Persistance of circulating tumor cells (CTCs) in peripheral blood of breast cancer patients two years after primary diagnosis

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Background

In metastatic breast cancer, CTCs have shown to predict treatment efficacy and reduced survival. Recent data also indicate a potential prognostic relevance of CTCs after adjuvant chemotherapy. The SUCCESS trial evaluates the role of persisting CTCs two years after diagnosis in primary BC patients treated with zoledronate.

Methods

We analyzed 23 ml of peripheral blood in N+ and high risk N- primary breast cancer patients receiving 3 x FEC (500/100/500) – 3 x Doc100 q3w vs. 3 x FEC (500/100/500) – 3 x DocGemcitabine (75/1000 d1+8) chemotherapy followed by 2 years (4 mg q 3m x 24m) vs. 5 years (4 mg q 3m x 24m followed by q 6m x 36m) of zoledronate. CTC results after two years are shown. CTCs were assessed with the CellSearchSystem (Veridex, Warren, USA). After immunomagnetic enrichment with an anti-Epcam-antibody, cells were labelled with anti-cytokeratin (8,18,19) and anti-CD45 antibodies. Patients were examined after a mean of 29 months (range 20 - 43).

Results

The data of 579 patients two years after diagnosis are available. 4.3% of patients (n = 25) presented with > 1 CTC in peripheral blood. In patients with the detection of CTCs, the mean number of cells was 1 (range 1 - 29). While we found 1 CTC in 5.9% and 2 CTCs in 1.6% of patients, 1,5% had 3 - 5 CTCs, 1.2% > 5 CTCs. The presence of > 1 CTC did not correlate with tumor size (p = 0.41), nodal status (p = 0.41), grading (p = 0.45), hormonal receptor status (p = 0.92) or Her2-Status of the tumor (p = 0.59).

In this patient group, 9.7% and 6.9% of patients had presented with > 1 CTC at primary diagnosis and after chemotherapy, respectively. While the presence of CTCs at diagnosis was associated with CTCs after two years (p = 0.03), there was no correlation of CTCs after chemotherapy with the results at primary diagnosis (p = 0.08) or at two years (p = 0.23).

In 184 postmenopausal HR+ patients endocrine treatment data was analyzed. CTCs at two years were detected in 6.8% of patients on tamoxifen (n = 9), while 1.9% of patients were positive on anastrozole treatment (n = 1; p = 0.19).

Conclusions

CTCs persisting cytostatic, endocrine and zoledronate treatment, can be observed in a relevant number of clinically recurrence-free breast cancer patients. Longer follow-up within the German SUCCESS study will give further insight in their prognostic relevance and show whether they can be used for real time tumor phenotyping or serve as treatment target.

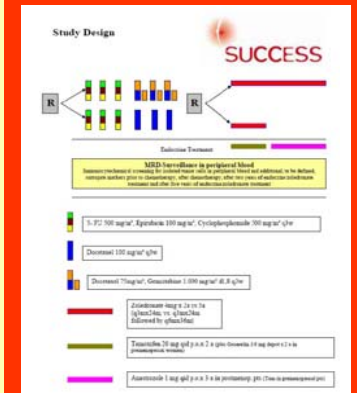

Figure 1: Study design of the SUCCESS-Trial

	CTC+	CTC-	p-value
Number of patients	59	520	
Tumor size			0.41
pT1	26 (44.1 %)	229 (44.0 %)	
pT2 - 4	33 (55.9 %)	291 (56.0 %)	
Lymph node status			0.41
pN0	19 (32.2 %)	187 (36.0 %)	
pN1-3	40 (67.8 %)	333 (64.0 %)	
Histopathological grading			0.45
G1	4 (6.8 %)	24 (4.6 %)	
G2 - 3	55 (93.2 %)	496 (95.4 %)	
Hormonal receptor status			0.92
Positive	45 (76.3 %)	367 (70.6 %)	
Negative	14 (23.7 %)	153 (29.4 %)	
Her2/neu-Status			0.59
Positive	16 (27.1 %)	148 (28.9 %)	
Negative	43 (72.9 %)	364 (71.1 %)	

Table 1: Tumor characteristics at primary diagnosis in relation to CTC status at 2 years

Figure 2: 251 active SUCCESS study centers in Germany

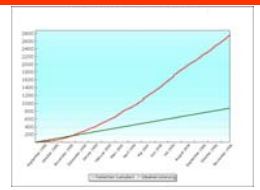

Figure 3: Planned recruitment of 3754 patients has been completed in March 2007

Figure 4: Detection of cytokeratin positive cells in peripheral blood using the CellSearchSystem (Veridex, USA)

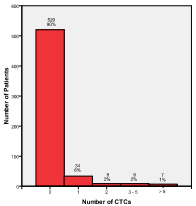

Figure 5: Number of CTCs in peripheral blood two years after primary diagnosis

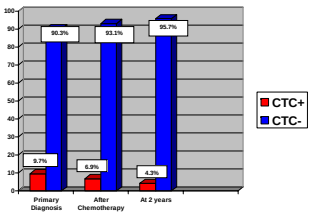

Figure 6: CTC positivity rate at primary diagnosis, after completion of chemotherapy and at two years

	Patients after CT	
	CTC - 533 (95%)	CTC + 25 (5%)
Patients before CT		
CTC - 504 (90%)	481 (86%)	23 (4%)
CTC + 54 (10%)	52 (9%)	2 (1%)

Table 2: CTC status in patients before chemotherapy and at two years

	Patients at 2 years	
	CTC - 478 (95 %)	CTC + 22 (5 %)
Patients before CT		
CTC - 466 (93%)	446 (89 %)	20 (4 %)
CTC + 34 (7 %)	32 (6 %)	2 (1 %)

Table 3: CTC status in patients after chemotherapy and at two years