Supplementary

Table S1 Subgroup analysis for frequency of treatment-related adverse events

ADCs	No. of RCTs	Statistical results			Heterogeneity test	
		Pooled OR (95% CI)	Pooled P value	Weight (%)	I^2	P value
Frequency of any grade toxicity						
SG	2	1.50 (0.87, 2.60)	0.145	25.19	97.4	<0.001
GV	2	1.40 (1.04, 1.88)	0.028	24.51	78.9	0.030
TE	4	0.73 (0.66, 0.81)	<0.001	50.29	67.7	0.026
Overall	8	1.03 (0.75, 1.41)	0.849	100.00	98.1	<0.001
Frequency of any grade hematologic toxicity						
SG	1	1.48 (1.22, 1.81)	<0.001	14.87	NA	NA
GV	2	1.20 (0.16, 9.19)	0.857	27.29	97.3	<0.001
TE	4	0.83 (0.37, 1.87)	0.653	57.84	96.6	<0.001
Overall	7	1.01 (0.58, 1.75)	0.982	100.00	95.6	<0.001
Frequency of any grade non-hematologic toxicity						
SG	1	2.23 (1.96, 2.53)	<0.001	14.44	NA	NA
GV	2	1.48 (1.31, 1.67)	<0.001	28.12	0.0	0.683
TE	4	0.74 (0.56, 0.97)	0.027	57.45	94.6	<0.001
Overall	7	1.06 (0.70, 1.61)	0.781	100.00	98.5	<0.001
Frequency of grade ≥3 toxicity						
SG	2	1.54 (1.26, 1.88)	<0.001	22.72	21.3	0.260
GV	2	1.26 (0.65, 2.42)	0.497	21.26	81.6	0.020
TE	4	0.53 (0.38, 0.72)	<0.001	44.78	81.0	0.001
TD	1	0.78 (0.59, 1.04)	0.088	11.24	NA	NA
Overall	9	0.83 (0.57, 1.21)	0.342	100.00	94.0	<0.001
Frequency of grade ≥3 hematologic toxicity						
SG	1	1.74 (1.35, 2.24)	<0.001	14.93	NA	NA
GV	2	1.50 (0.20, 11.35)	0.697	27.57	95.1	<0.001
TE	4	0.52 (0.17, 1.64)	0.266	57.50	96.4	<0.001
Overall	7	0.84 (0.38, 1.83)	0.656	100.00	95.8	<0.001
Frequency of grade ≥3 non-hematologic toxicity						
SG	1	1.63 (1.08, 2.45)	0.019	14.76	NA	NA
GV	2	1.33 (1.00, 1.77)	0.049	27.04	0.0	0.400
TE	4	0.78 (0.28, 2.14)	0.624	58.20	95.7	<0.001
Overall	7	1.04 (0.52, 2.09)	0.908	100.00	94.9	<0.001

ADC, antibody-drug conjugate; SG, sacituzumab govitecan; GV, glembatumumab vedotin; TE, trastuzumab emtansine; TD, trastuzumab deruxtecan.

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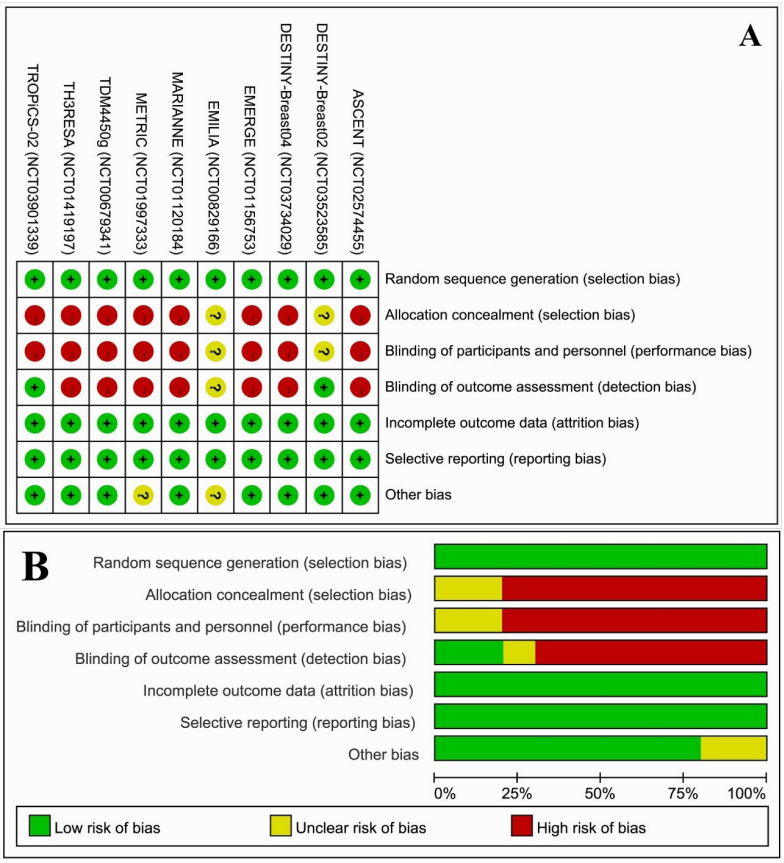

Figure S1 The judgements of risk of bias summary and risk of bias graph. (A) Shows the judgement of risk of bias summary and (B) shows the judgement of risk of bias graph.

Table S2 The funnel plot of publication bias

Analyzed label	P value*
Overall response rate	0.532
Clinical benefit rate	0.647
Progression-free survival	0.597
Overall survival	0.137
Frequency of any grade AEs	0.522
Frequency of grade ≥3 AEs	0.704

*, significant level: P<0.05.

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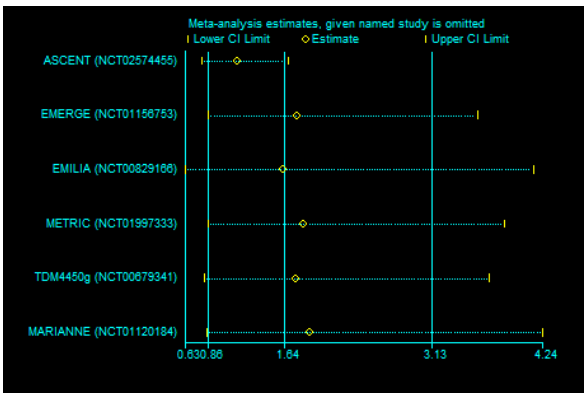

Figure S2 Sensitivity analysis for overall survival rate.

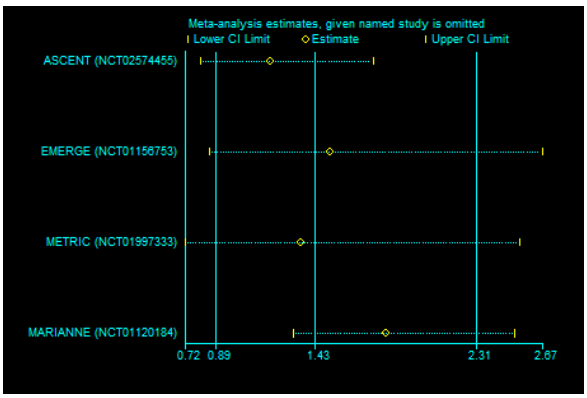

Figure S3 Sensitivity analysis for clinical benefit rate.

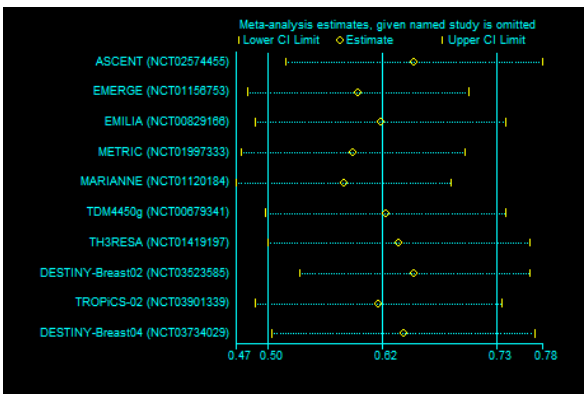

Figure S4 Sensitivity analysis for progression-free survival.

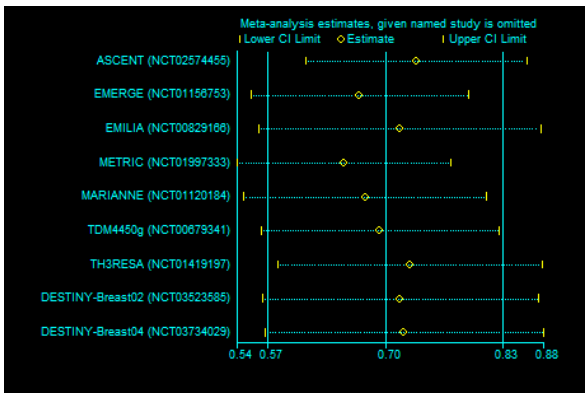

Figure S5 Sensitivity analysis for overall survival.

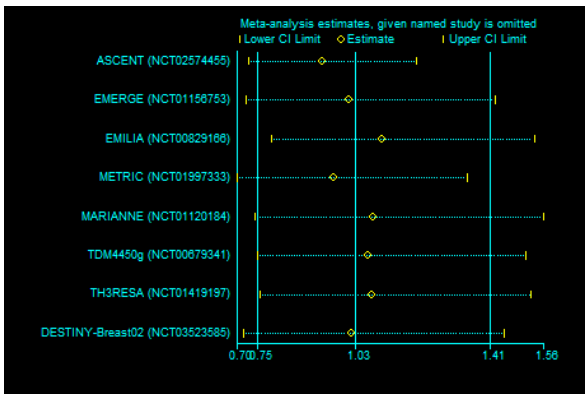

Figure S6 Sensitivity analysis for the frequency of any grade adverse events.

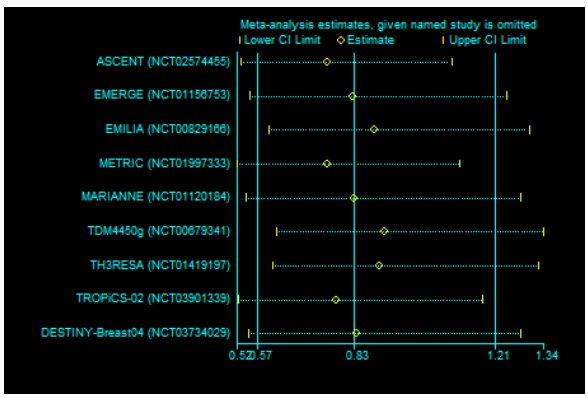

Figure S7 Sensitivity analysis for the frequency of grade ≥3 adverse events.

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Table S3 The detailed risk of bias assessments

Risk of bias	Risk of bias summary	Proportion of low risk (%)
Random sequence generation	All studies are described as randomized.	100
Allocation concealment	None of the studies have described the method of allocation concealment. Two studies do not provide sufficient information to accurately assess the method, therefore are at unclear risk of bias. The other nine studies are at high risk of bias.	0
Blinding of participants and personnel	None of the studies have described the method of allocation concealment. Two studies do not provide sufficient information to accurately assess the method, therefore are at unclear risk of bias. The other nine studies are at high risk of bias.	0
Blinding of outcome assessment	Two studies have described the method of blinding of outcome assessment. One study does not provide sufficient information to accurately assess the method, therefore is at unclear risk of bias. The other eight studies are at high risk of bias.	0–25
Incomplete outcome data	All studies are generally free of attrition bias.	100
Selective reporting	All studies are generally free of reporting bias. therefore is at unclear risk of bias.	100
Other bias	Nine studies are free of other bias, but the other two studies are at unclear risk of bias.	75–100

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ADCs	Physician's choice	Relative (95% CI)	Absolute (95% CI)		
Overall reponse rate												
10	randomised trials	not serious	very serious	not serious	not serious	all plausible residual confounding would reduce the demonstrated effect	691/2010 (34.4%)	443/1486 (29.8%)	**OR 1.78** (1.03 to 3.08)	**132 more per 1,000** (from 6 more to 269 more)	⨁⨁⨁◯ Moderate	IMPORTANT
Clinical benefit rate												
6	randomised trials	not serious	very serious	not serious	not serious	all plausible residual confounding would reduce the demonstrated effect	788/1251 (63.0%)	483/861 (56.1%)	**OR 1.62** (0.79 to 3.34)	**113 more per 1,000** (from 59 fewer to 249 more)	⨁⨁⨁◯ Moderate	IMPORTANT
Progression-free survival												
11	randomised trials	not serious	very serious	not serious	not serious	all plausible residual confounding would reduce the demonstrated effect	-/2585	-/1888	**HR 0.78** (0.61 to 0.94)	**-- per 1,000** (from -- to --)	⨁⨁⨁◯ Moderate	CRITICAL
Overall survival												
10	randomised trials	not serious	very serious	not serious	not serious	all plausible residual confounding would reduce the demonstrated effect	-/2538	-/1840	**HR 0.83** (0.64 to 1.02)	**-- per 1,000** (from -- to --)	⨁⨁⨁◯ Moderate	CRITICAL
Any grade adverse events												
11	randomised trials	not serious	very serious	not serious	not serious	all plausible residual confounding would reduce the demonstrated effect	-/2591	-/1795	**HR 1.07** (0.81 to 1.39)	**-- per 1,000** (from -- to --)	⨁⨁⨁◯ Moderate	IMPORTANT
Grade ≥ 3 adverse events												
11	randomised trials	not serious	very serious	not serious	not serious	all plausible residual confounding would reduce the demonstrated effect	-/2591	-/1795	**HR 0.77** (0.51 to 1.17)	**-- per 1,000** (from -- to --)	⨁⨁⨁◯ Moderate	IMPORTANT

Grade evidence by GRADEpro system.
Abbreviations: ADCs, antibody-drug conjugates; CI, confidence interval; HR, hazard Ratio; OR, odds ratio.

Figure S8 Grade evidence by GRADEpro system.

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