HER2 expression on circulating tumor cells (CTC) in patients with early HER2-positive breast cancer: Results of the German SUCCESS B trial.

B. Jaeger (1), B. Rack (1), J. Neugebauer (1), U. Andergassen (1), C. Melcher (2), D. Mouarrawy (3), G. Ziemendorff (4), M. Clemens (5), E. v. Abel (6), G. Heinrich (7), K. Schueller (8), A. Schneeweiss (9), W. Lichtenegger (10), M. W. Beckmann (11), K. Pantel (12), H. Sommer (1), K. Friese (1), W. Janni (2) - on behalf of the SUCCESS study group -

1) Department of Gynecology and Obstetrics, Ludwig-Maximilians-University, Munich; 2) Department of Gynecology and Obstetrics, Heinrich Heine University, Duesseldorf, Germany; 3) Klinikum Bremerhaven-Reinkenheide, Bremerhaven, Germany; 4) Klinikum Ludwigsburg, Ludwigsburg, Germany; 5) Krankenanstalten Mutterhaus der Borromäerinnen, Trier, Germany; 6) Klinikum Schwäbisch Gmuend, Mutlangen, Germany; 7) Gynäkologisch-onkologische Schwerpunktpraxis , Fürstenwalde, Germany; 8) Stat-up Statistische Beratung und Dienstleistung, Munich, Germany; 9) National Center for Tumor Diseases, Heidelberg, Germany; 10) Department of Gynecology, Charité Medical University of Berlin, Berlin, Germany;11) Frauenklinik der Universität Erlangen, Erlangen, Germany; 12) Institute for Tumor Biology, Center of Experimental Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Background

Recent reports showed a discrepancy in the Her2-status of metastases or minimal residual disease in blood and bone marrow compared to the primary tumor in patients with breast cancer. The Her2-status of CTC was prospectively evaluated in the German multicenter SUCCESS B study.

Trial Design

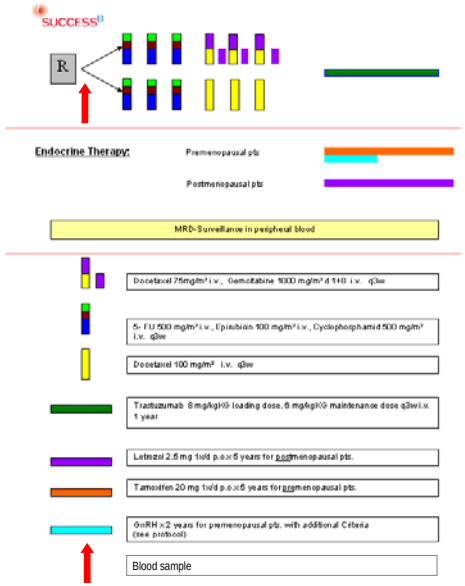

Figure 1: Clinical Trial Design

Methods

The SUCCESS B trial is a randomized Phase III study comparing FEC-Docetaxel (Doc) vs. FEC-Docetaxel-Gemcitabine (Doc-G) as well as Her2 targeted therapy with Trastuzumab as adjuvant treatment in patients with early, Her2 positive, node positive or high risk node negative primary breast cancer (Fig. 1 and Tab. 1). As part of the translational research program, 23ml of peripheral blood were drawn before adjuvant chemotherapy. In 638 samples CTC and Her2-status were assessed using the CellSearch System (Veridex, USA). After immunomagnetic enrichment with an anti-Epcam-antibody, cells were labeled with anti-CK8/18/19, anti-CD45 antibodies as well as a fluorescein conjugate antibody for Her2 phenotyping (Fig. 2). Cutoff for CTC-positivity was ≥1 CTC and for Her2 ≥1 CTC with strong Her2-staining (+++).

Clinical variable at baseline	Total no. of patients analyzed, N = 638 (%)	CTC negative, N =382 (%)	CTC positive, N =256 (%)
pT			
1	304 (47.65)	188 (49.21)	116 (45.31)
2	260 (40.75)	147 (38.48)	113 (44.14)
3	24 (3.76)	15 (3.93)	9 (3.52)
4	8 (1.25)	3 (0.79)	5 (1.95)
missing	8 (1.25)	29 (7.59)	13 (5.08)
pN			
0	334 (52.35)	202 (52.88)	132 (51.56)
1	187 (29.31)	114 (29.84)	73 (28.52)
2	49 (7.68)	22 (5.76)	27 (10.55)
3	27 (4.23)	15 (3.93)	12 (4.69)
missing	41 (6.43)	29 (7.59)	12 (4.69)
Histology			
ductal	233 (36.52)	127 (33.25)	106 (41.41)
lobular	22 (3.45)	12 (3.14)	10 (3.91)
other	338 (52.98)	211 (55.24)	127 (49.61)
missing	45 (7.05)	32 (8.38)	13 (5.08)
Grading			
1	6 (0.94)	5 (1.31)	1 (0.39)
2	219 (34.33)	128 (33.51)	91 (35.55)
3	365 (57.21)	216 (56.54)	149 (58.20)
missing	48 (7.52)	33 (8.64)	15 (5.86)
ER status			
neg.	364 (57.05)	215 (56.28)	149 (58.20)
pos.	232 (36.36)	137 (35.86)	95 (37.11)
missing	42 (6.58)	30 (7.85)	12 (4.69)
PR status			
neg.	325 (50.94)	193 (50.52)	132 (51.56)
pos.	269 (42.16)	158 (41.36)	111 (43.36)
missing	44 (6.90)	31 (8.12)	13 (5.08)
Menopause			
pre-menopausal	240 (37.62)	133 (34.82)	107 (41.80)
post-menopausal	398 (62.38)	249 (65.18)	149 (58.20)
Chemotherapy			0
FEC-DG	318 (49.84)	191 (50.00)	127 (49.61)
FEC-Doc	320 (50.16)	191 (50.00)	129 (50.39)

Table 1: Patient characteristics

Results

40.2% of pts (n=257) were positive for CTC (mean 4.52; range 0-1689). The number of detected CTC was distributed as follows: 1 CTC (n=112; 43.6%), 2 CTC (n=65; 25.3%), 3 CTC (n=36; 14.0%), 4 CTC (n=12; 4.7%) and ≥5 CTC (n=31; 12.1%) (Fig. 3). Her2 status on CTC was negative or weak in 12.5% (n=32) and 8.9% (n=23) of CTC positive patients respectively and therefore categorized as Her2 negative. In 21.4% (n=55) we detected moderate and in 57.2% (n=147) strong Her2-staining of ≥1 CTC per sample. Therefore 57.2% of CTC-positive samples were diagnosed as Her2 positive and 21.4% as questionable (Fig. 4). No association was found between the detection of CTC or the Her2-status on CTC with tumor size, histopathological grading, hormone receptor status or axillary lymph node involvement.

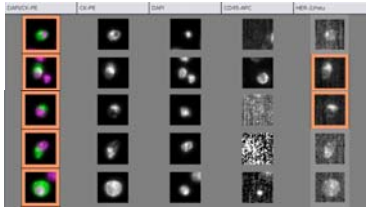

Figure 2: Sample Picture of Her2 positive CTCs

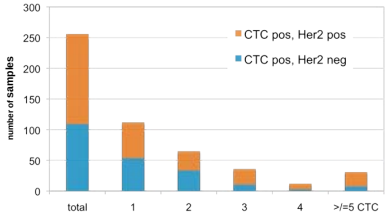

Figure 3: Fraction of blood-samples with Her2 positive CTCs

Results

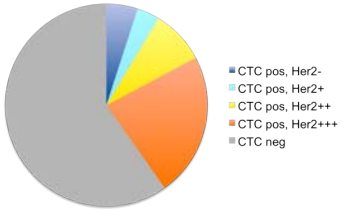

Figure 4: Intensity of Her2-Staining on CTCs (- = negative, + = weak, ++ = moderate, +++ = strong)

Conclusion

The data of this trial confirms the frequent discordance of Her2 expression on CTC compared to the primary tumor. Survival data within the Success B trial will give further insight into the tumor biology of Her2 positive disease and the role of the Her2-status on CTC to predict treatment efficacy.

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