

ENDOMETRIAL CARCINOMA TREATMENT REGIMENS (Part 1 of 2)

Clinical Trials: The NCCN recommends cancer patient participation in clinical trials as the gold standard for treatment.

Cancer therapy selection, dosing, administration, and the management of related adverse events can be a complex process that should be handled by an experienced healthcare team. Clinicians must choose and verify treatment options based on the individual patient; drug dose modifications and supportive care interventions should be administered accordingly. The cancer treatment regimens below may include both U.S. Food and Drug Administration-approved and unapproved indications/regimens. These regimens are only provided to supplement the latest treatment strategies.

These Guidelines are a work in progress that may be refined as often as new significant data becomes available. The NCCN Guidelines® are a consensus statement of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

Systemic Therapy for Recurrent, Metastatic, or High-Risk Endometrial Carcinoma¹

Note: All recommendations are category 2A unless otherwise indicated.

Chemotherapy Regimens

REGIMEN	DOSING
Carboplatin + paclitaxel^{2,3}	Day 1: Carboplatin AUC 5–6mg•min/mL IV over 1 hour + paclitaxel 175mg/m ² IV over 3 hours. Repeat cycle every 3 weeks for 6 to 9 cycles.
Cisplatin + doxorubicin^{4,5a}	Day 1: Doxorubicin 60mg/m ² IV followed by cisplatin 50mg/m ² over 1 hour Day 2–11 (optional): Granulocyte colony-stimulating factor 5mcg/kg/day subcutaneously. Repeat every 3 weeks for maximum of 7 cycles.
Cisplatin + doxorubicin + paclitaxel^{4,5b}	Day 1: Doxorubicin 45mg/m ² IV + cisplatin 50mg/m ² IV Day 2: Paclitaxel 160mg/m ² IV over 3 hours Days 3–12: Filgrastim 5mcg/kg SQ (or pegfilgrastim 6mg on day 3 only). Repeat every 3 weeks for 6–7 cycles.
Carboplatin + docetaxel^{6–8c}	Day 1: Docetaxel 60–75mg/m ² IV over 1 hour; followed by carboplatin AUC 6mg•min/mL IV over 1 hour. Repeat every 3 weeks for 6 cycles.
Ifosfamide + paclitaxel (Category 1 for carcinosarcoma)⁹	Day 1: Paclitaxel 135mg/m ² IV over 3 hours Days 1–3: Ifosfamide 1.6g/m ² /day IV (reduced to 1.2g/m ² /day if patient received prior radiation). Repeat cycle every 3 weeks for 8 cycles.
Cisplatin + ifosfamide (for carcinosarcoma)¹⁰	Days 1–4: Cisplatin 20mg/m ² /day IV over 15 minutes + ifosfamide 1.5g/m ² /day IV over 1 hour Day 1: Mesna 120mg/m ² IV bolus over 15 minutes (loading dose) Days 1–4: Mesna 1.5g/m ² /day continuous IV infusion. Repeat cycle every 3 weeks for 3 cycles.
Cisplatin¹¹	Day 1: Cisplatin 50mg/m ² IV. Repeat cycle every 3 weeks.
Carboplatin¹²	Day 1: Carboplatin 400mg/m ² IV. Repeat cycle every 3 weeks
Doxorubicin¹³	Day 1: Doxorubicin 60mg/m ² IV. Repeat cycle every 4 weeks.
Liposomal doxorubicin¹⁴	Day 1: Liposomal doxorubicin 50mg/m ² IV over 1 hour. Repeat cycle every 4 weeks.
Paclitaxel¹⁵	Day 1: Paclitaxel 110–200mg/m ² IV. Repeat cycle every 3 weeks.
Topotecan¹⁶	Days 1–5: Topotecan 1.5mg/m ² /day IV (reduced to 1.2mg/m ² if patients received prior pelvic radiation). Repeat cycle every 3 weeks.
Bevacizumab¹⁷	Day 1: Bevacizumab 15mg/kg IV. Repeat cycle every 3 weeks.
Temsirolimus¹⁸	Temsirolimus 25mg IV weekly. Repeat cycle every 4 weeks.
Docetaxel (Category 2B)¹⁹	Days 1, 8, and 15: Docetaxel 36mg/m ² IV over 1 hour. Repeat cycle every 4 weeks.
Ifosfamide (for carcinosarcoma)⁹	Days 1–3: Ifosfamide 2g/m ² /day IV + mesna 2g IV beginning 15 minutes before ifosfamide infusion. Repeat cycle every 3 weeks for 8 cycles.

continued

ENDOMETRIAL CARCINOMA TREATMENT REGIMENS (Part 2 of 2)

Systemic Therapy for Recurrent, Metastatic, or High-Risk Endometrial Carcinoma¹

Hormonal Therapy^d

REGIMEN	DOSING
Megestrol + alternating tamoxifen ²⁰	Megestrol acetate 80mg orally twice daily for 3 weeks alternating with tamoxifen 20mg orally twice daily for 3 weeks.
Tamoxifen ²¹	Tamoxifen 20mg orally twice daily until disease progression or unacceptable toxicity.
Progesterone agents	This regimen was included in the NCCN guidelines but no reference was provided to indicate appropriate agents or dosages, as no particular dose, drug, or schedule has been found to be superior.
Aromatase inhibitors	This regimen was included in the NCCN guidelines but no reference was provided to indicate appropriate agents or dosages, as no particular dose, drug, or schedule has been found to be superior.

General treatment notes:

- Participation in clinical trial is strongly recommended.
- Multi-agent chemotherapy regimens preferred over single agents, if tolerated.
- Cisplatin, carboplatin, liposomal doxorubicin, paclitaxel, and docetaxel may cause drug reactions.
- Chemotherapy regimens can be used for all carcinoma histologies. Carcinosarcomas are now considered and treated as high-grade carcinomas. However, ifosfamide-based regimens were previously used for carcinosarcomas.

^a Patients who have received prior pelvic radiotherapy or who are older than 65 years should receive a reduction in the starting dose of doxorubicin, to 45mg/m².

^b The cisplatin/doxorubicin/paclitaxel regimen is not widely used because of concerns about toxicity.

^c Docetaxel may be considered for patients in whom paclitaxel is contraindicated.

^d Hormonal therapy may be used for lower grade endometrioid histologies only (ie, not for G3 endometrioid, serous carcinoma, clear cell carcinoma, or carcinosarcoma), preferably in patients with small tumor volume or an indolent growth pace.

References

1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology™. Uterine Neoplasms. v 2.2016. Available at: http://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed March 22, 2016.
2. Miller D, Filiaci V, Fleming G, et al. Randomized phase III noninferiority trial of first line chemotherapy for metastatic or recurrent endometrial carcinoma: a Gynecologic Oncology Group study [abstract]. *Gynecol Oncol*. 2012;125:771.
3. Sorbe B, Andersson H, Boman K, et al. Treatment of primary advanced and recurrent endometrial carcinoma with a combination of carboplatin and paclitaxel-long-term follow-up. *Int J Gynecol Cancer*. 2008;18(4):803-808.
4. Fleming GF, Brunetto VL, Cella D, et al. Phase III trial of doxorubicin plus cisplatin with or without paclitaxel plus filgrastim in advanced endometrial carcinoma: a Gynecologic Oncology Group Study. *J Clin Oncol*. 2004;22(11):2159-2166.
5. 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.
6. Scribner DR Jr, Puls LE, Gold MA. A phase II evaluation of docetaxel and carboplatin followed by tumor volume directed pelvic plus or minus paraaortic irradiation for stage III endometrial cancer. *Gynecol Oncol*. 2012;125(2):388-393.
7. Geller MA, Iy JJ, Ghebres R, et al. A phase II trial of carboplatin and docetaxel followed by radiotherapy given in a "Sandwich" method for stage III, IV, and recurrent endometrial cancer. *Gynecol Oncol*. 2011;121(1):112-117.
8. Nomura H, Aoki D, Takahashi F, et al. Randomized phase II study comparing docetaxel plus cisplatin, docetaxel plus carboplatin, and paclitaxel plus carboplatin in patients with advanced or recurrent endometrial carcinoma: a Japanese Gynecologic Oncology Group study (JGOG2041). *Ann Oncol*. 2011;22(3):636-642.
9. Homesley HO, Filiaci V, Markman M, et al. Phase III trial of ifosfamide with or without paclitaxel in advanced uterine carcinosarcoma: a Gynecologic Oncology Group Study. *J Clin Oncol*. 2007;25(5):526-531.
10. Wolfson AH, Brady MF, Rocereto TF, et al. A gynecologic oncology group randomized trial of whole abdominal irradiation (WAI) vs cisplatin-ifosfamide-mesna (CIM) in optimally debulked stage I-IV carcinosarcoma (CS) of the uterus. *J Clin Oncol*. 2006;24(18S):5001.
11. Thigpen JT, Blessing JA, Lagasse LD. Phase II trial of cisplatin as first-line chemotherapy in patients with advanced or recurrent endometrial carcinoma: a Gynecologic Oncology Group study. *Gynecol Oncol*. 1989;33(1):68-70.
12. Van Wijk FH, Lhomme C, Bolis G, et al. Phase II study of carboplatin in patients with advanced or recurrent endometrial carcinoma: a trial of the EORTC Gynaecological Cancer Group. *Eur J Cancer*. 2003;39(1):78-85.
13. Aapro MS, van Wijk FH, Bolis G, et al. Doxorubicin versus doxorubicin and cisplatin in endometrial carcinoma: definitive results of a randomized study (55872) by the EORTC Gynaecological Cancer Group. *Ann Oncol*. 2003;14(3):441-448.
14. 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.
15. Lincoln S, Blessing JA, Lee RB, Rocereto TF. Activity of paclitaxel as second-line chemotherapy in endometrial carcinoma: a Gynecologic Oncology Group study. *Gynecol Oncol*. 2003;88(3):277-281.
16. Wadler S, Levy DE, Lincoln ST, et al. Topotecan is an active agent in the first-line treatment of metastatic or recurrent endometrial carcinoma: Eastern Cooperative Oncology Group Study E3E93. *J Clin Oncol*. 2003;21(11):2110-2114.
17. Aghajanian C, Sill MW, Darcy KM, et al. Phase II trial of bevacizumab in recurrent or persistent endometrial: a Gynecologic Oncology Group study. *J Clin Oncol*. 2011;29(16):2259-2265.
18. 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.
19. Garcia AA, Blessing JA, Nolte S, Mannel RS. A phase II evaluation of weekly docetaxel in the treatment of recurrent or persistent endometrial carcinoma: a study by the Gynecologic Oncology Group. *Gynecol Oncol*. 2008;111(1):22-26.
20. 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(1):10-14.
21. Thigpen T, Brady MF, Homesley HD, Soper JT, Bell J. Tamoxifen in the treatment of advanced or recurrent endometrial carcinoma: a Gynecologic Oncology Group study. *J Clin Oncol*. 2001;19(2):364-367.

(Revised 4/2016)

© 2016 by Haymarket Media, Inc.