Circulating tumor cells (CTC) in peripheral blood of breast cancer patients two years after adjuvant chemotherapy depending on endocrine treatment - The German SUCCESS-Trial

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Background:

The prognostic significance of CTC in metastatic, as well as in primary breast cancer has been demonstrated (Rack et al., ASCO 2010). The optimal endocrine treatment strategy for postmenopausal patients (pts) with hormone sensitive breast cancer remains unclear.We analyzed the prevalence of CTC two years after primary diagnosis in patients with tamoxifen or anastrozole treatment.

Methods:

As part of the translational research project of the German SUCCESS-trial, we analyzed 23ml of peripheral blood from 307 N+ and high risk N- postmenopausal pts with hormone sensitive breast cancer two years after adjuvant taxane based chemotherapy and with tamoxifen or anastrozole treatment. The presence of CTCs was assessed with the CellSearchSystem (Veridex, USA). After immunomagnetic enrichment with an anti-Epcam-antibody, cells were labelled with anti-cytokeratin (8,18,19) and anti-CD45 antibodies to distinguish between epithelial cells and leukocytes. Standard within the study was early switch treatment (tamoxifen for 2 years, followed by anastrozle), while pts with contraindications against tamoxifen were allowed to receive anastrozole up-front.

Results:

In 10.1% of pts (n=31) >1 CTC was detected after the completion of chemotherapy (range 2-33), while 7.8% (n=24) presented with >1 CTC (range 2-99) two years after completion of chemotherapy. The median age in the tamoxifen group was 59.9 years and 59.8 in the anastrozole group. In the tamoxifen group, 33.0% of the pts had a pT1 tumor, 5.3 % G1 grading and 21.6% of the pts were node negative. In the anastrozole group, 30.0% of the pts had a pT1 tumor, 7.5 % G1 grading and 22.5% of the pts were node negative, respectively. None of these differences were statistically significant. After the completion of chemotherapy, 9.7% of the pts were CTC positive in the tamoxifen group (range number of cells: 2-33) and 11.3% in the anastrozole group (range of cells: 2-24), p=0.69. Two years after primary diagnosis, 7.9% of the pts were CTC positive in the tamoxifen group (range number of cells:2-99) and 7.5% in the anastrozole group (range cells: 2-5), p=0.90.

Conclusions

The prognostic relevance of CTC in peripheral blood of early breast cancer patients both before and after chemotherapy has been demonstrated. The presented data will add information on the monitoring potential of CTC during adjuvant endocrine treatment.

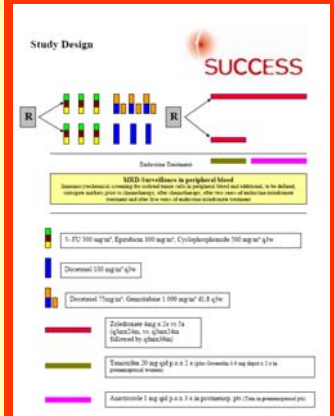


Fig 1: Study design of the SUCCESS A Study

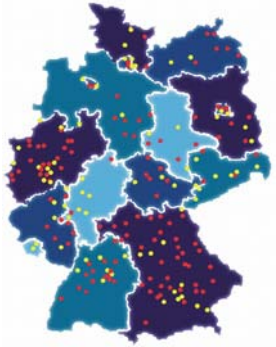
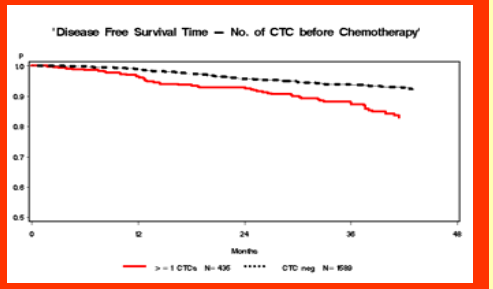


Fig. 2: Participating Centers of the SUCCESS A Study in Germany



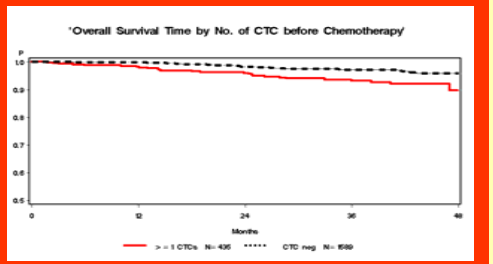


Table 3: Incidence of CTC

	Arimidex (%)	Tamoxifen (%)	P-Value
Number of Patients	80 (17.3)	227 (83.4)	
after chemotherapy			
0	59 (73.8)	172 (75.8)	
≥ 1	21 (26.3)	55 (24.2)	**0.719**
≥ 2	9 (11.3)	22 (9.7)	**0.691**
≥ 5	2 (2.5)	5 (2,2)	**0.878**
2 yrs. after end of chemotherapy			
0	69 (86.3)	185 (81.5)	
≥ 1	11 (13.8)	42 (18.5)	**0.334**
> 2	6 (7.5)	18 (7.9)	**0.902**
≥ 5	0	3 (1.3)	**0.302**

Table 4. Multivariate Proportional Hazard Model for disease-free and overall survival for different CTC cut-offs

	Hazard-Ratios adjusted for treatment					
	0 vs. 1 or more		0,1 vs. 2 or higher		0-5 vs. 6 or higher	
	OS	DFS	OS	DFS	OS	DFS
CTC before Therapy	1.907 *	1.878 *	2.242 *	2.025 *	4.040 *	4.730 *
Hormone Receptor Status (pos. vs. neg.)	3.326 *	2.073 *	3.287 *	2.020 *	3.632 *	2.232 *
Lymph node involvement (pos. vs. neg.)	1.835 *	1.698 *	1.825 *	1.664 *	1.936 *	1.751 *
Grading (G1 vs. G2-3)	3.287 *	2.961 *	3.476 *	3.182 *	3.378 *	3.018 *
Tumor size (T1 vs. T2-4)	1.879 *	1.629 *	1.863 *	1.655 *	1.801 *	1.587 *

Table 1: Patient Characteristics

	Arimidex (%)	Tamoxifen (%)	P-Value
Number of Patients	80 (17.3)	227 (83.4)	
Age (mean +- STD)	59.9 +- 6.4	59.8 +- 6.2	**0.689**
Tumor Size			
pT1	24 (30.0)	75 (33.0)	
pT2 - 4	55 (68.8)	152 (67.0)	
pTx	1 (1.2)	0	**0.219**
Lymph Node Metastases			
Absent (pN0)	18 (22.5)	49 (21.6)	
≥ 1 axillary LNM (pN1-pN3)	62 (77.5)	178 (78.4)	**0.865**
Grading			
GX	1 (1.2)	0	
G1	6 (7.5)	12 (5.3)	
G2-G3	73 (91.3)	215 (94.7)	**0.452**
Hormone Receptor Status			
Negative	1 (1.2)	2 (0.9)	
Positive	79 (98.8)	225 (99.1)	**0.773**
HER-2-neu Status			
undefined	4 (5.0)	6 (2.6)	
positiv	18 (22.5)	38 (16.7)	
negative	58 (72.5)	183 (80.6)	**0.212**
Histological Type			
Ductal	58 (72.5)	170 (74.9)	
Lobular	14 (17.5)	44 (19.4)	
Mixed ductal-lobular	7 (8.8)	13 (5.7)	
Other	1 (1.2)	0	**0.612**
Menopausal Status			
Perimenopausal	0	0	
Postmenopausal	80 (100)	227 (100)	
Primary Operation			
Breast Conserving	54 (67.5)	152 (67.0)	
Mastectomy	25 (31.3)	73 (33.0)	
Unknown	1 (1.2)	0	**0.820**
Radiotherapy			
Performed	64 (80.0)	189 (83.3)	
Not performed	16 (20.0)	38 (16.7)	**0.975**
Systemic Therapy			
Chemotherapy – FEC-D	38 (47.5)	104 (45.8)	
Chemotherapy – FEC-DG			

Table 2. Numbers of CTC before Chemotherapy

Numbers of CTC	No. of patients	% of all patients
0	1591	78.5
1	245	12.1
2	86	4.2
3-5	56	2.7
6-10	21	1.0
>10	27	1.3
ALL	2026	100.0

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