SUPPLEMENTARY MATERIAL

Supplementary Tables

Supplementary Figures

This supplementary material has been provided by the authors to give readers additional information about their work

Supplementary Table 1. Multivariable Cox Proportional Hazards Model: Effect of Temporary Ovarian Suppression, Tumor Size, Axillary Nodes, and Hormone Receptor Status on Disease-free Survival[a] (N = 281)[b]

Variable	Patients/Events[c]	HR (95% CI)	*P* [d]
Random assignment			
Control arm	133/39	1 [Reference]	.68
GnRHa arm	148/48	1.10 (0.72-1.68)	
Tumor size (T)			
pT1	166/47	1 [Reference]	.48
pT2-4	115/40	1.17 (0.76-1.80)	
Axillary nodes (N)			
pN0	130/31	1 [Reference]	.01
pN1-2	151/56	1.74 (1.11-2.72)	
Hormone receptor status			
ER-negative and PR-negative	55/19	1 [Reference]	.23
ER-positive and/or PR-positive	226/68	0.72 (0.43-1.21)	

[a] Disease-free survival interval was computed from the date of randomization to the date of the occurrence of an event. Observation times of patients without a disease-free survival event were censored on the date of last contact. HR = hazard ratio; CI = confidence interval; GnRHa = gonadotropin-releasing hormone analogs; ER = estrogen receptor; PR = progesterone receptor.
[b] After single imputation of missing values on at least one covariate in seven patients.
[c] Disease-free survival event was defined by the occurrence of local recurrence, distant metastases, contralateral or ipsilateral breast tumor, second primary malignancy, or death from any cause, whichever occurred first.
[d] Two-sided likelihood-ratio test.

Supplementary Table 2. Multivariable Cox proportional hazards model: effect of temporary ovarian suppression, tumor size, axillary nodes, hormone receptor status, type of chemotherapy, timing of chemotherapy, and use of GnRHa after the end of chemotherapy on disease-free survival[a]

Variable	HR (95% CI)	*P*[b]
Random assignment		
Control arm	1 [Reference]	.50
GnRHa arm	1.16 (0.75-1.81)	
Tumor size (T)		
pT1	1 [Reference]	.54
pT2-4	1.15 (0.73-1.82)	
Axillary nodes (N)		
pN0	1 [Reference]	.01
pN1-2	1.92 (1.14-3.22)	
Hormone receptor status		
ER-negative and PR-negative	1 [Reference]	.33
ER-positive and/or PR-positive	0.72 (0.37-1.40)	
Type of chemotherapy		
Anthracycline- and taxane-based	1 [Reference]	
Anthracycline-based	1.04 (0.61-1.78)	.10
CMF-based	3.07 (1.19-7.90)	
Timing of chemotherapy		
Adjuvant therapy	1 [Reference]	.09
Neoadjuvant therapy	1.83 (0.95-3.52)	
Use of GnRHa after the end of chemotherapy[c]		
No	1 [Reference]	.68
Yes	1.12 (0.65-1.95)	

[a] Disease-free survival interval was computed from the date of randomization to the date of the occurrence of an event. Observation times of patients without a disease-free survival event were censored on the date of last contact. HR = hazard ratio; CI = confidence interval; GnRHa = gonadotropin-releasing hormone analogs; ER = estrogen receptor; PR = progesterone receptor; CMF = cyclophosphamide, methotrexate, fluorouracil.
[b] Two-sided likelihood-ratio test.
[c] Time-dependent.

Supplementary Table 3. Multivariable Cox Proportional Hazards Model: Effect of Temporary Ovarian Suppression, Tumor Size, Axillary Nodes, and Hormone Receptor Status on Overall Survival[a] (N = 281)[b]

Variable	Patients/Events	HR (95% CI)	*P*[c]
Random assignment			
Control arm	133/23	1 [Reference]	.83
GnRHa arm	148/28	1.06 (0.61-1.85)	
Tumor size (T)			
pT1	166/24	1 [Reference]	.14
pT2-4	115/27	1.53 (0.87-2.68)	
Axillary nodes (N)			
pN0	130/15	1 [Reference]	.01
pN1-2	151/36	2.14 (1.16-3.94)	
Hormone receptor status			
ER-negative and PR-negative	55/13	1 [Reference]	.19
ER-positive and/or PR-positive	226/38	0.64 (0.34-1.22)	

[a] Overall survival interval was computed from the date of randomization to the date of the death. Observation times of patients without an overall survival event were censored on the date of last contact. HR = hazard ratio; CI = confidence interval; GnRHa = gonadotropin-releasing hormone analogs; ER = estrogen receptor; PR = progesterone receptor.
[b] After single imputation of missing values on at least one covariate in seven patients.
[c] Two-sided likelihood-ratio test.

Supplementary Table 4. Multivariable Cox Proportional Hazards Model: Effect of Temporary Ovarian Suppression, Tumor Size, Axillary Nodes, Hormone Receptor Status, Type of Chemotherapy, Timing of chemotherapy, and Use of GnRHa after the end of chemotherapy on Overall Survival[a]

Variable	HR (95% CI)	*P*[b]
Random assignment		
Control arm	1 [Reference]	.60
GnRHa arm	1.16 (0.65-2.08)	
Tumor size (T)		
pT1	1 [Reference]	.15
pT2-4	1.54 (0.85-2.79)	
Axillary nodes (N)		
pN0	1 [Reference]	.02
pN1-2	2.22 (1.09-4.51)	
Hormone receptor status		
ER-negative and PR-negative	1 [Reference]	.90
ER-positive and/or PR-positive	1.05 (0.47-2.35)	
Type of chemotherapy		
Anthracycline- and taxane-based	1 [Reference]	
Anthracycline-based	0.87 (0.42-1.80)	.28
CMF-based	2.49 (0.78-7.95)	
Timing of chemotherapy		
Adjuvant therapy	1 [Reference]	.02
Neoadjuvant therapy	2.61 (1.24-5.48)	
Use of GnRHa after the end of chemotherapy[c]		
No	1 [Reference]	.25
Yes	0.66 (0.33-1.32)	

[a] Overall survival interval was computed from the date of randomization to the date of the death. Observation times of patients without an overall survival event were censored on the date of last contact. HR = hazard ratio; CI = confidence interval; GnRHa = gonadotropin-releasing hormone analogs; ER = estrogen receptor; PR = progesterone receptor; CMF = cyclophosphamide, methotrexate, fluorouracil.
[b] Two-sided Likelihood-ratio test.
[c] Time-dependent.

Supplementary Table 5. Pregnancy outcome according to treatment arm

Pregnancy outcome	Control arm (n = 133) No. (%)	GnRHa arm (n = 148) No. (%)
No pregnancy	129 (97.0)	139 (93.9)
At term	3 (2.3)	4 (2.7)
Spontaneous abortion	0 (0)	2 (1.4)
Induced abortion	0 (0)	2 (1.4)
Preterm birth	0 (0)	1 (0.7)
Unknown	1 (0.8)	0 (0)

[a]GnRHa = gonadotropin-releasing hormone analogs

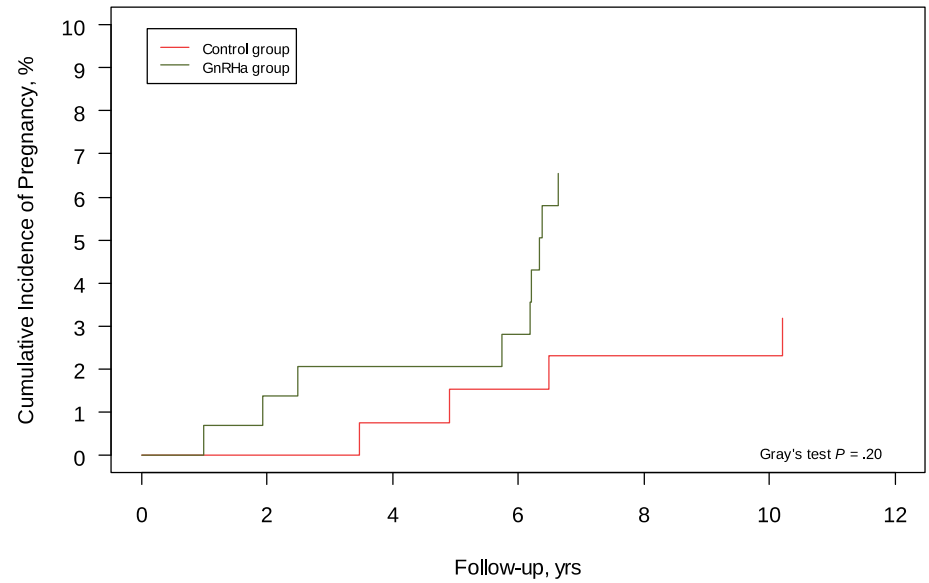
Supplementary Table 6. Baseline patient and tumor characteristics according to *BRCA* status

Characteristics	*BRCA*-mutated (n = 10)	*BRCA*-not mutated (n = 33)	*BRCA*-not tested (n = 238)
Median age (range), y	34.5 (29-44)	36 (24-44)	40 (24-45)
Tumor size (T) , No. (%)			
pT1	6 (60.0)	25 (75.8)	134 (56.3)
pT2-4	4 (40.0)	8 (24.2)	98 (41.2)
Unknown	0 (0)	0 (0)	6 (2.5)
Axillary nodes (N), No. (%)			
pN0	3 (30.0)	20 (60.6)	105 (44.1)
pN1-2	7 (70.0)	13 (39.4)	127 (53.4)
Unknown	0 (0)	0 (0)	6 (2.5)
Hormone receptor status, No. (%)			
ER-negative and PR-negative	3 (30.0)	9 (27.3)	39 (16.4)
ER-positive, PR-positive, or both	7 (70.0)	24 (72.7)	195 (81.9)
Unknown	0 (0)	0 (0)	4 (1.7)
Timing of chemotherapy, No. (%)			
Adjuvant therapy	9 (90.0)	30 (90.9)	211 (88.7)
Neoadjuvant therapy	1 (10.0)	3 (9.1)	19 (8.0)
Not begun	0 (0)	0 (0)	8 (3.4)
Type of chemotherapy, No. (%)			
Anthracycline-based	3 (30.0)	11 (33.3)	99 (41.6)
Anthracycline- and taxane-based	7 (70.0)	19 (57.6)	122 (51.3)
CMF-based	0 (0)	3 (9.1)	9 (3.8)
Median cumulative cyclophosphamide dose (IQR), mg/m^2	3660.5 (3350-3840)	3920 (3600-5390)	4100 (3710-5627)
Median duration of chemotherapy (IQR), wk	20.9 (16-21)	19 (15.1-21.3)	16.4 (15-21.3)
Type of adjuvant endocrine therapy in hormone receptor–positive patients[a], No. (%)			
No treatment	0 (0)	0 (0)	10 (5.1)
GnRHa alone	0 (0)	1 (4.2)	8 (4.1)
GnRHa + tamoxifen	4 (57.1)	17 (70.8)	105 (53.9)
GnRHa + aromatase inhibitor	0 (0)	0 (0)	4 (2.1)
Tamoxifen	1 (14.3)	2 (8.3)	49 (25.1)
Tamoxifen followed by aromatase inhibitor	2 (28.6)	4 (16.7)	19 (9.7)

Median duration of endocrine therapy (IQR), y	5.0 (5.0-5.2)	5.0 (4.96-5.06)	5.0 (4.8-5.1)
Median duration of adjuvant GnRHa (IQR), y	3.4 (3.2-5.0)	4.6 (3.8-5.0)	3.9 (2.0-5.0)

[a] Percentages calculated on the total number of patients with hormone receptor–positive disease (24 in the *BRCA* not mutated group, 7 in the *BRCA* mutated group, 195 in the *BRCA* not tested group). CMF = cyclophosphamide, methotrexate, fluorouracil; ER = estrogen receptor; PR = progesterone receptor; IQR = interquartile range; GnRHa = gonadotropin-releasing hormone analogs; NA = not applicable.

Supplementary Figure 1. Cumulative incidence of pregnancy after breast cancer according to treatment arm. GnRHa = gonadotropin-releasing hormone analogs.



No. at risk													
Control group	133	127	125	116	113	105	103	96	90	83	80	77	54
GnRHa group	148	142	129	124	120	110	100	92	90	86	84	78	50