Late Relapse a Concern in Tamoxifen/Radiotherapy

BY KATE JOHNSON
Montreal Bureau

CHICAGO — Late breast cancer recurrence may be emerging as a new concern in patients participating in a study on tamoxifen versus tamoxifen plus radiotherapy treatment, according to a Canadian expert.

Researchers from Toronto's Princess Margaret Hospital recently showed that the 5-year breast cancer relapse rate was significantly lower in 386 women over age 50 who were treated with the combination of radiation and tamoxifen after lumpectomy, compared with 383 women who were treated with lumpectomy and tamoxifen alone (N. Engl. J. Med. 2004;351:963-70).

"But the 5-year results may not be the whole story," lead investigator Anthony W. Fyles, M.D., reported at the annual meeting of the Radiological Society of North America.

Eight years of follow-up show a rise in breast cancer relapse rates in both the tamoxifen-only group and the group receiving tamoxifen and radiotherapy.

A small cohort of the study subjects now have been followed for 8 years, and preliminary data from these 87 women suggest that late relapse rates may be creeping up in both treatment groups, said Dr. Fyles, professor of radiation oncology at the University of Toronto.

"It's quite a small number of women, and we need to follow more of them for longer lengths of time, but we are concerned that we are starting to see quite a few more relapses, Dr. Fyles told this newspaper.

The published study showed that at 5 years, the relapse rate was 0.6% in the combination therapy group versus 7.7% in the tamoxifen-only group. But the 8-year data, although still showing a distinct advantage to the combination therapy, reveal increased relapse rates in both groups: 3.5% in the combination therapy group, compared with 18% in the tamoxifen-only group, he said.

Of particular concern in the 8-year follow-up are patients over aged 70 with tumor sizes of 1-2 cm, Dr. Fyles said. In this group, women who received combination therapy had no relapses. However women who received tamoxifen alone had a relapse rate of 17.6%.

The study design involved treatment with tamoxifen for 5 years, and the sudden increase in relapses could be partly explained by the termination of tamoxifen therapy at the 5-year mark, Dr. Fyles said.

"Of course, now what we do in current practice is that we often add an aromatase inhibitor after patients stop the tamoxifen. We don't know yet whether this reduces the risk of relapse, but the available data on these agents suggest that they will lower the risk of late relapse," for breast cancer patients, Dr. Fyles said at the meeting. ■

Tamoxifen Alone Not Enough In Node-Positive Breast Ca

BY BRUCE JANCIN
Denver Bureau

SAN ANTONIO — Postmenopausal women with node-positive, estrogen- and/or progesterone-receptor–positive breast cancer have a 25% better long-term outcome with a postsurgical regimen of chemotherapy followed by tamoxifen than with adjuvant tamoxifen alone, Kathy S. Albain, M.D., said at a breast cancer symposium sponsored by the Cancer Therapy and Research Center.

Ten-year results when chemotherapy and tamoxifen are given concurrently are significantly worse than with sequential therapy but better than with tamoxifen alone, added Dr. Albain, professor of medicine, hematology, and oncology and director of the breast cancer research program at Loyola University Chicago, Maywood, Ill.

She presented 10-year follow-up data from the Breast Cancer Intergroup of North America Trial 0100, in which 1,477 postmenopausal women with node-positive, endocrine-responsive disease were randomized to one of three postsurgical treatment regimens.

Ten-year disease-free survival was 48% in the tamoxifen arm; 53% in women who received concurrent cyclophosphamide, doxorubicin, 5-fluorouracil, and tamoxifen; and 60% in those who started on tamoxifen only after completing the triple-drug chemotherapy regimen.

The use of adjunctive chemotherapy in postmenopausal endocrine-responsive, node-positive disease has been controversial. But this study showed chemotherapy not only adds significant benefit to tamoxifen in terms of disease-free survival, but in overall survival as well, especially when given sequentially. The 10-year overall survival rate of women who received sequential chemotherapy followed by tamoxifen was 68%, compared with 62% with concurrent chemotherapy plus tamoxifen and 60% for tamoxifen alone.

A secondary purpose of the long-term analysis was to ascertain the value of tumor molecular biomarkers for prognosis as well as prediction of benefit from chemotherapy. Chemotherapy showed no benefit in the subset of patients whose tumor had a high estrogen-receptor score, had a low or intermediate nuclear grade, or was HER2 negative in the setting of one to three positive lymph nodes. In contrast, chemotherapy strongly enhanced disease-free survival in patients with low or intermediate levels of estrogen receptor in their tumor. ■

Obesity Linked to Poor Breast Cancer Outcomes

BY KATE JOHNSON
Montreal Bureau

CHICAGO — Women who are obese when they are diagnosed with early stage breast cancer have poorer outcomes than do women of normal weight—yet another reason for physicians to encourage weight control in their patients, according to Penny R. Anderson, M.D., a radiation oncologist at Fox Chase Cancer Center in Philadelphia.

"Obesity at the time of diagnosis significantly predicts poorer outcomes," she reported at the annual meeting of the Radiological Society of North America. "We found an increased risk of breast cancer death and distant metastases in obese women, compared with normal-weight patients, although they did not present with more advanced-stage disease."

The study included more than 2,000 women with stage I/II breast cancer who underwent lumpectomy, axillary dissection, and radiation therapy with or without systemic therapy.

The median age of the women was 58 years, with 22% considered normal weight, 43% considered overweight, and 35% considered obese.

The study, which had a median follow-up of 61 months, compared women in the three weight categories to determine independent predictors of local failure, distant metastases, cause-specific survival, and overall survival.

It found that the actuarial 5-year rates of distant metastases, cause-specific survival, and overall survival were the worst in obese women.

There were some statistically significant baseline differences between the weight groups, with the obese group comprising more women who were older and postmenopausal. However, there were no statistically significant differences between the groups in terms of tumor size or number of involved lymph nodes, she said. In addition, the local failure rate was no worse in the obese women. ■

Tamoxifen Does Not Appear to Increase The Risk of Stroke or Heart Attack

BY BRUCE JANCIN
Denver Bureau

SAN ANTONIO — Tamoxifen does not appear to increase the risk of either stroke or acute MI in women with breast cancer, Ann M. Geiger, Ph.D., reported at a breast cancer symposium sponsored by the Cancer Therapy and Research Center.

Previously, two large, randomized National Surgical Adjuvant Breast and Bowel Project studies—the P-1 Breast Cancer Prevention Trial and the B-24 trial involving treatment of patients with ductal carcinoma in situ—had suggested tamoxifen increased stroke risk. But such randomized trials are vulnerable to volunteer bias.

Dr. Geiger's nested case-control population-based study involving 532 breast cancer patients in a large HMO concluded that stroke risk should not enter into clinical decision-making about tamoxifen use in breast cancer patients.

On the other hand, although there were signals in prior studies that tamoxifen might have a cardioprotective effect, no such benefit was found in a separate Kaiser study involving 396 women with breast cancer. In this study, use of the nonsteroidal hormone didn't affect MI risk, said Dr. Geiger of Kaiser Permanente of Southern California, Pasadena.

What does matter a great deal in terms of preventing stroke and MI in women with a history of breast cancer is appropriate management of hypertension and diabetes, she stressed. In the Kaiser studies, hypertension that required medication was associated with 2.1-fold increased risk of MI and a 2.0-fold risk of stroke in breast cancer survivors. Diabetes requiring medication boosted stroke risk 2.4-fold and MI risk 3.0-fold.

Other key findings in the pair of studies were that chemotherapy for breast cancer was an independent risk factor for stroke, conferring a 2.7-fold increased risk, while radiation therapy was associated with a subsequent 2.9-fold increased risk of MI, she said

One study involved 179 Kaiser patients with a first invasive breast cancer followed by a first stroke during 1980-2001, along with 353 matched controls who were treated for breast cancer but did not have a stroke. Although the study identified chemotherapy as a risk factor for stroke, it wasn't possible to differentiate the impact of the various chemotherapy regimens used.

The other study involved 134 patients with invasive breast cancer who subsequently experienced a first MI and 262 matched controls with breast cancer who didn't.

In the two studies, neither cumulative dose of tamoxifen, duration of use, nor length of time since use was associated with stroke or MI.

Tamoxifen has been the leading hormonal therapy for patients with estrogen receptor–and/or progesterone receptor–positive breast cancer for nearly 3 decades. It has been shown to decrease the risks of ipsilateral recurrences as well as contralateral breast cancer. ■