Prognostic value of CA27.29 trend during adjuvant chemotherapy and until two years thereafter in patients with primary breast cancer

Brigitte Rack(2), Philip Hepp(1), Ulrich Andergassen(2), Julia Neugebauer (2), Jessica Salmen(1), Georg Heinrich (3), Jörg Schreier (4) Arnd Hönig (5) Dominique Finas (9) Thomas Zwingers(6), Rolf Kreienberg (10) Matthias W. Beckmann(7), Werner Lichtenegger(8), Klaus Friese(2), Wolfgang Janni(1)

(1) Universitätsfrauenklinik Düsseldorf (2) Universitätsfrauenklinik München (3) Praxis Dr. Heinrich, Fürstenwalde (4) DRK – Kliniken Köpenick (5) DRK – Kliniken Köpenick (6) Estimate GmbH Augsburg (7) Universitätsfrauenklinik Erlangen (8) Charitè Berlin (9) Universitätsklinik Lübeck (10) Universitätsfrauenklinik Ulm
-- SUCCESS Study Group --

Background

Several trials have shown that the use of tumor markers can lead to an early diagnosis of tumor recurrence in breast cancer. While tumor markers are frequently used in routine clinical practice, it is still unclear whether the prognosis of breast cancer patients can be improved by early treatment induction.

Methods

The SUCCESS Trial compares a FEC-Docetaxel (Doc) vs. FEC-Doc-Gemcitabine (Doc-G) regime and two versus five years of treatment with Zoledronat in patients with primary breast cancer (N+ or high risk N-). CA27.29 has been measured before and after chemotherapy and at 2 years with the ST AIA-PACK Ca27.29 reagent using MUC-1 for AIA-600II (Tosoh Bioscience, Tessenderlo, Belgium). The course of Ca27.29 from pre-chemotherapy baseline to 2 years was evaluated in this analysis.

Results

CA27.29 data is available of 3202 patients before and 2015 patients two years after chemotherapy. 20.2% of patients had increasing (≥ 1 U/ml), 59.7% had decreasing and 20.1% had stable CA27.29 levels from before chemotherapy to two years thereafter. For a difference of ≥ 5 U/ml 6.1% of patients had increasing values, 23.5% had decreasing and 70.4% had stable CA27.29 levels from before chemotherapy to two years.

Patients with increasing CA27.29 levels from before chemotherapy to two years after chemotherapy had a significantly worse DFS (HR 1.016; [95%CI 1.011-1.021] for ≥ 1 U/ml each $p < 0.001$) and OS (HR 1.02; [95%CI 1.004-1.037] $p < 0.001$) than patients with stable or decreasing levels. Between those with stable and decreasing levels there was no significant difference in terms of prognosis [figure Kaplan-Meier DFS]. Patients with an increase ≥ 5 U/ml had an 81% increased risk for recurrence (HR=1.810 (CI: 1.111 – 2.948)).

In the multivariate analysis taking into account tumor size, nodal status, grading, age, hormonal and Her2/neu receptor status increasing CA27.29 levels were an independent prognostic marker.

Conclusions

A small increase of the tumor marker CA27.29 compared to pre-chemotherapy baseline was associated with a worse prognosis. Therefore, changes in tumor marker values compared to baseline in the individual patient could result in a more accurate and clinically relevant interpretation of tumor markers.

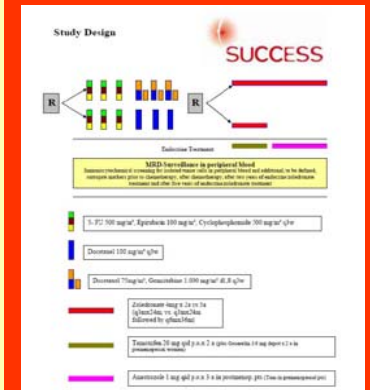

Figure 1: Study design of the SUCCESS-Trial

Figure 2: 251 active SUCCESS study centers in Germany

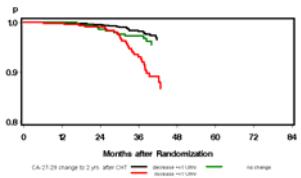

Figure 4: Disease-free survival as a function of tumor marker change (>= 1 U/ml)

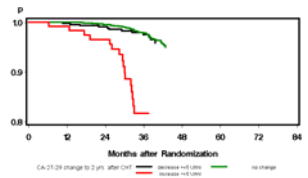

Figure 5: Disease-free survival as a function of tumor marker change (≥ 5 U/ml)

	CA27.29 increase (%)	CA27.29 no change/ decrease (%)	P-Value
Number of Patients	123 (6.1)	1892 (93.9)	
Tumor Size			
pT1	51 (41.5%)	764 (40.4%)	0.918
pT2 - 4	71 (57.7%)	1117 (59.0%)	
pTx	1 (0.8%)	11 (0.6%)	
Lymph Node status			0.088
Absent (pN0) / X	51 (41.5%)	624 (33.9%)	
Present (pN1-3)	72 (58.5%)	1250 (66.1%)	
Grading			0.070
G1	3 (2.5%)	98 (5.2%)	
G2-3	119 (97.5%)	1783 (94.8%)	
Hormone Receptor Status			0.111
Negative	41 (33.3%)	506 (26.7%)	
Positive	82 (66.7%)	1386 (73.3%)	
Her2-neu Status			0.006
Negative	101 (85.6%)	1374 (74.2%)	
Positive	17 (14.4%)	478 (25.8%)	
Histological Type			0.631
Ductal	96 (78.7%)	1535 (81.5%)	
Lobular	15 (12.3%)	220 (11.7%)	
Mixed ductal-lobular	11 (9.0%)	129 (6.8%)	
Systemic Therapy			0.741
Chemotherapy – FEC-D	60 (48.8%)	953 (49.7%)	
Chemotherapy - FEC - DG	63 (51.2%)	940 (50.3%)	

Table 1: Patient characteristics at the time of primary diagnosis

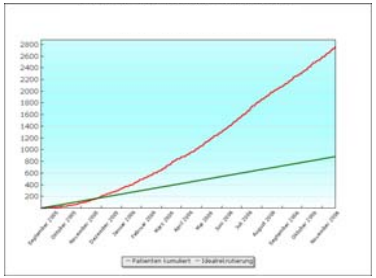

Figure 3: Planned recruitment of 3754 patients has been completed in March 2007

	Hazard-Ratios adjusted for treatment (95%-confidence interval)	
	OS	DFS
Change in CA27.29 (<= 5 U/l)	**0.102* (0.028 – 0.374)**	**0.337* (0.201 – 0.562)**
Hormone Receptor Status (pos. vs. neg.)	**0.374 (0.099 – 1.414)**	**0.866 (0.492 – 1.527)**
Her2-neu status (pos. vs. neg.)	**0.615 (0.151 – 2.507)**	**1.176 (0.644 – 2.147)**
Grading (G1 vs. G2-3)	**2.140 (0.580 – 7.898)**	**2.076* (1.254 – 3.435)**
Tumor size (T1 vs. T2-4)	**0.970 (0.411 – 2.288)**	**1.347 (0.950 – 1.911)**
Lymphnode status (N0 – N1-3)	**2.307* (1.230 – 4.327)**	**1.560* (1.200 – 2.028)**

* $P < 0.05$

Table 2: Multivariate Proportional Hazard Model for disease-free and overall survival for change in CA27.29