Supplementary

Table S1 The effects of clinical factors on PFS (n=482)

Covariates	Level	Univariate Cox regression		Multivariate Cox regression	
		Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value
Age at diagnosis (years)[#]		1.004 (0.99, 1.02)	0.63	1.019 (0.99, 1.05)	0.15
Menopause	No	Ref		Ref	
	Yes	0.91 (0.65, 1.29)	0.60	0.67 (0.40,1.13)	0.14
Neo-adjuvant therapy	No	Ref		Ref	
	Yes	1.06 (0.72, 1.56)	0.78	1.09 (0.73, 1.62)	0.68
Surgery	No	Ref		Ref	
	Yes	0.78 (0.40, 1.52)	0.46	0.81 (0.40, 1.64)	0.56
ER	Negative	Ref		Ref	
	Positive	0.97 (0.70, 1.32)	0.83	1.21 (0.81, 1.82)	0.35
PR	Negative	Ref		Ref	
	Positive	0.75 (0.55, 1.02)	0.07	0.59 (0.40, 0.89)	0.01
HER2	Negative	Ref		Ref	
	Positive	0.71 (0.50, 1.02)	0.06	0.66 (0.46, 0.96)	0.03
Subtype	Triple negative	Ref		Ref	
	HR+/HER2–	0.75 (0.51, 1.11)	0.15	0.70 (0.47, 1.04)	0.08
	HER2+/HR–	0.70 (0.41, 1.20)	0.19	0.67 (0.38, 1.15)	0.14
	HR+/HER2+	0.50 (0.30, 0.86)	0.01	0.48 (0.28, 0.82)	0.007
Prior treatment lines	1	0.79 (0.57, 1.08)	0.14	0.82 (0.59, 1.14)	0.24
	≥2	Ref		Ref	
Prior capecitabine-based treatment response	SD	Ref		Ref	
	PR	0.90 (0.65, 1.24)	0.51	0.90 (0.65, 1.26)	0.55
	CR	0.62 (0.23, 1.68)	0.35	0.71 (0.26, 1.96)	0.51
Capecitabine maintenance	No	Ref		Ref	
	Yes	1.07 (0.74, 1.55)	0.71	1.17 (0.81, 1.71)	0.40

Age at diagnosis (years)[#] represented as the average age at diagnosis with standard deviation and the median age at diagnosis with IQR. PFS, progression-free survival; CI, confidence interval; HR, hormone receptor; ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; SD, stable disease; PR, partial response; CR, complete response; IQR, interquartile range.

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Table S2 The clinical characteristics of propensity score-matched patients with MBC stratified by capecitabine maintenance treatment

Variables	Levels	Total (n=388)	Capecitabine maintenance		
			Yes (n=194)	No (n=194)	P value*
Age at diagnosis (years)#		45±9/45 (39, 51)	45±9/46 (39, 52)	45±9/45 (38, 50)	0.42
Menopause, n (%)	No	258 (66.49)	123 (63.40)	135 (69.59)	0.20
	Yes	130 (33.51)	71 (36.60)	59 (30.41)	
Neo-adjuvant therapy, n (%)	Yes	77 (19.85)	40 (20.62)	37 (19.07)	0.70
	No	311 (80.15)	154 (79.38)	157 (80.93)	
Surgery, n (%)	Yes	368 (94.85)	186 (95.88)	182 (93.81)	0.36
	No	20 (5.15)	8 (4.12)	12 (6.19)	
ER, n (%)	Positive	233 (60.05)	115 (59.28)	118 (60.82)	0.76
	Negative	155 (39.95)	79 (40.72)	76 (39.18)	
PR, n (%)	Positive	207 (53.35)	103 (53.09)	104 (53.61)	0.92
	Negative	181 (46.65)	91 (46.91)	90 (46.39)	
HER2, n (%)	Positive	108 (27.84)	56 (28.87)	52 (26.80)	0.65
	Negative	280 (72.16)	138 (71.13)	142 (73.20)	
Subtype, n (%)	Triple negative	89 (22.94)	45 (23.20)	44 (22.68)	0.84
	HR+/HER2–	191 (49.23)	93 (47.94)	98 (50.52)	
	HR–/HER2+	45 (11.60)	24 (12.37)	21 (10.82)	
	HR+/HER2+	63 (16.24)	32 (16.49)	31 (15.98)	
Prior chemotherapy lines, n (%)	1	239 (61.60)	122 (62.89)	117 (60.31)	0.46
	2	112 (28.87)	55 (28.35)	57 (29.38)	
	≥3	37 (9.54)	17 (8.76)	20 (10.31)	
Prior chemotherapy response, n (%)	CR	15 (3.87)	6 (3.09)	9 (4.64)	0.66
	PR	141 (36.34)	76 (39.18)	65 (33.51)	
	SD	232 (59.79)	112 (57.73)	120 (61.86)	

*, for quantitative variables, P values were calculated by Student's *t*-test; for categorical variables, P values were calculated by chi-squared test (Mantel-Haenszel for >2 levels comparison) or Fisher's exact test (n<5). Age at diagnosis (years)# represented as the average age at diagnosis with standard deviation and the median age at diagnosis with IQR. MBC, metastatic breast cancer; ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; CR, complete response; PR, partial response; SD, stable disease; IQR, interquartile range.

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Table S3 The effects of clinical factors on PFS in propensity score-matched MBC patients (n=388)

Covariates	Level	Univariate Cox regression		Multivariate Cox regression	
		Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value
Age at diagnosis (years)[#]		0.99 (0.97, 1.01)	0.25	1.01 (0.98, 1.04)	0.59
Menopause, n (%)	No	Ref		Ref	
	Yes	0.77 (0.52, 1.12)	0.17	0.68 (0.39,1.18)	0.17
Neo-adjuvant therapy, n (%)	No	Ref		Ref	
	Yes	1.11 (0.72, 1.72)	0.63	1.17 (0.75, 1.84)	0.49
Surgery, n (%)	No	Ref		Ref	
	Yes	0.87 (0.41, 1.86)	0.72	0.91 (0.41, 2.01)	0.81
ER	Negative	Ref		Ref	
	Positive	0.98 (0.69, 1.38)	0.89	1.20 (0.75, 1.93)	0.45
PR	Negative	Ref		Ref	
	Positive	0.82 (0.59, 1.16)	0.27	1.20 (0.75, 1.93)	0.45
HER2	Negative	Ref		Ref	
	Positive	0.67 (0.45, 1.00)	0.05	0.64 (0.42, 0.96)	0.03
Subtype, n (%)	triple negative	Ref		Ref	
	HR+/HER2–	0.78 (0.52, 1.17)	0.23	0.72 (0.47, 1.10)	0.13
	HER2+/HR–	0.61 (0.33, 1.14)	0.12	0.59 (0.31, 1.13)	0.11
	HR+/HER2+	0.53 (0.30, 0.94)	0.03	0.49 (0.27, 0.89)	0.02
Prior treatment lines	1	0.87 (0.61, 1.24)	0.45	0.88 (0.61, 1.27)	0.48
	≥2	Ref		Ref	
Prior capecitabine-based treatment response	SD	Ref		Ref	
	PR	1.01 (0.71, 1.44)	0.97	1.00 (0.70, 1.43)	1.00
	CR	0.45 (0.11, 1.85)	0.27	0.44 (0.11, 1.84)	0.26
Capecitabine maintenance	No	Ref		Ref	
	Yes	1.12 (0.79, 1.75)	0.42	1.22 (0.82, 1.82)	0.33

Age at diagnosis (years)[#] represented as the average age at diagnosis with standard deviation and the median age at diagnosis with IQR. PFS, progression-free survival; MBC, metastatic breast cancer; CI, confidence interval; ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; CR, complete response; SD, stable disease; PR, partial response; IQR, interquartile range.

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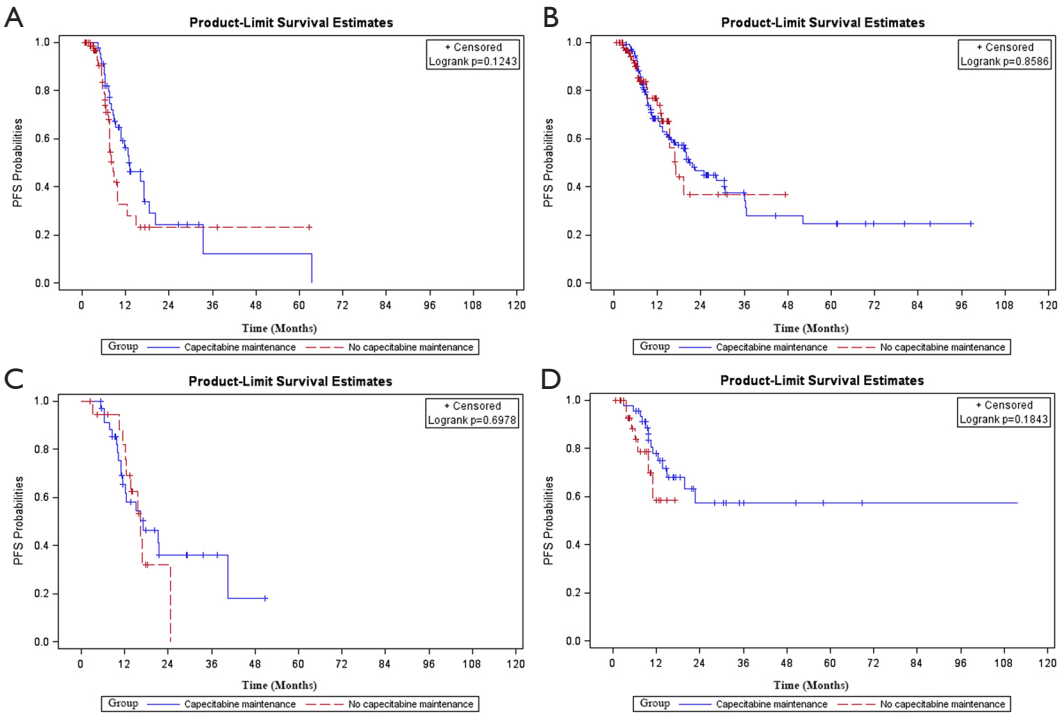

Figure S1 KM curves of PFS in capecitabine maintenance group and non-capecitabine maintenance group with TNBCs (A), HR+/HER2– (B), HR–/HER2+ (C) and HR+/HER2+ (D) breast cancers. PFS, progression-free survival; KM, Kaplan-Meier; TNBC, triple-negative breast cancer; HR, hormone receptor; HER2, human epidermal growth factor receptor 2.

Table S4 ctDNA analysis of *TP53* aberrations in capecitabine maintenance patients with different HR/HER2 subtypes

Subtype	*TP53*		P value*
	Wild-type (n=40)	Aberrant (n=17)	
TNBC	1 (16.67)	5 (83.33)	0.01
HR+/HER2–	29 (72.5)	11 (27.50)	
HR–/HER2+	2 (100.00)	0 (0.00)	
HR+/HER2+	8 (88.89)	1 (11.11)	

*, P values were calculated using a chi-squared test (Mantel-Haenszel for >2 levels of comparison) or Fisher's exact test (n<5). ctDNA, circulating tumour DNA; TNBC, triple-negative breast cancer; HR, hormone receptor; HER2, human epidermal growth factor receptor 2.

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Table S5 Side effects

Variables	Levels	Total (n=669)	Capecitabine maintenance		
			Yes	No	P value*
WBC decrease, n (%)					0.63
	No	317 (65.77)	171 (66.80)	146 (64.60)	
	Yes	165 (34.23)	85 (33.20)	80 (35.40)	
Neutropenia, n (%)					0.11
	No	356 (73.86)	197 (76.95)	159 (70.35)	
	Yes	126 (26.14)	59 (23.05)	67 (29.65)	
Skin adverse reactions, n (%)					0.63
	No	478 (99.17)	253 (98.83)	225 (99.56)	
	Yes	4 (0.83)	3 (1.17)	1 (0.44)	
Hand-foot syndrome, grade, n (%)					<0.0001
	0	458 (95.02)	232 (90.63)	226 (100.00)	
	1	9 (1.87)	9 (3.52)	0 (0.00)	
	2	6 (1.24)	6 (2.34)	0 (0.00)	
	3	9 (1.87)	9 (3.52)	0 (0.00)	
Neurotoxicity, n (%)					0.38
	No	477 (98.96)	252 (98.44)	225 (99.56)	
	Yes	5 (1.04)	4 (1.56)	1 (0.44)	
Nausea, n (%)					0.55
	No	471 (97.72)	249 (97.27)	222 (98.23)	
	Yes	11 (2.28)	7 (2.73)	4 (1.77)	

*, P values were calculated using a chi-squared test (Mantel-Haenszel for >2 levels of comparison) or Fisher's exact test (n<5). WBC, white blood cell.

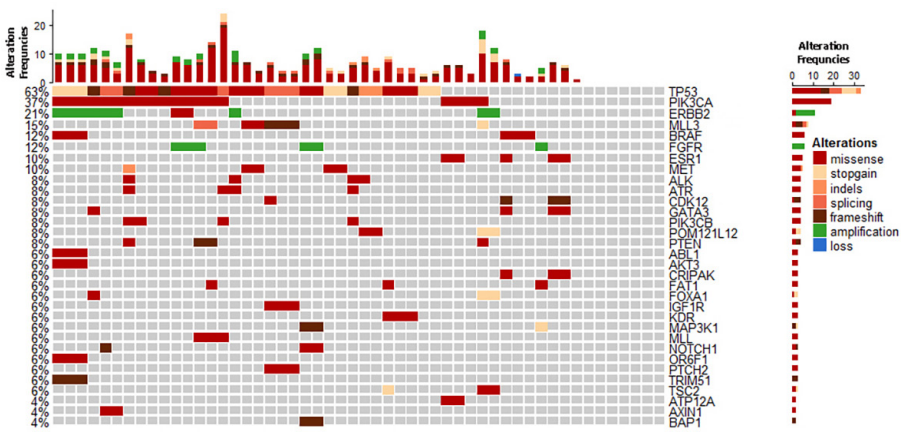

Figure S2 A heatmap of the circulating tumour DNA alterations in patients who had progressive disease during prior capecitabine-based chemotherapy.

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