

Toxicity was slightly higher with the addition of docetaxel, attributable mainly to the occurrence of several cases of bowel perforation. This complication was virtually eliminated when the premedication steroid dose was reduced. Docetaxel recipients had more grade 4 toxicities (24% vs. 10%) and deaths (six patients vs. two patients) than those who did not receive it, but there was no difference in rate of infection.

Aberdeen Neoadjuvant Study: Increased Survival By Adding Docetaxel

Results were reported at this meeting from a Phase III neoadjuvant study conducted by investigators at the University of Aberdeen, Aberdeen, UK. At a median follow-up of 38 months, the sequential use of docetaxel after response to anthracycline-based primary chemotherapy (CVAP) resulted in significantly higher clinical and pathologic response rates, as well as higher three-year overall and disease-free survival rates, than were achieved by four further cycles of CVAP therapy.

The study included 167 patients with large (>3 cm) and locally advanced breast cancer (T3, T4, or Tx N2) who received four cycles of CVAP. The 104 patients with a clinical response were randomized to receive either four additional cycles of CVAP (n=52) or four cycles of docetaxel 10 mg/m² (n=52). Ninety-seven patients were evaluable for pathologic response, which was reviewed by two pathologists blinded to treatment.

Andrew Hutcheon, MD, Consultant Medical Oncologist, Aberdeen Royal Infirmary, Aberdeen, UK, reported the following results favoring the docetaxel arm after among 97 evaluable patients:

- Clinical response: 94% vs. 66% (p=0.001)
- Substantial overall pathologic response (grades 4 and 5): 53% vs. 34% (p=0.035)
- Complete pathologic response: 34% vs. 18% (p=0.001)
- Breast conserving surgery: 67% vs. 48% (p=0.01)
- Three-year disease-free survival rate: 90% vs. 77% (p=0.03)
- Three-year overall survival rate: 97% vs. 84% (p=0.05)

Dr. Hutcheon speculated on the improvement in survival: "I think when you give the doxorubicin regimen, you destroy a lot of cancer cells. But if you then give docetaxel, you kill the cells that are resistant to doxorubicin and this will give you better survival."

Similar Results in H. Lee Moffit Cancer Center Study

Researchers at H. Lee Moffit Cancer Center & Research Institute, at the University of South Florida, Tampa, Florida, also found a high rate of pCR with doxorubicin and docetaxel given sequentially in a dose-dense fashion. In their Phase II study of 42 women with Stage III disease, 24% achieved a pCR, and 30%

of women initially node-positive had no evidence of residual disease in the nodes, reported Susan Minton, D.O., lead investigator and Assistant Professor at the H. Lee Moffit Cancer Center.

Patients received 80 mg/m² of doxorubicin every two weeks for a total of three cycles. After a three-week rest period, they received 100 mg/m² of docetaxel every two weeks for a total of three cycles.

Neoadjuvant Chemotherapy with CMF: Clinical Outcomes

Another neoadjuvant study evaluated 181 Stage II breast cancer patients (T2, N0-1, M0) treated with two cycles of CMF (cyclophosphamide/methotrexate/5FU). After assessment of tumor response, the groups were randomized to either wide quadrantectomy and mastoplasticity (for tumors < 3.5 cm) or modified radical mastectomy (for tumors > 3.5 to 5 cm); both groups then received irradiation and adjuvant chemotherapy and/or hormonal therapy.

V.M. Ostapenko, MD, and colleagues from the Lithuanian Oncology Center, Vilnius, Lithuania, reported that the partial and complete tumor response after two cycles of neoadjuvant CMF in the whole group was 19.33%. For the quadrantectomy and mastectomy groups, respectively, the local recurrence rates were 3.23% and 2.76%, and the distant metastasis rates were 7.53% and 7.54%. Node-positive patients in both groups had statistically higher rates of metastases compared with node-negative patients: for quadrantectomy patients, 11.4% versus 5.1% and for mastectomy patients, 9.5% versus 2.8%, Dr. Ostapenko reported.

Conclusion

Emerging data show the value of using taxanes in the neoadjuvant setting, including a possible survival benefit. In the NSABP B-27 trial, reported at the San Antonio Breast Cancer Symposium, a regimen of AC followed by docetaxel essentially doubled the complete pathologic response rate over AC alone, from 13.7% to 25.6%. Similar improved responses were seen in studies from Aberdeen, UK, and the H. Lee Moffit Cancer Center, with enhanced survival also shown in the Aberdeen study. Investigators using the sequential regimen expressed optimism that longer follow-up will translate these pathologic complete responses into a survival benefit.

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