgical cytoreduction (>2 cm residual disease); Group III consisted of 10 patients (18%) who had unresectable carcinomatosis and had no cytoreduction at all. There were no statistically significant differences between the 3 groups with respect to median age at diagnosis, tumor grade, histologic subtype, or the presence of extra-abdominal metastases. The median survival rates for the 3 groups were I, 31 months; II, 12 months; and III, 3 months ($P<0.01$). Within Group I, there was no statistically significant difference in survival between the 8 patients who were found at laparotomy to have metastatic disease ≤2 cm and the 16 patients who initially had metastatic disease >2 cm and were subsequently cytoreduced to optimal status. On multivariate analysis only the extent of surgical cytoreduction had prognostic significance on survival.	2
46. Nezhat F, Prasad Hayes M, Peiretti M, Rahaman J. Laparoscopic radical parametrectomy and partial vaginectomy for recurrent endometrial cancer. *Gynecol Oncol.* 2007;104(2):494-496.	Review/Other-Tx	1 patient	To describe a case of a second recurrence of EC isolated to the vaginal apex that was treated with a laparoscopic radical parametrectomy and partial vaginectomy.	Laparoscopic radical parametrectomy and partial vaginectomy may be an option for patients with small central recurrences of EC.	4
47. Cho JE, Liu C, Gossner G, Nezhat FR. Laparoscopy and gynecologic oncology. *Clin Obstet Gynecol.* 2009;52(3):313-326.	Review/Other-Tx	N/A	To present the application of laparoscopy in cervical, endometrial, and ovarian cancer.	No results stated in abstract.	4
48. Lee YS, Lee TH, Koo TB, Cho YL, Park IS. Laparoscopic-assisted radical parametrectomy including pelvic and/or paraaortic lymphadenectomy in women after prior hysterectomy-three cases. *Gynecol Oncol.* 2003;91(3):619-622.	Review/Other-Tx	3 patients	To report on the cases of 2 patients with invasive cervical cancer found after a simple hysterectomy and 1 patient with recurrent EC in the vaginal stump.	A laparoscopic radical parametrectomy including a pelvic and/or para-aortic lymphadenectomy is a viable technique for women with invasive cervical cancer or recurrent endometrial vaginal cancer after a prior hysterectomy.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
49. Barber HR, Brunschwig A. Treatment and results of recurrent cancer of corpus uteri in patients receiving anterior and total pelvic exenteration 1947-1963. *Cancer.* 1968;22(5):949-955.	Review/Other-Tx	36 patients	To question whether further therapy in the form of exenteration should be offered to patients with recurrent or persistent disease.	Of 36 patients receiving pelvic exenteration 5 or more years ago, 7 received their initial treatment <1 year prior to treatment for recurrence and none survived more than 15 months. Of the 29 patients who were free of disease for at least 1 year after initial treatment and before receiving exenteration for recurrence, 5 lived 5 or more years. It is concluded that there is a limited place for pelvic exenteration in the treatment of recurrent EC.	4
50. Morris M, Alvarez RD, Kinney WK, Wilson TO. Treatment of recurrent adenocarcinoma of the endometrium with pelvic exenteration. *Gynecol Oncol.* 1996;60(2):288-291.	Observational-Tx	20 patients	To reevaluate the role of pelvic exenteration in selected women with recurrent adenocarcinoma of the endometrium.	The median patient age was 65 years (range 44–79 years). At most recent follow-up, 8 patients were alive and disease free, 2 were alive with disease, 6 had died of disease, and 4 had died of other causes. The median follow-up of living patients is 89 months. 12/20 patients experienced major complications, the most common of which was neovaginal flap necrosis. Of the 20 patients, 1 patient (5%) died in 1963 of surgical complications. The Kaplan-Meier estimate of 5-year DFS is 45%.	3
51. Ferenschild FT, Vermaas M, Verhoef C, et al. Total pelvic exenteration for primary and recurrent malignancies. *World J Surg.* 2009;33(7):1502-1508.	Observational-Tx	69 patients	To study preoperative morbidity and mortality, local recurrence, DFS, and OS rates, and to analyze prognostic factors for LC or survival.	The median follow-up was 43 (range, 1–196) months. Median duration of surgery was 448 (range, 300–670) minutes, median blood loss was 6,300 (range, 750–21,000) mL, and hospitalization was 17 (range, 4–65) days. Overall major and minor complication rates were 34% and 57%, respectively. The in-hospital mortality rate was 1%. A complete resection was possible in 75% of all patients, a microscopically incomplete resection (R1) in 16%, and a macroscopically incomplete resection (R2) in 9%. 5-year LC for primary locally advanced rectal cancer, recurrent rectal cancer, and cervical cancer was 89%, 38%, and 64%, respectively. OS after 5 years for primary locally advanced rectal cancer, recurrent rectal cancer, and cervical cancer was 66%, 8%, and 45%, respectively.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
52. Barakat RR, Goldman NA, Patel DA, Venkatraman ES, Curtin JP. Pelvic exenteration for recurrent endometrial cancer. *Gynecol Oncol.* 1999;75(1):99-102.	Observational-Tx	44 patients	To review our experience with pelvic exenteration performed in patients with recurrent endometrial adenocarcinoma from 1947 through 1994.	A total of 44 patients were identified, with a mean age of 60 years (range 35–69 years). Primary therapy usually consisted of total abdominal hysterectomy with bilateral salpingo-oophorectomy; with most receiving either pre- or postoperative RT. Prior to exenteration, 10/44 (23%) patients had never received any form of RT. The median interval between initial surgery and exenteration was 28 months (range 2–189 months). The type of exenteration performed was total in 23 patients (52%), anterior in 20 patients (46%), and posterior in 1 patient. Major postoperative complications occurred in 35 patients (80%) and included urinary/intestinal tract fistulas, pelvic abscess, septicemia, pulmonary embolism, and cerebrovascular accident. Median survival for the entire group of patients was 10.2 months. 9 patients (20%) achieved long-term survival (>5 years). Pelvic exenteration for recurrent EC is associated with a high operative morbidity and poor OS.	2
53. de Wilt JH, van Leeuwen DH, Logmans A, et al. Pelvic exenteration for primary and recurrent gynaecological malignancies. *Eur J Obstet Gynecol Reprod Biol.* 2007;134(2):243-248.	Observational-Tx	42 patients	To analyze the outcome of pelvic exenteration for gynecological malignancies in a tertiary referral center, including postoperative in-hospital morbidity, long-term morbidity, disease free and OS rates.	A pelvic exenteration was performed in 14 patients for primary and 28 patients for recurrent gynecological cancers. In-hospital complications occurred in 19 patients (45%) of whom 7 patients needed a reoperation (17%). Late complications occurred in 31 patients (75%); 21 reinterventions were performed (50%). 5-year DFS and OS was, respectively, 48% and 52%. Age, type of surgery, histology, localization of the tumor, lateral wall involvement, completeness of resection and primary vs recurrent cancer were not identified as prognostic factors for recurrence or survival.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
54. Sharma S, Odunsi K, Driscoll D, Lele S. Pelvic exenterations for gynecological malignancies: twenty-year experience at Roswell Park Cancer Institute. *Int J Gynecol Cancer.* 2005;15(3):475-482.	Observational-Tx	48 patients	To review the experience with pelvic exenterations for gynecological malignancies at our cancer institute.	Charts of 48 women who underwent a pelvic exenteration between January 1980 and December 1999 were reviewed, and several outcomes were analyzed. Majority of patients had received prior RT. The median survival was 35 months, and the DFS was 32 months. Mortality from the procedure was 4.2%. Early and late postoperative complication rates were 27% and 75%, respectively. Recurrence rate was 60%. 8 patients received IOERT. Median survival in this group was 11.3 vs 35 months (P=0.003). Univariate analysis failed to show an association between type of pelvic exenteration, type of fecal and urinary diversion, outcome, need for reoperation, and recurrence.	2
55. Roos EJ, Van Eijkeren MA, Boon TA, Heintz AP. Pelvic exenteration as treatment of recurrent or advanced gynecologic and urologic cancer. *Int J Gynecol Cancer.* 2005;15(4):624-629.	Observational-Tx	62	To determine morbidity, DFS and OS after pelvic exenteration for gynecological and urologic cancer in the University Medical Center Utrecht from 1989 to 1999.	The operative mortality was 1.6%. 75% of the patients had postoperative complications of which ileus and urinary tract infection were the most common. Late complications occurred in 83% of the patients. Recurrent disease was observed in 38% of the women, whereas 50% had died on January 1, 2000. 5-years DFS and OS were 42% (CI 5 +/- 14%) and 46% (CI +/- 14%), respectively.	2
56. Burke TW, Stringer CA, Morris M, et al. Prospective treatment of advanced or recurrent endometrial carcinoma with cisplatin, doxorubicin, and cyclophosphamide. *Gynecol Oncol.* 1991;40(3):264-267.	Experimental-Tx	102 patients	To present updated and final results concerning the effectiveness of cisplatin, doxorubicin, and cyclophosphamide as a salvage combination.	Of the 87 patients with measurable disease, 12 had a complete clinical response, while 27 had a partial clinical response, for an overall objective response rate of 45%. No differences in response rates between primary and recurrent disease patients were noted. Median time to response was 2.5 months with median response duration of 4.8 months. Nonresponders included 33 patients with stable disease and 15 with progression. Median PFS for all patients was 6 months. Dose escalation was possible in 25% of patients; however, 52% of patients required dose reductions during treatment. Clinically significant toxicities included neutropenia (65%), anemia (47%), emesis (21%), nephrotoxicity (17%), and neurotoxicity (4%).	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
57. Gallion HH, Brunetto VL, Cibull M, et al. Randomized phase III trial of standard timed doxorubicin plus cisplatin versus circadian timed doxorubicin plus cisplatin in stage III and IV or recurrent endometrial carcinoma: a Gynecologic Oncology Group Study. *J Clin Oncol.* 2003;21(20):3808-3813.	Experimental-Tx	169 patients standard timed arm; 173 patients circadian timed arm	To determine if circadian timed chemotherapy results in improved response, PFS, OS, and lower toxicity, when compared with standard timed chemotherapy.	The objective response rate (complete responses plus partial responses) was 46% in the standard timed group compared with 49% in the circadian timed group (P =.26, one tail). Median PFS and OS were 6.5 and 11.2 months, respectively, in the standard timed group; and 5.9 and 13.2 months, respectively, in the circadian timed group (PFS: *P*=.31; OS: *P*=.21, 1 tail). Median total doses were 209 mg/m2 doxorubicin and 349 mg/m2 cisplatin in the standard timed group, vs 246 mg/m2 doxorubicin and 354 mg/m2 cisplatin in the circadian timed group. Grade 3 or 4 leukopenia occurred in 73% of patients in the standard timed arm and in 63% of patients in the circadian timed arm. There were 8 treatment-related deaths.	1
58. Muggia FM, Blessing JA, Sorosky J, Reid GC. Phase II trial of the pegylated liposomal doxorubicin in previously treated metastatic endometrial cancer: a Gynecologic Oncology Group study. *J Clin Oncol.* 2002;20(9):2360-2364.	Experimental-Tx	42 patients	To determine whether pegylated liposomal doxorubicin has antitumor activity in pretreated patients with persistent or recurrent EC and to define the nature and degree of toxicity of pegylated liposomal doxorubicin.	Of 46 patients entered, 42 were assessable for response, as 3 were declared ineligible on central pathology review and 1 was not assessable for response. 40 had received prior chemotherapy, 11 hormonal therapy, and 29 RT. Doxorubicin had been given to 32 patients, carboplatin with paclitaxel to 6, carboplatin to 1, and fluorouracil to 1. 4 patients had partial responses lasting 1.1, 2.1, 3.3, and 5.4 months; the overall response rate was 9.5% (95% CI, 2.7% to 22.6%). 3 of these responses (in liver and in lymph node) occurred in patients who had progressed after doxorubicin with either paclitaxel or cisplatin. The median number of courses was 2.5 (range, 1 to 14). Toxicity was generally mild: only 25 patients experienced leukopenia, with a median white-blood cell count of 2,900 (range, 800 to 3,900) at nadir. The only grade 4 toxicities were 1 episode each of esophagitis, hematuria, and vomiting. The median OS was 8.2 months.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
59. Pierga JY, Dieras V, Beuzeboc P, et al. Phase II trial of doxorubicin, 5-fluorouracil, etoposide, and cisplatin in advanced or recurrent endometrial carcinoma. *Gynecol Oncol.* 1997;66(2):246-249.	Experimental-Tx	20 patients	To describe the preliminary results of a combination of adriamycin (doxorubicin), 5-fluorouracil, etoposide, and cisplatin (AFEP) in a series of 20 patients as a first-line chemotherapy in advanced or recurrent EC.	From August 1992 to January 1996, 20 consecutive patients were treated with a monthly combination chemotherapy consisting of doxorubicin 30 mg/m2 i.v. Day 1, 5-fluorouracil 600 mg/m2 i.v. Days 1 to 3, etoposide 80 mg/m2 i.v. Days 1 to 3, and cisplatin 35 mg/m2 i.v. Days 1 to 3. All patients were evaluable for response and toxicity. Median age was 62 years (range 45–72). 2 to 8 cycles were delivered (median 5). 2 of 20 patients had complete response and 7 of 20 had partial response. The objective response rate was 45% (CI 95%: 23%–68%). The median survival duration was 17 months. The median PFS was 8 months. Major toxic effect was myelosuppression: 75% of grade 3 and 4 leukopenia and 20% of grade 3 and 4 thrombocytopenia. 7 patients (35%) developed infection and 4 (20%) were hospitalized once or more for toxicity.	2
60. Scudder SA, Liu PY, Wilczynski SP, et al. Paclitaxel and carboplatin with amifostine in advanced, recurrent, or refractory endometrial adenocarcinoma: a phase II study of the Southwest Oncology Group. *Gynecol Oncol.* 2005;96(3):610-615.	Experimental-Tx	47 patients	To evaluate the response rate and PFS and OS of patients with advanced EC treated with paclitaxel, carboplatin and amifostine. To evaluate the toxicity of amifostine when used in combination with carboplatin and paclitaxel.	There were 4 complete responses (8%) (2 confirmed, 2 unconfirmed) and 15 partial responses (32%) (9 confirmed, 6 unconfirmed) for a total response rate of 40% (95% CI, 26% to 56%). The median PFS was 7 months (95% CI, 6–9 months) and a 6-month PFS rate of 64% (95% CI, 50% to 78%). The median OS was 14 months (95% CI, 12 to 17 months). Toxicity was tolerable. While 79% of patients developed Grade 3/4 neutropenia (30% Grade 3, 49% Grade 4), there were no episodes of Grade 4 febrile neutropenia and one episode of infection with grades 3-4 neutropenia.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
61. Thigpen JT, Blessing JA, DiSaia PJ, Yordan E, Carson LF, Evers C. A randomized comparison of doxorubicin alone versus doxorubicin plus cyclophosphamide in the management of advanced or recurrent endometrial carcinoma: A Gynecologic Oncology Group study. *J Clin Oncol.* 1994;12(7):1408-1414.	Experimental-Tx	276 patients	To compare doxorubicin with or without cyclophosphamide in patients with advanced or recurrent EC no longer amenable to therapy with surgery, RT, or progestins.	Among 132 patients treated with doxorubicin alone, there were 7 complete responses (5%), 22 partial responses (17%), 73 with stable disease (55%), and 30 with increasing disease within 2 months of study entry (23%). For the 144 patients who received the combination, there were 18 complete responses (13%), 25 partial responses (17%), 75 with stable disease (52%), and 26 with increasing disease (18%). The median progression-free interval for those patients who received doxorubicin alone was 3.2 months, while it was 3.9 months for those who received the combination. The median survival duration for doxorubicin patients was 6.7 months, while it was 7.3 months for the combination patients. None of the unadjusted estimates of treatment differences are statistically significant. Prognostic features that had an impact on outcome included one factor associated with an increased likelihood of response (presence of measurable lung metastases) and 4 features associated with a poorer survival (poor performance status of 2 or 3, high pathologic grade, and presence of liver metastases or other intra-abdominal disease). If these features are taken into account in multivariate analyses, there is no statistically significant evidence for differences in response rates (relative odds of response, 1.58; P=.06, one-tailed test), and survival duration is slightly longer in the combination regimen (17% reduction in death rate; P=.048).	1

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
62. Guckenberger M, Bachmann J, Wulf J, et al. Stereotactic body radiotherapy for local boost irradiation in unfavourable locally recurrent gynaecological cancer. *Radiother Oncol.* 2010;94(1):53-59.	Observational-Tx	19 patients	To evaluate outcome of RT for locally recurrent cervical and EC.	After median follow-up of 22 months, 3-year OS was 34% with systemic progression the leading cause of death (7/10). Median time to systemic progression was 16 months. 3 local recurrences resulted in a LC rate of 81% at 3 years. No correlation between survival, systemic or LC and any patient or treatment characteristic was observed. The rate of late toxicity >grade II was 25% at 3 years: 2 patients developed a grade IV intestino-vaginal fistula and 1 patient suffered from a grade IV small bowel ileus.	2
63. Deodato F, Macchia G, Grimaldi L, et al. Stereotactic radiotherapy in recurrent gynecological cancer: a case series. *Oncol Rep.* 2009;22(2):415-419.	Experimental-Tx	11 patients (12 lesions)	To analyze the results of our preliminary experience with extracranial SBRT in locally or distantly recurrent gynecological tumors.	11 patients (12 lesions), were included in the analysis. SBRT was delivered as first RT treatment (5 patients), or as retreatment (6 patients). Complete clinical response was achieved in 8/12 lesions (66.6%), while partial response was documented in 2/12 lesions (16.6%). With a median follow-up of 19 months (range, 2–37 months), 7 patients (63%) experienced local and/or distant progression of disease. The 2-year local PFS was 81.8%, while the 2-year metastases-free survival was 54.4%. The 2-year OS was 63.6%. Acute and late toxicities were grade 2 or less. There was no difference in quality of life scores between the data collected before extracranial SBRT and at first follow-up evaluation.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
64. Aghajanian C, Sill MW, Darcy KM, et al. Phase II trial of bevacizumab in recurrent or persistent endometrial cancer: a Gynecologic Oncology Group study. *J Clin Oncol.* 2011;29(16):2259-2265.	Experimental-Tx	52 patients	To assess the activity and tolerability of single-agent bevacizumab in recurrent or persistent EC.	56 patients were enrolled. 52 patients were eligible and evaluable. Median age was 62 years, and prior treatment consisted of 1 or 2 regimens in 33 (63.5%) and 19 (36.5%) patients, respectively. 29 patients (55.8%) received prior radiation. Adverse events were consistent with those expected with bevacizumab treatment. No gastrointestinal perforations or fistulae were seen. 7 patients (13.5%) experienced clinical responses (1 complete response and 6 partial responses; median response duration, 6.0 months), and 21 patients (40.4%) survived progression free for at least 6 months. Median PFS and OS times were 4.2 and 10.5 months, respectively. Suggested associations were observed between high VEGF-A and adjusted hazard of death or tumor response when evaluated in tumor/plasma or plasma, respectively.	2
65. Oza AM, Elit L, Tsao MS, et al. Phase II study of temsirolimus in women with recurrent or metastatic endometrial cancer: a trial of the NCIC Clinical Trials Group. *J Clin Oncol.* 2011;29(24):3278-3285.	Experimental-Tx	60 patients (33 in Group A; 27 in Group B)	To investigate the efficacy of temsirolimus in patients with locally advanced, recurrent, and/or metastatic EC.	In the chemotherapy-naive group, 33 patients received a median of 4 cycles (range, 1 to 23 cycles). Of the 29 patients evaluable for response, 4 (14%) had an independently confirmed partial response and 20 (69%) had stable disease as best response, with a median duration of 5.1 months (range, 3.7 to 18.4 months) and 9.7 months (range, 2.1 to 14.6 months). Only 5 patients (18%) had progressive disease. In the chemotherapy-treated group, 27 patients received a median of 3 cycles (range, 1 to 6 cycles). Of the 25 patients evaluable for response, 1 (4%) had an independently confirmed partial response, and 12 patients (48%) had stable disease, with a median duration of 4.3 months (range, 3.6 to 4.9 months) and 3.7 months (range, 2.4 to 23.2 months). PTEN loss (immunohistochemistry and mutational analysis) and molecular markers of PI3K/Akt/mTOR pathway did not correlate with the clinical outcome.	2

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
66. Decruze SB, Green JA. Hormone therapy in advanced and recurrent endometrial cancer: a systematic review. *Int J Gynecol Cancer.* 2007;17(5):964-978.	Review/Other-Tx	2,471 patients (5 randomized control trials; 29 phase II studies)	To identify which populations should be considered for hormone interventions.	In previously untreated patients with grade 1 or grade 2 tumors, the response rate for progestogens and the PFS is in the range of 11%–56% and 2.5–14 months, respectively. Higher response rates are seen in progesterone receptor-positive cases. Phase II studies comprise the majority of the data and many are of poor quality. There was considerable heterogeneity in patient selection, prior treatment, and type of regimen, and meta-analysis was not possible. Grade 3 or 4 toxicity was < 5%.	4
67. Dellinger TH, Monk BJ. Systemic therapy for recurrent endometrial cancer: a review of North American trials. *Expert Rev Anticancer Ther.* 2009;9(7):905-916.	Review/Other-Tx	N/A	To discuss the developments of systemic therapy in recurrent EC, focusing on North American trials, in particular those documenting recent progress in new drug developments, as well as the future of individualized treatment regimens.	No results stated in abstract.	4
68. Rose PG, Brunetto VL, VanLe L, Bell J, Walker JL, Lee RB. A phase II trial of anastrozole in advanced recurrent or persistent endometrial carcinoma: a Gynecologic Oncology Group study. *Gynecol Oncol.* 2000;78(2):212-216.	Experimental-Tx	23 patients	To evaluate anastrozole in recurrent EC.	23 patients were entered on this trial. On central pathology review, 9 of them had grade 2 and 14 had grade 3 tumors. 1 to 24 courses (median: 1) of therapy were administered. 2 partial responses were noted (9%; 90% CI, 3 to 23%). 2 additional patients had short-term stable disease. With the exception of 1 case of venous thrombosis, the toxicity profile was mild. Median durations of PFS and OS are 1 and 6 months, respectively.	2

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
69. McMeekin DS, Gordon A, Fowler J, et al. A phase II trial of arzoxifene, a selective estrogen response modulator, in patients with recurrent or advanced endometrial cancer. *Gynecol Oncol.* 2003;90(1):64-69.	Experimental-Tx	34 patients	To determine response rate and evaluate toxicity of LY353381 (arzoxifene) in patients with recurrent or advanced EC.	From February 1999 through April 2001, 37 patients were entered of whom 34 received treatment. Efficacy was evaluated for the 29 patients who received at least 4 weeks of therapy and at least 1 tumor response assessment. Safety was assessed in all 34 patients who received any drug. 30 patients were defined as progestogen sensitive, and 4 patients were defined as progestogen failures. 26 patients were estrogen receptor+, and 22 were progesterone receptor+. 9 (1 complete response + 8 partial response) of 29 patients responded (31%, CI 25%–51%), with a median duration of response of 13.9 months. All 9 responses occurred in progestogen-sensitive patients. 2 additional patients (1 from each progestogen cohort) had stable disease for ≥6 months. The median progression-free interval was 3.7 months (CI 1.9–6.6 months) for all 29 patients. Toxicity was minimal with no grade 3-4 toxic effects, and 9 patients had only grade 1-2 toxic effects (7 grade 1, 2 grade 2). Hot flashes were the most common toxic effect and, in all 3 reported cases, were grade 1.	2
70. Piura B, Rabinovich A, Apel-Sarid L, Shaco-Levy R. Splenic metastasis from endometrial carcinoma: report of a case and review of literature. *Arch Gynecol Obstet.* 2009;280(6):1001-1006.	Review/Other-Tx	1	To describe only the 12th case of splenic metastasis from EC and review pertinent literature.	A 58-year-old woman had surgery and RT for stage IIB EC. 18 months later, PET scan discovered a hypermetabolic splenic mass and 2 hypermetabolic lung nodules. Spleen biopsy showed metastasis from EC. Chemotherapy with 6 cycles of cyclophosphamide, adriamycin and cisplatin effected a partial response of the splenic and lung metastasis. After few months, however, splenectomy was performed because of substantial growth of the splenic metastasis and it confirmed that the splenic metastasis was of endometrial origin and solitary in the peritoneal cavity. After splenectomy, the patient received chemotherapy with six cycles of paclitaxel. To date, 6 months after splenectomy, she is alive with no intraperitoneal disease and with few stable lung metastases.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
71. Tangjitgamol S, Levenback CF, Beller U, Kavanagh JJ. Role of surgical resection for lung, liver, and central nervous system metastases in patients with gynecological cancer: a literature review. *Int J Gynecol Cancer.* 2004;14(3):399-422.	Review/Other-Tx	N/A	To review the published literature, regarding surgical management of metastatic disease in patients with gynecological cancer.	Some prognostic factors in the patients with metastatic lesions from these three different cancers were found in common. Favorable prognostic factors for a prolonged survival were good performance status of the patients, long disease-free interval, absence of other systemic disease, and the resectability, preferably with a clear margin. These factors should be considered as the criteria for surgery. In well-selected patients, survival could be extended from the surgical procedure with minimal complications. Other types of treatment such as RT or chemotherapy could also be given in conjunction with surgery, depending on tumor type and disease status of the primary cancer, other systemic diseases, and residual metastatic lesions after surgery.	4
72. Salama JK, Milano MT. Radical irradiation of extracranial oligometastases. *J Clin Oncol.* 2014;32(26):2902-2912.	Review/Other-Tx	N/A	No abstract available.	No abstract available.	4
73. Higginson DS, Morris DE, Jones EL, Clarke-Pearson D, Varia MA. Stereotactic body radiotherapy (SBRT): Technological innovation and application in gynecologic oncology. *Gynecol Oncol.* 2011;120(3):404-412.	Review/Other-Tx	N/A	To provide an introduction and review of SBRT with regard to its use in gynecologic malignancies, and to present preliminary results from our experience for the purpose of illustrating the range of SBRT applications in gynecologic oncology.	6 case series are published that report results of SBRT for gynecologic malignancies. 16 gynecologic patients have been treated with SBRT at our institution. Treatment sites include pelvic and periaortic nodes (9 patients), oligometastatic disease (2), and cervical or endometrial primary tumors when other conventional external radiation or brachytherapy techniques were unsuitable (5). Preliminary follow-up at a median of 11 months (range, 0.3–33 months) demonstrates 79% locoregional control, 43% distant failure, and 50% OS.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
74. Baschnagel AM, Mangona VS, Robertson JM, Welsh RJ, Kestin LL, Grills IS. Lung metastases treated with image-guided stereotactic body radiation therapy. *Clin Oncol (R Coll Radiol)*. 2013;25(4):236-241.	Experimental-Tx	32 patients (47 lung metastases)	To evaluate outcomes after treatment with image-guided SBRT using daily online cone beam CT for malignancies metastatic to the lung.	The median follow-up was 27.6 months (7.6–57.1 months). The 1, 2 and 3 year actuarial LC rates for all treated lesions were 97%, 92% and 85%, respectively. 2 patients with colorectal primaries (4 lesions in total) had local failure. The median OS was 40 months. The 1, 2 and 3 year OS from the time of SBRT completion was 83%, 76% and 63%, respectively. There were no grade 4 or 5 toxicities. Grade 3 toxicities (1 instance of each) included pneumonitis, dyspnoea, cough, rib fracture and pain.	2
75. Lo SS, Lutz ST, Chang EL, et al. ACR Appropriateness Criteria (R) spinal bone metastases. *J Palliat Med.* 2013;16(1):9-19.	Review/Other-Tx	N/A	Evidence-based guidelines to assist referring physicians and other providers in making the most appropriate imaging or treatment decision for a specific clinical condition.	No results stated in abstract.	4

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
76. Nag S, Erickson B, Parikh S, Gupta N, Varia M, Glasgow G. The American Brachytherapy Society recommendations for high-dose-rate brachytherapy for carcinoma of the endometrium. *Int J Radiat Oncol Biol Phys*. 2000;48(3):779-790.	Review/Other-Tx	N/A	To develop recommendations for use of HDR brachytherapy in patients with EC.	The American Brachytherapy Society (ABS) endorses the National Comprehensive Cancer Network (NCCN) guidelines for indications for RT for patients with EC and the guidelines on HDR quality assurance of the American Association on Physicists in Medicine (AAPM). The ABS made specific recommendations for HDR applicator selection, insertion techniques, target volume definition, dose fractionation, and specifications for postoperative adjuvant vaginal cuff therapy, for vaginal recurrences, and for medically inoperable primary EC patients. The ABS recommends that applicator selection should be based on patient and target volume geometry. The dose prescription point should be clearly specified. The treatment plan should be optimized to conform to the target volume whenever possible while recognizing the limitations of computer optimization. Suggested doses were tabulated for treatment with HDR alone, and in combination with EBRT, when applicable. For intravaginal brachytherapy, the largest diameter applicator should be selected to ensure close mucosal apposition. Doses should be reported both at the vaginal surface and at 0.5 cm depth irrespective of the dose prescription point. For vaginal recurrences, intracavitary brachytherapy should be restricted to patients with nonbulky (<0.5 cm thick) disease. Patients with bulky (>0.5 cm thick) recurrences should be treated with interstitial techniques. For medically inoperable patients, an appropriate applicator that will allow adequate irradiation of the entire uterus should be selected.	4
77. Elshaikh MA, Yashar CM, Wolfson AH, et al. ACR appropriateness Criteria(R) advanced stage endometrial cancer. *Am J Clin Oncol.* 2014;37(4):391-396.	Review/Other-Tx	N/A	Evidence-based guidelines to assist referring physicians and other providers in making the most appropriate imaging or treatment decision for advanced stage EC.	N/A	4

Evidence Table Key

Study Quality Category Definitions

- *Category 1* The study is well-designed and accounts for common biases.
- *Category 2* The study is moderately well-designed and accounts for most common biases.
- *Category 3* There are important study design limitations.
- *Category 4* The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:
  a) the study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
  b) the study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
  c) the study is an expert opinion or consensus document.

Dx = Diagnostic

Tx = Treatment

Abbreviations Key

CI = Confidence interval

CT = Computed tomography

DFS = Disease-free survival

DSS = Disease-specific survival

EBRT = External beam radiation therapy

EC = Endometrial cancer

FDG-PET = Fluorine-18-2-fluoro-2-deoxy-D-glucose-positron emission tomography

HDR = High-dose-rate

HR = Hazard ratio

IOERT = Intraoperative electron radiation therapy

KPS = Karnofsky Performance Status

LC = Local control

LRR = Locoregional recurrence

OS = Overall survival

PFS = Progression-free survival

RT = Radiation therapy

SBRT = Stereotactic body radiotherapy