Small HER2-Positive Breast Ca Needs Adjuvant Tx

BY BRUCE JANCIN

SAN ANTONIO — Women with HER2-positive breast cancers 1 cm or less in size have a surprisingly high 23% risk of relapse within 5 years, according to a first-of-its-kind study from the University of Texas M.D. Anderson Cancer Center, Houston.

That's a recurrence rate more than threefold greater than in similarly sized HER2-negative tumors. This new finding indicates that women with small HER2-positive tumors should be considered candidates for adjuvant systemic therapy, which is not now the case, Dr. Ana M. Gonzalez-Angulo said at the San Antonio Breast Cancer Symposium.

The recurrence risk associated with small HER2-positive breast cancers has not been evaluated previously in a large study. Affected women were excluded from the major clinical trials of trastuzumab (Herceptin) in HER2-positive breast cancer. The assumption has been that the recurrence risk is low enough not to warrant routine adjuvant therapy.

Indeed, current National Comprehensive Cancer Network guidelines don't recommend adjuvant systemic therapy for any T1a tumors—that is, those 1-5 mm—and merely suggest discussing treatment with patients who have 6- to 10-mm T1b tumors without specifying what type of treatment should be considered.

"We found there's no difference in risk of these HER2-positive tumors based on a size of 1-5 mm or 6-10 mm," according to Dr. Gonzalez-Angulo, a breast medical oncologist at M.D. Anderson. She presented a retrospective study of 965 patients with T1a or b breast cancers diagnosed at the cancer center. None received adjuvant systemic therapy. Overall, 10% of the women had HER2-positive tumors.

The 5-year recurrence-free survival rate was 77.1% in patients with HER2-positive tumors and 93.7% in those with HER2-negative tumors. The distant recurrence-free survival rate was 86.4% in women with HER2-positive tumors, compared with 97.2% in patients with HER2-negative tumors.

In a multivariate analysis adjusted for age at diagnosis along with tumor grade, size, and hormone receptor status, HER2 status was the strongest independent predictor of recurrence risk. Women with HER2-positive tumors were at 2.7-fold greater risk of recurrence than were those with similarly sized HER2-negative tumors and at 5.3-fold increased risk of distant recurrences.

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DR. GONZALEZ-ANGULO

Compared with women who had hormone receptor-positive small tumors, those with HER2-positive tumors were at 5.1 times greater risk of recurrence and 7.8-fold greater risk of distant recurrence over 5 years of follow-up, Dr. Gonzalez-Angulo continued.

In a confirmatory analysis involving 350 breast cancer patients at two European centers, the 5-year relapse-free survival rate was 87.4% in women with HER2-positive T1a,b tumors and 97% in those with HER2-negative cancers.

Dr. Powel H. Brown, who was not involved in the study, said that although these small HER2-positive tumors will "absolutely" respond to trastuzumab, thereby reducing recurrence risk, he'd like to see patients with such tumors enrolled in clinical treatment trials.

"Is the toxicity of treatment worth the benefit? That's the issue that's not clear yet," noted Dr. Brown, professor of medicine at Baylor College of Medicine, Houston, and deputy editor of Cancer Prevention Research.

Dr. Gonzalez-Angulo agreed that opening up clinical trials to these patients is the best way to figure out optimal treatment regimens. She added that a Harvard University study is now recruiting 400 women. She reported having no financial conflicts of interest in this institutionally funded study. ■