

## Cancer Chemotherapy Update

# Docetaxel and Estramustine for Prostate Cancer

Dominic A. Solimando, Jr, MA, FAPhA, FASHP, BCOP;  
J. Aubrey Waddell, PharmD, FAPhA, BCOP; and Andrew J. Watts\*

The complexity of cancer chemotherapy requires that pharmacists be familiar with the complicated regimens and highly toxic agents used. This column reviews various issues related to preparing, dispensing, and administering antineoplastic therapy and to the agents, commercially available and investigational, used to treat malignant diseases. Questions or suggestions for topics should be addressed to Dominic A. Solimando, Jr, President, Oncology Pharmacy Services, Inc, 4201 Wilson Blvd #110-545, Arlington, VA 22203, e-mail: OncRxSvc@aol.com; or J. Aubrey Waddell, Associate Professor, University of Tennessee College of Pharmacy; Oncology Pharmacist, Pharmacy Department, Blount Memorial Hospital, 907 E Lamar Alexander Parkway, Maryville, TN 37804, e-mail: waddfour@charter.net.

**Regimen Name:** Docetaxel and estramustine  
**Origin of Name:** The regimen is named for the 2 drugs it contains: docetaxel and estramustine.

### INDICATION(S)

The docetaxel and estramustine regimen has been studied for the treatment of hormone-resistant metastatic and nonmetastatic prostate cancer.<sup>1-21</sup> Current guidelines do not recommend use of estramustine for the therapy of prostate cancer.<sup>22-24</sup> See Table 1 for treatment regimen.

### DRUG PREPARATION

#### A. Docetaxel

1. Follow institutional policies for preparation of hazardous medications when preparing docetaxel.
2. Use docetaxel injection 40 mg/mL.
3. Prepare docetaxel according to package instructions, using the provided diluent to

make a concentration of 10 mg/mL.

4. Exercise caution when preparing docetaxel.
  - a. The Institute for Safe Medication Practices has reported instances in which the diluent was accidentally dispensed instead of the reconstituted drug because the label on the diluent vial emphasizes the name of the active drug.<sup>25</sup>
  - b. Errors in the reconstitution of docetaxel related to overfill in the drug and diluent vials also have been reported. The 20 and 80 mg vials contain 23.6 and 94.4 mg of docetaxel, respectively. The diluent vials are also overfilled. When reconstituted properly, the final solution contains 10 mg/mL of docetaxel. The proper volume needed to obtain the required dose should be measured, rather than merely withdrawing the entire contents of the vial.<sup>7</sup>
5. Dilute with 0.9% sodium chloride injection or 5% dextrose injection. The final concentration should be 0.3 to 0.9 mg/mL.
6. Contact of undiluted docetaxel with plasticized polyvinyl chloride (PVC) equipment or devices is not recommended. Docetaxel solutions should be dispensed in glass, polypropylene, or polyolefin containers.

#### B. Estramustine

1. Follow institutional policies for handling of hazardous medications when dealing with estramustine.
2. Estramustine is available as a 140 mg capsule.

### DRUG ADMINISTRATION

- A. Docetaxel is administered by intravenous (IV) infusion over 60 to 90 minutes through a non-PVC (low-sorbing) infusion set.
- B. Estramustine is given orally (PO) on an empty stomach, usually in 2 or 3 divided doses each day.

\*Doctor of pharmacy candidate, School of Pharmacy, College of Pharmacy, Nursing & AHS, Howard University, Washington, DC.

**Table 1. Docetaxel and Estramustine Regimen<sup>1-6</sup>**

<i>Drug</i>	<i>Dose</i>	<i>Route of Administration</i>	<i>Administered on Day(s)</i>	<i>Total Dose/Cycle</i>
Docetaxel	70 mg/m <sup>2</sup>	IV	2	70 mg/m <sup>2</sup>
Estramustine	280 mg 3 times per day	PO	1 through 5	4,300 mg
Cycle repeats every 21 days.				
<b>Variations</b>				
1. Savarese et al used estramustine 10 mg/kg/day PO on days 1 through 5 and docetaxel 70 mg/m <sup>2</sup> IV on day 2 every 3 weeks. <sup>7</sup>				
2. Sinibaldi et al used estramustine 280 mg PO every 6 hours for 5 doses, beginning on day 1, and docetaxel 70 mg/m <sup>2</sup> IV on day 2 every 3 weeks. <sup>8,9</sup>				
3. Sitka Copur et al used estramustine 420 mg PO 3 times a day for 4 doses and then 280 mg 3 times a day for 5 doses, beginning on days 1 and 8, and docetaxel 35 mg/m <sup>2</sup> IV on days 2 and 9 every 3 weeks. <sup>10</sup>				
4. Walczak et al, Petrylak et al, and Berry et al used estramustine 280 mg PO 3 times a day on days 1 through 5 and docetaxel 60 mg/m <sup>2</sup> IV on day 2 every 3 weeks. <sup>11-13</sup>				
5. Hussain et al and Cocco et al used estramustine 280 mg PO 3 times a day on days 1 through 3 and docetaxel 70 mg/m <sup>2</sup> IV on day 2 every 3 weeks. <sup>14,15</sup>				
6. Hainsworth et al used estramustine 140 mg PO 3 times a day for 7 doses, beginning days 1, 8, and 15; and docetaxel 35 mg/m <sup>2</sup> IV on days 2, 9, and 16 every 4 weeks. <sup>16</sup>				
7. Chittoor et al used estramustine 140 mg PO twice a day on days 1 through 3, 8 through 10, and 15 through 17 and docetaxel 25 mg/m <sup>2</sup> IV on days 2, 9, and 16 every 4 weeks. <sup>17</sup>				
8. Carles et al used estramustine 280 mg PO twice a day on days 1 through 3, 8 through 10, and 15 through 17 and docetaxel 25 mg/m <sup>2</sup> IV on days 2, 9, and 16 every 4 weeks. <sup>18</sup>				
9. Eymard et al and Caffo et al used estramustine 280 mg PO twice a day on days 1 through 5 and docetaxel 70 mg/m <sup>2</sup> IV on day 2 every 3 weeks. <sup>19,20</sup>				
10. Takenaka et al used estramustine 560 mg PO daily for 6 weeks and docetaxel 30 mg/m <sup>2</sup> IV weekly for 6 weeks every 8 weeks. <sup>21</sup>				
IV = intravenous; PO = oral.				

**SUPPORTIVE CARE**

**A. Acute Emesis Prophylaxis:** It is predicted that the docetaxel-estramustine regimen will cause acute emesis in 60% to 90% of patients.<sup>26</sup> According to current guidelines, appropriate acute emesis prophylaxis includes a serotonin antagonist, a corticosteroid, and a neurokinin antagonist.<sup>26-29</sup> The studies reviewed reported nausea or vomiting in 3% to 31% of patients, with moderate to severe (grade 3) nausea or vomiting in only 3% of patients.<sup>1,5,6</sup> For many patients receiving docetaxel and estramustine, any nausea

that is experienced is generally mild to moderate. Aggressive combination antiemetic regimens may not be necessary; less complicated regimens, such as those listed here, or single-agent regimens may be sufficient<sup>27-29</sup>:

1. Ondansetron 16 to 24 mg PO and dexamethasone 20 mg PO on day 2, given 30 minutes before docetaxel.
2. Granisetron 2 mg PO and dexamethasone 20 mg PO on day 2, given 30 minutes before docetaxel.
3. Dolasetron 100 to 200 mg PO and dexamethasone 20 mg PO on day 2, given 30

minutes before docetaxel.

4. Palonosetron 0.5 mg PO and dexamethasone 20 mg PO on day 2 only, given 30 minutes before docetaxel.

The antiemetic therapy should continue for at least 3 days. A meta-analysis of several trials of serotonin antagonists recommended against prolonged (greater than 24 hours) use of these agents, making a steroid or steroid and dopamine antagonist combination most appropriate for follow-up therapy.<sup>30</sup> One of the following regimens is suggested:

1. Dexamethasone 4 mg PO twice a day for 3 days, ±

metoclopramide 0.5 to 2 mg/kg PO every 4 to 6 hours, ± diphenhydramine 25 to 50 mg PO every 6 hours if needed, starting on day 3 of the docetaxel-estramustine regimen.

2. Dexamethasone 4 mg PO twice a day for 3 days, ± prochlorperazine 10 mg PO every 4 to 6 hours, ± diphenhydramine 25 to 50 mg PO every 6 hours if needed, starting on day 3 of docetaxel-estramustine regimen.
3. Dexamethasone 4 mg PO twice a day for 3 days, ± promethazine 25 to 50 mg PO every 4 to 6 hours, ± diphenhydramine 25 to 50 mg PO every 6 hours if needed, starting on day 3 of docetaxel-estramustine regimen.

One of the previously listed regimens also would be appropriate on the days when estramustine is taken alone if the patient routinely requires an antiemetic while receiving estramustine.

Patients who experience significant nausea or vomiting with one of these regimens should receive an agent from a different pharmacologic category.<sup>27-29</sup> A few small studies suggested substituting granisetron for ondansetron in subsequent treatment cycles; however, none of these reports found the improvement statistically significant.<sup>31-35</sup>

**B. Breakthrough Nausea and Vomiting<sup>26-29</sup>:** Patients should receive an antiemetic prescription to treat breakthrough nausea. One of the following regimens is suggested:

1. Metoclopramide 0.5 to 2 mg/kg PO every 4 to 6

hours if needed ± diphenhydramine 25 to 50 mg PO every 6 hours if needed.

2. Prochlorperazine 10 mg PO every 4 to 6 hours if needed ± diphenhydramine 25 to 50 mg PO every 6 hours if needed.
3. Prochlorperazine 25 mg rectally every 4 to 6 hours if needed ± diphenhydramine 25 to 50 mg PO every 4 to 6 hours if needed.
4. Promethazine 25 to 50 mg PO every 4 to 6 hours if needed ± diphenhydramine 25 to 50 mg PO every 4 to 6 hours if needed.

A few small studies suggested that higher doses of granisetron (3 mg IV or 40 to 240 mcg/kg IV)<sup>31-35</sup> may be effective in treating breakthrough nausea; however, none of these reports found the improvement statistically significant.

**C. Hydration:** No special precautions are required.

**D. Hypersensitivity Precautions<sup>36,37</sup>:** Although it is less likely that docetaxel will cause hypersensitivity reactions than paclitaxel, the manufacturer recommends administration of dexamethasone 8 mg PO twice daily for 3 days, beginning the day before the docetaxel infusion. Some clinicians administer a histamine 2 antagonist ± a histamine 1 antagonist in addition to the steroid. If additional prophylaxis against hypersensitivity is chosen, the following regimen is suggested:

1. Cimetidine 300 mg or ranitidine 50 mg
  2. Diphenhydramine 50 mg
- All given IV over 30 minutes before docetaxel.

**E. Hematopoietic Growth Factors:** Accepted practice guide-

lines and pharmacoeconomic analysis suggest that antineoplastic regimens have a greater than 20% incidence of febrile neutropenia before prophylactic use of colony-stimulating factors is warranted. For regimens with an incidence of febrile neutropenia between 10% and 20%, use of colony-stimulating factors should be considered. For regimens with an incidence of febrile neutropenia less than 10%, routine prophylactic use of colony-stimulating factors is not recommended.<sup>38,39</sup>

Because grade 3 or 4 febrile neutropenia was reported in 5% to 14% of patients in the trials reviewed,<sup>1,3,6</sup> prophylactic use of colony-stimulating factors may not be necessary in all patients. Because patients with prostate cancer are generally older and age is one of the factors for which growth factor support is indicated in regimens with an incidence of neutropenic fever between 10% and 20%, prophylactic filgrastim would be appropriate for some patients.<sup>38,39</sup>

Any patient who experiences febrile neutropenia following a cycle of the docetaxel-estramustine regimen should receive filgrastim with subsequent treatment cycles.<sup>38,39</sup>

**F. Extravasation:** No special precautions are required.<sup>40-42</sup>

**G. Pulmonary:** Docetaxel can cause fluid retention, including pleural effusion, ascites, and peripheral edema, in up to 27% of patients.<sup>36</sup> In the docetaxel-estramustine trials reviewed, moderate-to-severe (grade 3 or 4) fluid retention or edema was reported for 2% to 8% of patients.<sup>3,5</sup> Patients should be treated with a steroid

(eg, dexamethasone 8 to 10 mg PO twice daily) for 3 to 5 days, beginning the day before docetaxel administration.<sup>36,37</sup>

**MAJOR TOXICITIES**

Most of the toxicities listed below are presented according to their degree of severity. Higher grades represent more severe toxicities. Although there are several grading systems for cancer chemotherapy toxicities, all are similar. One of the frequently used systems is the National Cancer Institute Common Terminology Criteria for Adverse Events. (For more information, go to <http://ctep.info.nih.gov>.) Oncologists generally do not adjust doses or change therapies for grade 1 or 2 toxicities but they make or consider dosage reductions or therapy changes for grade 3 or 4 toxicities. Incidence values are rounded to the nearest whole percent unless incidence was 0.5% or less.

- A. Cardiovascular:** Cerebral vascular accident (grade 4) 5%<sup>1</sup>; edema (grade 3) 5% to 8%,<sup>1,3,5</sup> (grade 4) 2% to 8%<sup>1,3,5</sup>; phlebitis/thrombosis (grade 1 or 2) 3%,<sup>5</sup> (grade 3) 3%,<sup>5</sup> (grade 4) 3%.<sup>5</sup>
- B. Dermatologic:** Alopecia (grade 1 or 2) 61%,<sup>5</sup> (grade 1 or 2) 45%<sup>5</sup>; onycholysis (grade 1 or 2) 13%,<sup>5</sup> (grade 3) 16%.<sup>1</sup>
- C. Gastrointestinal:** Anorexia (grade 1 or 2) 21%,<sup>5</sup> (grade 3) 3%,<sup>5</sup> (grade 4) 3%<sup>5</sup>; constipation (grade 3) 5% to 8%<sup>1,3</sup>; diarrhea (grade 1 or 2) 19%,<sup>5</sup> (grade 3) 3%<sup>5</sup>; esophagitis (grade 3) 3%<sup>2</sup>; nausea (grade 1 or 2) 31%,<sup>5</sup> (grade 3) 3% to 5%<sup>1,5</sup>; nausea or vomiting (grade 2) 9%<sup>6</sup>; stomatitis (grade 1 or 2) 15%,<sup>5</sup> (grade 3) 3% to 5%<sup>1,5</sup>; vomiting (grade 1 or 2) 11%.<sup>5</sup>
- D. Hematologic:** Anemia (grade 1 or 2) 71%,<sup>5</sup> (grade 3) 11%,<sup>5</sup>

- (grade 4) 6%<sup>5</sup>; granulocytopenia (grade 4) 12%<sup>2</sup>; leukopenia (grade 1 or 2) 13%,<sup>5</sup> (grade 3) 31%,<sup>5</sup> (grade 4) 3%<sup>5</sup>; neutropenia (grade 3) 26% to 33%,<sup>1,3</sup> (grade 3 or 4) 64%,<sup>6</sup> (grade 4) 16% to 33%<sup>1,3</sup>; neutropenic fever 5% to 14%,<sup>1,6</sup> (grade 4) 8%<sup>3</sup>; thrombocytopenia (grade 1 or 2) 35%,<sup>5</sup> (grade 3) 18%,<sup>5</sup> (grade 4) 2%.<sup>5</sup>
- E. Hepatic:** Transaminitis (grade 3) 3% to 16%<sup>1,2</sup>; unspecified (grade 2) 9%.<sup>6</sup>
- F. Metabolic:** Fatigue/malaise/asthenia (grade 1 or 2) 29%,<sup>5</sup> (grade 3) 16% to 23%,<sup>1,5</sup> (grade 4) 5%<sup>5</sup>; hypocalcemia (grade 3) 8%<sup>3</sup>; hypokalemia (grade 2) 5%<sup>6</sup>; hyponatremia (grade 2) 5%<sup>6</sup>; hyperglycemia (grade 3) 8%<sup>3</sup>; hypersensitivity reactions (grade 3) 3%.<sup>5</sup>
- G. Neurologic:** Asthenia (grade 3) 33%<sup>3</sup>; neuropathy unspecified (grade 1 or 2) 29%,<sup>5</sup> (grade 2) 9%,<sup>6</sup> (grade 3) 5%.<sup>5</sup>
- H. Pulmonary:** Dyspnea (grade 1 or 2) 16%,<sup>5</sup> (grade 3) 5%,<sup>5</sup> (grade 4) 5%.<sup>5</sup>
- I. Renal:** Increased serum creatinine (grade 1 or 2) 21%,<sup>5</sup> (grade 3) 5%.<sup>5</sup>

**PRETREATMENT LABORATORY STUDIES NEEDED**

- A. Baseline**
  - 1. Aspartate aminotransferase/alanine aminotransferase (AST/ALT)
  - 2. Total bilirubin
  - 3. Serum creatinine and creatinine clearance (CrCl)
  - 4. Complete blood count (CBC) with differential
- B. Before Each Treatment:** CBC with differential
- C. Recommended Pretreatment Values:** The minimally acceptable pretreatment CBC values required for beginning a cycle

with full-dose therapy in the protocols reviewed were as follows:

- 1. Absolute granulocyte count
  - a. Greater than 1,500 cells/mcL<sup>2,5</sup>
  - b. Greater than or equal to 1,500 cells/mcL<sup>6</sup>
- 2. Absolute neutrophil count: Greater than 1,500 cells/mcL<sup>3</sup>
- 3. Platelet count
  - a. Greater than 100,000 cells/mcL<sup>2,3,5</sup>
  - b. Greater than or equal to 100,000 cells/mcL<sup>6</sup>
- 4. Hemoglobin: Greater than or equal to 9 g/dL<sup>6</sup>
- 5. Serum creatinine
  - a. Less than 2.2 mg/dL<sup>2</sup>
  - b. Less than 2.4 mg/dL<sup>3</sup>
  - c. Less than 1.5 mg/dL<sup>6</sup>
- 6. CrCl less than 1.5 times the upper limit of normal (ULN)<sup>5</sup>
- 7. Serum bilirubin
  - a. Less than or equal to the ULN<sup>2</sup>
  - b. Less than the ULN<sup>3,5</sup>
  - c. Less than 1.5 mg/dL<sup>6</sup>
- 8. Serum AST
  - a. Less than or equal to 2.5 times the ULN<sup>2</sup>
  - b. Less than or equal to 2 times the ULN<sup>3</sup>
  - c. Less than or equal to 1.5 times the ULN<sup>5</sup>
  - d. Less than 60 mg/dL.<sup>6</sup>

In clinical practice, a pretreatment absolute neutrophil count of 1,000 cells/mcL and platelets of 75,000 cells/mcL are usually considered acceptable.

**DOSAGE MODIFICATIONS**

- A. Renal Function:** No adjustments necessary.<sup>43,44</sup>
- B. Liver Function:** Docetaxel
  - 1. AST or ALT 1.6 to 6 times ULN: Reduce dose by 25%.<sup>45</sup>

2. AST or ALT greater than 6 times ULN: Use clinical judgement.<sup>45</sup>

## REFERENCES

- Weitzman A, Shelton G, Zuech N, et al. Phase II study of estramustine (E) combined with docetaxel (D) in patients with androgen-independent prostate cancer (AIPCA). *Proc Am Soc Clin Oncol*. 1999;abstract 1369. [http://www.asco.org/ASCO/Abstracts+%26+Virtual+Meeting/Abstracts?&vmview=abstract\\_detail\\_view&confID=17&abstractID=15619](http://www.asco.org/ASCO/Abstracts+%26+Virtual+Meeting/Abstracts?&vmview=abstract_detail_view&confID=17&abstractID=15619). Accessed February 10, 2009.
- Petrylak DP, Macarthur RB, O'Connor J, et al. Phase I trial of docetaxel with estramustine in androgen-independent prostate cancer. *J Clin Oncol*. 1999;17(3):958-967.
- Weitzman AL, Shelton G, Zuech N, et al. Dexamethasone does not significantly contribute to the response rate of docetaxel and estramustine in androgen independent prostate cancer. *J Urol*. 2000;163(3):834-837.
- Eastham JA, Kelly WK, Grossfeld GD, et al. Cancer and Leukemia Group B (CALGB) 90203: a randomized phase 3 study of radical prostatectomy alone versus estramustine and docetaxel before radical prostatectomy for patients with high-risk localized disease. *Urology*. 2003;62(suppl 1):55-62.
- Nelius T, Reiher F, Lindenmeier T, et al. Characterization of prognostic factors and efficacy in a phase-II study with docetaxel and estramustine for advanced hormone refractory prostate cancer. *Onkologie*. 2005;28(11):573-578.
- Sella A, Zisman A, Kovel S, et al. Neoadjuvant chemohormonal therapy in poor-prognosis localized prostate cancer. *Urology*. 2008;71(2):323-327.
- Savarese D, Taplin ME, Halabi S, et al. A phase II study of docetaxel (*Taxotere*), estramustine, and low-dose hydrocortisone in men with hormone-refractory prostate cancer: preliminary results of Cancer and Leukemia Group B Trial 9780. *Semin Oncol*. 1999;26(5)(suppl 17):39-44.
- Sinibaldi VJ, Carducci M, Laufer M, et al. Preliminary evaluation of a short course of estramustine phosphate and docetaxel (*Taxotere*) in the treatment of hormone-refractory prostate cancer. *Semin Oncol*. 1999;26(5)(suppl 17):45-48.
- Sinibaldi VJ, Carducci MA, Moore-Cooper S, et al. Phase II evaluation of docetaxel plus one-day oral estramustine phosphate in the treatment of patients with androgen independent prostate carcinoma. *Cancer*. 2002;94(5):1457-1465.
- Sitka Copur M, Ledakis P, Lynch J, et al. Weekly docetaxel and estramustine in patients with hormone-refractory prostate cancer. *Semin Oncol*. 2001;28(4)(suppl 15):16-21.
- Walczak JR, Carducci MA; Eastern Cooperative Oncology Group E1899. Phase 3 randomized trial evaluating second-line hormonal therapy versus docetaxel-estramustine combination chemotherapy on progression-free survival in asymptomatic patients with a rising prostate-specific antigen level after hormonal therapy for prostate cancer: an Eastern Cooperative Oncology Group (E1899), Intergroup/Clinical Trials Support Unit study. *Urology*. 2003;62(suppl 1):141-146.
- Petrylak DP, Tangen CM, Hussain MH, et al. Docetaxel and estramustine compared with mitoxantrone and prednisone for advanced refractory prostate cancer. *N Engl J Med*. 2004;351(15):1513-1520.
- Berry DL, Moynour CM, Jiang CS, et al; Southwest Oncology Group. Quality of life and pain in advanced stage prostate cancer: results of a Southwest Oncology Group randomized trial comparing docetaxel and estramustine to mitoxantrone and prednisone. *J Clin Oncol*. 2006;24(18):2828-2835.
- Hussain M, Smith DC, El-Rayes BF, et al. Neoadjuvant docetaxel and estramustine chemotherapy in high-risk/locally advanced prostate cancer. *Urology*. 2003;61(4):774-780.
- Coccaro M, Tartarone A, Romano G, et al. Dose-finding study of weekly docetaxel plus estramustine in patients with hormone-refractory metastatic prostate cancer. *Tumori*. 2005;91(4):314-316.
- Hainsworth JD, Meluch AA, Spigel DR, et al. Weekly docetaxel/estramustine phosphate in patients with increasing serum prostate-specific antigen levels after primary treatment for prostate cancer: a phase II trial of the Minnie Pearl Cancer Research Network. *Clin Genitourin Cancer*. 2006;4(4):287-292.
- Chittoor S, Berry W, Loesch D, et al. Phase II study of low-dose docetaxel/estramustine in elderly patients or patients aged 18-74 years with hormone-refractory prostate cancer. *Clin Genitourin Cancer*. 2006;5(3):212-218.
- Carles J, Font A, Mellado B, et al. Weekly administration of docetaxel in combination with estramustine and celecoxib in patients with advanced hormone-refractory prostate cancer: final results from a phase II study. *Br J Cancer*. 2007;97(9):1206-1210.
- Eymard JC, Priou F, Zannetti A, et al. Randomized phase II study of docetaxel plus estramustine and single-agent docetaxel in patients with metastatic hormone-refractory prostate cancer. *Ann Oncol*. 2007;18(6):1064-1070.
- Caffo O, Sava T, Comploj E, et al. Docetaxel, with or without estramustine phosphate, as first-line chemotherapy for hormone-refractory prostate cancer: results of a multicentre, randomized phase II trial. *BJU Int*. 2008;102(9):1080-1085.
- Takenaka A, Yamada Y, Kurahashi T, et al. Combination chemotherapy with weekly docetaxel and estramustine for hormone refractory prostate cancer in Japanese patients. *Int J Urol*. 2008;15(1):106-109.
- National Comprehensive Cancer Network clinical practice guidelines in oncology—prostate cancer. V.2.2009. National Comprehensive Cancer Network Web site. <http://www.nccn.org/index.asp>. Accessed April 26, 2009.
- Winqvist E, Waldron T, Berry S, et al. Non-hormonal systemic therapy in men with hormone-refractory prostate cancer: a clinical practice guideline. [www.cancercare.on.ca/pdf/pebc3-15s.pdf](http://www.cancercare.on.ca/pdf/pebc3-15s.pdf). Published November 1, 2005. Accessed February 10, 2009.
- Basch EM, Somerfield MR, Beer TM, et al. American Society of Clinical Oncology endorsement of the Cancer Care Ontario Practice Guideline on non-hormonal therapy for men with metastatic hormone-refractory (castration-resistant) prostate cancer. *J Clin Oncol*. 2007;25(33):5313-5318.
- Cohen MR, Smetzer J. Preparing for a damaging medication error. *ISMP Medication Safety Alert!* 1999;4(14):26.
- Hesketh PJ, Kris MG, Grunberg SM, et al. Proposal for classifying the acute emetogenicity of cancer chemotherapy. *J Clin Oncol*. 1997;15(1):103-109.

27. National Comprehensive Cancer Network clinical practice guidelines—antiemesis. V.3.2009. National Comprehensive Cancer Network Web site. <http://www.nccn.org/index.asp>. Accessed April 26, 2009.
28. Kris MG, Hesketh PJ, Somerfield MR, et al. American Society of Clinical Oncology guideline for antiemetics in oncology: update 2006. *J Clin Oncol*. 2006;24(18):2932-2947.
29. Antiemetic guidelines: 2007. Multi-national Association for Supportive Care in Cancer Web site. [http://www.mascc.org/media/Resource\\_centers/MASCC\\_Guidelines\\_Update.pdf](http://www.mascc.org/media/Resource_centers/MASCC_Guidelines_Update.pdf). Accessed February 10, 2009.
30. Geling O, Eichler HG. Should 5-hydroxytryptamine-3 receptor antagonists be administered beyond 24 hours after chemotherapy to prevent delayed emesis? Systematic re-evaluation of clinical evidence and drug cost implications. *J Clin Oncol*. 2005;23(6):1289-1294.
31. Terrey JP, Aapro MS. The activity of granisetron in patients who had previously failed ondansetron antiemetic therapy. *Eur J Clin Res*. 1996;8:281-288.
32. Carmichael J, Keizer HJ, Cupissol D, et al. Use of granisetron in patients refractory to previous treatment with antiemetics. *Anticancer Drugs*. 1998;9(5):381-385.
33. de Wit R, de Boer AC, vd Linden GH, et al. Effective cross-over to granisetron after failure to ondansetron, a randomized double blind study in patients failing ondansetron plus dexamethasone during the first 24 hours following highly emetogenic chemotherapy. *Br J Cancer*. 2001;85(8):1099-1101.
34. Smith IE. A dose-finding study of granisetron, a novel antiemetic, in patients receiving cytostatic chemotherapy. The Granisetron Study Group. *J Cancer Res Clin Oncol*. 1993;119(6):350-354.
35. Soukop M. A dose-finding study of granisetron, a novel antiemetic, in patients receiving high-dose cisplatin. Granisetron Study Group. *Support Care Cancer*. 1994;2(3):177-183.
36. *Taxotere* [package insert]. Bridgewater, NJ: sanofi-aventis Pharmaceuticals, Inc; 2008. <http://products.sanofi-aventis.us/Taxotere/taxotere.html>. Accessed February 10, 2009.
37. Zanotti KM, Markman M. Prevention and management of antineoplastic-induced hypersensitivity reactions. *Drug Saf*. 2001;24(10):767-779.
38. Smith TJ, Khatcheressian J, Lyman GH, et al. 2006 update of recommendations for the use of white blood cell growth factors: an evidence-based clinical practice guideline. *J Clin Oncol*. 2006;24(19):3187-3205.
39. National Comprehensive Cancer Network clinical practice guidelines in oncology—myeloid growth factors. V.1.2009. National Comprehensive Cancer Network Web site. <http://www.nccn.org/index.asp>. Accessed February 10, 2009.
40. Larson DL. Treatment of tissue extravasation by antitumor agents. *Cancer*. 1982;49(9):1796-1799.
41. Larson DL. What is the appropriate management of tissue extravasation by antitumor agents? *Plast Reconstr Surg*. 1985;75(3):397-402.
42. Mullin S, Beckwith MC, Tyler LS. Prevention and management of antineoplastic extravasation injury. *Hosp Pharm*. 2000;35(1):57-74.
43. Kintzel PE, Dorr RT. Anticancer drug renal toxicity and elimination: dosing guidelines for altered renal function. *Cancer Treat Rev*. 1995;21(1):33-64.
44. Aronoff GR, Bennett WM, Berns JS, et al. *Drug Prescribing in Renal Failure*. 5th ed. Philadelphia, PA: American College of Physicians; 2007.
45. Floyd J, Mirza I, Sachs, Perry MC. Hepatotoxicity of chemotherapy. *Semin Oncol*. 2006;33(1):50-67. ■