Research To Practice: HER2-Positive Disease

27TH ANNUAL San Antonio Breast Cancer Symposium 24

Availability of the humanized monoclonal antibody trastuzumab makes it critical to accurately determine HER2 tumor status in all patients with metastatic breast cancer. About three fourths of oncologists accept IHC results of 3+ as HER2-positive, but others require FISH confirmation. The 2004 Patterns of Care Study demonstrated that, in the first-line metastatic setting, trastuzumab is generally combined with chemotherapy — usually a taxane. Although no randomized clinical trial data are available addressing the questions of continuation of trastuzumab upon disease progression, this is a common practice pattern both in tertiary care centers and community oncology practice. In the adjuvant setting, trastuzumab is rarely utilized outside the context of a clinical trial.

INTERPRETATION OF HER2 TEST RESULTS

How would you interpret the following HER2 test results?

	IHC 3+	IHC 2+	IHC 1+
HER2-positive	78%	4%	0%
HER2-positive only with FISH confirmation	22%	96%	48%
HER2-negative	0%	0%	52%

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

TREATMENT OF PATIENTS WITH HER2-POSITIVE ASYMPTOMATIC METASTATIC DISEASE

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

	Age 40 (premenopausal)		Age 57		Age 75	
	First line	Second line	First line	Second line	First line	Second line
Chemotherapy alone	7%	17%	6%	17%	8%	18%
Trastuzumab alone	19%	3%	20%	3%	23%	10%
Trastuzumab + chemotherapy	70%	77%	71%	77%	61%	68%
No therapy	4%	3%	3%	3%	8%	4%

If you would use first-line trastuzumab (with or without chemotherapy), would you continue trastuzumab upon disease progression?

	Age 40 (premenopausal)	Age 57	Age 75
Yes, continue	84%	85%	86%

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

CHEMOTHERAPY REGIMENS USED WITH TRASTUZUMAB

Which chemotherapy regimen do you generally utilize with trastuzumab?

	First line	Second line	Third line
Docetaxel	40%	26%	10%
Paclitaxel	24%	6%	2%
Carboplatin/docetaxel	8%	16%	5%
Carboplatin/paclitaxel	6%	4%	4%
Vinorelbine	14%	34%	33%
Gemcitabine	6%	4%	22%
Other/none	2%	10%	24%

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

SCHEDULE OF TRASTUZUMAB

What trastuzumab schedule do you generally utilize?	Percent of physicians
Weekly	88%
Every three weeks	12%
Other	—

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

CLINICAL USE OF ADJUVANT TRASTUZUMAB

The patient is a woman in average health with a 1.2-cm, ER-positive, Grade II tumor and 3 positive lymph nodes. Tumor is HER2-positive as confirmed by FISH. Would you utilize trastuzumab for this patient? (Percent responding "yes")

	35 years old	65 years old
Trastuzumab off protocol	6%	4%
Trastuzumab clinical trial	75%	70%

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

SELECT PUBLICATIONS

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TREATMENT ALGORITHM FOR PATIENTS WITH HER2-POSITIVE METASTATIC DISEASE

I tend to put patients into three categories — low risk, intermediate risk and high risk. I look at the low-risk category as an opportunity to give trastuzumab by itself. As the risk increases, I add more agents. My double-agent combination has generally been a taxane and trastuzumab, while my three-drug combination has been taxane/platinum/trastuzumab.

If a patient is fairly asymptomatic and doesn't have much disease, I offer her trastuzumab by itself and see how it goes. I have had some patients do very well with trastuzumab monotherapy. We conducted a trial in which patients had the opportunity to have a lead-in induction with trastuzumab. Patients who had stable disease (or better) remained on trastuzumab for eight weeks and then received an additional eight weeks of treatment.

In patients who had evidence of progressive disease, paclitaxel and carboplatin were added to the trastuzumab. It was a small trial of 63 patients, but if you look back and see how the patients fared, we didn't lose any ground during those first eight weeks in patients who didn't benefit from trastuzumab.

For a patient who clearly has visceral metastases and is symptomatic, I use the three-drug combination with a platinum included. The other patients fall in the mix, and we discuss which one to start with and how aggressive to be.

— Howard A Burris III, MD

I have been using carboplatin/docetaxel/trastuzumab frequently, especially in patients with bulky disease and visceral crises. My choice of which chemotherapeutic agent to use is guided by the toxicities a patient is willing to tolerate. A woman with newly diagnosed metastatic disease may feel absolutely violated by the idea of hair loss with the use of a weekly taxane. I also like the vinorelbine/trastuzumab combination. It's well-tolerated and generates good responses.

Once a patient reaches an optimal response on combination therapy, I discontinue the chemotherapy and maintain them on trastuzumab almost indefinitely. Some of my patients have been on monotherapy for three or four years, if only to avoid the possibility of upregulating proliferative mechanisms when trastuzumab is stopped.

Trastuzumab monotherapy is a reasonable option for patients with small-volume, HER2-positive disease who are not open to the idea of chemotherapy. Chuck Vogel demonstrated a 47 percent clinical benefit with trastuzumab monotherapy in chemotherapy-naïve patients with measurable metastatic disease. I tend to use trastuzumab with chemotherapy up front and then apply trastuzumab alone as maintenance treatment.

— Maria Theodoulou, MD

SELECTION AND INTERPRETATION OF HER2 TESTING

Every patient with metastatic breast cancer in my practice has her tumor evaluated for HER2 gene amplification by FISH. Tumors with an IHC score of 3+ should be evaluated by FISH, because they may not have gene amplification. In tumors with an IHC score of 0 or 1+, three percent and seven percent, respectively, will have HER2 gene amplification by FISH. We need to determine HER2 status accurately because it is a matter of life or death.

— Melody A Cobleigh, MD

We recommend an algorithm that starts with immunohistochemistry because it is an easier, less expensive test to do. If the tumor is IHC 0, 1+ or 3+, no further testing is necessary. If the tumor is IHC 2+, reflex FISH testing is recommended. At our facility, the pathologists automatically perform the FISH analysis. We believe perhaps it's not a good idea to do FISH testing for every tumor because the majority will be negative.

— Edith A Perez, MD