

# Prognostic Value of Relative Change in Tumor Marker CA 27.29 in Early Stage Breast Cancer – The SUCCESS trial

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## Background

MUC1 based tumor markers like CA27.29 (TM) in breast cancer are routinely used in metastatic disease as early marker for treatment efficacy. However, in early stage disease data is sparse. In this analysis, we looked at the impact of individual change in CA27.29 on prognosis instead of using a threshold.

## Methods

The SUCCESS Trial is a phase III trial comparing FEC-docetaxel (Doc) vs. FEC-Doc-Gemcitabine (Doc-G) regime and two vs. five year treatment with Zoledronat in 3754 patients at 251 study centers in Germany (Fig. 2) with primary breast cancer N+ or high risk N0 (Fig. 1). We measured CA27.29 after surgery but before chemotherapy (CHT) as baseline and compared it to CA27.29 levels 2 years thereafter with the ST AIA-PACK Ca27.29 reagent using MUC-1 for AIA-600II (Tosoh Bioscience, Tessenderlo, Belgium).

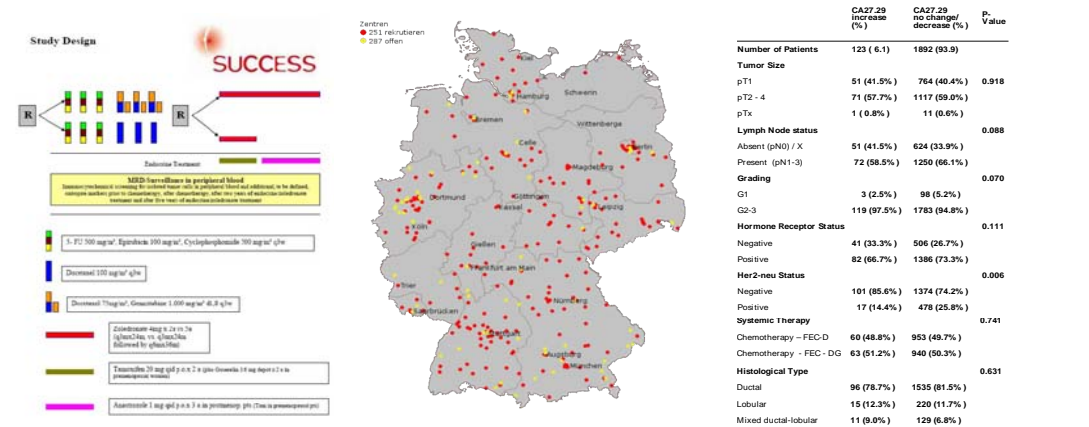


Fig. 1 Design of the SUCCESS trial | Fig. 2 Participating study centers

	CA27.29 increase (%)	CA27.29 no change/decrease (%)	p-Value
<b>Number of Patients</b>	123 (6.1)	1892 (93.9)	
<b>Tumor Size</b>			
pT1	51 (41.5%)	764 (40.4%)	0.918
pT2 - 4	71 (57.7%)	1117 (59.0%)	
pTx	1 (0.8%)	11 (0.6%)	
<b>Lymph Node status</b>			0.088
Absent (pN0) / X	51 (41.5%)	624 (33.9%)	
Present (pN1-3)	72 (58.5%)	1250 (66.1%)	
<b>Grading</b>			0.070
G1	3 (2.5%)	98 (5.2%)	
G2-3	119 (97.5%)	1793 (94.8%)	
<b>Hormone Receptor Status</b>			0.111
Negative	41 (33.3%)	506 (26.7%)	
Positive	82 (66.7%)	1386 (73.3%)	
<b>Her2-neu Status</b>			0.006
Negative	101 (85.6%)	1374 (74.2%)	
Positive	17 (14.4%)	478 (25.8%)	
<b>Systemic therapy</b>			0.741
Chemotherapy – FEC-D	60 (48.8%)	953 (49.7%)	
Chemotherapy – FEC-DG	63 (51.2%)	940 (50.3%)	
<b>Histological Type</b>			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%)	

Tab. 1 Patient characteristics

## Results

CA27.29 data is available of 2,015 patients (for patient characteristics and correlation to CA 27.29 see Tab. 1). 119 pts (5.9%) had TM over the threshold of 32U/ml before CHT and 56 (2.8%) two years thereafter. To examine the relative change of tumor marker, patients were divided into 3 groups: increase: change  $\geq 5$  U/ml; stable: change  $< \pm 5$  U/ml; decrease: change  $\geq -5$  U/ml.

123 (6.1%) patients had increasing ( $\geq 5$  U/ml), 1419 (70.4%) had stable, 473 (23.5%) had decreasing TM levels from before CHT to 2 years thereafter. The majority of patients with increasing TM (86 pts; 69.9%) had levels below the usual threshold of 32U/ml at all times (Tab. 2). Patients with an increase  $\geq 5$  U/ml had an increased risk for recurrence (HR=4.017 [CI: 2.621-6.156]; Fig. & Tab. 3a) and reduced overall survival (HR=6.920 [CI: 4.109-11.654]; Fig. 3c; Tab. 3b). Among patients always below 32U/ml those with an increase  $\geq 5$  U/ml had an even reduced disease free survival (HR 5.838 [3.607-9.448]; Fig. 3b).

In multivariate analysis taking into account tumor size, nodal status, grading, age, menopausal-, hormonal- and HER2/neu receptor status increasing CA27.29 levels were an independent prognostic marker (Tab. 3a&b).

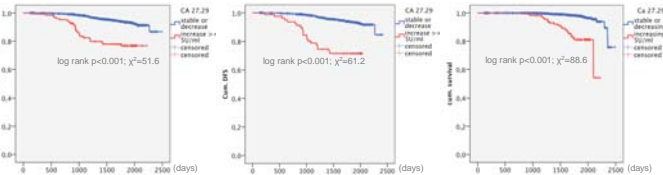


Fig. 3a: Kaplan-Meier chart disease free survival (DFS) all patients | Fig. 3b: Kaplan-Meier chart DFS: patients always below 32U/ml | Fig. 3c: Kaplan-Meier chart overall survival (OS) all patients

	Change 2yrs. after Chemo			p-value	prop. HR	95.0% CI	
	decrease $\geq -5$ U/ml	no change $< \pm 5$ U/ml	increase $\geq 5$ U/ml			low	high
<b>before Chemo</b>							
<32 U/ml	n	381	1396	86			
	%	80.5%	98.4%	69.9%			
$\geq 32$ U/ml	n	3	30	24.2%			
	%	0.2%	2.2%				
<b><math>\geq 32</math> U/ml</b>	n	88	8	5.7%			
	%	18.6%	0.6%				
<b>total</b>	n	473	1419	123			
	%	100.0%	100.0%				

Tab. 2 Patient distribution

	decrease $\geq -5$ U/ml	no change $< \pm 5$ U/ml	increase $\geq 5$ U/ml
before Chemo			
<32 U/ml	n	381	1396
	%	80.5%	98.4%
$\geq 32$ U/ml	n	3	30
	%	0.2%	2.2%
<b><math>\geq 32</math> U/ml</b>	n	4	12
	%	0.8%	0.8%
<b>total</b>	n	473	1419
	%	100.0%	100.0%

Tab. 2 Patient distribution

Tab. 3a Cox regression proportional hazards DFS

	p-value	prop. HR	95.0% CI	
CA27.29 increase $\geq 5$ U/ml (cat)	<0.001	4.017	2.621	6.156
grading	<0.001	1.875	1.369	2.569
nodal status (TNM)	<0.001	1.703	1.438	2.018
tumor size (TNM)	0.024	1.314	1.037	1.665
hormon receptor status (cat)	0.236	1.254	0.862	1.824
age (y)	0.107	1.021	0.996	1.047
HER2/neu status (cat)	0.544	0.895	0.625	1.281
menopausal status (cat)	0.657	0.889	0.528	1.495

Tab. 3a Cox regression proportional hazards DFS

Tab. 3b Cox regression proportional hazards OS

	p-value	prop. HR	95.0% CI	
CA27.29 increase $\geq 5$ U/ml (cat)	<0.001	6.920	4.109	11.654
nodal status (TNM)	<0.001	1.910	1.499	2.435
tumor size (TNM)	0.006	1.560	1.137	2.141
grading	0.091	1.457	0.942	2.255
hormon receptor status (cat)	0.499	1.219	0.687	2.164
HER2/neu status (cat)	0.642	1.140	0.656	1.983
menopausal status (cat)	0.964	1.019	0.460	2.257
age (y)	0.654	1.009	0.971	1.048

Tab. 3b Cox regression proportional hazards OS