

Prognostic relevance of circulating tumor cells (CTCs) before adjuvant chemotherapy in breast cancer patients – Results of the German SUCCESS-trial

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Background

The prognostic significance of CTCs in primary breast cancer has been demonstrated for 2026 patients of the German SUCCESS-study (Rack et al., in press). In this analysis the prognostic relevance of CTCs in peripheral blood at primary diagnosis in a different cohort of patients of the same trial with node positive or high risk N0 breast cancer in respect of disease free survival (DFS) and overall survival (OAS) was investigated.

Patients and Methods

As part of the translational research project we analyzed 23ml of peripheral blood from 1247 patients with breast cancer before adjuvant taxane based chemotherapy. Cells were separated by Oncoquick® (greiner bio-one, Frickenhausen, Germany) followed by labelling of epithelial cells with the anti-cytokeratine-antibody A45-B/B3 (Micromet, Munich, Germany), directed against cytokeratines 8, 18 and 19, and immunohistochemically staining with neu-fuchsin. All cytopspins were screened by two independent persons.

Results

In 21.1% of all patients (n=263) at least 1 CTC was detected (median 1.8, range 1-28), while 78.9% of the patients (n=984) were negative for CTCs before adjuvant chemotherapy. 38.3% of the patients had a pT1 tumor, 4.7% G1 grading and 27.4% of the patients were node negative. None of these factors were statistically significant for CTC detection. Survival data analyses showed a disease recurrence rate of 7.6% and a mortality rate of 3.8% (n=48). With a median follow up of 32 months 9.9% of the patients (n=26) showing CTCs relapsed, compared to 7.0% of the patients (n=69) who were CTC negative (p=.124). There was no statistically significant difference seen in OAS: 15 deaths (5.7%) occurred in patients with CTCs vs. 33 deaths (3.4%) in patients without CTCs (p=.11). In multivariate analyses only larger tumor size, detection of lymph node metastases and negative hormone receptor status were associated with reduced DFS and OAS (p<.05, respectively).

Conclusions

In contrast to our previous findings, in this cohort with a median follow up of 32 months the detection of CTCs in peripheral blood of early breast cancer patients before chemotherapy was not statistically associated with DFS or OAS maybe due to the small number of events and short follow up in this cohort. Further follow up will show, if this method can be used for risk stratification and monitoring of treatment efficacy in adjuvant breast cancer.

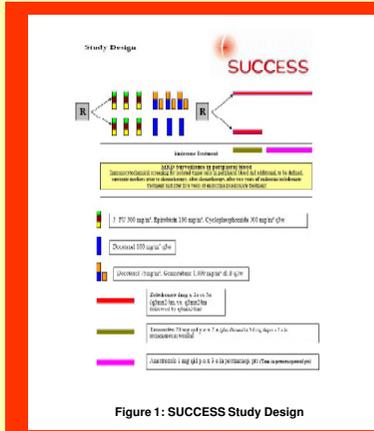


Figure 1: SUCCESS Study Design

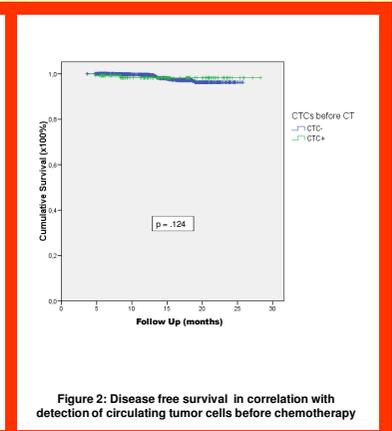


Figure 2: Disease free survival in correlation with detection of circulating tumor cells before chemotherapy

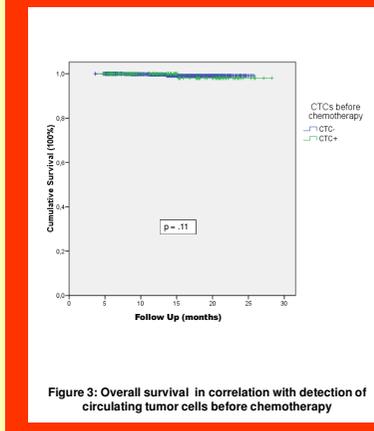


Figure 3: Overall survival in correlation with detection of circulating tumor cells before chemotherapy

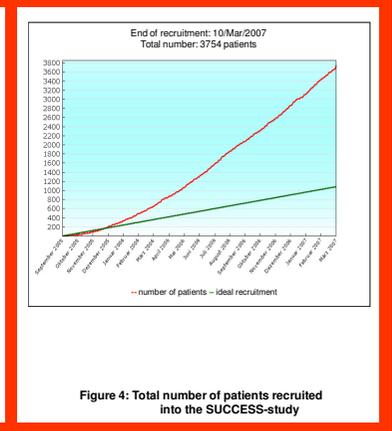


Figure 4: Total number of patients recruited into the SUCCESS-study



Supporting investigational industry: AstraZeneca, Chugai, Greiner bio-one, Lilly, Micromet, Novartis, Sanofi-Aventis, Tosoh, Veridex