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THE PROGNOSTIC RELEVANCE OF SERUM Ca27.29 LEVEL IN PRIMARY BREAST CANCER PATIENTS BEFORE ADJUVANT CHEMOTHERAPY – RESULTS OF THE GERMAN **SUCCESS** TRIAL



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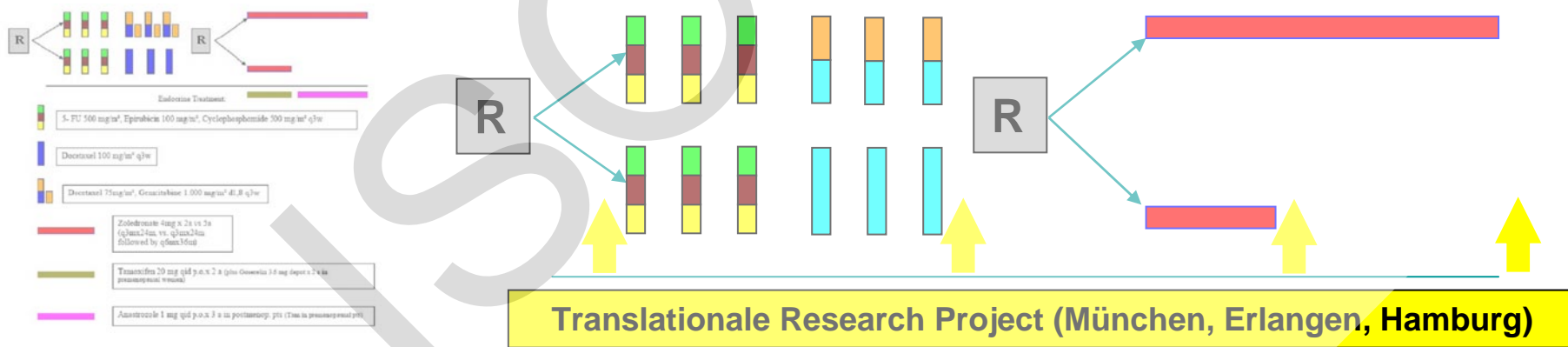
Mucin MUC-1 is physiologically present at the **luminal surface of glandular epithelia**. Since this **glycoprotein is upregulated in many adenocarcinomas and released into the bloodstream** in higher amounts than in healthy individuals, it has been investigated extensively in **breast cancer patients**. Several studies identified **MUC-1 markers such as Ca15-3 and Ca27.29** at primary diagnosis as being independent **predictors for disease outcome**, in addition to the traditional prognostic markers such as tumor size and nodal status (1- 3). After primary therapy, the level of these **markers can predict disease recurrence** about six months earlier than available methods.

While tumor markers are frequently used for the evaluation of treatment efficacy in metastatic breast cancer, the role of Muc-1 markers in primary disease and during recurrence-free follow-up is still under discussion.

In the German multicenter SUCCESS trial we evaluated Ca27.29 in 3754 patients before and after adjuvant chemotherapy and 2 and 5 years after primary diagnosis.

SUCCESS - Study Design

(Simultaneous Study of Docetaxel-Gemcitabine Combination adjuvant treatment, as well as Extended Bisphosphonate and Surveillance-Trial)
An initiative of the ADEBAR-Study Group



- The SUCCESS Trial compares FEC-Docetaxel (Doc) vs. FEC-Doc-Gemcitabine (Doc-G) regime and two vs. five year treatment with Zoledronat in patients with primary breast cancer (N+ or high risk N-).

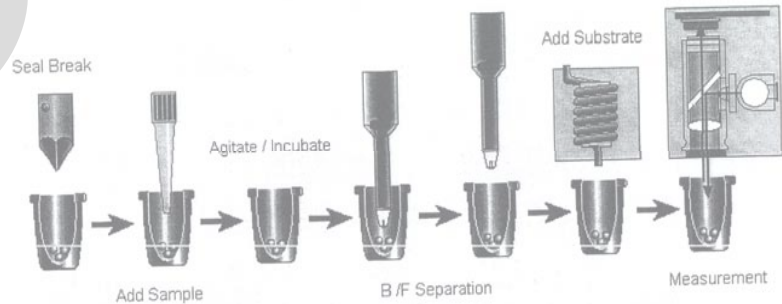
- n=3.658 patients

Detection of the Tumor Marker Ca27.29

- Ca 27.29 is shedded from the cell surface of epithelial tumor cells.
- Ca 27.29 is detected in serum samples within 72 hours after blood collection.
- Immunoassay for the detection of circulating Muc-1 Antigen Ca 27.29 (Tosoh Bioscience, Belgium).
- Samples with more than 31 U/ml are regarded as positive.

Peripheral Blood Sampling (60ml)

- Before start of chemotherapy
- After completion of chemotherapy
(before the start of endocrine and zoledronate treatment)
- Two years after completion of chemotherapy
- Five years after completion of chemotherapy



A competitive immunoassay is used for the detection of **Ca27.29**, a specific part of the MUC1 coded glycoprotein. **The labeled antibody binds to an 8-amino acid sequence**, which corresponds to amino acids Ser-Ala-Pro-Asp-Thr-Arg-Pro-Ala.

The combination of the labeled B27.29 antibody and the solidphase antigen purified from breast cancer cells forms a competitive assay with a decreasing exponential doseresponse curve. **CA27.29** has been **measured** with **ST AIA-PACK CA27.29** reagent using **MUC-1 for AIA-600II (Tosoh Bioscience, Tessenderlo, Belgium)**.

Patients' characteristics

Tumorstage *	
T1	40%
T2	50%
T3	6%
T4	1%

Nodal status	
N0	34%
N1	46%
N2	14%
N3	6%

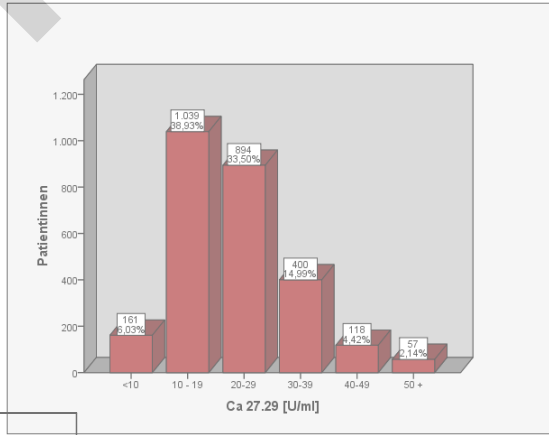
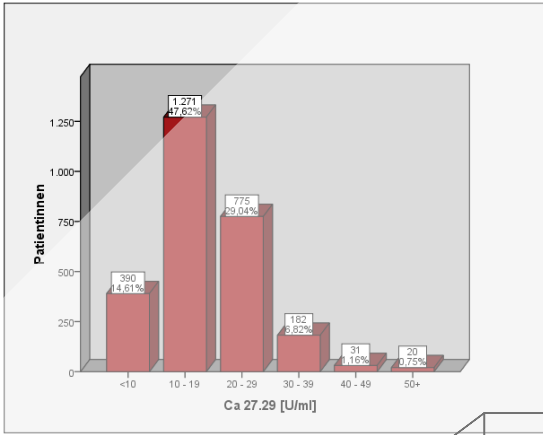
Menopausal status	
pre	43%
post	57%

Her2/neu status *	
positive	21%
negative	75%

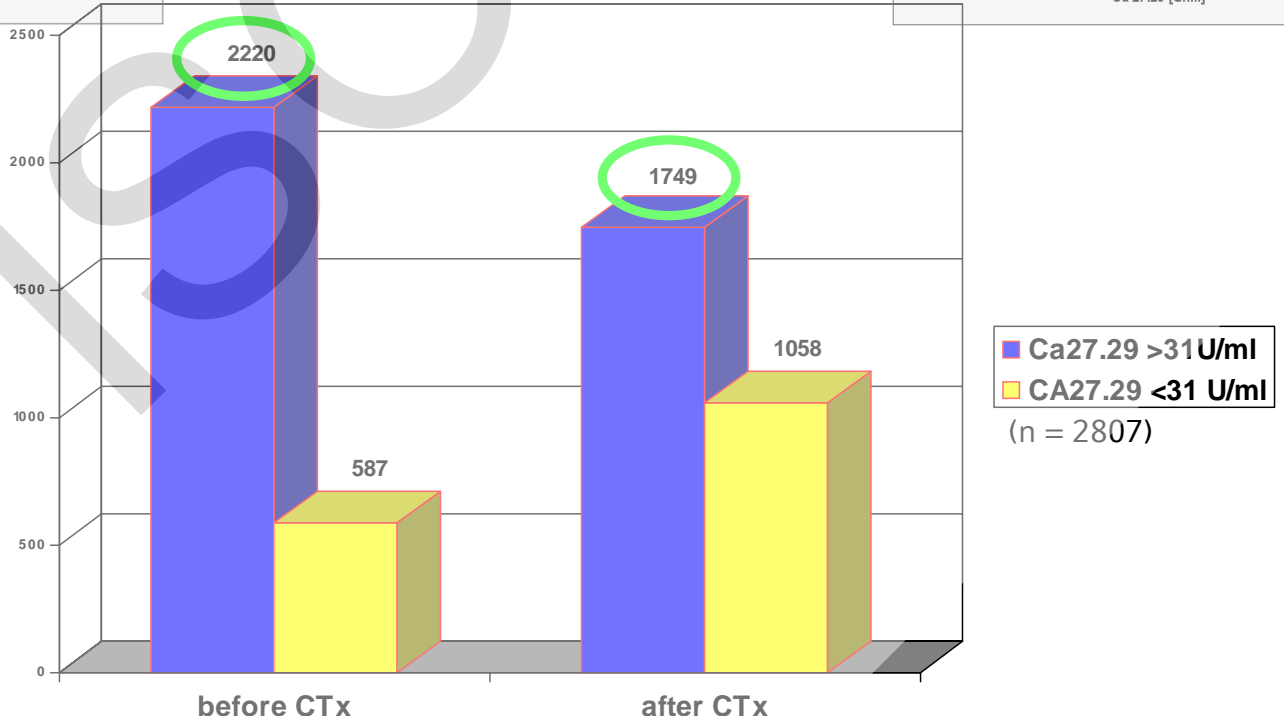
Hormone sensitive	
yes	79%
no	21%

Avg. age at diagnosis
53 years

* Difference to 100%: missing value



Ca27.29 before and after chemotherapy



CA 27-29 before and after chemotherapy (CHT) in 2669 pat.

		After CHT	
		negativ	positiv
Before CHT	Negativ	91% 2436 pat.	75% 2009 pat.
	positiv	9% 233 pat.	4% 85 pat.
			21% 575 pat.
			16% 427 pat.
			5% 148 pat.

p < 0.0001

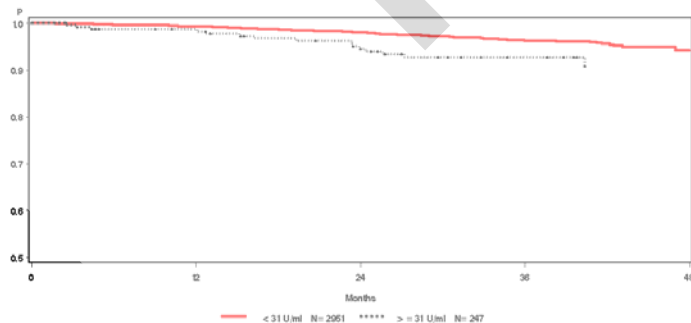
Follow up 18 months after chemotherapy

138pts with recurrence of disease

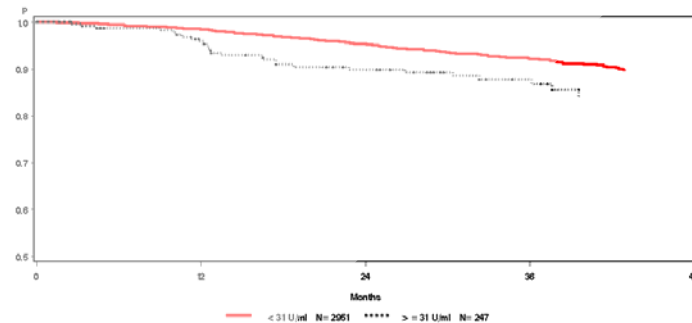
	before CTx	after CTx
CA 27.29 > 31U/ml	17	22

	before CTx		after CTx	
07 pts	CA27.29 > 31 U/ml	(+)	CA27.29 < 31 U/ml	(-)
109 pts	CA27.29 < 31 U/ml	(-)	CA27.29 < 31 U/ml	(-)
12 pts	CA27.29 < 31 U/ml	(-)	CA27.29 > 31 U/ml	(+)
10 pts	CA27.29 > 31 U/ml	(+)	CA27.29 > 31 U/ml	(+)

*Overall Survival Time by CA-27-29 before Chemotherapy



*Disease Free survival time by CA-27-29 before Chemotherapy



Correlation of Ca27.29 with other Prognostic Factors

Ca 27.29 correlates with:

- tumor size ($p < 0,022$)
- nodal status ($p < 0,022$)

Ca 27.29 doesn't correlate with:

- grading ($p < 0,565$)
- Her2/neu status ($p < 0,308$)
- estrogen receptor status ($p < 0,323$)
- progesterone receptor status
($p < 0,078$)

Conclusions

- These results could indicate a close relation between elevated Ca27.29 levels and tumor mass at primary diagnosis.
- Longer follow-up of the SUCCESS trial will indicate, whether Ca27.29 can be used as
 - as early predictive marker for treatment response
 - as prognostic marker for early detection of disease recurrence
- Treatment intervention trials are necessary to determine the value of tumor markers to tailor more individualized treatment approaches.



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3754 breast cancer patients

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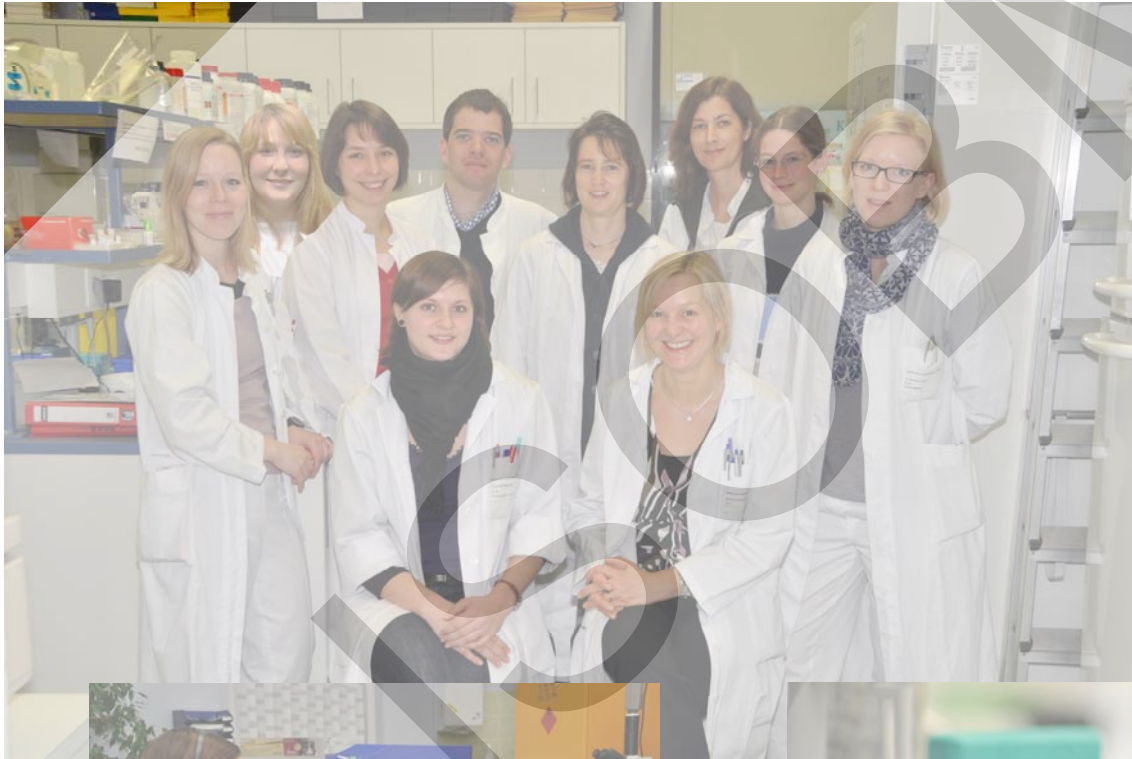
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Thank you for your attention

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