

**[77] BCIRG 005 main efficacy analysis: a phase III randomized trial comparing docetaxel in combination with doxorubicin and cyclophosphamide (TAC) versus doxorubicin and cyclophosphamide followed by docetaxel (AC→T) in women with Her-2/neu negative axillary lymph node positive early breast cancer.**

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*Background:* The relative benefits of adjuvant breast cancer chemotherapy with docetaxel in combination with anthracycline, or given sequentially after an anthracycline-based regimen, are unknown.

*Material and Methods:* We randomized women with axillary lymph node positive, central HER-2 nonamplified, breast cancer to either TAC (75/50/500 mg/m<sup>2</sup> q3wk x 6 cycles) or AC (60/600 mg/m<sup>2</sup> q3wk x 4 cycles) followed by T (100 mg/m<sup>2</sup> q3wk x 4 cycles). Patients were prospectively stratified by number of positive nodes (1-3 vs. 4+) and hormone receptor status. Patients with ER and/or PR positive (HR+) tumors received hormonal therapy after chemotherapy. The primary endpoint was disease-free survival (DFS) with 80% power to detect an absolute difference of 5%. Secondary endpoints included overall survival and safety.

*Results:* A total of 3298 patients (1649 per arm) were recruited between August 2000 and February 2003. Baseline characteristics were well balanced: age < 50 yrs 47%, 1-3 nodes 61%, HR+ 82%, T > 2 cm 58%. The planned 6 cycles of TAC were given to 93.5% of patients and 8 cycles of AC-T to 90.5%. Febrile neutropenia (17.9% vs. 8.5%) was more frequent with TAC, while grade 3 / 4 neutropenic infections were equivalent (8.7% with TAC vs. 8.0%). One septic death occurred in the TAC arm. Grade 3 / 4 non-hematological toxicity rates were fatigue (5.2% vs. 6.3%), nausea (4.5% vs. 4.1%), vomiting

(4.2% vs. 4.1%), diarrhea (2.9% vs. 3.1%), stomatitis (2.6% vs. 3.0%), peripheral edema (1.3% vs. 2.6%), neuropathy-sensory (0.6% vs. 2.0%) and CHF (0.1% vs. 0.4%) in the TAC and AC-T arms, respectively. The other Grade 3 / 4 docetaxel specific toxicities (nail and skin toxicities were observed in less than 0.5% in both arms. The protocol specified main efficacy analysis triggered by 688 DFS events will be presented, with a median follow-up of 60 months.

*Discussion:* The safety profile of the two docetaxel-based adjuvant chemotherapy regimens is comparable with the exception of a higher incidence of febrile neutropenia with TAC. This analysis will define the relative efficacy of combination vs. sequential docetaxel-containing chemotherapy in the adjuvant treatment of women with node positive, HER-2 negative breast cancer.