Persistence of HER2-overexpression on circulating tumor cells (CTC) in patients after systemic treatment for HER2-positive breast cancer – Follow up results of the German SUCCESS B trial

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Background

The discordance between HER2-expression on circulating tumor cells (CTC) in peripheral blood and the primary tumor has already been shown by our study group for early breast cancer patients with HER2-positive tumors. Here, we compare the results to CTC prevalence and Her2-status of CTC after adjuvant chemotherapy.

Materials & Methods

The SUCCESS B trial compares FEC-Docetaxel (Doc) vs. FEC-Docetaxel-Gemcitabine (Doc-G) and Her2-targeted therapy with Trastuzumab as adjuvant treatment for patients with early, HER2-positive, node positive or high risk node negative primary breast cancer.

We prospectively analyzed 23ml peripheral blood before and 28 days after chemotherapy. CTC and HER2-status were assessed with the CellSearchSystem (Veridex, USA). After immunomagnetic enrichment with an anti-Epcam-antibody, cells were labeled with anti-Cytokeratin 8/18/19, anti-CD45 antibodies and a fluorescein conjugate antibody for HER2-phenotyping. Cutoff for CTC positivity was ≥ 1 CTC. HER2-positivity of CTC was assigned if at least one CTC showed strong HER2 staining (3+).

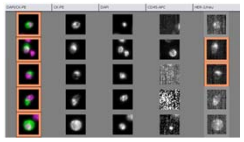


Figure 1: detected HER2 positive CTC

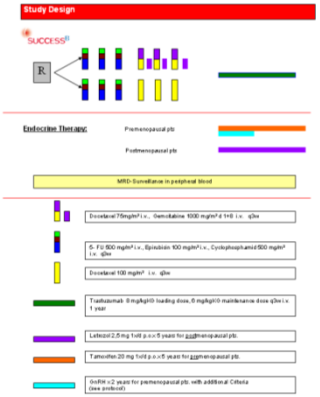


Figure 2: study design

Results

Valid data on CTC and their HER2-status both before and after chemotherapy were available for 392 patients. In 179 (45.7%) patients no CTC were detected before and after chemotherapy. CTC status changed from positive before to negative after chemotherapy in 104 (26.5%) patients and from negative before to positive after chemotherapy in 69 (17.6%) patients, while 40 (10.2%) patients had a consistently positive CTC status.

Patients were significantly more likely to change their CTC status from positive to negative than from negative to positive (McNemar test for related samples, p = 0.01). Of the 40 patients with CTC both before and after chemotherapy, 14 (35%) patients had HER2-positive CTC before and after therapy, and 9 (22%) patients had HER2-negative CTC at both time points. 7 (18%) patients had HER2-positive CTC before but not after chemotherapy, while 10 (25%) patients showed the reverse pattern (McNemar test, p = 0.63).

Table 1: Patient characteristics (n=392)

Age (years)	Mean	54.3
	Range	19 - 76
Menopausal status	premenopausal	153 (39.0%)
	postmenopausal	239 (61.0%)
Tumor stage	pT1	192 (49.0%)
	pT2	163 (41.6%)
	pT3	16 (4.1%)
	pT4	5 (1.3%)
	unknown	16 (4.1%)
Nodal stage	pN0	213 (54.3%)
	pN+	162 (41.3%)
	unknown	17 (4.3%)
Histological grading	G1	3 (0.8%)
	G2	142 (36.2%)
	G3	228 (58.2%)
	unknown	19 (4.8%)
Estrogen receptor status	negative	131 (33.4%)
	positive	245 (62.5%)
	unknown	16 (4.1%)
Progesteron receptor status	negative	152 (38.8%)
	positive	222 (56.6%)
	unknown	18 (4.6%)

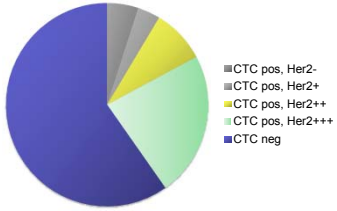
Table 2: Prevalence of CTC before and after chemotherapy (*p=0.01)

		CTC after chemotherapy		
		neg. (%)	pos. (%)	Total (%)
CTC before chemotherapy	neg. (%)	179 (45.7)	69 (17.6)	**248 (63.3)**
	pos. (%)	104 (26.5)	40 (10.2)	**144 (36.7)**
	Total (%)	**283 (72.2)**	**109 (27.8)**	**392 (100)***

Table 3: HER2 status of CTC in 40 Patients with persisting tumor cells (p=0.63)

		HER2 status of CTC after chemotherapy		
		neg. (%)	pos. (%)	Total (%)
HER2 status of CTC before chemotherapy	neg. (%)	9 (22.5)	10 (25.0)	**248 (47.5)**
	pos. (%)	7 (17.5)	14 (35.0)	**144 (52.5)**
	Total (%)	**283 (40)**	**109 (60)**	**40 (100)**

Tables and Figures



CAVE: Figure 2 und 3 analog den aktuellen Zahlen stehen noch aus!

Figure 2: Intensity of HER2-Staining on CTC before chemotherapy (- = negative, + = weak, ++ = moderate, +++ = strong)

Figure 3: Intensity of HER2-Staining on CTC after chemotherapy (- = negative, + = weak, ++ = moderate, +++ = strong)

Conclusion

Cytotoxic treatment does not seem to influence the HER2-status on CTC. Follow up data within the Success B trial will analyze the relevance of the HER2-expression of CTC to predict the efficacy of targeted treatment.

Acknowledgments

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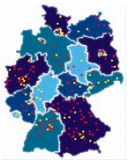

251 active SUCCESS study centers in Germany