Research To Practice: Systemic Therapy of Metastatic Disease

28TH ANNUAL San Antonio Breast Cancer Symposium 24

Selection of systemic therapy in patients with metastatic disease is a multi-faceted decision which is frequently influenced by the patient's age, prior adjuvant systemic therapy and a variety of other biopsychosocial considerations. Data from the *Breast Cancer Update* Patterns of Care Study, a telephone survey conducted in September 2005 of randomly selected medical oncologists in the United States, are presented here. For patients with minimally symptomatic metastatic disease, single-agent docetaxel is a common choice, and in older patients, capecitabine is commonly utilized. In addition, bevacizumab is a common consideration, particularly in patients receiving paclitaxel as first-line treatment. As more postmenopausal women receive adjuvant aromatase inhibitors, the selection of first-line endocrine therapy for metastatic disease is changing. In postmenopausal women, fulvestrant is a popular choice after progression on adjuvant anastrozole, while the aromatase inhibitors are commonly utilized after progression on adjuvant tamoxifen.

CHEMOTHERAPY FOR METASTATIC DISEASE AFTER PRIOR ADJUVANT AC → PACLITAXEL

The patient was treated two years ago with adjuvant AC → paclitaxel for an ER/PR-negative, HER2-negative tumor and now has bone and lung metastases with minimal symptoms. What first-line treatment are you likely to recommend for this patient?

	Age 40	Age 57	Age 75
Paclitaxel	10%	10%	2%
Docetaxel	24%	26%	24%
Nanoparticle paclitaxel	8%	8%	10%
Capecitabine	14%	14%	34%
Gemcitabine	2%	2%	8%
Vinorelbine	—	—	8%
Capecitabine + docetaxel	10%	6%	—
Gemcitabine + paclitaxel	8%	8%	2%
Gemcitabine + docetaxel	4%	6%	2%
Carboplatin + docetaxel	12%	12%	4%
Carboplatin + paclitaxel	2%	2%	—
AC	2%	2%	—
AC + paclitaxel	2%	2%	2%
AC + docetaxel	2%	2%	—
No chemotherapy	—	—	4%
Would you recommend bevacizumab for this patient?			
Percent responding "yes"	36%	36%	18%

SOURCE: *Breast Cancer Update* Patterns of Care Survey, September 2005. (n = 50)

CHEMOTHERAPY FOR METASTATIC DISEASE (NO PRIOR CHEMOTHERAPY)

The patient has received no prior systemic therapy for an ER/PR-negative, HER2-negative tumor and bone and lung metastases with minimal symptoms. What first-line treatment are you likely to recommend for this patient?

	Age 40	Age 57	Age 75
Paclitaxel	14%	14%	12%
Docetaxel	22%	24%	24%
Nanoparticle paclitaxel	—	—	10%
Capecitabine	12%	14%	26%
Gemcitabine	—	2%	4%
Vinorelbine	—	—	4%
Capecitabine + docetaxel	6%	4%	2%
Gemcitabine + paclitaxel	2%	—	—
Gemcitabine + docetaxel	4%	4%	—
AC	22%	18%	8%
AC + docetaxel	8%	12%	—
AC + paclitaxel	8%	6%	2%
Other chemotherapy	2%	2%	6%
No chemotherapy	—	—	2%
Would you recommend bevacizumab for this patient?			
Percent responding "yes"	32%	34%	20%

SOURCE: *Breast Cancer Update* Patterns of Care Survey, September 2005. (n = 50)

HORMONE THERAPY FOR METASTATIC DISEASE AFTER ADJUVANT TAMOXIFEN

The patient has been on adjuvant tamoxifen for four years for an ER/PR-positive, HER2-negative tumor and now has bone and lung metastases with minimal symptoms. What first-line endocrine treatment are you likely to recommend for this patient?

	Age 57	Age 75
Anastrozole	62%	60%
Exemestane	2%	6%
Letrozole	30%	30%
Tamoxifen	—	—
Fulvestrant	2%	—
No therapy	4%	4%
Would you recommend bevacizumab for this patient?		
Percent responding "yes"	14%	8%

SOURCE: *Breast Cancer Update* Patterns of Care Survey, September 2005. (n = 50)

HORMONE THERAPY FOR METASTATIC DISEASE AFTER ADJUVANT ANASTROZOLE

The patient has been on adjuvant anastrozole for four years for an ER/PR-positive, HER2-negative tumor and now has bone and lung metastases with minimal symptoms. What first-line treatment are you likely to recommend for this patient?

	Age 57	Age 75
Exemestane	10%	12%
Letrozole	2%	8%
Tamoxifen	26%	24%
Fulvestrant	50%	46%
No therapy	12%	10%

SOURCE: *Breast Cancer Update* Patterns of Care Survey, September 2005. (n = 50)

CLINICAL USE OF FULVESTRANT

Do you generally use a loading dose with fulvestrant? (percent responding "yes")	16%
What percentage of patients with metastatic breast cancer do you believe would prefer a monthly injection rather than a daily oral endocrine agent? (mean)	31%

SOURCE: *Breast Cancer Update* Patterns of Care Survey, September 2005. (n = 50)

SELECT PUBLICATIONS

Carrick S et al. **Single agent versus combination chemotherapy for metastatic breast cancer.** *Cochrane Database Syst Rev* 2005;(2):CD003372.

Ghersi D et al. **Taxane containing regimens for metastatic breast cancer.** *Cochrane Database Syst Rev* 2005;(2):CD003366.

Gralow JR. **Optimizing the treatment of metastatic breast cancer.** *Breast Cancer Res Treat* 2005;89(Suppl 1):9-15.

Jones SE, Pippen J. **Effectiveness and tolerability of fulvestrant in postmenopausal women with hormone receptor-positive breast cancer.** *Clin Breast Cancer* 2005;6(Suppl 1):9-14.

Miller KD et al. **E2100: A randomized phase III trial of paclitaxel versus paclitaxel plus bevacizumab as first-line therapy for locally recurrent or metastatic breast cancer.** Presentation. ASCO 2005.

Wong ZW, Ellis MJ. **First-line endocrine treatment of breast cancer: Aromatase inhibitor or antioestrogen?** *Br J Cancer* 2004;90(1):20-5.

CHEMOTHERAPY FOR METASTATIC DISEASE

I decide whether a patient should receive combination chemotherapy or sequential single agents based on the burden and pace of the disease. For example, women with quite a bit of visceral involvement — particularly liver involvement — may need combination therapy. For the patient with much more indolent disease, particularly the patient with a long disease-free interval who may have had sequential hormonal therapy and is now hormone therapy refractory, I use sequential single agents. Many of my patients receive capecitabine as the first chemotherapy in this situation because it's orally administered, does not cause alopecia and is extremely well tolerated. It is similar to taking a hormone pill.

— *Joanne L Blum, MD, PhD.* Breast Cancer Update *2005 (1)*

Many times in metastatic disease, we use all of the available therapies, so what we're really deciding on is the order — what to start with. Many patients make that decision based on their personal values. I find many of my older patients are attracted to capecitabine because it is an oral agent. Some of my younger patients think of intravenous therapy as more aggressive, and they prefer that strategy. However, this perception is based on gut reaction rather than reality. I am a big fan of capecitabine. Maybe it comes from being a "hormonal therapy person" who prefers pills to begin with because I use capecitabine a lot for salvage chemotherapy in women who have already had an anthracycline and a taxane for metastatic disease. In oncology, we tend to remember our successes, but I have seen several impressive responses with capecitabine in dire circumstances. I have had women on capecitabine for a considerable period of time with relatively good quality of life.

— *Nancy E Davidson, MD.* Breast Cancer Update *2005 (5)*

ENDOCRINE THERAPY FOR POSTMENOPAUSAL WOMEN WITH METASTATIC DISEASE

Previously, patients received tamoxifen in the adjuvant setting, so we would use an aromatase inhibitor as front-line therapy in the metastatic setting. Fulvestrant was used second line, or we could use megestrol acetate, but for many women fulvestrant has a more convenient side-effect profile. Now that more women receive aromatase inhibitors in the adjuvant setting, we're using tamoxifen or fulvestrant as first-line treatment in the metastatic setting.

— *Harold J Burstein MD, PhD.* Patterns of Care *2005 (1)*

In my experience, patients tolerate the fulvestrant injections just fine. We have randomized data comparing fulvestrant versus anastrozole in patients who have already received tamoxifen, but the optimal sequence for using fulvestrant is still undetermined. In choosing between an aromatase inhibitor and fulvestrant, I ask my patients whether they prefer an injection or a pill. If they have transportation problems, then I use an oral agent. However, for the Medicare population, these drugs are very expensive. If the patient does not have adequate insurance coverage and can't afford them, a monthly injection may be better. Compliance is also an issue to be considered when choosing between a daily oral agent and a monthly injection.

— *Joanne L Blum, MD, PhD.* Patterns of Care *2005 (1)*

I use fulvestrant as third-line therapy in patients whose disease has progressed on tamoxifen and an aromatase inhibitor. That's the current indication, but it wouldn't surprise me to see it moved up because data from the randomized trials clearly suggest it is as effective as aromatase inhibitors in patients who progressed after tamoxifen. The clinical question is whether the patient prefers a pill versus a parenteral injection. For some patients, the injection is easier, but most patients prefer taking a pill. In my experience, the tolerability of fulvestrant is similar to that of the aromatase inhibitors.

— *Daniel F Hayes, MD.* Breast Cancer Update *2004 (6)*