Research To Practice: Chemotherapy for Metastatic Disease

27TH ANNUAL San Antonio Breast Cancer Symposium 22

The Patterns of Care Study indicates that key factors determining choice of systemic treatment in the metastatic setting are patient age, performance status, site of disease and ER and HER2 receptor assay results. Endocrine therapy alone is generally utilized in patients with good performance status and ER-positive tumors. Trastuzumab, usually in combination with chemotherapy, is widely utilized as first-line therapy for women with HER2-positive disease. A key issue in selection of chemotherapy is the choice between sequential single agents and combinations. Oncologists often use single agents for patients with good performance status, and the decisions regarding sequencing varies. Side-effect profiles alter choices in individual situations. Anthracycline-based regimens are commonly utilized in patients who have not previously received adjuvant chemotherapy. The combination of docetaxel and capecitabine is frequently utilized in women who have previously received chemotherapy.

TREATMENT OF ASYMPTOMATIC CHEMOTHERAPY-NAÏVE PATIENTS WITH RECEPTOR-NEGATIVE DISEASE

The patient is a woman with no prior systemic therapy who has an ER-negative, HER2-negative tumor with rising tumor markers and asymptomatic bone metastases. What are your first- and second-line treatment recommendations?

	Age 40 (premenopausal)		Age 57		Age 75	
	1st line	2nd line	1st line	2nd line	1st line	2nd line
Capecitabine + docetaxel	6%	5%	4%	4%	1%	2%
Docetaxel	16%	16%	16%	17%	10%	15%
Paclitaxel	17%	9%	18%	8%	19%	8%
Platinum + taxane	4%	5%	4%	5%	1%	1%
Capecitabine	12%	17%	14%	19%	27%	26%
Gemcitabine	—	16%	—	18%	4%	15%
Vinorelbine	—	16%	—	16%	5%	15%
AC	15%	8%	15%	5%	6%	2%
AC + docetaxel	14%	—	13%	—	3%	—
Other chemotherapy	8%	5%	10%	5%	6%	3%
No chemotherapy	8%	3%	6%	3%	18%	13%

SOURCE: *Breast Cancer Update* Patterns of Care Study, 2004.

TREATMENT OF SYMPTOMATIC CHEMOTHERAPY-NAÏVE PATIENTS WITH RECEPTOR-NEGATIVE DISEASE

The patient is a woman with no prior systemic therapy who has an ER-negative, HER2-negative tumor with bone and lung metastases and is symptomatic. What are your first- and second-line treatment recommendations?

	Age 40 (premenopausal)		Age 57		Age 75	
	1st line	2nd line	1st line	2nd line	1st line	2nd line
Capecitabine + docetaxel	15%	9%	14%	5%	12%	4%
Docetaxel	4%	15%	7%	15%	15%	18%
Paclitaxel	2%	8%	3%	10%	15%	8%
Platinum + taxane	16%	12%	17%	8%	12%	—
Capecitabine	—	9%	—	11%	12%	21%
Gemcitabine	—	13%	—	15%	4%	17%
Vinorelbine	—	8%	—	10%	5%	23%
AC	23%	8%	22%	9%	15%	3%
AC + docetaxel	30%	1%	27%	1%	6%	—
AC + paclitaxel	4%	1%	4%	1%	1%	—
Other chemotherapy	6%	16%	6%	15%	3%	6%

SOURCE: *Breast Cancer Update* Patterns of Care Study, 2004.

TREATMENT OF ASYMPTOMATIC PATIENTS WITH RECEPTOR-NEGATIVE DISEASE AFTER ADJUVANT AC-PACLITAXEL

The patient is a woman treated two years ago with adjuvant AC → paclitaxel for an ER-negative, HER2-negative tumor with rising tumor markers and asymptomatic bone metastases. What are your first- and second-line treatment recommendations?

	Age 40 (premenopausal)		Age 57		Age 75	
	1st line	2nd line	1st line	2nd line	1st line	2nd line
Capecitabine + docetaxel	11%	3%	9%	2%	3%	2%
Docetaxel	29%	14%	29%	14%	15%	12%
Paclitaxel	8%	4%	8%	4%	6%	3%
Platinum + taxane	6%	4%	6%	3%	1%	—
Capecitabine	18%	20%	20%	19%	36%	24%
Gemcitabine	8%	25%	9%	26%	8%	25%
Vinorelbine	8%	14%	7%	18%	11%	18%
Other chemotherapy	5%	12%	5%	10%	3%	2%
No chemotherapy	7%	4%	7%	4%	17%	14%

SOURCE: *Breast Cancer Update* Patterns of Care Study, 2004.

TREATMENT OF SYMPTOMATIC PATIENTS WITH RECEPTOR NEGATIVE DISEASE AFTER ADJUVANT AC-PACLITAXEL

The patient is a woman treated two years ago with adjuvant AC → paclitaxel for an ER-negative, HER2-negative tumor who now has bone and lung metastases and is symptomatic. What are your first- and second-line treatment recommendations?

	Age 40 (premenopausal)		Age 57		Age 75	
	1st line	2nd line	1st line	2nd line	1st line	2nd line
Capecitabine + docetaxel	41%	9%	41%	7%	17%	4%
Docetaxel	9%	5%	10%	5%	18%	8%
Paclitaxel	1%	—	1%	1%	7%	1%
Platinum + taxane	24%	2%	24%	4%	9%	—
Capecitabine	1%	16%	1%	17%	17%	30%
Gemcitabine	6%	29%	6%	31%	15%	29%
Vinorelbine	—	22%	—	21%	8%	22%
AC	1%	2%	1%	1%	—	—
AC + docetaxel	4%	—	4%	—	—	—
Other chemotherapy	13%	15%	12%	13%	9%	6%

SOURCE: *Breast Cancer Update* Patterns of Care Study, 2004.

SELECT PUBLICATIONS

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CHEMOTHERAPY IN THE METASTATIC SETTING

I believe that single-agent sequential therapy is still the best way to manage metastatic breast cancer in most patients. It is less toxic, you're not lowering dose — and perhaps efficacy — below a threshold level, and survival is identical. Additionally, other drugs can be offered later. I believe single-agent sequential therapy is the way to go, and I start with capecitabine first in most patients.

I don't believe vast differences exist with regard to responses and confidence intervals; however, there are exceptions, such as the patient with terrible bone pain or in whom another doubling of their liver or pulmonary metastases will be catastrophic. While achieving a faster response is helpful in these cases, these are the minority of patients. When I use combinations, I use agents like capecitabine and docetaxel. In chemotherapy-naïve patients, anthracyclines and taxanes have high response rates, but in the last several years in my practice I have started with a combination regimen in only about 10 percent of patients. Breast cancer is not high-grade lymphoma or acute myeloid leukemia. We have time to work with the patients. This is a tough problem for which all of our therapy is palliative.

— Hyman B Muss, MD

In the metastatic setting, I generally use sequential single agents rather than combination therapy, except when an early response is vital, such as lymphangitic pulmonary disease. The sequence depends on the patient's prior therapy, comorbid conditions and lifestyle, so it's extremely variable.

I usually use a taxane, as most of the patients who are relapsing have not previously been treated with a taxane. I believe docetaxel is superior to paclitaxel, so for a younger or more seriously ill patient, I tend to use docetaxel every three weeks. In an older patient, I prefer weekly paclitaxel. If a patient has received a taxane and progresses, I generally use capecitabine, starting at two grams per meter squared per day for two weeks, then one week off. Some patients do fine, but some develop toxicity during the second week, so I shorten the duration of treatment with subsequent cycles.

I have become more liberal with combination therapy and if a patient is quite ill, I generally use capecitabine/docetaxel. Paclitaxel/gemcitabine is less toxic; however, docetaxel/capecitabine may be superior in terms of survival. Docetaxel has a survival advantage over paclitaxel, paclitaxel plus gemcitabine has a survival advantage over paclitaxel alone, and docetaxel plus capecitabine has been shown to be superior to docetaxel. In my experience the majority of patients I have treated with capecitabine/docetaxel have derived benefit, although they have also experienced significant toxicity.

— G Thomas Budd, MD

In metastatic disease, I believe sequential single-agent chemotherapy is a gentler approach than combination therapy and offers equivalent survival. Capecitabine is probably my favorite drug in this setting because it's oral, very active and extremely well tolerated as long as patients are properly educated about side effects. I prefer capecitabine before an anthracycline or a taxane in a patient who hasn't received either one.

— Melody A Cobleigh, MD

Patients with ER-negative, HER2-negative disease can only benefit from chemotherapy. I use combination chemotherapy when I need a quick response and sequential single agents when I don't. In a patient who has recently received adjuvant AC and a taxane and has relapsed, I would probably use capecitabine as my first choice for a sequential single agent. We don't know which drug is better in this situation, but women tend to like an oral drug and many would choose capecitabine. Interestingly, an ongoing EORTC trial (EORTC-10001) is comparing capecitabine and vinorelbine in these women.

— Martine J Piccart-Gebhart, MD, PhD