Circulating Tumor Cells (CTC) may Express HER2/neu in Patients With Early HER2/neu Negative Breast Cancer – Results of the German SUCCESS C Trial

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Background

There is growing evidence that the HER2/neu-status of distant metastases or minimal residual disease in blood and bone marrow may differ from the primary tumor in patients with breast cancer. The HER2/neu-status of CTCs was prospectively evaluated in patients with HER2/neu negative primary breast cancer randomized into the German multicenter SUCCESS C study.

Patient Characteristics

Clinical variable at baseline	CTC negative	CTC positive	p value
Age (Y)			.023*
<50	265 (71.8)	83 (61.0)	
>=50	104 (28.2)	53 (39.0)	
Menopausal status			0,051
pre-menopausal	137 (37.1)	64 (47.1)	
post-menopausal	232 (62.9)	72 (52.9)	
pT			0,11
1	141 (38.2)	65 (47.8)	
2	196 (53.1)	66 (48.5)	
3	25 (6.8)	4 (2.9)	
4	7 (1.9)	1 (0.7)	
pN			0,644
0	117 (31.7)	46 (33.8)	
1	209 (56.6)	75 (55.1)	
2	27 (7.3)	12 (8.8)	
3	16 (4.3)	3 (2.2)	
Histology			0,566
ductal	59 (16)	21 (15.4)	
lobular	5 (1.4)	0 (0.0)	
other	295 (79.9)	112 (82.4)	
missing	10 (2.7)	3 (2.2)	
Grading			0,587
1	31 (8.4)	8 (5.9)	
2	221 (59.9)	81 (59.6)	
3	117 (31.7)	47 (34.6)	
ER status			0,393
neg.	365 (98.9)	133 (97.8)	
pos.	4 (1.1)	3 (2.2)	
PR status			0,867
neg.	333 (90.2)	122 (89.7)	
pos.	36 (9.8)	14 (10.3)	

*significant at alpha=.05

Methods

The SUCCESS C trial is a randomized Phase III study comparing FEC-Docetaxel (FEC-Doc) vs. Docetaxel-Cyclophosphamid (DC) as well as 2 years of a lifestyle-intervention in patients with early, HER2/neu negative, node positive or high-risk node negative primary breast cancer.

As part of the translational research program, 23ml peripheral blood were drawn after adjuvant chemotherapy. In 505 samples, the prevalence of CTCs and their HER2/neu-status were assessed using the CellSearch System (Veridex, USA). After immunomagnetic enrichment with an anti-Epcam-antibody, cells were labelled with anti-CK8/18/19 and anti-CD45 antibodies. A fluorescein conjugate antibody with anti-CK-Fluorescein Isothiocyanate (FITC) was used for HER2/neu phenotyping. The cut-off for CTC-positivity was 1 CTC and for HER2/neu 1 CTC with strong HER2/neu-staining (+++).

Trial Design

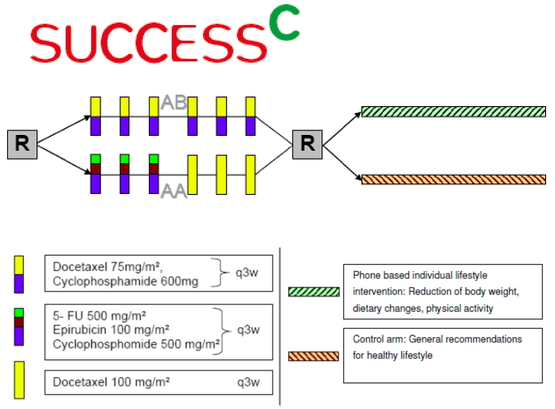

Figure 1: Clinical Trial Design

Results

26,9% of pts (n=136) were positive for CTCs (mean 1.78; range 1-7; median = 1). The number of detected CTC was distributed as follows: 1 CTC (n=76; 55.9%), 2 CTCs (n=35; 25.7%), 3 CTCs (n=13; 9.6%), 4 CTCs (n=7; 5.2%) and 5 CTCs (n=5; 3.7%). HER2/neu staning of CTCs was not detectable or weak in 26.5% (n=36) and 4.4% (n=6) of CTC positive patients respectively and therefore categorized as HER2/neu negative. In 32.4% of the CTC-positive patients (n=44), we detected moderate and in 36.8% (n=50) strong HER2/neu-staining of 1 CTC per sample. No association was found between CTCs or the HER2/neu-status of CTCs with tumor size, histopathological grading, hormone receptor status or axillary lymph node involvement.

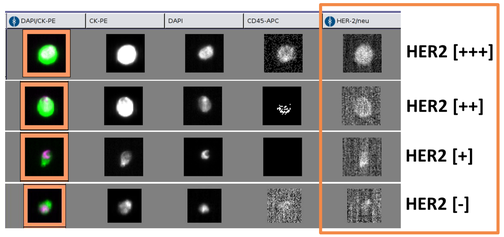

Figure 2: Sample Picture of HER2 positive CTCs

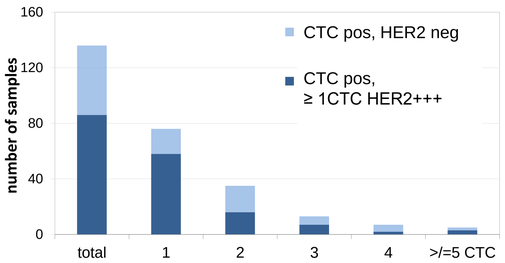

Figure 3: Fraction of blood-samples with HER2 positive CTCs

Results

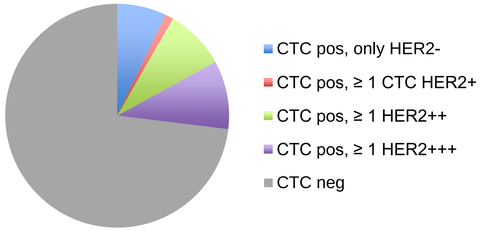

Figure 4: Intensity of HER2-Staining on CTCs (- = negative, + = weak, ++ = moderate, +++ = strong)

Conclusion

The data of this trial confirm previous findings that patients with HER2/neu negative primary breast cancer can show HER2/neu positive minimal residual disease. These results underline the importance of frequent HER2/neu determination during follow up and disease progression. Survival data within the Success C trial will give further insight into the tumor biology of HER2/neu negative disease.

Acknowledgment

Universitätsklinikum Erlangen
Universitätsklinikum Hamburg-Eppendorf
NOGGO
AGO
BNGO
SUCCESS BIG-Member

AACR Scholar-in-Training Award 2012

This abstract was selected for an AACR Scholar-in-Training Award supported by The American Association for Cancer Research.