Common Breast Cancer Regimen Comes In Third

BY BRUCE JANCIN
Denver Bureau

SAN ANTONIO — One of the most commonly used breast cancer chemotherapy regimens—the combination of doxorubicin and cyclophosphamide followed by paclitaxel—proved "significantly inferior" to two others in a major randomized trial, Dr. Margot Burnell said at a breast cancer symposium sponsored by the Cancer Therapy and Research Center.

The MA.21 study involved 2,104 women, from either Canada or the United States, with axillary lymph node–positive or high-risk node-negative operable breast cancer who were randomized to one of three 6-month intravenous chemotherapy regimens: doxorubicin and cyclophosphamide followed by paclitaxel, known as AC/T; another commonly used regimen consisting of cyclophosphamide, epirubicin, and fluorouracil (CEF); or 3 months of dose-dense epirubicin and cyclophosphamide followed by 3 months of paclitaxel (EC/T). (Dose-dense chemotherapy is delivered with briefer-than-standard intervals between doses.)

The hypothesis was that EC/T—the most recently developed and least widely used of the regimens—would prove superior.

An earlier trial in women with locally advanced breast cancer had established that 3 months of dose-dense EC was equivalent to 6 months of CEF, and the thinking was that tacking on 3 months of paclitaxel after EC would further enhance the dose-dense approach, explained Dr. Burnell, an oncologist who practices in St. John, N.B.

She presented a prespecified interim analysis showing that at a median 30.4 months, the primary study end point—recurrence-free survival—was significantly worse in the AC/T arm. (See table below.)

The AC/T arm also had more deaths, although this end point won't be formally analyzed until after another 2-3 years of follow-up.

In adjusted paired comparisons, patients in the AC/T arm were 49% more likely to have a recurrence than were those assigned to CEF, and 68% more likely to develop a recurrence than were those who received EC/T.

There was no significant difference in risk between the CEF and EC/T groups. Additional follow-up will be required to determine whether adding a taxane to dose-dense EC is worthwhile.

With regard to toxicities, patients on CEF or EC/T had substantially more febrile neutropenia than did those on AC/T. They also had more thromboembolic events, probably because of greater use of central lines.

Cardiotoxicity was similar across all three groups.

Neurotoxicity occurred primarily in conjunction with paclitaxel.

The trial was supported by the Canadian Cancer Society, the National Cancer Institute of Canada, the U.S. National Cancer Institute, Pfizer Inc., Bristol-Myers Squibb Co., Amgen Inc., Janssen-Ortho Inc., and Ortho Biotech Products L.P. ■

Interim Analysis of Major Breast Cancer Chemotherapy Trial

	Recurrence-free survival	Number of deaths
CEF	90.1%	50
EC/T	89.5%	47
AC/T	85.0%	65

Note: Based on a study of 2,104 women at a median 30.4 months' follow-up.
Source: Dr. Burnell

ELSEVIER GLOBAL MEDICAL NEWS

Affect, Quality of Life Predict Chronic Distress in Ca Patients

BY JEFF EVANS
Senior Writer

WASHINGTON — Breast cancer patients who are at risk of developing chronic distress may be identified at diagnosis by their low quality of life and high level of negative affectivity, Steven C. Palmer, Ph.D., reported at the annual meeting of the Society of Behavioral Medicine.

Psychological distress appears in approximately 25%-35% of women with breast cancer and is generally predicted by younger age, lower optimism, increased pessimism, declining functional status, and greater illness burden.

Most patients lose the feeling of distress over time, but few studies have examined the subset of patients who remain chronically distressed.

Dr. Palmer and his colleagues at the Abramson Cancer Center at the University of Pennsylvania, Philadelphia, are conducting an ongoing study of 154 patients with a mean age of about 53 years who had newly diagnosed ductal carcinoma in situ or breast cancer.

None of the patients had yet received chemotherapy. Most of the patients were white American (75%) and married (68%); 46% were college educated.

At diagnosis, 33% of the patients reported elevated distress on the Hopkins Symptom Checklist, but this decreased to 20% after 3 months and 21% after 6 months.

Most patients (58%) never reported feeling distressed, whereas 21% had a single episode of distress and another 21% had chronic distress (defined as two or more episodes).

Low baseline quality of life and high negative affectivity were independent predictors of chronic distress in a multivariate analysis. Together, they predicted 40% of the variance in chronicity of distress, according to Dr. Palmer.

The level of distress of women who experienced a single episode tended to decline to a nonclinically significant level by 3 months. These women also could not be differentiated from women with chronic distress, based on their baseline level of distress, which would make it difficult to conduct an interventional study on only chronically distressed women.

"You need another stratifier to be able to differentiate how these two" groups will respond to distress over time, Dr. Palmer said.

Women who were never distressed and those who had a single episode slowly improved throughout the 6-month period, whereas women with chronic distress remained at the same level of distress the whole period.

Overall, about 59% of women who were distressed at baseline recovered by 3 months.

"It's both significant and striking that women who have no distress have very high levels of baseline quality of life," Dr. Palmer said.

Those women had a significantly higher quality of life at baseline than women with one episode of distress. Those with one episode also had significantly higher quality of life than chronically distressed women did.

By the end of 6 months, quality of life had increased slightly among women who were never distressed and had substantially increased in women who had one episode of distress.

Quality of life declined, however, among women with chronic distress even though they started with a low level, he said.

The amount of supportive services that were used by women in each group also seemed to increase with the level of distress.

The study is planned to continue for another 6 months of follow-up. ■

Mammographic Density Confers Steep Rise in Breast Cancer Risk

BY MARY ANN MOON
Contributing Writer

Density on mammography accounts for "a substantial proportion of cases of breast cancer, particularly in younger women"—to the extent that 26% of all breast cancers and 50% of all those detected within 1 year of a negative screen result occur in women whose mammograms show extensive breast density.

"The marked increase in the risk of breast cancer associated with extensive mammographic density … is probably due to cancers that were present at the time of screening but were not detected because of masking by dense breast tissue," researchers reported in the New England Journal of Medicine.

Dr. Norman F. Boyd of the Ontario Cancer Institute, Toronto, and his associates assessed the relationship between mammographic density and the risk of breast cancer developing during follow-up.

The researchers used data from three large case-control studies: the Canadian National Breast Screening Study, the Screening Mammography Program of British Columbia, and the Ontario Breast Screening Program.

A total of 1,112 case-control pairs were followed for up to 8 years after baseline mammography. Mammographic density was determined by two independent methods, and results were similar in all three patient populations.

Women who developed breast cancer showed a higher percentage of dense tissue on baseline mammograms than did those who did not develop breast cancer, Dr. Boyd and his associates said (N. Engl. J. Med. 2007;356:227-36).

Women who had density in 75% or more of the mammogram had a rate of breast cancer that was nearly five times higher (odds ratio 4.7) than that for women who had density in less than 10% of the mammogram.

For the subgroup of women who were found to have cancer within 1 year of a negative screening result, those with density in 75% or more of the mammogram had a breast cancer rate nearly 18 times (odds ratio 17.8) higher than that of women with density in less than 10% of the mammogram.

These results indicate that masking, rather than rapid growth of tumors in dense breast tissue, is the most probable mechanism at work here, the investigators said. Thus, the best estimate of breast cancer incidence tied to mammographic density is "by combining cancers that were detected by screening with those that were diagnosed up to 12 months after a screening examination," they wrote.

In an editorial comment accompanying this report, Dr. Karla Kerlikowske of the University of California, San Francisco, said that more frequent mammographic screenings probably would not improve cancer detection among women with extensive breast density, "because the tumors are not visible, because the tumors may grow quickly between examinations, or both."

"The time has come to acknowledge breast density as a major risk factor for breast cancer and to determine, develop, and test the best ways to measure breast density in clinical practice and use this measurement to maximize primary and secondary prevention of breast cancer," Dr. Kerlikowske commented (N. Engl. J. Med. 2007;356:297-300). ■