

Supplementary Table S1. Demographic characteristics of the HER2-IHC0 and HER2 low groups in the whole cohort

Characteristic	Overall N = 999 ¹	HER2 IHC 0 N = 152 ¹	HER2 low N = 847 ¹	P value ²
Age	49.00 (43.00, 59.00)	49.00 (42.75, 61.25)	50.00 (43.00, 59.00)	0.9
Age group, years				0.070
< 40	138 (14%)	25 (16%)	113 (13%)	
40–59	622 (62%)	82 (54%)	540 (64%)	
> 59	239 (24%)	45 (30%)	194 (23%)	
BMI, kg/m ²				0.7
≤ 25	553 (55%)	82 (54%)	471 (56%)	
> 25	446 (45%)	70 (46%)	376 (44%)	
Menopausal				0.8
premenopausal	549 (55%)	82 (54%)	467 (55%)	
postmenopausal	450 (45%)	70 (46%)	380 (45%)	
Histology ³				0.13
IDC	903 (90%)	133 (88%)	770 (91%)	
ILC	33 (3.3%)	4 (2.6%)	29 (3.4%)	
Others	63 (6.3%)	15 (9.9%)	48 (5.7%)	
Grade				0.2
1	59 (5.9%)	10 (6.6%)	49 (5.8%)	
2	665 (67%)	92 (61%)	573 (68%)	
3	275 (28%)	50 (33%)	225 (27%)	
T				> 0.9
1	538 (54%)	83 (55%)	455 (54%)	
2	431 (43%)	65 (43%)	366 (43%)	
3	30 (3.0%)	4 (2.6%)	26 (3.1%)	
N				> 0.9
0	596 (60%)	89 (59%)	507 (60%)	
1	241 (24%)	38 (25%)	203 (24%)	
2	102 (10%)	17 (11%)	85 (10%)	
3	60 (6.0%)	8 (5.3%)	52 (6.1%)	
Stage				0.7
I	402 (40%)	59 (39%)	343 (40%)	
II	450 (45%)	67 (44%)	383 (45%)	
III	147 (15%)	26 (17%)	121 (14%)	
ER ⁴ , %				< 0.001
0	220 (22%)	56 (37%)	164 (19%)	
1–10	45 (4.5%)	9 (5.9%)	36 (4.3%)	
> 10	734 (73%)	87 (57%)	647 (76%)	

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Characteristic	Overall N = 999 ¹	HER2 IHC 0 N = 152 ¹	HER2 low N = 847 ¹	P value ²
PR ⁵				< 0.001
negative	256 (26%)	60 (39%)	196 (23%)	
positive	743 (74%)	92 (61%)	651 (77%)	
Ki67				0.5
< 14%	216 (22%)	36 (24%)	180 (21%)	
≥ 14%	783 (78%)	116 (76%)	667 (79%)	
TOP2A, %				0.8
< 30	866 (87%)	134 (88%)	732 (86%)	
30–60	97 (9.7%)	13 (8.6%)	84 (9.9%)	
> 60	36 (3.6%)	5 (3.3%)	31 (3.7%)	
Radiotherapy				0.9
No	798 (80%)	122 (80%)	676 (80%)	
Yes	201 (20%)	30 (20%)	171 (20%)	
Chemotherapy				> 0.9
No	372 (37%)	56 (37%)	316 (37%)	
Yes	627 (63%)	96 (63%)	531 (63%)	
Endocrine therapy				< 0.001
No	272 (27%)	103 (68%)	169 (20%)	
Yes	727 (73%)	49 (32%)	678 (80%)	

Note. ¹Median (IQR); *n* (%); ²Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test; ³ IDC, invasive ductal carcinoma; ILC: invasive lobular carcinoma; ⁴ER: estrogen receptor; ⁵PR: progesterone receptor. T, T stage; N, N stage.

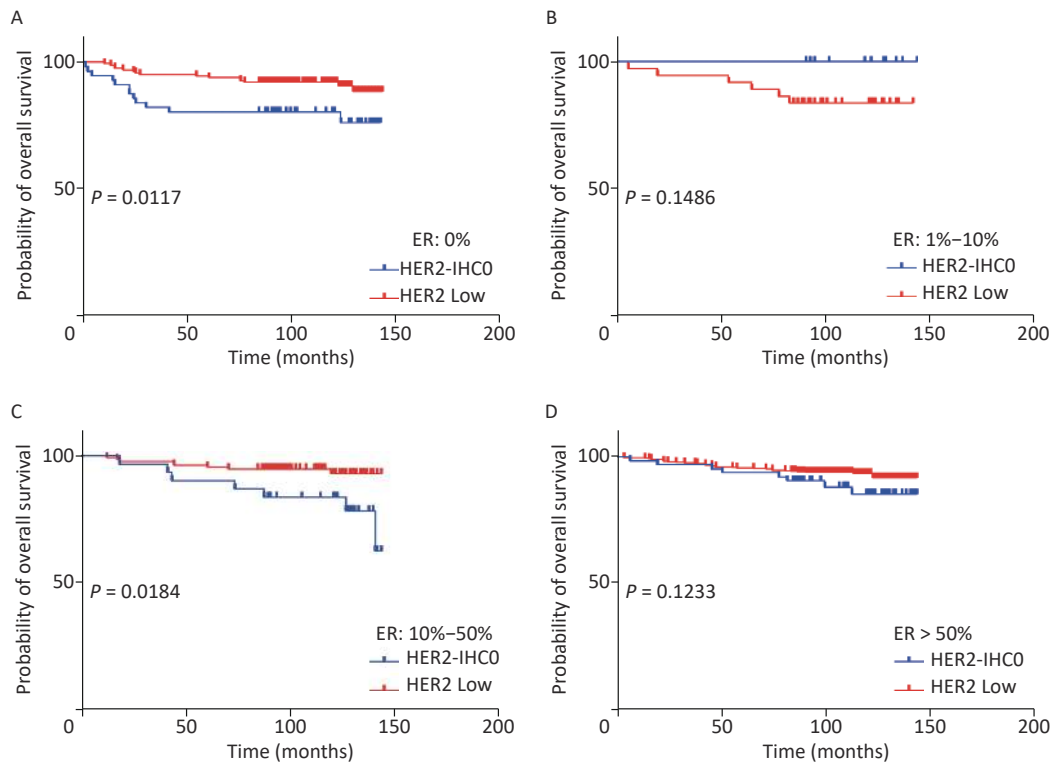
Supplementary Table S2. Univariate and multivariate Cox analyses of DFS between the HER2 low and HER-IHC0 groups

Characteristics	Univariate			Multivariate		
	HR	95% CI	P value	HR	95% CI	P value
Age, years						
< 40	–	–	–	–	–	–
40–59	0.42	0.28–0.62	< 0.001	0.47	0.32–0.70	< 0.001
> 59	0.69	0.44–1.06	0.088	0.81	0.52–1.25	0.334
BMI, kg/m ²						
≤ 25	–	–	–			
> 25	0.91	0.66–1.25	0.555			
Menopausal						
postmenopausal	–	–	–			
premenopausal	0.90	0.66–1.23	0.502			
histology						
IDC	–	–	–			
ILC	0.76	0.28–2.06	0.594			
Others	0.90	0.46–1.77	0.769			

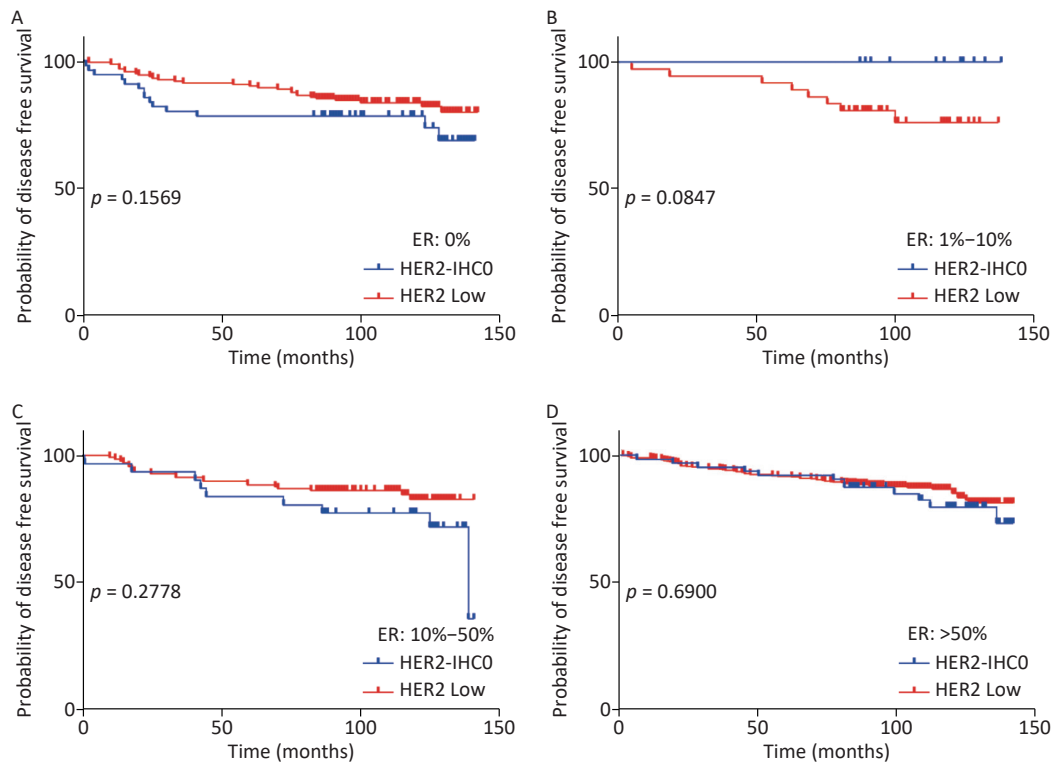
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Characteristics	Univariate			Multivariate		
	HR	95% CI	P value	HR	95% CI	P value
Grade						
1	–	–				
2	0.86	0.45–1.65	0.653			
3	1.35	0.69–2.64	0.383			
T						
1	–	–	–	–	–	–
2	1.86	1.35–2.57	< 0.001	1.35	0.85–2.15	0.201
3	1.41	0.57–3.52	0.457	0.70	02.6–1.91	0.488
N						
0	–	–	–	–	–	–
1	1.7	1.17–2.47	0.005	1.13	0.70–1.80	0.62
2	2.06	1.29–3.31	0.003	0.87	0.31–2.46	0.791
3	3.44	2.11–5.61	< 0.001	1.23	0.39–3.84	0.726
Stage						
I	–	–	–	–	–	–
II	1.91	1.30–2.83	0.001	1.25	0.66–2.36	0.502
III	3.42	2.20–5.31	< 0.001	2.1	0.64–6.94	0.222
ER						
Negative	–	–	–			
Positive	0.79	0.56–1.13	0.202			
PR						
Negative	–	–	–			
Positive	0.76	0.54–1.06	0.105			
HER2						
0	–	–	–			
Low	0.81	0.54–1.20	0.295			
Ki67, %						
< 14	–	–	–			
≥ 14	2.33	1.41–3.85	< 0.001	2.07	1.24–3.43	0.005
TOP2A, %						
< 30	–	–	–			
30%–60	1.09	0.67–1.78	0.732			
> 60	1.11	0.52–2.37	0.796			
Chemotherapy						
No	–	–	–			
Yes	1.35	0.97–1.89	0.078			
Radiotherapy						
No	–	–	–			
Yes	2.3	1.66–3.21	< 0.001	1.81	1.27–2.60	0.001
Endocrine therapy						
No	–	–	–			
Yes	0.86	0.62–1.21	0.383			

Note. T, T stage; N, N stage.



Supplementary Figure S1. OS of HER2 low and HER2-IHCO in different ER levels. (A) ER: 0%; B. ER: 1%–10%; (C) ER: 10%–50%; (D) ER > 50%. HER2 low group showed a longer OS in ER 0 and ER 10%–50% groups [ER: 0% group: $HR = 0.319$ (95% CI : 0.132–0.776), $P = 0.0117$; ER: 10%–50% group: $HR = 0.2183$ (95% CI : 0.06159–0.7737), $P = 0.0291$]. P -values were calculated using the stratified log-rank test.



Supplementary Figure S2. DFS for HER2 low and HER2-IHC0 in different ER levels. (A) ER: 0%; (B) ER: 1%–10%; (C) ER: 10%–50%; (D) ER > 50%. HER2 low group showed a longer OS than the ER 0 and ER 10%–50% groups. No significant differences were found between the HER2-IHC0 and HER2 low groups. P -values were calculated using the stratified log-rank test.