

# BREAST CANCER:

## INCREASING PATHOLOGICAL RESPONSE RATES WITH EFFECTIVE THERAPY

*The sequential use of docetaxel [Taxotere; Aventis Oncology] after Adriamycin [Pharmacia]/cyclophosphamide (AC) as a neoadjuvant regimen in primary operable breast cancer essentially doubles the rate of pathologic complete responses, according to final response data from the National Surgical Adjuvant Breast and Bowel Project (NSABP) Protocol B-27 reported at the San Antonio Breast Cancer Symposium. The Aberdeen neoadjuvant study also found improved clinical and pathologic response rates with sequential docetaxel following CVAP (cyclophosphamide, doxorubicin, vincristine, and prednisolone), compared with further cycles of CVAP, and showed a three-year overall and disease-free survival advantage for the docetaxel regimen. These findings signal the movement of taxanes to earlier in the treatment setting, and suggest the possibility of extending survival by using docetaxel neoadjuvantly.*

The sequential use of docetaxel after preoperative AC (AC/T) increased the breast tumor pathologic complete response (pCR) rate by 87%, clinical complete response rate by 60%, and lymph node-negative status by 15%, reported Harry D. Bear, MD, PhD, Professor of Surgery at Virginia Commonwealth University, Richmond, Virginia. Dr. Bear, Protocol Chair of the study, presented the data for the NSABP at the opening session of the conference.

While there are no survival data yet, Dr. Bear commented regarding the long-term effect of AC/T, "I am very optimistic." NSABP B-27 evaluated neoadjuvant AC (60/600mg/m<sup>2</sup> every three weeks) and docetaxel (100mg/m<sup>2</sup> every three weeks) in 2411 patients with large operable tumors. The schema for the three-arm trial was as follows:

- Group 1: four cycles of AC followed by surgery
- Group 2: four cycles of AC followed by four cycles of docetaxel and then surgery
- Group 3: four cycles of AC, then surgery followed by four cycles of docetaxel

For purposes of the response rate analyses, groups 1 and 3 were combined as the AC group and compared with group 2 the AC/T group.

The prior NSABP B-18 trial showed that patients achieving pCRs had improved survival. However, neoadjuvant AC in that trial only produced a 13% pathologic complete response rate. The aim of B-18 was to determine whether the addition of a taxane to AC neoadjuvant therapy (AC/T) would improve pCR rates and multiple outcomes.

### High Pathologic Complete Response Achieved

As anticipated, NSABP B-27 doubled the pCR rate with the addition of docetaxel, from 13.7% to 25.6%. No tumor was identified in 18.7% of surgical speci-

mens in the AC/T group versus 9.8% of specimens from AC patients; ductal carcinoma *in situ* was the only remaining lesion in 7% and 3.9% respectively. These differences were highly statistically significant (p<0.001), reported Dr. Bear.

Chairman of the Breast Committee for the NSABP, Terri Mamounas, MD, Associate Professor of Surgery, Northeastern Ohio Universities College of Medicine, Canton, Ohio, put the two trials into perspective. "We don't have overall survival figures for NSABP B-27, but we are encouraged. When we designed B-27, the 'unofficial' expectation was, hopefully, that we would see a 25% pathologic complete response, and indeed we did, compared to about 14% in NSABP B-18. So, in essence, we almost doubled the pathologic complete response rate.

"The leap of faith is whether this increase in pathologic complete response will translate into survival. We know that response to AC correlates with survival, but we don't know if response to AC followed by Taxotere will correlate in the same way. We expect it to be the case, however," he said in an interview.

### Other Outcomes

Nodal status was also positively influenced by docetaxel, though more modestly. After neoadjuvant therapy, negative nodes were found in about 58% of AC/T recipients, compared with 51% of AC patients, a statistically significant difference. Having a pCR was associated with a higher likelihood of achieving negative nodal status.

The AC/T regimen did not, however, significantly improve the rate of breast-conserving surgery. Lumpectomy was performed on 61.4% of patients after AC and 63.1% after AC/T. In Dr. Bear's view, the already high rate of lumpectomies in this optimally treated population is difficult to improve upon.