

Table S1 NAT schemes and response to treatment in NAT-insensitive group (N=63)

Variables	n (%)
Treatment 1	
No. of cycles for treatment 1	
2	11 (17.4)
3–4	25 (39.7)
5–6	22 (34.9)*
7–8	5 (7.9)
Response to treatment 1	
SDa	37 (58.7)
SD	3 (4.8)
SDb	19 (30.2)
PD	4 (6.3)
Treatment 2	
Treatment regimen 2	
SDa (n=37)	
Surgery	8 (21.6)
Medication change	13 (35.1)
No change	16 (43.2)
SD (n=3)	
Surgery	1 (33.3)
Medication change	1 (33.3)
No change	1 (33.3)
SDb (n=19)	
Surgery	3 (15.8)
Medication change	12 (63.2)
No change	4 (21.0)
PD (n=4)	
Surgery	0 (0)
Medication change	4 (100)
No change	0 (0)
Response to treatment 2 (n=30)	
Yes	10 (33.3)
No	12 (40.0)
Missing	8 (26.7)

*, Six patients switched regimens, and 16 continued without modification. NAT, neoadjuvant therapy; SD, stable disease; SDa, SD with slight improvement; SDb, SD with tumor enlargement; PD, progression disease.

Table S2 Postoperative pathological characteristics and treatment in NAT-insensitive group (N=63)

Characteristic and treatment	n (%)
Postoperative Miller-Payne grading	
1–2	30 (47.6)
3	21 (33.3)
4	6 (9.5)
5	3 (4.8)
Missing	3 (4.8)
pCR	
Yes	3 (4.8)
No	60 (95.2)
Postoperative adjuvant chemotherapy	
Yes	30 (47.6)
No	31 (49.2)
Missing	2 (3.2)
HER2 treatment post-surgery	
Monotherapy	
Trastuzumab	18 (28.6)
Pyrotinib	3 (4.8)
T-DM1	5 (7.9)
Trastuzumab deruxtecan	1 (1.6)
Combination therapy	
HP	14 (22.2)
T-DM1 plus pertuzumab	1 (1.6)
Trastuzumab plus pyrotinib	6 (9.5)
Sequential combination therapy	
HP followed by neratinib	2 (3.1)
T-DM1 followed by neratinib	3 (4.8)
No	3 (4.8)
Missing	7 (11.1)

NAT, neoadjuvant therapy; pCR, pathological complete response; HER2, human epidermal growth factor receptor 2; T-DM1, trastuzumab emtansine; HP, trastuzumab plus pertuzumab.

Table S3 Standardized mean differences before and after PSM

Characteristic	SMD (before PSM)	SMD (after PSM)
cT stage (0/1/2 vs. 3/4)	0.084	0.101
Clinical stage (II vs. III)	0.188	0.040
HR (negative vs. positive)	0.305	0.035
HER2 (2+/FISH+ vs. 3+)	0.268	0.057
Anti-HER2 therapy (monotherapy vs. dual-therapy)	0.336	0.082

PSM, propensity score matching; HR, hormone receptor; HER2, human epidermal growth factor receptor 2; SMD, standardized mean difference.

Table S4 Characteristics of patients included in HER2 heterogeneity assessment

Characteristic	n		P
	NAT-insensitive group (N=36)	NAT-sensitive group (N=46)	
cT stage			0.901
0/1/2	23	30	
3/4	13	16	
Clinical stage			0.498
II	5	9	
III	31	37	
HR			0.741
Negative	9	13	
Positive	27	33	
HER2			0.628
2+/FISH+	7	11	
3+	29	35	
Anti-HER2 therapy			0.937
Monotherapy	13	17	
Dual-therapy	23	29	

HER2, human epidermal growth factor receptor 2; HR, hormone receptor; NAT, neoadjuvant therapy.