Common Breast Cancer Regimen Comes In Third

BY BRUCE JANCIN
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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; an alternative 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 CEF would further enhance the dose-dense approach, explained Dr. Burnell, an oncologist who practices in St. John, N.B.

She presented a pre-specified 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 may be influenced by an azytely until after another 2.5 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 chemotherapy 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.

Neurotoxicity was similar across all three groups.

Cardiotoxicity was maximal in the CEF arm and the AC/T arm had more neurotoxicity, but few patients had neurotoxicity.

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

<table>
<thead>
<tr>
<th>Recurrence-free survival</th>
<th>Number of deaths</th>
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<tbody>
<tr>
<td>CEF</td>
<td>90.1%</td>
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<tr>
<td>EC/T</td>
<td>89.5%</td>
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<tr>
<td>AC/T</td>
<td>85.0%</td>
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Note: Based on a study of 2,104 women at a median 30.4 months follow-up.

Source: Dr. Burnell

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 their last mammogram than did those who did not develop breast cancer, Dr. Boyd and his associates noted (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 reason 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 minimize primary and secondary prevention of breast cancer,” Dr. Kerlikowske commented (N. Engl. J. Med. 2007;356:297-300).