

Chemotherapy-induced amenorrhea in premenopausal breast cancer patients treated with adjuvant anthracycline and taxane based chemotherapy within the **SUCCESS** study.

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Background

Chemotherapy induced amenorrhea (CIA) is often used as a surrogate marker for cytotoxic gonadal damage. The aim of this analysis was to identify predictive factors for CIA in premenopausal breast cancer patients treated with adjuvant chemotherapy.

Materials & Methods

The German multicenter, phase III SUCCESS trial compared 3 cycles of FEC (500/100/500mg/m²) q3w followed by 3 cycles of Docetaxel (100mg/m²) q3w vs.

FEC followed by Doc + Gemcitabine (1000mg/m² d1,8 q3w) as adjuvant treatment in patients with node positive or high risk node negative primary breast cancer.

Premenopausal patients with hormone receptor positive tumors underwent endocrine treatment with Tamoxifen (Tam) for 5 years. Goserelin (GnRH) was additionally administered for the first 2 years if one of the following criteria were met: Patients < 40 years at study entry, premenopausal hormone status or regular menses within 6 months after last chemotherapy application.

We retrospectively investigated CIA rates of 1.189 initially premenopausal patients during disease-free follow-up.

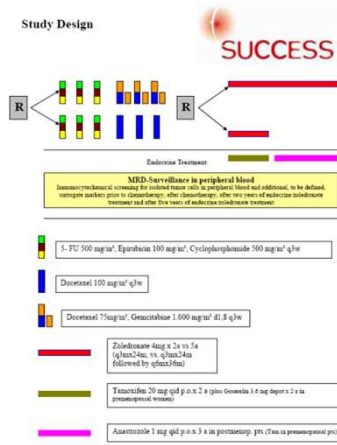


Fig. 1: The SUCCESS study design

Results

Median age at diagnosis was 44 years (range 21-50). The median follow up time was 44 months (range 1-62). 791 patients (66.5%) received endocrine treatment after the completion of chemotherapy. Tam intake was reported in 370 patients, GnRH in 29 patients, Tam + GnRH in 392 patients.

In 963 patients (81.0%) CIA occurred for ≥ 3 months after chemotherapy, while in 22.7% of initially amenorrheic patients CIA was temporary. 192 patients (16.2%) had continuous menstrual bleeding.

In multivariate analysis the risk of CIA was significantly higher in older patients, increasing by factor 1.32 per life year ($p < 0.0001$). Tam intake was also associated with increased CIA rates ($p = 0.0032$). Patients with combined Tam + GnRH were more likely to resume menses compared to patients without endocrine therapy ($p = 0.0056$).

Factors like the cytotoxic regimen, tumor stage, grading, the patient's BMI or the use of GnRH analogues as ovarian protectants during chemotherapy did not correlate with CIA rates.

Table 1: Patient characteristics

	n=1189	%
tumor stage		
pT1	549	46.2
pT2	575	48.4
pT3	52	4.4
pT4	9	0.8
unknown	4	0.3
nodal stage		
pN0	481	40.5
pN1	519	43.7
pN2	124	10.4
pN3	61	5.1
unknown	4	0.3
grading		
G1	56	4.7
G2	555	46.7
G3	577	48.5
unknown	1	0.1
her2/neu status		
positive	296	24.9
negative	879	73.9
unknown	14	1.2
hormone receptor status		
positive	862	72.5
negative	324	27.3
unknown	3	0.3
adjuvant endocrine therapy		
tamoxifen (TAM)	370	31.1
TAM+GnRH	392	33.0
GnRH	29	2.4
none	360	30.3
unknown	38	3.2
ovarian protection during CTX		
yes	46	3.9
no	1143	96.1

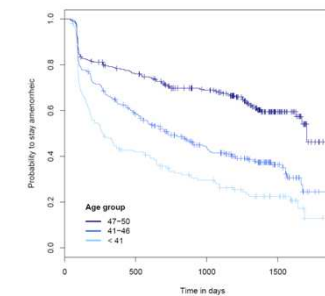


Fig. 1: Kaplan-Meier analysis for the incidence of CIA within different age groups

Table 2: Generalized additive mixed model for the risk of CIA for ≥ 3 months

variable	p-value	OR (95% CI)
age per life year	< 0.0001	1.237 - 1.395
endocrine therapy (TAM vs. none)	0.0032	1.149 - 1.989
endocrine therapy (TAM+GnRH vs. none)	0.0056	0.408 - 0.857
tumor stage (pT1 vs. pT2-4)	0.1628	0.389 - 1.173
lymphnode involvement (pN0 vs. pN+)	0.0179	1.122 - 3.406
ovarian protection during CTX (yes vs. no)	0.2784	0.439 - 17.321
BMI (normal weight vs. obesity)	0.3019	0.697 - 3.207
CTX regimen (FEC-Doc+G vs. FEC-Doc)	0.4062	0.467 - 1.362

Conclusion

Age was the strongest predictor for CIA. Tam administered alone increased CIA rates. Opposite effects were observed for patients who received Tam+GnRH. The addition of Gemcitabine to sequential anthracycline-taxane based chemotherapy did not influence CIA rates.

Acknowledgments



251 active SUCCESS study centers in Germany