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

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9th International Symposium on Minimal Residual Cancer
September 25-27, 2013
Paris, France

Background

- Circulating tumor cells (CTCs) in blood are associated with reduced progression-free and overall survival in metastatic and early breast cancer
- Disseminated tumor cells persisting after chemotherapy in early BC are an independent prognostic factor for disease free survival, distant disease free survival, and overall survival
- Marker for treatment monitoring might improve patient care
- The HER2 status may chance during disease progression.
- Frequent discrepancy between the primary tumor und metastasis

Cristofanilli et al, N Engl J Med 2004; 351(8):781-791.
Hayes et al, Clin Cancer Res 2006; 12(14 Pt 1):4218-4224
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Hayes et al., Prog Mol Biol Transl Sci 2010; 95:95-112
Janni, W. et al. Clinical cancer research 2011; **17,** 2967□2976
Shin, S. J., et al., International Journal of Surgical Pathology 14, 279□284 (2006).
Sz□ll□si, J., et al., Cancer Research 55, 5400□5407 (1995).

HER2-Status on CTCs in MBC

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Total **n=245**
CTC+ **n=122 (50%)**

n=122	**Primärtumor**		
CTC	HER2 neg	HER2 pos	HER2 unknown
HER2 neg	51 (67%)	13 (42%)	8 (53%)
HER2 pos	**25 (33%)**	18 (58%)	7 (47%)
Total	78 (100%)	31 (100%)	15 (100%)

Fehm et al., Breast Cancer Res Treat. 2010

Issue

Lack of data for CTCs in early BC

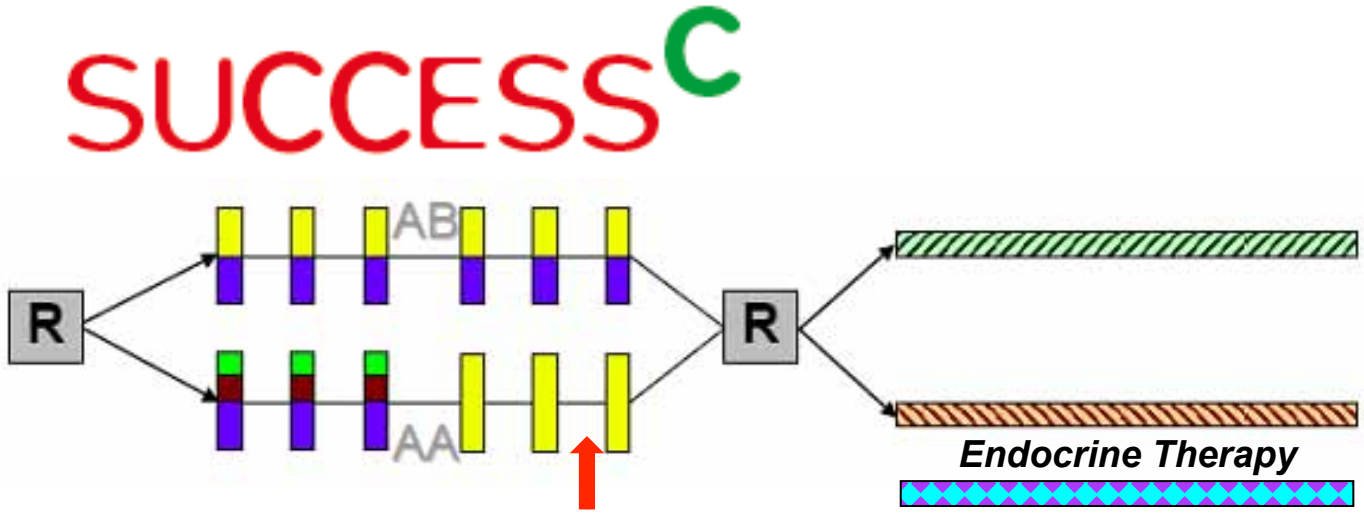
as well as phenotype and molecular characterisation of CTCs

Do CTCs persist after adjuvant Chemotherapy?

Do patients with early HER2 negative breast cancer have HER2 positive CTCs?

Will these patients benefit from a HER2 targeted therapy?

The SUCCESS C trail

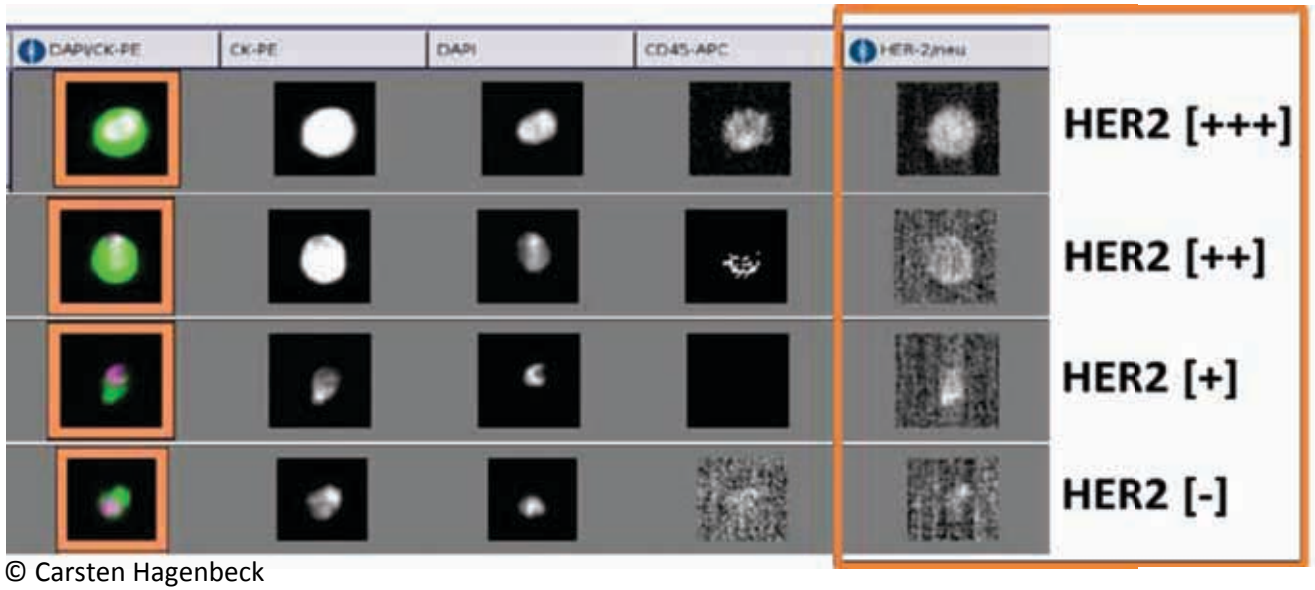


MRD-Surveillance in peripheral blood

Docetaxel 75mg/m², Cyclophosphamide 600mg	q3w	Phone based individual lifestyle intervention: Reduction of body weight, dietary changes, physical activity
5- FU 500 mg/m² Epirubicin 100 mg/m² Cyclophosphomide 500 mg/m²	q3w	Control arm: General recommendations for healthy lifestyle
Docetaxel 100 mg/m²	q3w	

HER2 phenotyping using CellSearch¨

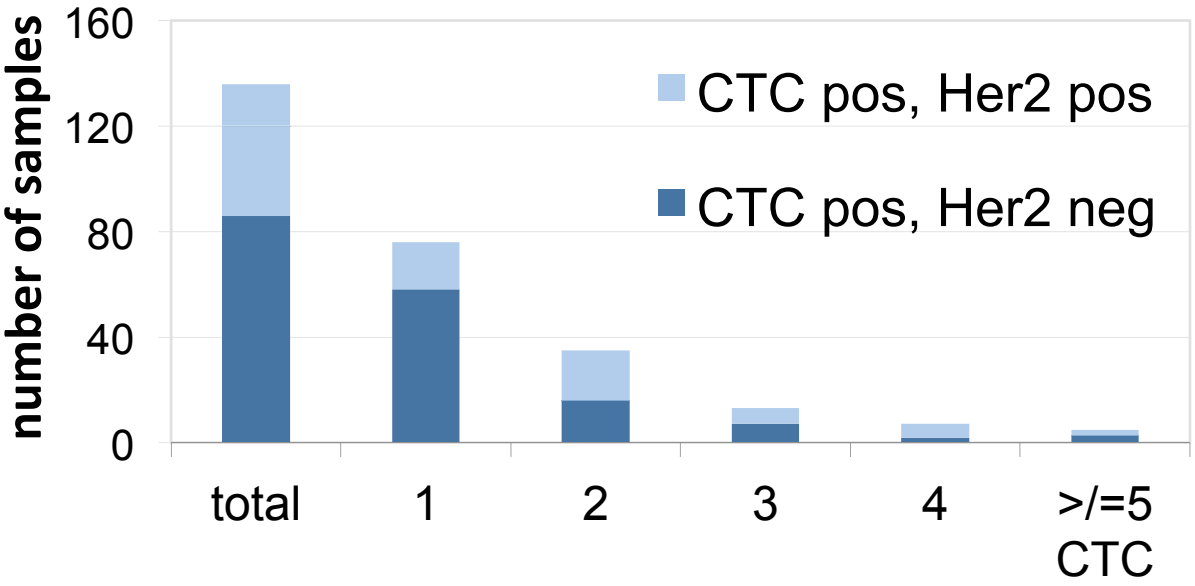
- Analysis of 23 ml of peripheral blood
- Anti-CK-Fluorescein Isothiocyanate (FITC) was used for HER2 phenotyping
- Categorization of HER2-Signal:



- Cut-off: 1 >/=CTC, >/=1 CTC HER2+++

HER2-Status on CTCs in SUCCESS C

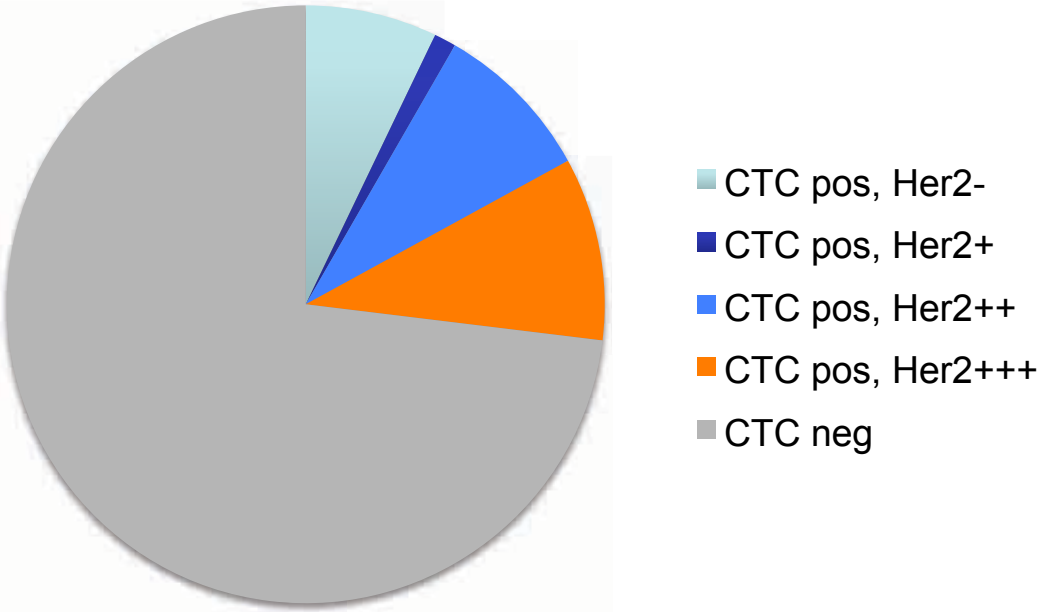
- 505 samples
- ≥ 1 CTC in 26.9% (n = 136)
- Median 0.48; Range 1-7
- Distribution of CTC pos samples:
  - 1 CTC (n=76; 55.9%)
  - ≥ 5 CTCs (n=5; 3.7%)

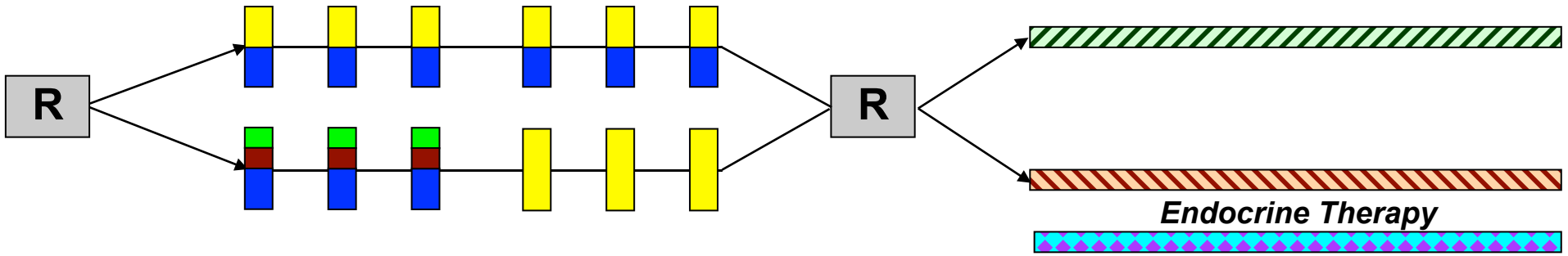


- HER2-status of the sample:
  - ≥ 1 HER2 pos (+++) CTC in 9,9% of all samples
  - ≥ 1 HER2 pos (+++) CTC in 36,8% of all CTC pos samples

HER2-Status on CTCs in SUCCESS C

- HER2-status on CTCs of CTC positive patients
  - Negative 26.5% (n=36)
  - Weak 4.4% (n=6)
  - Moderate in 32.4% (n=44)
  - Strong 36.8% (n=50)



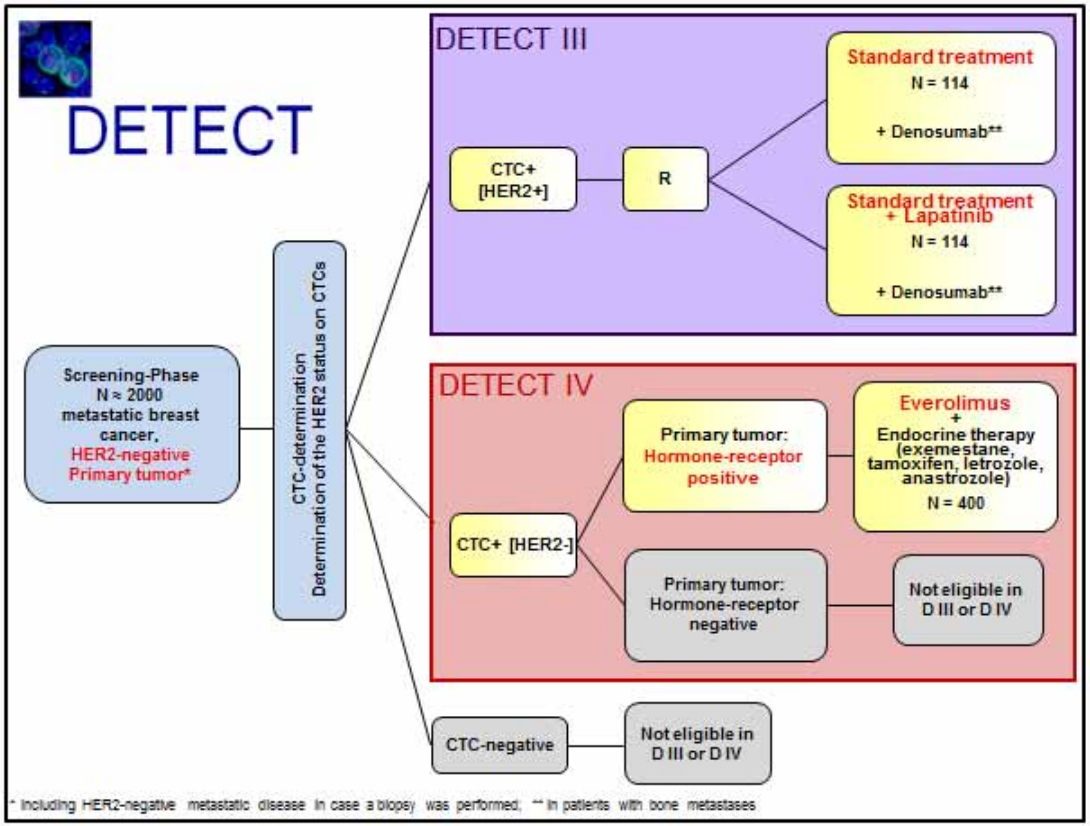


MRD-Surveillance in peripheral blood

	Premenopausal women: Tamoxifen 20 mg qid p.o.x 5 a
	Postmenopausal women without circulating tumor cells: Exemestane qid p.o.x 5 a
	Postmenopausal women with circulating tumor cells: Randomization to Exemestane qid p.o.x 5 a or Tamoxifen 20mg qid p.o.x 2a and Switch to Exemestane qid p.o.x 3a
	GnRH x 2 a in premenopausal women with additional criteria as described in the protocol

DETECT III

A multicenter, randomized, phase III study to compare standard therapy alone versus standard therapy plus Lapatinib in patients with initially HER2-negative metastatic breast cancer and HER2-positive circulating tumor cells



TREAT CTC - FLOW CHART

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Screening: blood draw after chemo (N=2150)

↓ ≥1CTC/15mL ~8%

Women with positive Blood Test

↓ 10% Drop out

Eligible for randomization / analysis (N=156)

↙ ↘

Trastuzumab **Observation**

Stratification for ER, center, chemo (adj vs neoadj)

EORTC
European Organisation for Research and Treatment of Cancer

Conclusion

- CTCs are prognostic factors in metastatic and early breast cancer

  → Identification of patients at higher risk of relapse

- Phenotyping of CTCs

  •HER2-Status on CTCs may be different compared to the primary tumor even in early breast cancer

  •10 % of HER2 negative early breast cancer have ≥ 1 HER2 positive CTC

  → CTCs target of personalized therapy (DETECT III, TREAT CTC)