



Evaluation of prevalence, number and temporal changes of circulating tumor cells as assessed after 2 and 5 years of follow-up in patients with early breast cancer in SUCCESS A study

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Background

Recent studies revealed that temporal changes in circulating tumor cells (CTC) prevalence assessed before and immediately after adjuvant chemotherapy (CT) might indicate treatment response in early breast cancer (EBC). However, there is limited knowledge on CTC status one or more years after chemotherapy treatment. Here we present descriptive data on CTC status prospectively evaluated 2 and 5 years after primary diagnosis in the German SUCCESS A study.

Methods

The SUCCESS A trial is a large, randomized, open-label, 2x2 factorial design Phase III study comparing disease free survival (DFS) in patients with EBC treated with 3 cycles of Epirubicin-Fluorouracil-Cyclophosphamide (FEC) followed by either 3 cycles of Docetaxel (D) or 3 cycles of Gemcitabine-Docetaxel (DG), and comparing DFS in patients treated with 2 years or 5 years of Zoledronate. CTC status at various time points was assessed using either the FDA-approved CellSearch® system (Veridex, USA) or Immunocytochemistry. The CellSearch® system detects CTCs by immunomagnetic enrichment with an EPCAM-antibody followed by labeling with monoclonal antibodies to differentiate between CTCs (cytokeratin 8, 18 and 19) and leukocytes (CD45). CTCs detected by manual immunocytochemistry were identified by staining with the monoclonal pancytokeratin antibody A45-B/B3 (CK 8, CK 18 and CK 19) and the APAAP technique. Stained cells were detected using conventional light field microscopy.

Trial Design

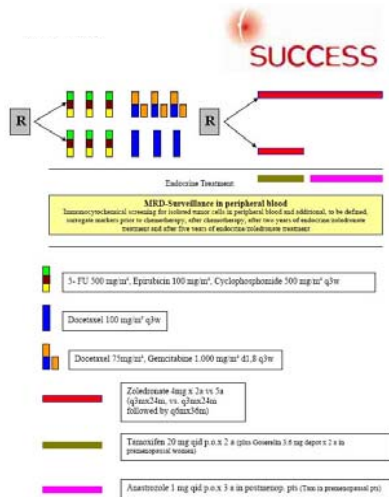


Figure 1: Study Design SUCCESS A

Results

Data on CTC status both at 2 years and at 5 years after primary diagnosis were available for 983 (26.2%) out of 3754 randomized patients. Both methods combined, CTCs were found after 2 years in 132 (13.4%; median 1; range 1 – 99) and after 5 years in 88 (9.0%; median 1; range 1 – 60) patients, respectively. The majority of patients (n = 779; 79.2%) had no CTCs at any of the two time points. CTCs were found at 2 years but not at 5 years after primary diagnosis in 116 (11.8%) patients, at 5 years but not at 2 years of follow-up in 72 (7.3%) patients, and both at 2 and at 5 years of follow-up in 16 (1.6%) patients. The corresponding numbers for cases in which CTC assessment at both time points was performed either only by the CellSearch® system (n = 567) or only by immunocytochemistry (n = 292) are shown in Table 1. In the remaining 124 cases (not shown) the method used for CTC assessment at the two time points was not the same.

Table 1: Prevalence of CTCs 2 and 5 years after primary diagnosis as assessed by (A) CellSearch® system only, (B) immunocytochemistry only, and (C) any of the two methods. N = Number (%) of patients.

| A: CellSearch® system | | Prevalence of CTCs after 5 years | | |
|--|-------|----------------------------------|----------|------------|
| | | CTC - | CTC + | Total |
| Prevalence of CTCs after 2 years | CTC - | 430 (75.8) | 38 (6.7) | 468 (82.5) |
| | CTC + | 85 (15.0) | 14 (2.5) | 99 (17.5) |
| | Total | 515 (90.8) | 52 (9.2) | 567 (100) |
| B: Immunocytochemistry | | Prevalence of CTCs after 5 years | | |
| | | CTC - | CTC + | Total |
| Prevalence of CTCs after 2 years | CTC - | 257 (88.0) | 18 (6.2) | 275 (94.2) |
| | CTC + | 16 (5.5) | 1 (0.3) | 17 (5.8) |
| | Total | 273 (93.5) | 19 (6.5) | 292 (100) |
| C: CellSearch® and Immunocytochemistry | | Prevalence of CTCs after 5 years | | |
| | | CTC - | CTC + | Total |
| Prevalence of CTCs after 2 years | CTC - | 779 (79.2) | 72 (7.3) | 851 (86.6) |
| | CTC + | 116 (11.8) | 16 (1.6) | 132 (13.4) |
| | Total | 895 (91.0) | 88 (9.0) | 983 (100) |

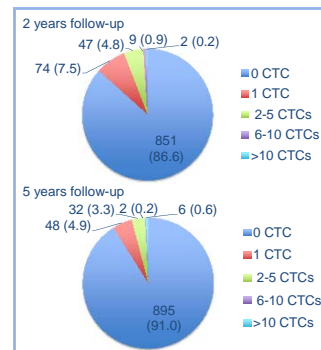


Figure 2: Number (%) of detected CTCs per sample at 2 and 5 years follow-up (n = 983), as assessed either with CellSearch® or immunocytochemistry.

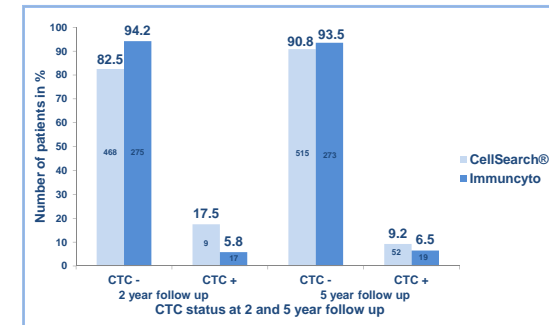


Figure 3: Percentage (and absolute numbers) of patients according to presence/absence of CTCs after 2 and 5 years follow-up for CTC assessment using either CellSearch® system or immunocytochemistry.

Conclusion

CTCs in peripheral blood were detected in a subset of early breast cancer patients without relapse up to five years after primary diagnosis. These CTCs may indicate the presence of occult "dormant" micrometastases.

Acknowledgement

