Supplementary

Regimen: Cycle No:

Name:	Patient No:	Sex:	Age:	Height:	Weight:	Body surface area:																	
Day:		-	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Date:																							
Drug																							
Laboratory test results and adverse events	Fatigue																						
	Nausea																						
	Vomiting																						
	Diarrhea																						
	Constipation																						
	Allergy																						
	Appetite																						
	Hand-foot syndrome																						
	Numb limbs																						
	Abdominal pain																						
	Headache																						
	WBC																						
	NEUT																						
	AST																						
	ALT																						
	HGB																						
	PLT																						
	Other AEs:																						

Figure S1 Medication and adverse events self-monitoring form. The form provided to patients is a Chinese version and more patient-friendly.

https://dx.doi.org/10.21037/tbcr-25-8

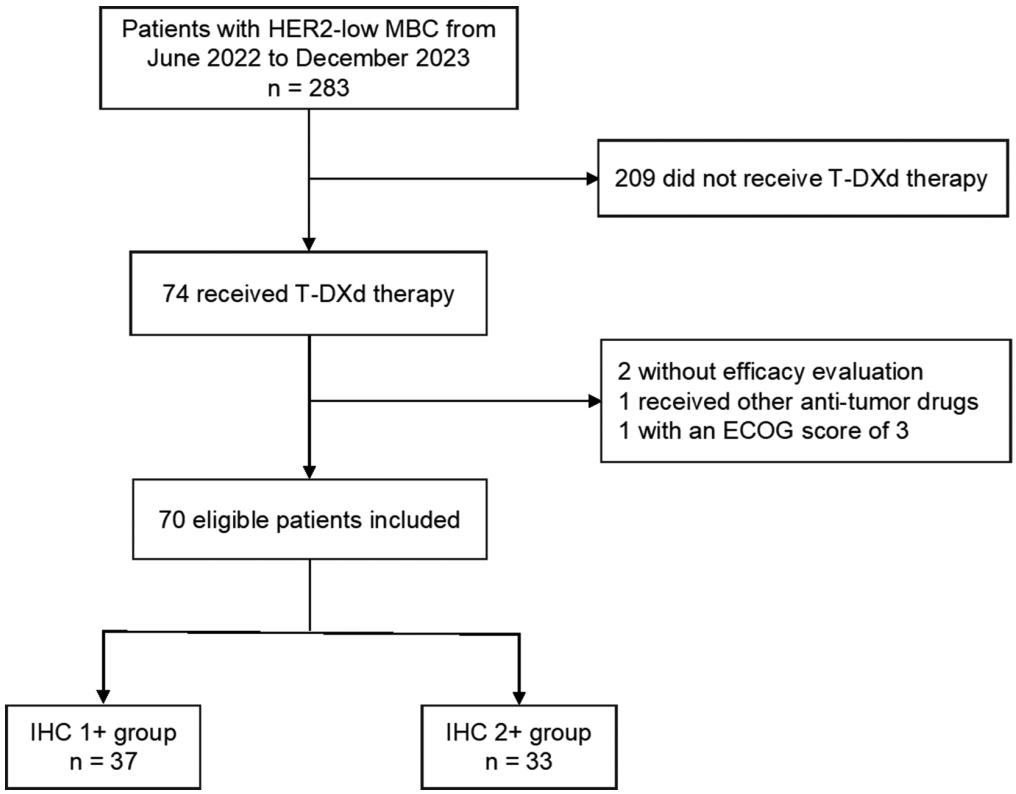

Figure S2 Flow chart of patient selection. ECOG, Eastern Cooperative Oncology Group; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; MBC, metastatic breast cancer; T-DXd, trastuzumab deruxtecan.

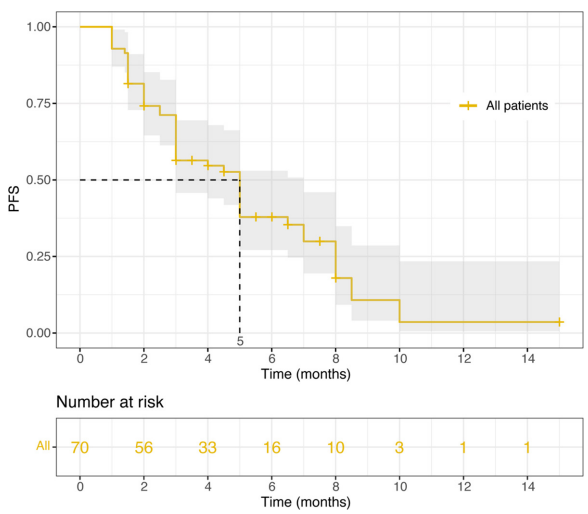

Figure S3 PFS curve of the total population. The median PFS was 5 months (95% confidence interval: 3–7). The shaded area represents the 95% confidence interval. Tick marks indicate data right-censored at the last follow-up. PFS, progression-free survival.

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Table S1 Comparison of clinical efficacy between IHC 1+ and 2+ groups according to the RECIST 1.1 criteria

	All patients (n=70)	IHC 1+ group (n=37)	IHC 2+ group (n=33)	P value
Clinical response, n (%)				
CR	0 (0)	0 (0)	0 (0)	
PR	15 (21.4)	6 (16.2)	9 (27.3)	
SD	38 (54.3)	20 (54.1)	18 (54.5)	
SD ≥6 months	6 (8.6)	3 (8.1)	3 (9.1)	
PD	17 (24.3)	11 (29.7)	6 (18.2)	
Response outcomes, n (%)				
ORR	15 (21.4)	6 (16.2)	9 (27.3)	0.404
CBR	21 (30)	9 (24.3)	12 (36.4)	0.403

CBR, clinical benefit rate; CR, complete response; IHC, immunohistochemistry; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

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Table S2 Univariate and multivariate Cox regression analyses of clinical factors affecting PFS in patients with HER2-low MBC receiving T-DXd

Characteristics	Univariate Cox analysis		Multivariate Cox analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
IHC status[†]				
1+	Reference		Reference	
2+, FISH-negative	0.48 (0.27–0.87)	0.015	0.51 (0.28–0.95)	0.034
Prior lines of chemotherapy				
≤2	Reference		Reference	
≥3	2.13 (1.19–3.81)	0.011	1.99 (1.10–3.58)	0.022
Initial T-DXd dose (mg/kg, q3w)	0.6 (0.43–0.84)	0.003	0.64 (0.45–0.89)	0.009
IHC score of primary lesion				
0	Reference			
1+	1.42 (0.71–2.84)	0.316		
2+, FISH-negative	0.64 (0.30–1.37)	0.247		
IHC score of metastatic lesion				
0	Reference			
1+	1.06 (0.37–3.08)	0.91		
2+, FISH-negative	0.48 (0.15–1.54)	0.22		
Not biopsied	0.88 (0.26–2.99)	0.841		
Line of treatment with T-DXd				
≤5th	Reference			
≥6th	1.76 (0.98–3.17)	0.058		
Age of receiving T-DXd (year)	0.97 (0.94–1.01)	0.104		
Menopausal status				
Premenopausal	Reference			
Postmenopausal	0.85 (0.48–1.51)	0.583		
HoR status				
Negative	Reference			
Positive	0.89 (0.38–2.12)	0.799		
Clinical stage at diagnosis				
I	Reference			
II	1.16 (0.49–2.75)	0.729		
III	0.77 (0.3–1.96)	0.581		
IV	1.26 (0.44–3.67)	0.667		
Visceral metastases				
No	Reference			
Yes	0.87 (0.31–2.43)	0.789		

Table S2 (*continued*)

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Table S2 (*continued*)

Characteristics	Univariate Cox analysis		Multivariate Cox analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Liver metastases				
No	Reference			
Yes	1.23 (0.59–2.55)	0.576		
Lung metastases				
No	Reference			
Yes	0.92 (0.53–1.61)	0.782		
Bone metastases				
No	Reference			
Yes	0.71 (0.37–1.34)	0.289		
Brain metastases				
No	Reference			
Yes	0.61 (0.3–1.26)	0.184		
Number of metastatic sites				
1–2	Reference			
≥3	0.83 (0.45–1.53)	0.547		
Prior lines of endocrine therapy				
≤2	Reference			
≥3	1.07 (0.59–1.95)	0.821		
Prior endocrine therapy				
Not received	Reference			
Received	0.79 (0.37–1.69)	0.539		
Prior CDK4/6i benefit				
Benefit[‡]	Reference			
Not benefit	1.52 (0.71–3.27)	0.284		
Not received	0.64 (0.31–1.28)	0.205		

[†], determined based on the higher IHC score between the primary lesion and pathologically examined metastatic lesions; [‡], defined as gained complete response or partial response or stable disease lasting ≥6 months from CDK4/6i treatment. CDK4/6i, cyclin-dependent kinase 4 and 6 inhibitors; CI, confidence interval; FISH, fluorescence *in situ* hybridization; HER2, human epidermal growth factor receptor 2; HoR, hormone receptor; HR, hazard ratio; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan.

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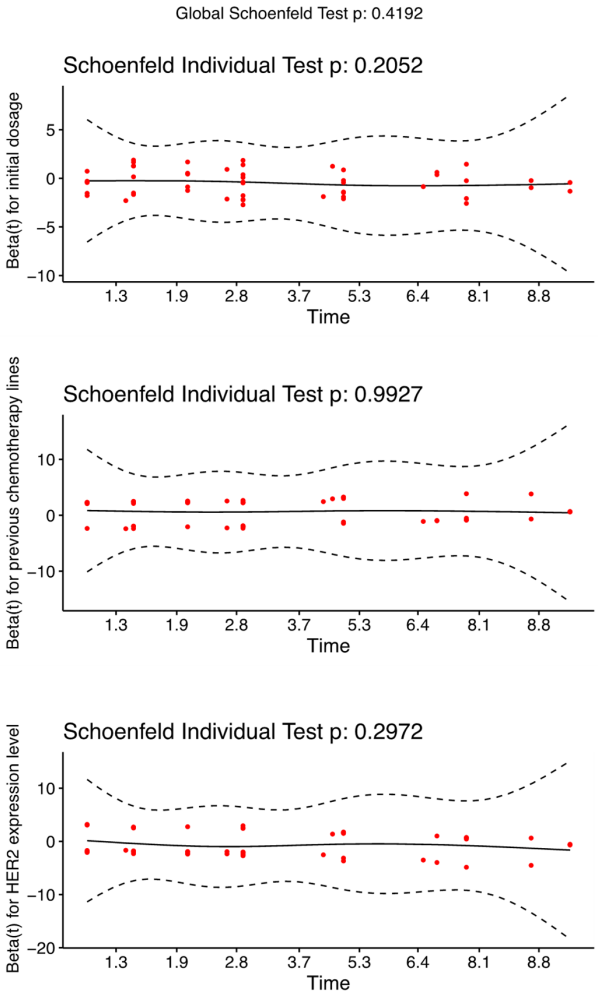

Figure S4 Schoenfeld residual plots to test whether variables in the multivariate Cox analysis meet the proportional hazard assumption: there was no significant correlation between the candidate variables and time (all P>0.05), thus all variables meet the proportional hazard assumption.

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Table S3 Treatment-related adverse events in all patients and different initial dose groups

Event, n (%)	All patients (n=70)		<4.4 mg/kg, q3w (n=29)		≥4.4 mg/kg, q3w (n=41)	
	Any grade	Grade 3–4	Any grade	Grade 3–4	Any grade	Grade 3–4
Hematological disorders						
Neutropenia	24 (34.3)	5 (7.1)	8 (27.6)	2 (6.9)	16 (39)	3 (7.3)
Anemia	23 (32.9)	5 (7.1)	8 (27.6)	2 (6.9)	15 (36.6)	3 (7.3)
Leukopenia	21 (30)	5 (7.1)	7 (24.1)	2 (6.9)	14 (34.1)	3 (7.3)
Thrombocytopenia	19 (27.1)	2 (2.9)	6 (20.7)	1 (3.4)	13 (31.7)	1 (2.4)
Gastrointestinal disorders						
Nausea	30 (42.9)	2 (2.9)	10 (34.5)	1 (3.4)	20 (48.8)	1 (2.4)
Vomiting	18 (25.7)	1 (1.4)	6 (20.7)	0 (0)	12 (29.3)	1 (2.4)
Diarrhea	12 (17.1)	2 (2.9)	4 (13.8)	1 (3.4)	8 (19.5)	1 (2.4)
Constipation	11 (15.7)	0 (0)	5 (17.2)	0 (0)	6 (14.6)	0 (0)
Increased aminotransferase levels	10 (14.3)	2 (2.9)	3 (10.3)	1 (3.4)	7 (17.1)	1 (2.4)
Fatigue	23 (32.9)	2 (2.9)	8 (27.6)	0 (0)	15 (36.6)	2 (4.9)
Decreased appetite	21 (30)	0 (0)	6 (20.7)	0 (0)	15 (36.6)	0 (0)
Interstitial lung disease	3 (4.3)	1 (1.4)	1 (3.4)	0 (0)	2 (4.9)	1 (2.4)

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