Supplementary material

Relationships between pathological factors and long-term outcomes in patients enrolled in two prospective randomized controlled trials comparing the efficacy of oral tegafur-uracil with CMF (N•SAS-BC 01 trial and CUBC trial)

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Supplementary Table 1. Characteristics of evaluable patients in the N•SAS-BC 01 and CUBC studies, and in the present study

Variables	N•SAS-BC 01 and CUBC studies[a] (N=1057)	The present study (N=689)	p value
CUBC, n (%)	350 (33.1)	158 (22.9)	<0.0001[b]
N•SAS-BC 01, n (%)	707 (66.9)	531 (77.1)	
Age (years)			0.687[c]
Median (range)	53.0 (31–75)	53.0 (32–75)	
<50, n (%)	416 (39.4)	267 (38.8)	0.800[b]
≥50	641 (60.6)	422 (61.2)	
Tumor size (cm)			0.038[c]
Median (range)	2.2 (0.4–12.0)	2.1 (0.5–10.0)	
<3 cm, n (%)	740 (70.0)	540 (73.1)	0.157[b]
≥3 cm	317 (30.0)	185 (26.9)	
Lymph nodes, n (%)			<0.0001[b]
0	707 (66.9)	531 (77.1)	
1–3	273 (25.8)	131 (19.0)	
4	77 (7.3)	27 (3.9)	
Histological type, n (%)			0.357[b]
Invasive ductal	975 (92.2)	627 (91.0)	
Other	82 (7.8)	62 (9.0)	
Estrogen receptor[d], n (%)			0.200[b]
Positive	534 (50.5)	380 (55.2)	
Negative	479 (45.3)	300 (43.5)	
Unknown	44 (4.2)	9 (1.3)	
Progesterone receptor[d], n (%)			0.358[b]
Positive	485 (45.9)	346 (50.2)	
Negative	501 (47.4)	326 (47.3)	
Unknown	71 (6.7)	17 (2.5)	
Human epidermal growth factor receptor 2, n (%)			

[a]Evaluable patients in the N•SAS-BC 01 (707 patients) and CUBC (350 patients) studies.

[b]χ^2 test

[c]*t*-test

[d]Based on the expression measured locally in the previous N•SAS-BC 01 and CUBC studies.

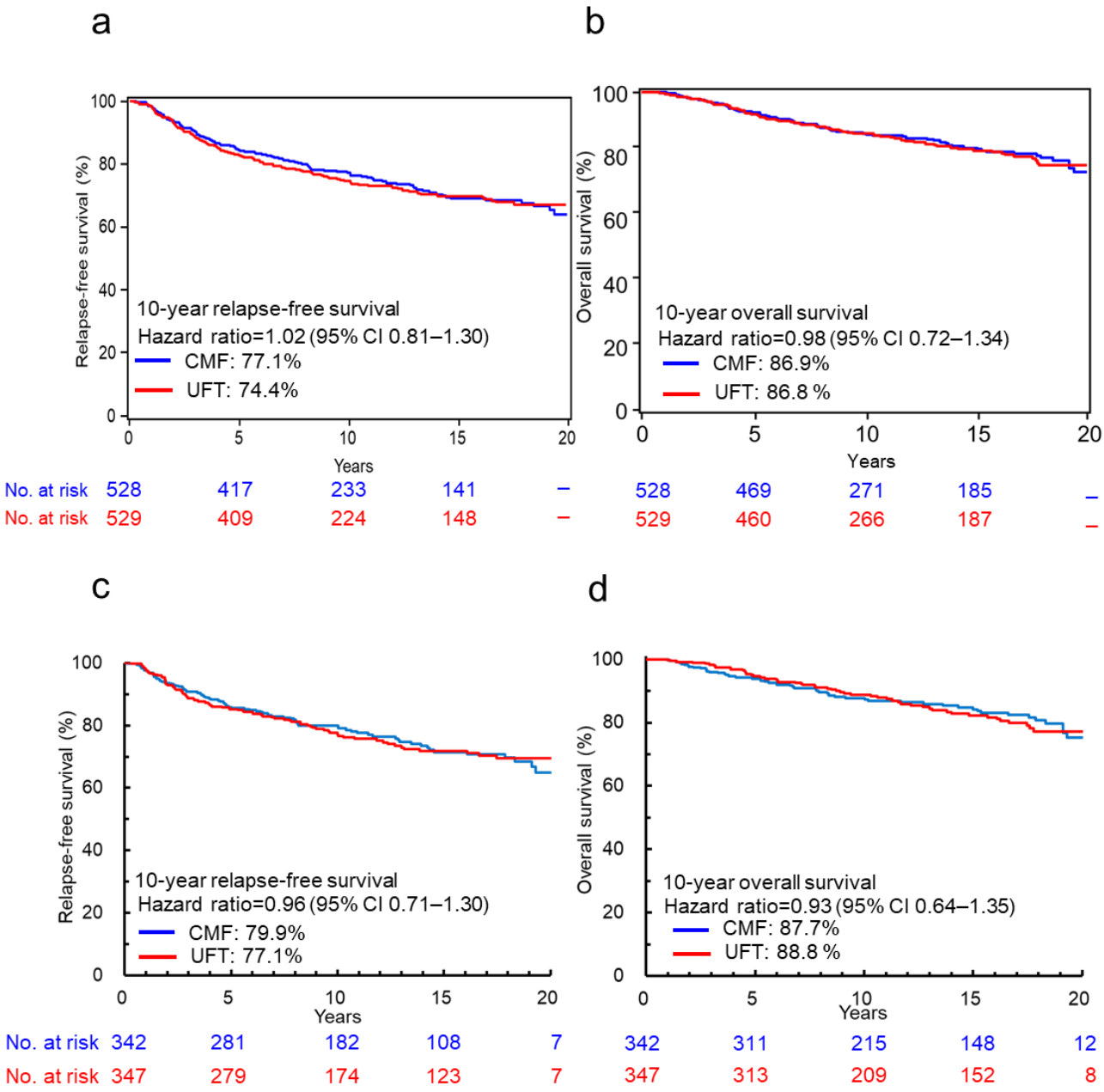
Supplementary Table 2. Patient characteristics according to HR/HER2 subtype

Variable	HR+/HER2−		HR−/HER2−		HR+/HER2+		HR−/HER2+	
	CMF (N=210)	UFT (N=210)	CMF (N=59)	UFT (N=73)	CMF (N=42)	UFT (N=26)	CMF (N=29)	UFT (N=29)
Patients, n (%)								
N•SAS-BC 01	157 (74.8)	150 (71.4)	52 (88.1)	62 (84.9)	35 (83.3)	20 (76.9)	22 (75.9)	23 (79.3)
CUBC	53 (25.2)	60 (28.6)	7 (11.9)	11 (15.1)	7 (16.7)	6 (23.1)	7 (24.1)	6 (20.7)
Age (years)								
Median (range)	52.0 (32–74)	52.0 (33–70)	53.0 (32–73)	52.0 (32–75)	52.5 (34–71)	55.0 (39–73)	54.0 (41–68)	56.0 (44–71)
<50, n (%)	90 (42.9)	90 (42.9)	21 (35.6)	25 (34.2)	15 (35.7)	12 (46.2)	5 (17.2)	5 (17.2)
≥50	120 (57.1)	120 (57.1)	38 (64.4)	48 (65.8)	27 (64.3)	14 (53.8)	24 (82.8)	24 (82.8)
Tumor size (cm)								
Median (range)	2.0 (0.7–8.0)	2.2 (0.5–9.5)	2.2 (0.9–8.0)	2.3 (0.5–7.8)	2.0 (0.5–4.5)	2.0 (0.5–10.0)	2.5 (0.7–6.0)	2.2 (0.9–5.0)
<3 cm, n (%)	161 (76.7)	150 (71.4)	40 (67.8)	51 (69.9)	35 (83.3)	17 (65.4)	19 (65.5)	20 (69.0)
≥3 cm	49 (23.3)	60 (28.6)	19 (32.2)	22 (30.1)	7 (16.7)	9 (34.6)	10 (34.5)	9 (31.0)
Lymph nodes, n (%)								
0	157 (74.8)	150 (71.4)	52 (88.1)	62 (84.9)	35 (83.3)	20 (76.9)	22 (75.9)	23 (79.3)
1–3	45 (21.4)	49 (23.3)	7 (11.9)	10 (13.7)	6 (14.3)	5 (19.2)	3 (10.3)	5 (17.2)
4	8 (3.8)	11 (5.2)	0	1 (1.4)	1 (2.4)	1 (3.8)	4 (13.8)	1 (3.4)
Histological type, n (%)								
Invasive ductal	188 (89.5)	186 (88.6)	55 (93.2)	65 (89.0)	42 (100.0)	25 (96.2)	29 (100.0)	26 (89.7)
Other	22 (10.5)	24 (11.4)	4 (6.8)	8 (11.0)	0	1 (3.8)	0	3 (10.3)
Estrogen receptor, n (%)								
Negative	5 (2.4)	4 (1.9)	59 (100.0)	73 (100.0)	1 (2.4)	0	29 (100.0)	29 (100.0)
Positive	205 (97.6)	206 (98.1)	0	0	41 (97.6)	26 (100.0)	0	0
Progesterone receptor, n (%)								
Negative	34 (16.2)	28 (13.3)	59 (100.0)	73 (100.0)	16 (38.1)	9 (34.6)	29 (100.0)	29 (100.0)
Positive	176 (83.8)	182 (86.7)	0	0	26 (61.9)	17 (65.4)	0	0
Ki67 (%)								
Median (range)	19.0 (0.0–90.8)	15.9 (0.0–83.7)	41.5 (0.0–97.2)	44.4 (0.0–86.0)	27.0 (0.0–69.7)	30.4 (2.4–57.3)	29.8 (0.0–60.7)	33.5 (0.0–67.7)
<20%	115 (54.8)	130 (61.9)	13 (22.0)	14 (19.2)	10 (23.8)	6 (23.1)	7 (24.1)	4 (13.8)
≥20%	95 (45.2)	80 (38.1)	46 (78.0)	59 (80.8)	32 (76.2)	20 (76.9)	22 (75.9)	25 (86.2)
Nuclear grade, n (%)								
Grade 1	81 (38.6)	85 (40.5)	4 (6.8)	2 (2.7)	2 (4.8)	3 (11.5)	2 (6.9)	0

Grade 2	59 (28.1)	76 (36.2)	7 (11.9)	5 (6.8)	10 (23.8)	6 (23.1)	4 (13.8)	2 (6.9)
Grade 3	70 (33.3)	49 (23.3)	48 (81.4)	66 (90.4)	29 (69.0)	17 (65.4)	23 (79.3)	27 (93.1)
Unknown	0	0	0	0	1 (2.4)	0	0	0
Histological grade, n (%)								
Grade 1	36 (17.1)	28 (13.3)	1(1.7)	0	1 (2.4)	2 (7.7)	0	0
Grade 2	109 (51.9)	136 (64.8)	14 (23.7)	9 (12.3)	15 (35.7)	7 (26.9)	8 (27.6)	4 (13.8)
Grade 3	65 (31.0)	46 (21.9)	44 (74.6)	64 (87.7)	25 (59.5)	17 (65.4)	21 (72.4)	25 (86.2)
Unknown	0	0	0	0	1 (2.4)	0	0	0
Tumor-infiltrating lymphocytes, n (%)								
Low	163 (77.6)	183 (87.1)	28 (47.5)	29 (39.7)	26 (61.9)	18 (69.2)	10 (34.5)	11 (37.9)
Intermediate	31 (14.8)	21 (10.0)	22 (37.3)	30 (41.1)	9 (21.4)	5 (19.2)	12 (41.4)	10 (34.5)
High	15 (7.1)	5 (2.4)	9 (15.3)	14 (19.2)	7 (16.7)	3 (11.5)	7 (24.1)	8 (27.6)
Unknown	1 (0.5)	1 (0.5)	0	0	0	0	0	0

CMF, cyclophosphamide, methotrexate, and fluorouracil; UFT, tegafur-uracil; HER2, human epidermal growth factor receptor 2; HR, hormone receptor

Supplementary Fig. 1 Kaplan–Meier survival curves for relapse-free survival (RFS) (a) and overall survival (OS) (b) adjusted for age, tumor size, nodal status, histological type, estrogen receptor (ER), and progesterone receptor (PgR) in all patients, and for RFS (c) and OS (d) adjusted for tumor size and nodal status in patients included in the final analysis. ER and PgR data used for the adjustment in all patients were measured at each study site, and those included in the final analysis were measured by central pathological review



CI, confidence interval, CMF, cyclophosphamide, methotrexate, and fluorouracil; UFT, tegafur-uracil