

Chemotherapy-induced ovarian failure (CIOF) in young women with early breast cancer

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Background

Patients <45 years with breast cancer have a risk of developing premature ovarian failure. The incidence of chemotherapy-induced amenorrhea (CIA) ranges between 45-61% among different studies.^{1,2} The wide range of CIA mainly reflects on the difference in the definition used, in follow-up periods and in patients characteristics included in the different studies.

Resumption of menses occurs often within two years of CIA,¹ with a median time of recovery of about 7 months.³

Awareness of CIOF is essential for young women. The combination of hormones such as the follicle-stimulating hormone (FSH), estradiol and the Anti-Müllerian Hormone (AMH) is assumed to be able to define the risk of premature ovarian failure and loss of fertility with modern therapeutic regimen for early breast cancer, including new taxanes and dose-dense chemotherapy.

Materials and Methods

Overall 740 patients aged ≤45 years treated with anthracycline or taxane-based chemotherapy for early breast cancer from 4 German neoadjuvant/adjuvant trials were included. Blood samples were collected at baseline (N=740), end of treatment (EOT n=740), 6 (n=177), 12 (n=113), 18 (n=69), 24 (n=47) months after EOT. Only samples collected in a time sequence were included.

Estradiol (E2), Follicle-Stimulating Hormone (FSH) and Anti-Müllerian Hormone (AMH) were centrally assessed. CIOF was defined as FSH >12.4IU/l and E2 <52.2ng/ml and was analysed per timepoint and according to clinical and treatment-related variables.

Objectives

The objectives of the current analysis are the following:

1. Describe basal level of FSH, estradiol and AMH
2. Describe the rate of CIOF at EOT, 6, 12, 18 and 24 months after EOT
3. Find clinical and treatment-related parameters that could have an influence on CIOF

Results

Table 1: Baseline characteristics

CHARACTERISTICS	<30 YEARS N (%)	30-<40 YEARS N (%)	≥40 YEARS N (%)	OVERALL N (%)
AGE (median [range])				40 [21-45]
CT REGIMEN				
PM	9 (14.5)	39 (12.8)	54 (14.5)	102 (13.8)
PMCb	9 (14.5)	48 (15.7)	47 (12.6)	104 (14.1)
P-EC	17 (27.4)	79 (25.9)	91 (24.4)	187 (25.3)
nP-EC	14 (22.6)	61 (20.0)	89 (23.9)	164 (22.2)
Cabazitaxel	1 (1.6)	13 (4.3)	17 (4.6)	31 (4.2)
Paclitaxel	3 (4.8)	17 (5.6)	9 (2.4)	29 (3.9)
iddEnPC	4 (6.5)	23 (7.5)	28 (7.5)	55 (7.4)
dtEC-dtD	5 (8.1)	25 (8.2)	38 (10.2)	68 (9.2)
CT DURATION				
12 weeks	4 (6.5)	30 (9.8)	26 (7.0)	60 (8.1)
16-18 weeks	27 (43.5)	135 (44.3)	167 (44.8)	329 (44.5)
24 weeks	31 (50.0)	140 (45.9)	180 (48.3)	351 (47.4)
CT DENSITY				
Conventional*	35 (56.5)	170 (55.7)	206 (55.2)	411 (55.5)
dose-dense#	27 (43.5)	135 (44.3)	167 (44.8)	329 (44.5)
HORMONE LEVELS (median [range])				
FSH	5.15 [0.10-25.50]	5.60 [0.05-61.10]	6.40 [0.05-142.70]	5.95 [0.05-142.70]
E2	101.00 [2.50-2375.00]	86.00 [2.50-2027.00]	88.00 [2.50-763.00]	88 [2.5-2375.00]
AMH	2.14 [0.21-11.69]	1.58 [0.02-16.18]	0.53 [0.02-10.59]	0.96 [0.02-16.18]

*P/nP-EC q3w, P, Cz; # dtEC-dtD, wPM(Cb), iddEnPC. Abbreviations: AMH, anti-müllerian hormone; BMI, body mass index; C, cyclophosphamide; Cb, carboplatin; D, docetaxel; dt, dose-tailored; E, epirubicin; FSH; Follicle-Stimulating Hormone; idd, intense dose-dense; M, doxorubicin; P, paclitaxel; nP, nab-paclitaxel

Figure 1: Rate of Chemotherapy-induced ovarian failure (CIOF) at different timepoints

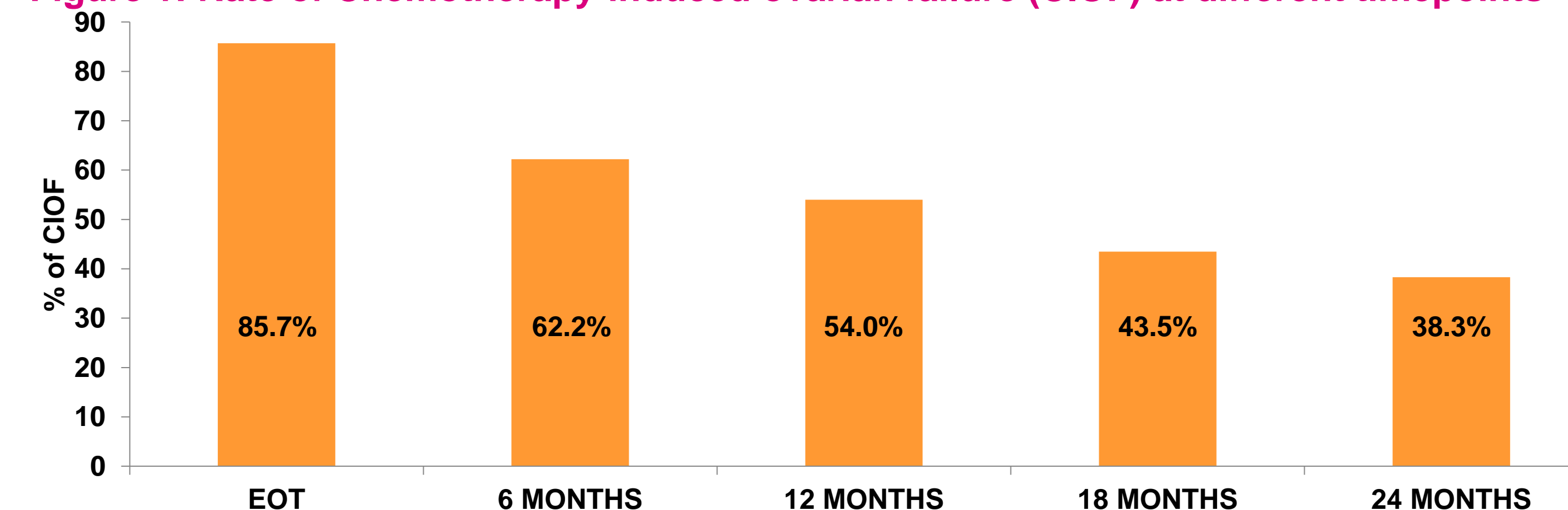
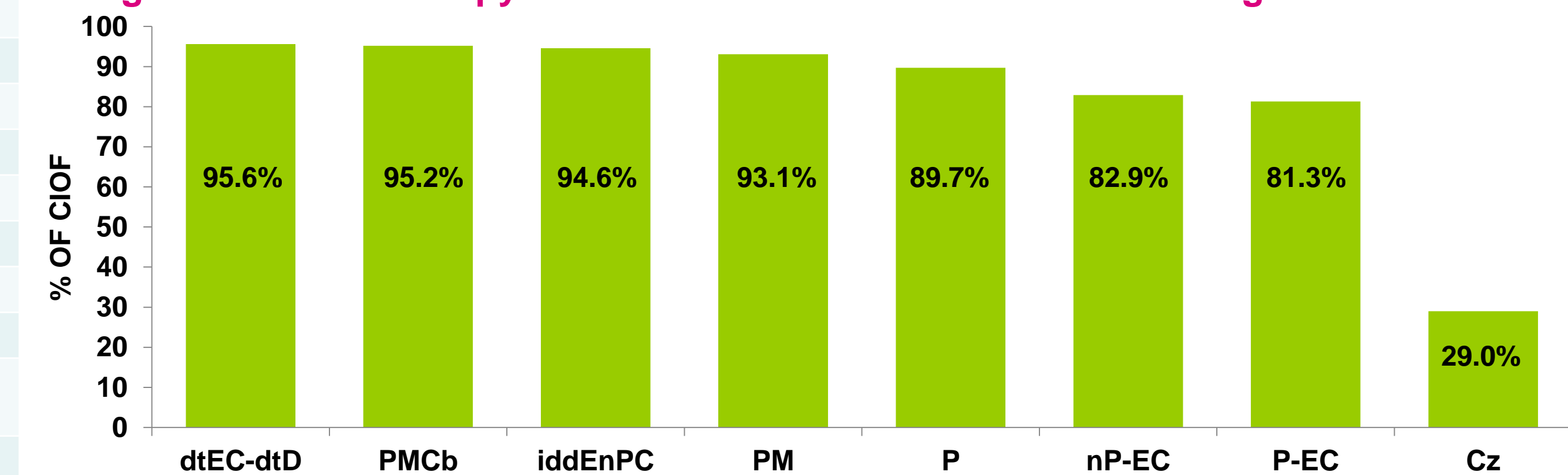


Table 2: Parameters influencing Chemotherapy-induced ovarian failure (CIOF) at EOT

PARAMETERS	RATE OF CIOF (%)	p-value	
AGE	≥40 years	94.6	<0.001
	30-40 years	82.0	
	<30 years	50.0	
CT AGENTS	See Figure 2	<0.001	
CT DURATION	24 weeks	82.1	<0.001
	16-18 weeks	94.5	
	12 weeks	58.3	
CT DENSITY	dose-dense	94.5	<0.001
	conventional dosed	78.6	

Figure 2: Chemotherapy-induced ovarian failure at EOT according to treatment



Conclusions

The majority of young women experienced CIOF after chemotherapy for early breast cancer. After 2 years 62% of the patients rendered premenopausal by hormone levels. Age, chemotherapy regimen, duration and density influenced the rate of CIOF and should be taken into account when counseling young women who desire to maintain ovarian function.

References

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