

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

W. Janni; Th. Zwingers, P. Hepp, U. Andergassen, A. Schneeweiss, W. Lichtenegger, M.W. Beckmann, H. Sommer, K. Pantel, J. Salmen, J. Jueckstock, B. K. Rack
Ludwig-Maximilians-University, Muenchen, Germany; University of Heidelberg, Heidelberg, Germany; Henriettenstiftung, Hannover, Germany;
Charité University Hospital, Berlin, Germany; University of Erlangen, Erlangen, Germany; University Medical Center Hamburg-Eppendorf, Hamburg, Germany;



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 anastrozole), 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.

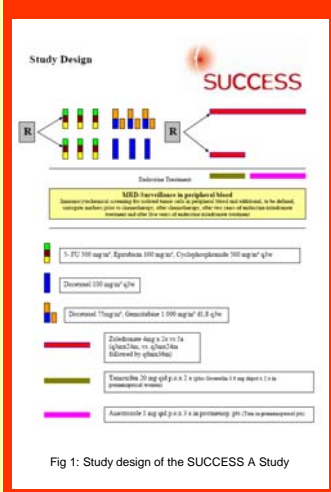


Fig 1: Study design of the SUCCESS A Study

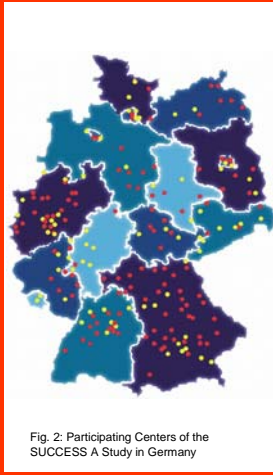


Fig. 2: Participating Centers of the SUCCESS A Study in Germany



Table 1: Patient Characteristics

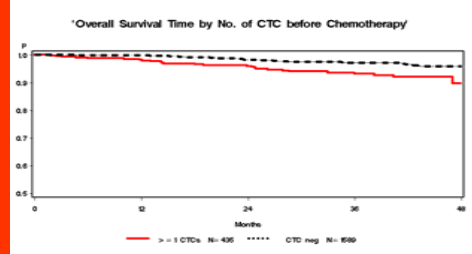
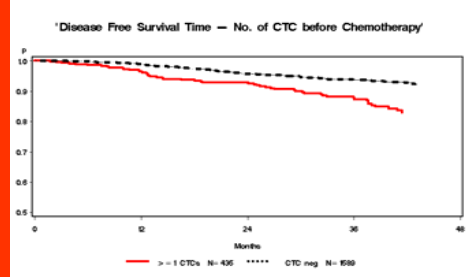
	Arimidex (%)	Tamoxifen (%)	P-Value
Number of Patients	80 (17.3)	227 (60.4)	
Age (mean ± STD)	59.9 ± 6.4	59.8 ± 6.2	0.889
Tumor Size			
pT1	24 (30.0)	71 (31.0)	
pT2 - 4	55 (68.0)	152 (67.0)	
pT5	1 (1.2)	0	0.229
Lymph-Node Metastases			
Absent (pN0)	18 (22.5)	49 (21.6)	
1 - 3 axillary LN (pN1-pN3)	62 (77.5)	178 (79.4)	0.960
Grading			
G1	1 (1.2)	0	
G2-G3	6 (7.5)	12 (5.3)	0.682
Hormone Receptor Status			
Negative	79 (98.8)	221 (96.1)	
Positive	1 (1.2)	6 (2.6)	0.773
HER-2-neu Status			
undefined	4 (5.0)	6 (2.6)	
positive	18 (22.5)	59 (26.0)	
negative	58 (72.5)	161 (71.4)	0.621
Histological Type			
Ductal	58 (72.5)	178 (79.4)	
Lobular	14 (17.5)	44 (19.4)	
Mixed ductal-lobular	7 (8.8)	15 (6.7)	
Other	1 (1.2)	0	0.042
Menopausal Status			
Premenopausal	0	0	
Postmenopausal	80 (100)	227 (100)	
Primary Operation			
Breast Conserving	54 (67.5)	152 (67.0)	
Mastectomy	26 (32.5)	75 (33.0)	0.620
Unknown	1 (1.2)	0	
Radiation Therapy			
Performed	64 (80.0)	189 (85.3)	
Not performed	16 (20.0)	38 (16.7)	0.075
Systemic Therapy			
Chemotherapy - FEC-4	78 (97.5)	223 (98.3)	

Table 3: Incidence of CTC

	Arimidex (%)	Tamoxifen (%)	P-Value
Number of Patients after chemotherapy	80 (17.3)	227 (63.4)	
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

	0 vs. 1 or more	1 vs. 2 or more	2 vs. 3 or more	3 vs. 4 or more	4 vs. 5 or more
Adjuvant Therapy	1.000	1.000	1.000	1.000	1.000
Endocrine Receptor Status (yes vs. no)	3.528*	2.893*	3.267*	2.923*	4.588*
Lymph node involvement (yes vs. no)	1.826*	1.628*	1.826*	1.864*	1.826*
Grading (G1 vs. G2-3)	3.282*	2.861*	3.476*	3.162*	3.378*
Tumor size (T1 vs. T2-4)	1.870*	1.623*	1.840*	1.855*	1.869*



Acknowledgements

3754 breast cancer patients participating in the SUCCESS trial
Unrestricted Research Grant by: Sanofi-Aventis, AstraZeneca, Amgen, Pfizer

All 251 participating study centers throughout Germany:

- Universitätsklinik Heidelberg
- Universitätsklinikum Erlangen
- Heinrich-Heine-Klinikum, Hannover
- Städtisches Klinikum Karlsruhe
- Klinikum Köln
- Städtisches Klinikum Krefeld
- Klinikum Mannheim
- Klinikum Regensburg
- Städtisches Klinikum Saarbrücken
- Städtisches Klinikum Schwerin
- Städtisches Klinikum Siegen
- Städtisches Klinikum Tübingen
- Städtisches Klinikum Ulm
- Städtisches Klinikum Weiden
- Städtisches Klinikum Würzburg
- Städtisches Klinikum Bayreuth
- Städtisches Klinikum Chemnitz
- Städtisches Klinikum Düsseldorf
- Städtisches Klinikum Gießen
- Städtisches Klinikum Jena
- Städtisches Klinikum Koblenz
- Städtisches Klinikum Konstanz
- Städtisches Klinikum Landshut
- Städtisches Klinikum Leipzig
- Städtisches Klinikum Magdeburg
- Städtisches Klinikum Mainz
- Städtisches Klinikum Merseburg
- Städtisches Klinikum München
- Städtisches Klinikum Nürnberg
- Städtisches Klinikum Oldenburg
- Städtisches Klinikum Osnabrück
- Städtisches Klinikum Passau
- Städtisches Klinikum Regensburg
- Städtisches Klinikum Rostock
- Städtisches Klinikum Salzburg
- Städtisches Klinikum Schwerin
- Städtisches Klinikum Siegen
- Städtisches Klinikum Tübingen
- Städtisches Klinikum Ulm
- Städtisches Klinikum Weiden
- Städtisches Klinikum Würzburg
- Städtisches Klinikum Bayreuth
- Städtisches Klinikum Chemnitz
- Städtisches Klinikum Düsseldorf
- Städtisches Klinikum Gießen
- Städtisches Klinikum Jena
- Städtisches Klinikum Koblenz
- Städtisches Klinikum Konstanz
- Städtisches Klinikum Landshut
- Städtisches Klinikum Leipzig
- Städtisches Klinikum Magdeburg
- Städtisches Klinikum Mainz
- Städtisches Klinikum Merseburg
- Städtisches Klinikum München
- Städtisches Klinikum Nürnberg
- Städtisches Klinikum Oldenburg
- Städtisches Klinikum Osnabrück
- Städtisches Klinikum Passau
- Städtisches Klinikum Regensburg
- Städtisches Klinikum Rostock
- Städtisches Klinikum Salzburg
- Städtisches Klinikum Schwerin
- Städtisches Klinikum Siegen
- Städtisches Klinikum Tübingen
- Städtisches Klinikum Ulm
- Städtisches Klinikum Weiden
- Städtisches Klinikum Würzburg
- Städtisches Klinikum Bayreuth
- Städtisches Klinikum Chemnitz
- Städtisches Klinikum Düsseldorf
- Städtisches Klinikum Gießen
- Städtisches Klinikum Jena
- Städtisches Klinikum Koblenz
- Städtisches Klinikum Konstanz
- Städtisches Klinikum Landshut
- Städtisches Klinikum Leipzig
- Städtisches Klinikum Magdeburg
- Städtisches Klinikum Mainz
- Städtisches Klinikum Merseburg
- Städtisches Klinikum München
- Städtisches Klinikum Nürnberg
- Städtisches Klinikum Oldenburg
- Städtisches Klinikum Osnabrück
- Städtisches Klinikum Passau
- Städtisches Klinikum Regensburg
- Städtisches Klinikum Rostock
- Städtisches Klinikum Salzburg
- Städtisches Klinikum Schwerin
- Städtisches Klinikum Siegen
- Städtisches Klinikum Tübingen
- Städtisches Klinikum Ulm
- Städtisches Klinikum Weiden
- Städtisches Klinikum Würzburg
- Städtisches Klinikum Bayreuth
- Städtisches Klinikum Chemnitz
- Städtisches Klinikum Düsseldorf
- Städtisches Klinikum Gießen
- Städtisches Klinikum Jena
- Städtisches Klinikum Koblenz
- Städtisches Klinikum Konstanz
- Städtisches Klinikum Landshut
- Städtisches Klinikum Leipzig
- Städtisches Klinikum Magdeburg
- Städtisches Klinikum Mainz
- Städtisches Klinikum Merseburg
- Städtisches Klinikum München
- Städtisches Klinikum Nürnberg
- Städtisches Klinikum Oldenburg
- Städtisches Klinikum Osnabrück
- Städtisches Klinikum Passau
- Städtisches Klinikum Regensburg
- Städtisches Klinikum Rostock
- Städtisches Klinikum Salzburg
- Städtisches Klinikum Schwerin
- Städtisches Klinikum Siegen
- Städtisches Klinikum Tübingen
- Städtisches Klinikum Ulm
- Städtisches Klinikum Weiden
- Städtisches Klinikum Würzburg