

TAC Improves Disease Free Survival

Over FAC in Node Positive Early Breast Cancer Patients: 55 Months Follow-up

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This study accrued 1,491 patients from June 1997 to June 1999. The 1st planned interim analysis with a median follow-up of 33 months and 289 events presented at ASCO 2002 (Abs.141) showed significant improvement in disease free survival (DFS) in favor of TAC. This is the 2nd interim analysis at a median follow-up of 55 months with 399 DFS events. A statistical boundary of 0.001 for DFS adjusted for nodal (N) status was defined for this analysis.

For DFS, there were 172 events on TAC and 227 on FAC: 80% and 75% of pts on

Intent-to-Treat Efficacy Analyses Prospectively Powered (n=1,491)

DFS	Hazard Ratio TAC/FAC (95% CI)	P-value
Adjusted for N status (Primary endpoint)	0.72 (0.59-0.88)	0.0010
1-3 nodes (n=923)	0.61 (0.46-0.82)*	0.0009
4+ nodes (n=568)	0.82 (0.63-1.08)*	0.1629
Hormone Receptor Positive†	0.73 (0.57-0.94)	0.0132
Hormone Receptor Negative†	0.66 (0.47-0.93)	0.0163
Overall Survival		
Adjusted for N status	0.70 (0.53-0.91)	0.0080

*Ratio of Hazard Ratios: 1.34 (0.90-2.00), p= 0.1476, †: Centrally reviewed

TAC were alive and disease-free at 4 and 5 years respectively, vs.71% and 68% on FAC. For OS, there were 91 events on TAC and 130 on FAC: 89% and 87% of pts on TAC were alive at 4 and 5 years respectively, vs.

85% and 81% on FAC. HER2neu amplification was centrally reviewed. TAC/FAC DFS hazard ratio was 0.61 (0.42-0.90; p=0.0118) in HER2+ pts, and 0.76 (0.58-0.99; p=0.0380) in HER2- pts. There were no changes in the toxicity profile since the first interim analysis.

Conclusion:

TAC significantly improves DFS and overall survival over FAC and should be considered to be one of the most active adjuvant treatments in patients with node positive early breast cancer.

A Five-Year Update of the Aberdeen Trial

Docetaxel Primary Chemotherapy in Breast Cancer

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Background

Primary chemotherapy has been increasingly used in the treatment of operable breast cancer. Clinical response rates of more than 80% occur, although complete pathological responses (pCR), a surrogate marker for survival, occur in less than 20%. The Aberdeen trial and the NSABP B27 trials have demonstrated that the addition of docetaxel to primary chemotherapy results in an increased cPR. We now report survival in the Aberdeen trial.

Patients and Methods

Patients with large or locally advanced (T₃, T₄, or N₂) breast cancers received 4 X CVAP (cyclophosphamide 1000mg/m², doxorubicin 50mg/m², vincristine 1.5mg/m², prednisolone 40mg for 5 days). Those who had responded

(CR or PR) were randomized to receive either further 4 X CVAP or 4 X DOC (docetaxel 100mg/m²). All patients who failed to respond, received 4 X DOC (100mg/m²). Clinical and pathological responses were obtained and patients followed for a median of 65 months.

Results

162 patients were enrolled. 145 patients completed 8 cycles of chemotherapy. The breast cancers in 102 patients (66%) achieved a clinical response (PR or CR) following 4 X CVAP. Following randomization 50 patients received 4 X CVAP and 47 patients received 4 X DOC. In patients who received 8 cycles of chemotherapy the cCR & cPR (94% vs 66%) and pCR (34% vs 16%) response rates were higher (p=0.001 and

p=0.04) in those who received further DOC. Intention to treat analysis demonstrated cCR & cPR (85% vs 64%, p=0.03) and pCR (31% vs 15%, p=0.06).

A median follow up of 65 months has now been reached. At this time survival are 93% in those randomized to DOC versus 78% in the CVAP group (p=0.04), with 12 deaths in the CVAP arm and 4 in the DOC arm.

Discussion

This study had previously demonstrated that docetaxel would increase pathological response rates to primary chemotherapy (subsequently confirmed by NSABP B27). This is the first study to demonstrate that primary chemotherapy with docetaxel significantly increases 5-year survival.