Sequential Treatment with Epirubicin/Cyclophosphamide, Followed by Docetaxel vs. FEC120 in the Adjuvant Treatment of N+ Breast Cancer Patients: Final Survival Analysis of the German ADEBAR Phase III Study

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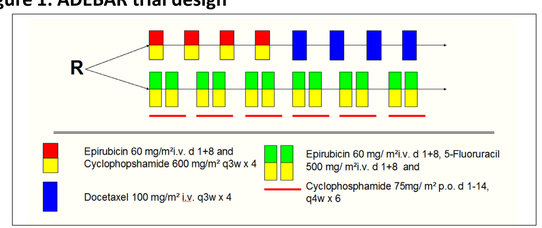
Background

Based on meta-analytic evidence, taxane containing adjuvant chemotherapy has been established as standard treatment in node-positive breast cancer. However, in the MA-21 study, adriamycin-cyclophosphamide, followed by paclitaxel (AC-P) was significantly inferior FEC120. We prospectively compared a sequential epirubicin-docetaxel chemotherapy regimen to FEC120.

Methods

The ADEBAR study was a multicenter phase III trial (n=1502) to evaluate whether breast cancer (BC) pts with > 3 axillary lymph node metastases benefit from a sequential anthracycline-docetaxel regimen (E90C–D: 4 cycles epirubicin [E] 90 mg/m2 plus cyclophosphamide [C] 600 mg/m2 q21 days followed by 4 cycles docetaxel [D] 100mg/m2 q21 days) compared to dose-intensive anthracycline-containing polychemotherapy (FE120C: 6 cycles E 60 mg/m² d 1+8, 5-FU 500mg/m² d 1+8 and C 75 mg/m² d 1-14, q4 weeks).(Fig 1) The Overall observation time (median – 95%CI) was 49.5 (47.4 – 51.3) months .

Figure 1: ADEBAR trial design



Results

Treatment was stopped prematurely in 3.7% of the pts in the E90C–D arm and in 8.0% in the FE120C arm due to toxicity (p=0.0009). Antibiotic treatment was given in 10.4% (E90C–D) vs. 19.7% (FE120C), G-CSF support in 39.2% vs 61.4 % and erythropoietin stimulation in 8.7% vs. 20.0%, respectively (p<0.0001). Haematological toxicity (leucopenia, neutropenic fever, thrombocytopenia, anemia) was significantly higher in the FE120C-arm.

At the time of the current analysis, 369 events of recurrence of breast cancer, were observed:

166 events in the FE120C group and 193 in the E90C–D group. The unadjusted hazard ratio (HR) was 0.877 (95 percent confidence interval, 0.722 to 1.065; p=0.3819, log-rank test). Overall survival in the two groups was not significantly different: (131 deaths with FE120C vs. 134 with E90C–D (HR 0.996, 0.783-1.267, p=0.9691). Subgroup analyses, stratifying for tumor size, lymph node involvement, hormone receptor and HER2-neu status showed no significant difference between the two treatment arms.

Table 1: Multivariate survival analysis

Factor	DSF		OS	
	HR	95%-CI	HR	95%-CI
Therapy (EC-DOC vs. FEC)	1.009	0.818 – 1.243	0.925	0.719 – 1.190
Tumor size (T1 vs. T2-4)	1.279 *	1.119 – 1.463	1.259 *	1.071 – 1.480
Lymph node involvement (N0. vs. N1-3.)	1.470 *	1.267 – 1.705	1.230 *	1.029 – 1.472
Grading (G1 vs. G2-3)	2.261	0.933 – 5.477	2.493	0.797 – 7.799
Hormone Receptor Status (neg. vs. pos.)	1.843 *	1.474 – 2.304	2.210 *	1.696 – 2.880
Her-2-neu (neg. vs. pos.)	0.803	0.640 – 1.007	1.060	0.972 – 1.156

Fig 3 a-d: Disease Free Survival Analysis in Subgroups

Fig 3a: DFS Subgroup HER2 neg/HR pos

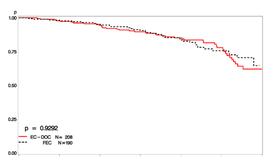


Fig 3b: DFS Subgroup HER2 neg/HR neg

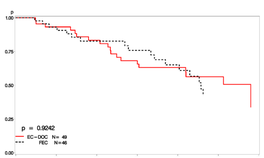


Fig 3c: DFS Subgroup HER2 pos/HR neg

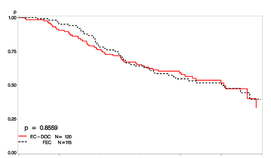


Fig 3d: DFS Subgroup HER2 pos/HR pos

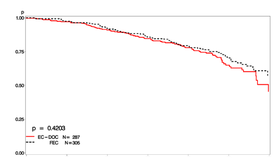
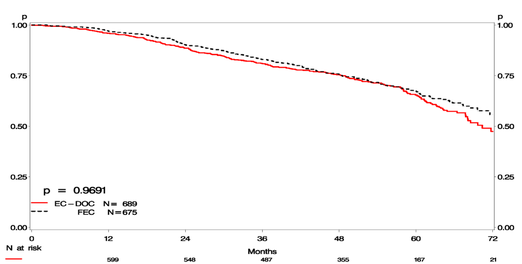


Figure 2: Disease free survival



Conclusion

Different toxicity profiles given, hematological toxicity in the FE120C group was more severe than in the E90C–D. In contrast to AC-P in earlier studies, EC-Doc provides a feasible and effective alternative option to dose-intensified FEC with different saftey profile in this high risk breast cancer cohort.

Acknowledgment

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