Dose dependent effects of G-CSF on CA 27.29 in early stagebreast cancer patients

P. Hepp [1], B. Rack [2], C. Schindlbeck [2], J. Jückstock [2], C. Jendereck [2], U. Andergassen [2], E.-M. Genss [2], H. Sommer [2], K. Pantel [3], K. Friese [2], W. Janni [1]

All the following institutions are located in Germany: (1) University of Düsseldorf; (2) University of Munich; (3) University of Hamburg

Background

13% of 2556 patients (pts) examined in the SUCCESS trial showed elevated levels of Ca27.29 only after chemotherapy (SABCS2008). Recently a possible relationship between the administration of G-CSF and a rise in the tumor marker could be demonstrated. This analysis focuses on the dose dependency of this effect.

Methods

The SUCCESS Trial is a phase III trial comparing FEC-Docetaxel vs. FEC-Doc-Gemcitabine regime and 2 vs. 5 years of treatment with zoledronate in 3754 patients with primary breast cancer and node positive or high risk for relapse disease. Blood samples for the analysis at hand are taken before and after chemotherapy (CHT). CA27.29 has been measured with ST AIA-PACK Ca27.29 reagent using MUC-1 for AIA-600II (Tosoh Bioscience, Tessenderlo, Belgium). The cutoff for Ca27.29 is 32 U/ml. For chi^2 analysis patients were grouped to CA27.29 raise or no raise and 1 to 6 cycles with G-CSF or no G-CSF at all. The difference of CA27.29 before and after CHT has then been correlated with the number of G-CSF cycles administered.

Results

The analysis of Ca27.29 is based on the data of 2556 pts. 1252 pts (49%) received at least one course of G-CSF. 338 pts (13%) exceeded the threshold for CA27.29 only after CHT. In this group 209 pts (62%) received G-CSF and 129 (38%) did not. 1043 pts with stable or decreased CA27.29 received G-CSF (47%) and 1175 did not (53%). This difference was highly significant ($p<0.0001$). Correlating the number of G-CSF cycles a patient got during CHT with the absolute difference in Ca27.29 levels before and after CHT showed a highly significant positive correlation of 0.13 (Spearman-Rho; $p<0.0001$[two-sided]).

Discussion and Conclusion

This analysis gives strong evidence that at least part of the elevation of CA27.29 post CHT is connected to the application of G-CSF during CHT. There is also a positive correlation of the increase in CA27.29 levels and the dose of G-CSF administered to the patient. This could be an important part of the explanation why MUC-1 based tumor markers tend to increase during CHT. Whether this effect is due to an increased liberation during leucopoiesis or direct or indirect effects on remaining tumor cells needs to be further evaluated.

Patients' characteristics

Tumorstage *		Nodal status	
T1	40%	N0	34%
T2	50%	N1	46%
T3	6%	N2	14%
T4	1%	N3	6%

Menopausal status		Her2/neu status *	
pre	43%	positive	21%
post	57%	negative	75%

Hormone sensitive		Avg. age at diagnosis	
yes	79%	53 years	
no	21%		

* Difference to 100%: missing value
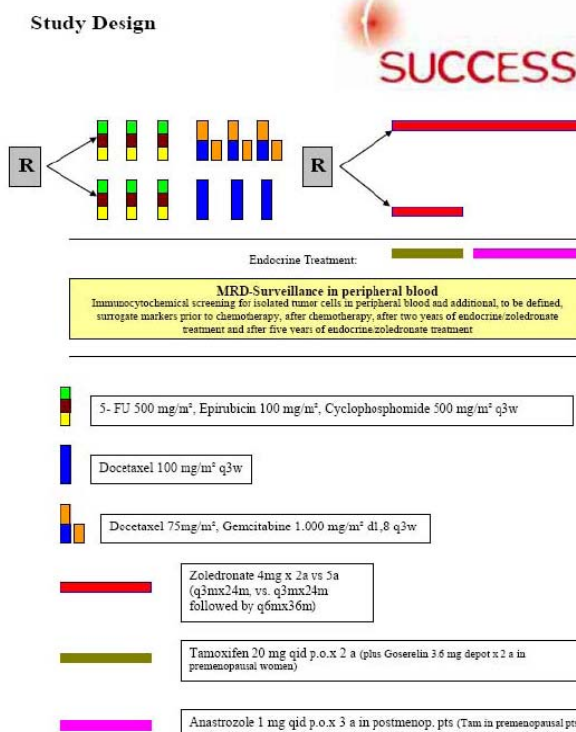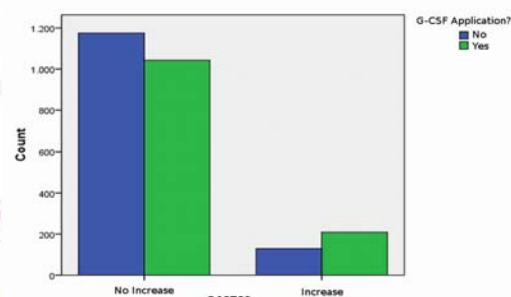
CA 27-29 before and after chemotherapy (CHT) in 2556 pat.

		After CHT	
		negative	positive
		83% 2117 pat.	17% 439 pat.
Before CHT	negative 93% 2388 pat.	80% 2050 pat.	13 % 338 pat.
	positive 7% 168 pat.	3% 67 pat.	4 % 101 pat.

Study Design

5- FU 500 mg/m², Epirubicin 100 mg/m², Cyclophosphomide 500 mg/m² q3w

Docetaxel 100 mg/m² q3w

Decetaxel 75mg/m², Gemcitabine 1.000 mg/m² d1,8 q3w

Zoledronate 4mg x 2a vs 5a (q3mx24m. vs. q3mx24m followed by q6mx36m)

Tamoxifen 20 mg qid p.o.x 2 a (plus Goserelin 3.6 mg depot x 2 a in premenopausal women)

Anastrozole 1 mg qid p.o.x 3 a in postmenop. pts (Tam in premenopausal pts)

Endocrine Treatment:

MRD-Surveillance in peripheral blood
Immunocytochemical screening for isolated tumor cells in peripheral blood and additional, to be defined, surrogate markers prior to chemotherapy, after chemotherapy, after two years of endocrine/zoledronate treatment and after five years of endocrine/zoledronate treatment

Bar Chart