

Effects of Granulocyte-colony stimulating factor (G-CSF) on circulating tumor cells (CTC) and CA 27.29 in breast cancer patients

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Background

Some publications showed that different types of tumors not only express receptors for G-CSF but are promoted in their growth or at least altered in their properties (1-4). In the SUCCESS Trial CTC and CA27.29 levels have been examined before and after adjuvant chemotherapy (CHT) in 3754 breast cancer patients (pts). This analysis focuses on the coherence between CTC and CA27.29 levels and an application of G-CSF in the course of CHT.

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 patients with primary breast cancer (BC) (N+ or high risk). Blood samples for this analysis are taken before and four weeks after completion of CHT. CTC were assessed with the CellSearchSystem (Veridex, Warren, USA). After immunomagnetic enrichment with an anti-Epcam-antibody, cells were labeled with anti-cytokeratin (8,18,19) and anti-CD45 antibodies to distinguish epithelial cells and leukocytes. 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 positivity is > 32 U/ml for CA27.29 and >1 cell for the CTC analysis. Patients were grouped to CTC/CA27.29 raise or no raise and 1 to 6 cycles with G-CSF or no G-CSF at all.

Results

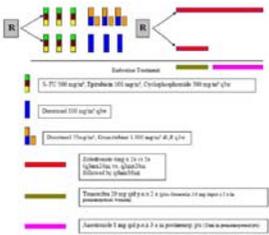
Complete data on 1510 pts are available for CTC analysis. 745 pts (49%) received at least one course of G-CSF. 117 pts (8%) showed an increase in CTC after CHT. In this group 52 (3%) pts received G-CSF and 65 (4%) did not. 693 pts with stable or even decreased CTC after CHT received G-CSF (46%) and 700 did not (46%). There was no significant difference in the chi-square test (p=0.29). The analysis of CA27.29 is based on the data of 2556 pts. Again 49% or 1252 pts received at least one course of G-CSF during CHT. 338 pts (13%) exceeded the threshold for CA27.29 only after CHT. In this group 209 pts (8%) received G-CSF and 129 (5%) did not. 1043 pts with stable or decreased CA27.29 received G-CSF (41%) and 1175 did not (46%). This difference was highly significant (p<0.0001).

Discussion

This analysis gives strong evidence that there might be a connection between elevated levels of CA27.29 post CHT and the application of G-CSF. This might be part of the explanation for the finding that tumor markers tend to increase in some pts directly after the completion of CHT (6). Whether this is an direct e.g. receptor mediated effect on residual tumor cells or unrelated to the disease at all cannot be answered by this examination and therefore needs to be further evaluated. Existence of CTC after completion of CHT has been shown to be of prognostic relevance. CTC therefore might be a valuable new instrument for treatment monitoring in early breast cancer (5). This analysis showed no influence of G-CSF application on CTC.

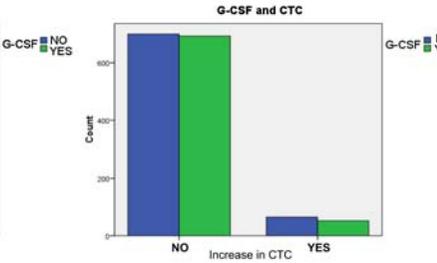
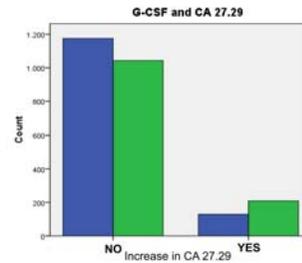
Conclusion

No evidence can be provided for a significant correlation between an increase in the number of CTC and the application of G-CSF over CHT. Nevertheless the results on CA27.29 showed a highly significant correlation between the administration of G-CSF and increased CA27.29 levels four weeks after CHT. This could be a possible explanation for the often observed increase of tumor markers after CHT.



	G-CSF Application			
	No	Yes	Total	
Increased Ca27.29 after Chemotherapy	No	46.0%	40.8%	86.8%
	Yes	5.0%	8.2%	13.2%
Total		51.0%	49.0%	100.0%

	G-CSF Application			
	No	Yes	Total	
Increased CTC after Chemotherapy	No	46.4%	45.9%	92.3%
	Yes	4.3%	3.4%	7.7%
Total		50.7%	49.3%	100.0%



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	

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