

# The prevalence and quantity of circulating tumor cells (CTCs) after adjuvant chemotherapy with and without anthracyclines in patients with HER2-negative early breast cancer (EBC).

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## Background

The use of anthracycline based chemotherapy in early breast cancer (EBC) patients has been well established. However, adverse effects like cardiotoxicity and efficacy in certain subgroups continue to be subjects of discussion. (Bird 2008; Gianni 2008). Based on data suggesting a limited benefit of anthracyclines in HER2-negative patients (Gennari 2008), the German SUCCESS C study randomly assigned patients with EBC to be treated with either anthracycline-containing or anthracycline-free chemotherapy. Since the prognostic value of CTCs in EBC has already been demonstrated in several trials (Lucci 2012; Rack 2010), we compared the prevalence of CTCs after the completion of chemotherapy between both treatment arms.

## Trial Design /Methods

The SUCCESS C trial was a randomized, open-label, Phase III study comparing disease free survival (DFS) in patients with HER2-negative EBC. Treatments were either 3 cycles epirubicin, 5-fluorouracil and cyclophosphamide followed by 3 cycles of docetaxel (FEC-DOC), or 6 cycles of an anthracycline-free regimen with docetaxel and cyclophosphamide (DOC-C). The CTC status at chemotherapy cycle 6 was prospectively evaluated using the FDA-approved CellSearch System (Veridex, USA).

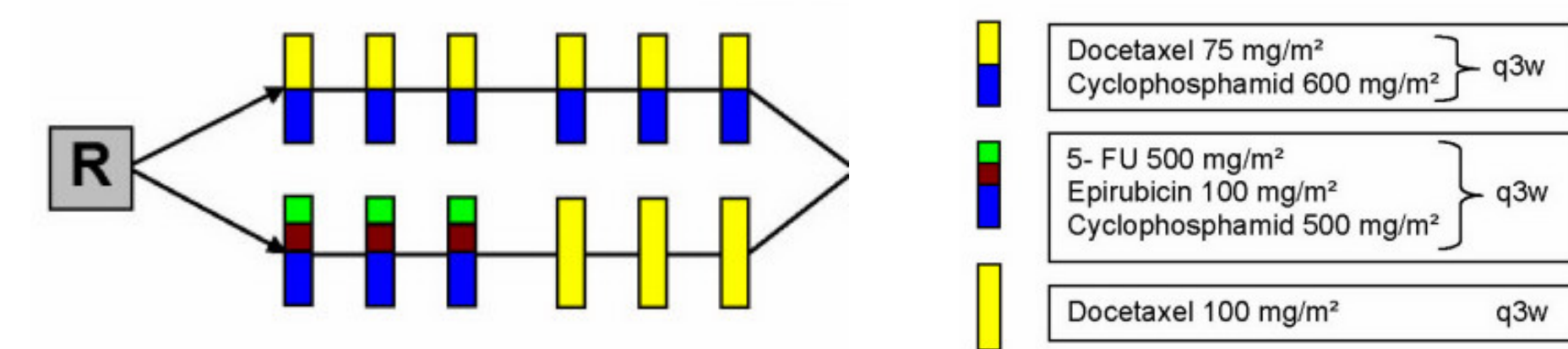


Figure 1: Clinical Trial Design – First Randomisation

## Results

Data on CTC status after chemotherapy are available for 1757 patients. Overall, CTCs were found in 220 (12.5%) patients (median 1, range 1 – 18 CTCs). One CTC was detected in 123 (55.9%), two CTCs in 53 (24.1%), three to five CTCs in 37 (16.8%), and more than five CTCs in 7 (3.2%) of these patients. Univariate analyses showed that CTC prevalence was not significantly associated with tumor size (pT1, pT2, pT3, pT4), nodal stage (pN0, pN1, pN2, pN3), grading (G1, G2, G3), histological type (ductal, lobular, other), estrogen-, or progesterone-receptor status (Chi-square tests, all  $p > 0.1$ ).

Variable	Total (N = 1757)	CTC positive (N = 220)	CTC negative (N = 1537)	p-value
Age (years)				0.499 <sup>1</sup>
Mean	55.1	55.6	55.0	
Range	24 - 79	30 - 77	24 - 79	
Tumor stage				0.107 <sup>2</sup>
pT1	700 (39.8%)	98 (44.5%)	602 (39.2%)	
pT2	936 (53.3%)	104 (47.3%)	832 (54.1%)	
pT3	96 (5.5%)	12 (5.5%)	84 (5.5%)	
pT4	25 (1.4%)	6 (2.7%)	19 (1.2%)	
Nodal stage				0.873 <sup>2</sup>
pN0	554 (31.5%)	70 (31.8%)	484 (31.5%)	
pN1	967 (55.0%)	117 (53.2%)	850 (55.3%)	
pN2	176 (10.0%)	24 (10.9%)	152 (9.9%)	
pN3	60 (3.4%)	9 (4.1%)	51 (3.3%)	
Histological grading				0.321 <sup>2</sup>
G1	135 (7.7%)	16 (7.3%)	119 (7.7%)	
G2	1084 (61.7%)	127 (57.7%)	957 (62.3%)	
G3	538 (30.6%)	77 (35.0%)	461 (30.0%)	
Histological type				0.992 <sup>2</sup>
ductal	292 (16.6%)	37 (16.8%)	255 (16.6%)	
lobular	1395 (79.4%)	174 (79.1%)	1221 (79.4%)	
other	70 (4.0)	9 (4.1%)	61 (4.0%)	
Estrogen receptor status				0.442 <sup>2</sup>
negative	36 (2.0%)	3 (1.4%)	33 (2.1%)	
positive	1719 (97.8%)	217 (98.6%)	1502 (97.7%)	
unknown	2 (0.1%)	0 (0.0%)	2 (0.1%)	
Progesteron receptor status				0.611 <sup>2</sup>
negative	185 (10.5%)	21 (9.5%)	164 (10.7%)	
positive	1572 (89.5%)	199 (90.5%)	1373 (89.3%)	

<sup>1</sup> Mann-Whitney U test    <sup>2</sup> Chi-square test

Table 1: Patient characteristics at baseline and association with CTC prevalence after adjuvant chemotherapy

## Results

There was no significant difference with respect to the prevalence of CTCs after chemotherapy between the two treatment arms (Chi-square test,  $p = 0.23$ ), as CTCs were detected in 11.6% (103 out of 889) of patients treated with the anthracycline-containing chemotherapy regimen and in 13.5% (117 out of 868) of patients treated with the anthracycline-free chemotherapy regimen.

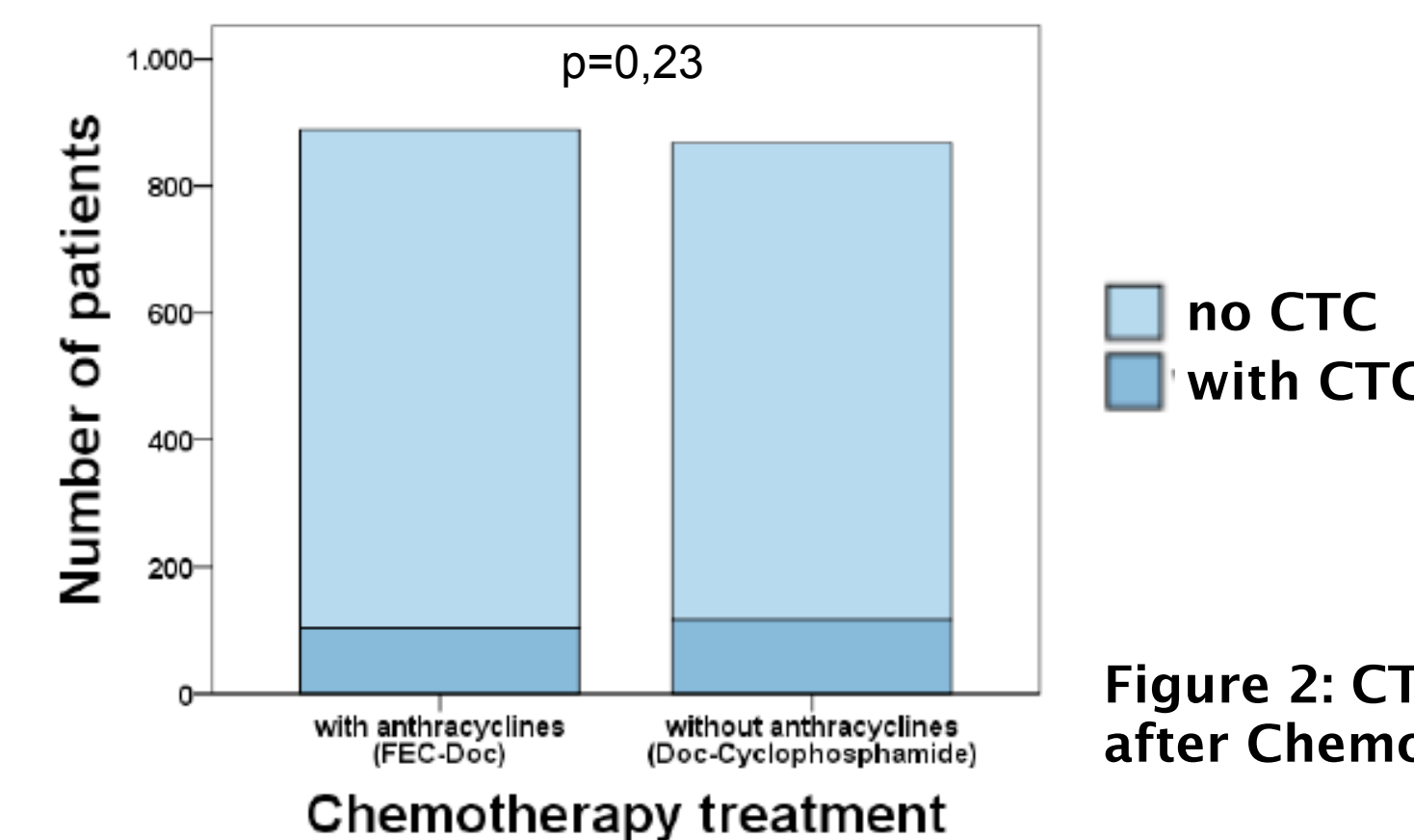


Figure 2: CTC prevalence after Chemotherapy

In addition, there was no significant difference between the two treatment arms with regard to the number of CTCs detected after chemotherapy in CTC-positive patients (FEC-DOC: median = 1, range 1 – 18; DOC-C: median = 1, range 1 – 8; Mann-Whitney U test,  $p = 0.30$ ).

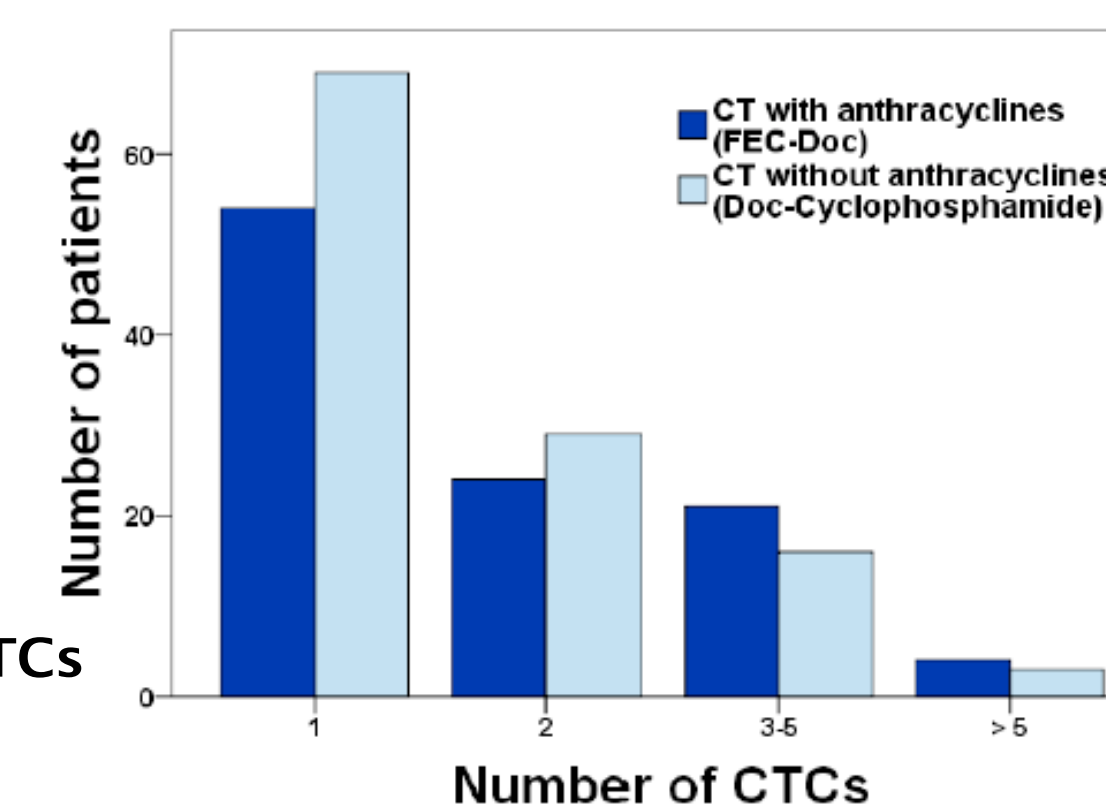


Figure 3: Number of CTCs found in 22 ml blood after chemotherapy

## Conclusion

The comparable prevalence and number of CTCs after the completion of chemotherapy may indicate that anthracycline-free chemotherapy is not inferior to anthracycline-containing chemotherapy in HER2-negative early breast cancer. This however, has to be confirmed by survival analyses.

## Acknowledgment



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