The SUCCESS-Trial – Toxicity analysis of a phase III study evaluating FEC-Doc vs. FEC-Doc in combination with Gemcitabine as adjuvant treatment for breast cancer

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Background

Taxane containing regimens have been established as standard of care for node-positive primary breast cancer patients and have shown superiority to mere anthracycline containing regimens. The SUCCESS-trial evaluates, whether adjuvant taxane based treatment can be further improved by the addition of Gemcitabine.

Methods

The SUCCESS-Study is an open-label randomized controlled, Phase III study comparing the disease free survival after randomisation in patients treated with 3 cycles of Epirubicin (100 mg/m²) – Fluorouracil (500) -Cyclophosphamide (500, FEC) -chemotherapy, followed by 3 cycles of Docetaxel(100 mg/mg², D) versus 3 cycles of FEC, followed by 3 cycles of Gemcitabine (1,000mg/m² d1,8) -Docetaxel (75 mg/m²) (DG) . Complete, monitored toxicity data of 2.691 pts were available for this analysis.

Results

Dose reduction >20% (3.97% vs 2.90%) and postponement of treatment cycles >7die (22,85% vs 14.19%) was rare, but more frequent in the FEC-DG arm (both p< .001). Cytostatic treatment was prematurely stopped in 119 pts (4,4%) receiving FEC-DG and in 103 pts (3,8%) with FEC-D (p=0,21). G-CSF support was applied in 850 (29.2%) vs. 602 pts (20.7%, p< .001). Toxicities NCI grade > 2 which occurred with incidence > 1% or significantly different in the two arms are depicted in Table 1. Afebrile and febrile neutropenia and anemia did not differ between the two arms, but thrombocytopenia was more frequent in FEC-DG (1.7%, p= .007). Hand-foot syndrome and neuropathy was more frequent in the FEC-D arm (p= .09 and p= .02, respectively).

Conclusions

No unexpected toxicities were observed and severe adverse effects were rare in both treatment arms. With the addition of gemcitabine to FEC-D adjuvant chemotherapy toxicity was moderately increased. Outcome data will have to be awaited to further interpret these findings.

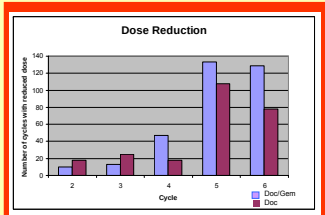


Fig. 1: Dose reduction for both study arms per chemotherapy cycle

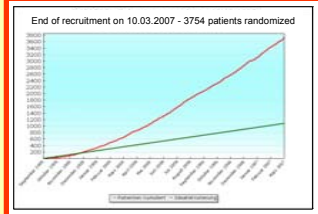
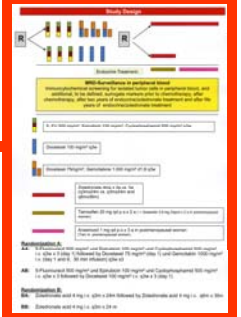


Fig. 2: Patient recruitment within the Success trial: actual recruitment in red, ideal recruitment in green



Success Study Design – Inclusion criteria (summary)

- pT1-4, pM0
- Axillary lymph node metastases (pN1-3) or 'high risk N0':
  pT ≥ 2 or ER/PR neg. or Grading G3
  or age < 35
- R0-Resection
- Female older than 18
- Performance Status ≤ 2 ECOG-Scale

Major Reasons to participate in the SUCCESS-Study

- Modern cytostatic treatment in conventional regimes
- All patients will receive bisphosphonates
- Agents beyond official registration status will be provided free of charge
- Easy Online-Documentation
- Intensive Flow of information (study meetings, newsletter, call center)
- Complementary electronic documentation system for all pts in participating centers
- Translational research results free of charge

Major toxicity

Toxicity	FEC-DG	FEC-D	Percentage		p-value
	Grad > 2	Grad > 2	FEC-DG	FEC-D	
Neutropenia	504	508	0,3490	0,3458	0,9984
Febrile neutropenia (fever of unknown origin without clinically or microbiologically documented infection) (ANC <1.0 x 10e9/L, fever >=38.5 degrees C)	42	59	0,0291	0,0402	0,4454
Anemia	31	20	0,0215	0,0136	0,4556
Thrombocytopenia	25	6	0,0173	0,0041	0,0070
SGPT (ALT) (serum glutamic pyruvic transaminase) elevation	68	28	0,0471	0,0191	0,0004
GGT (Gamma-Glutamyl transpeptidase)	45	34	0,0312	0,0231	0,6205
Vomiting	55	58	0,0381	0,0395	0,9981
Nausea	43	45	0,0298	0,0306	0,9994
Stomatitis/pharyngitis (oral/pharyngeal mucositis)	24	26	0,0166	0,0177	0,9971
Diarrhea patients without colostomy	41	39	0,0284	0,0265	0,9927
Fatigue (lethargy, malaise, asthenia)	40	46	0,0277	0,0313	0,9539
Bone pain	28	44	0,0194	0,0300	0,3381
Thrombosis/embolism	28	22	0,0194	0,0150	0,8396
Arthralgia (joint pain)	24	29	0,0166	0,0197	0,9409
Headache	21	10	0,0145	0,0068	0,2469
Myalgia	20	37	0,0139	0,0252	0,1809
Dyspnea	19	24	0,0132	0,0163	0,9175
Hand-foot skin reaction	15	33	0,0104	0,0225	0,0876
Neuropathy	9	28	0,0062	0,0191	0,0227