## 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 Carcinoma<sup>1</sup>

### **Chemotherapy and other Treatment Regimens**

REGIMEN		DOSING		
Carboplatin + paclitaxel <sup>2,3</sup>		<b>Day 1:</b> Carboplatin AUC 5–6* IV over 1 hour <u>plus</u> paclitaxel 175mg/m <sup>2</sup> IV over 3 hours. Repeat cycle every 3 weeks for 6 to 9 cycles.		
Cisplatin + doxorubicin <sup>4,5</sup>	doxorubicin <sup>4,5</sup>		Day 1: Doxorubicin <sup>†</sup> 60mg/m <sup>2</sup> followed by       cisplatin 50mg/m <sup>2</sup> over         1 hour. <sup>‡</sup> Day 2-11 (optional): Granulocyte colony-stimulating factor         5mcg/kg/day SQ <sup>§</sup> Repeat every 3 weeks for maximum of 7 cycles.	
Cisplatin + doxorubicin + paclitaxel <sup>4,5,  </sup>		Day 1: Doxorubicin 45mg/m <sup>2</sup> IV <u>plus</u> cisplatin 50mg/m <sup>2</sup> . <sup>‡</sup> Day 2: Paclitaxel 160mg/m <sup>2</sup> IV over 3 hours. <sup>‡</sup> Days 3-12: Filgrastim 5mcg/kg SQ (or pegfilgrastim 6mg <u>on day 3 only</u> ) Repeat every 3 weeks for 6-7 cycles.		
Carboplatin + docetaxel <sup>6-8,¶</sup>		Day 1: Docetaxel 60-75mg/m <sup>2</sup> IV over 1 hour; <u>followed by</u> carboplatin AUC 6 IV over 1 hour. Repeat every 3 weeks for 6 cycles.		
lfosfamide + paclitaxel <sup>9</sup>		Day 1: Paclitaxel 135mg/m <sup>2</sup> IV over 3 hours, <u>plus</u> Days 1-3: Ifosfamide 1.6g/m <sup>2</sup> /day IV (reduced to 1.2g/m <sup>2</sup> /day if patient received prior radiation). Repeat cycle every 3 weeks for 8 cycles.		
Cisplatin + ifosfamide (for carcinosarcoma) <sup>10</sup>		<ul> <li>Days 1-4: Cisplatin 20mg/m²/day IV; <u>followed by</u> ifosfamide 1.5g/m²/day IV over 1 hour.</li> <li>Day 1: Mesna 120mg/m² IV bolus over 15 minutes (loading dose), <u>followed by</u></li> <li>Days 1-4: Mesna 1.5g/m²/day continuous IV infusion. Repeat cycle every 3 weeks for 3 cycles.</li> </ul>		
Hormonal Regimens <sup>#</sup>		'		
Medroxyprogesterone acetate <sup>11</sup>		Medroxyprogesterone acetate 200mg PO once daily.		
Tamoxifen <sup>12</sup>		Tamoxifen 20mg PO twice daily.		
Anastrozole <sup>13**</sup>		Anastrozole 1mg/day PO for at least 28 days.		
Tamoxifen + medroxyprogesterone acetate <sup>14</sup>		Medroxyprogesterone acetate 80mg PO twice daily for 3 weeks alternating with tamoxifen 20mg orally twice daily. Repeat cycle every 3 weeks.		
Single Agents				
Cisplatin	<ul> <li>Liposomal doxorubicin</li> </ul>		•Temsirolimus	
•Carboplatin	•Pacli	taxel	•Docetaxel <sup>¶</sup>	
Doxorubicin     •Topot		tecan	<ul> <li>Ifosfamide (for carcinosarcoma)</li> </ul>	

# ENDOMETRIAL CARCINOMA TREATMENT REGIMENS (Part 2 of 2)

#### **General treatment notes:**

- · Participation in clinical trial is strongly recommended.
- 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.
- \* In 2008, initial doses of TC were reduced (135mg/m<sup>2</sup>, AUC 5) for those with a history of pelvic/spine irradiation.
- † Patients who have received prior pelvic RT or who are older than 65 years should receive a reduction in the starting dose of doxorubicin, to 45mg/m<sup>2</sup>.
- ‡ Maximum BSA of 2.0m<sup>2</sup> was used for dose calculations.
- § Following the expected chemotherapy induced neutrophil nadir, until ANC reaches 10,000/mm<sup>3</sup>.
- | The cisplatin/doxorubicin/paclitaxel regimen is not widely used because of concerns about toxicity.
- ¶ Docetaxel may be considered for patients in whom paclitaxel is contraindicated.
- # Hormonal therapy is for endometrioid histologies only (i.e., not for serous adenocarcinoma, clear cell adenocarcinoma, or carcinosarcoma).
- \*\* Anastrozole has minimal activity in an unselected population of patients with recurrent endometrial cancer.
- <sup>††</sup> Bevacizumab may be considered for use in patients who have progressed on prior cytotoxic chemotherapy.<sup>15</sup>

## References

- Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology<sup>IM</sup>. Uterine Neoplasms. v 1.2014. Available at: http://www.nccn.org/professionals/physician\_gls/ pdf/uterine.pdf. Accessed April 10, 2014.
- 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.
- 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.
- 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.
- Homesley HD, Filiaci V, Gibbons SK, et al. A randomized phase Ill 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.
- 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.
- Geller MA, Ivy JJ, Ghebre 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.
- 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.

- 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. 2007:25:526–531.
- 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.
- Thigpen JT, Brady MF, Alvarez RD, et al. Oral medroxyprogesterone acetate in the treatment of advanced or recurrent endometrial carcinoma: a dose-response study by the Gynecologic Oncology Group. J Clin Oncol. 1999;17:1736–1744.
- Thigpen T, Brady MF, Homesley HD, et al. Tamoxifen in the treatment of advanced or recurrent endometrial carcinoma: a Gynecologic Oncology Group study. J Clin Oncol. 2001;19: 364–367.
- Rose PG, Brunetto VL, VanLe L, et al. 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.
- 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.
- 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: 2259–2265.