Table S1 Risk of bias assessed using the Cochrane Collaboration Risk of Bias Tool

	random sequence generation	allocation concealment	blinding of patients and personnel	blinding of outcome assessment	incomplete outcome data	selective reporting	other bias
Cristofanilli,2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Tripathy,2018	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Sledge,2017	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Sonke,2018	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Goetz,2017	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Finn,2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Finn,2015	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Slamon,2018	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Baselga,2017	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Di Leo,2017	Unclear	Unclear	Yes	Yes	Yes	Yes	Unclear
Andre,2019	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Krop,2016	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Bachelot,2012	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Pritchard,2013	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Wolff,2013	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Mosulino,2017	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Cristofanilli,2010	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Osborne,2011	Yes	Yes	Yes	Yes	Yes	Yes	Unclear

Clemons,2014	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Dickler,2016	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Hyams,2013	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear
Martín,2015	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Jiang,2019	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Yardley,2013	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Robertson,2013	Yes	Yes	Yes	Yes	No	Yes	Unclear
Ibrahim,2011	Yes	Yes	No	No	No	Yes	Unclear

Each domain is rated as being at low (yes), moderate (unclear) or high (no) risk of bias.

Table S2 Characteristics and overall survival data of studies about cyclin-dependent kinase 4/6 inhibitors [a]

Study	Trial name	Size	Menopausal status	Study design				Overall survival (months)					
				intervention group	N	control group	N	intervention group	control group	HR	95% CI		P value
											LL	UL	
Cristofanilli,2016	PALOMA-3	521	any	palbociclib+fulvestrant	345	fulvestrant	172	34.9 (median)	28.0 (median)	0.81	0.64	1.03	0.09
Tripathy,2018 [b]	MONALEESA-7	672	premenopausal	ribociclib+TAM/AI+OFI	335	TAM/AI+OFI	337	70.2% (42-month)	46.0% (42-month)	0.71	0.54	0.95	0.0097
Sledge,2017	MONARCH 2	669	any	abemaciclib+fulvestrant	446	fulvestrant	223	46.7 (median)	37.3 (median)	0.757	0.606	0.945	0.01
Finn,2015	PALOMA-1	165	postmenopausal	palbociclib+letrozole	83	letrozole	77	37.5 (median)	33.3 (median)	0.813	0.492	1.345	0.42
Slamon,2018 [b]	MONALEESA-3	780	postmenopausal	ribociclib+fulvestrant	484	fulvestrant	242	57.8% (42-month)	45.9% (42-month)	0.72	0.57	0.92	0.005

CDK, cyclin-dependent kinase; TAM, tamoxifen; AI, aromatase inhibitor; NSAI, non-steroidal aromatase inhibitor; OFI, ovarian function inhibition.

[a] In all, this meta-analysis included eight trials about CDK4/6 inhibitors, with only five of them updating their overall survival data.

[b] In MONALEESA-3 and MONALEESA-7 trials median overall survival was not reached in the intervention arm and an estimated overall survival at 42 months was reported instead.

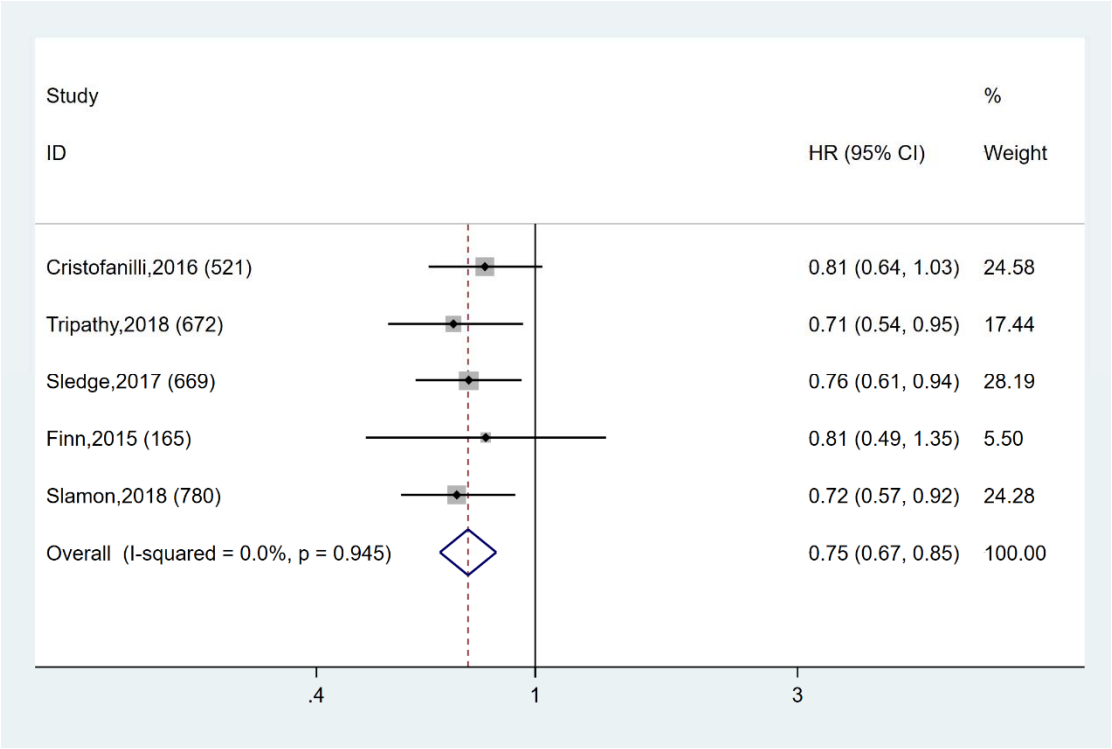

Figure S1 Forest plot of the analysis about efficacy of cyclin-dependent kinase (CDK) 4/6 inhibitors plus endocrine therapy (ET) compared with ET alone, in terms of overall survival (OS).

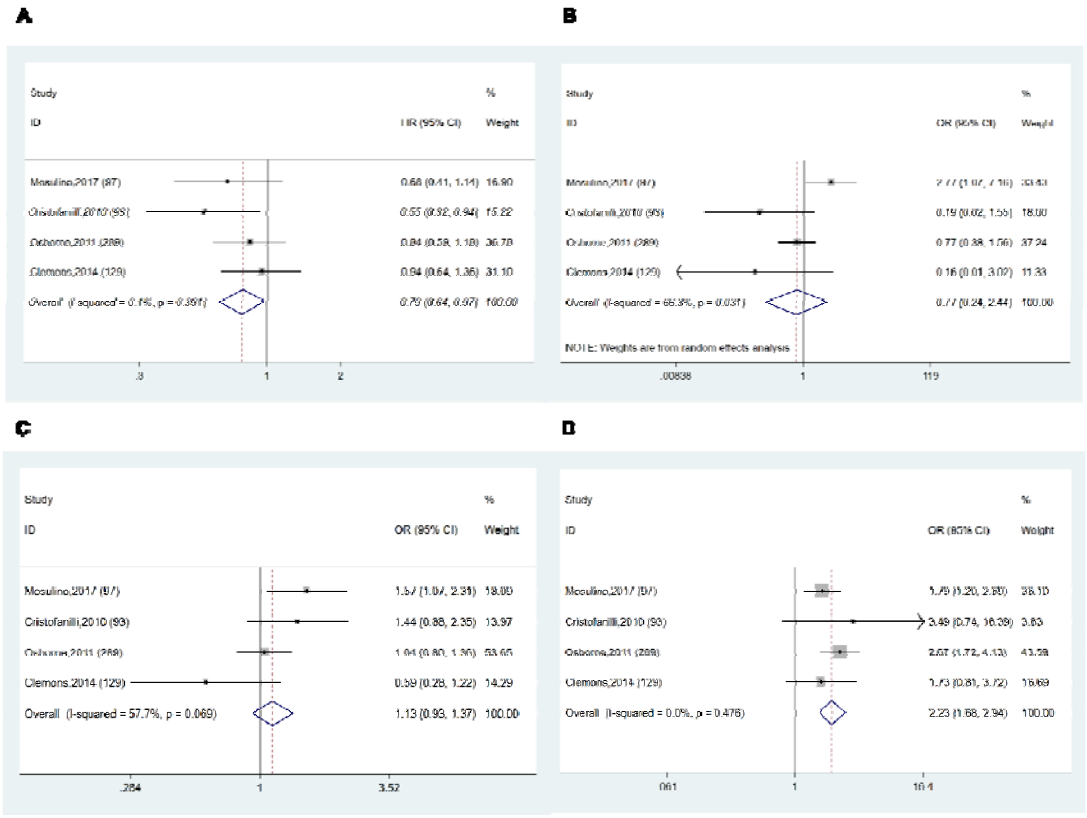

Figure S2 Forest plots of the analyses about efficacy of tyrosine kinase inhibitors (TKIs) plus endocrine therapy (ET) compared with ET alone, in terms of progression-free survival (PFS, A), objective response rate (ORR, B), clinical benefit rate (CBR, C) and toxicity (D). Fixed (A, C, D) and random (B) effect models were used as the pooling method respectively.

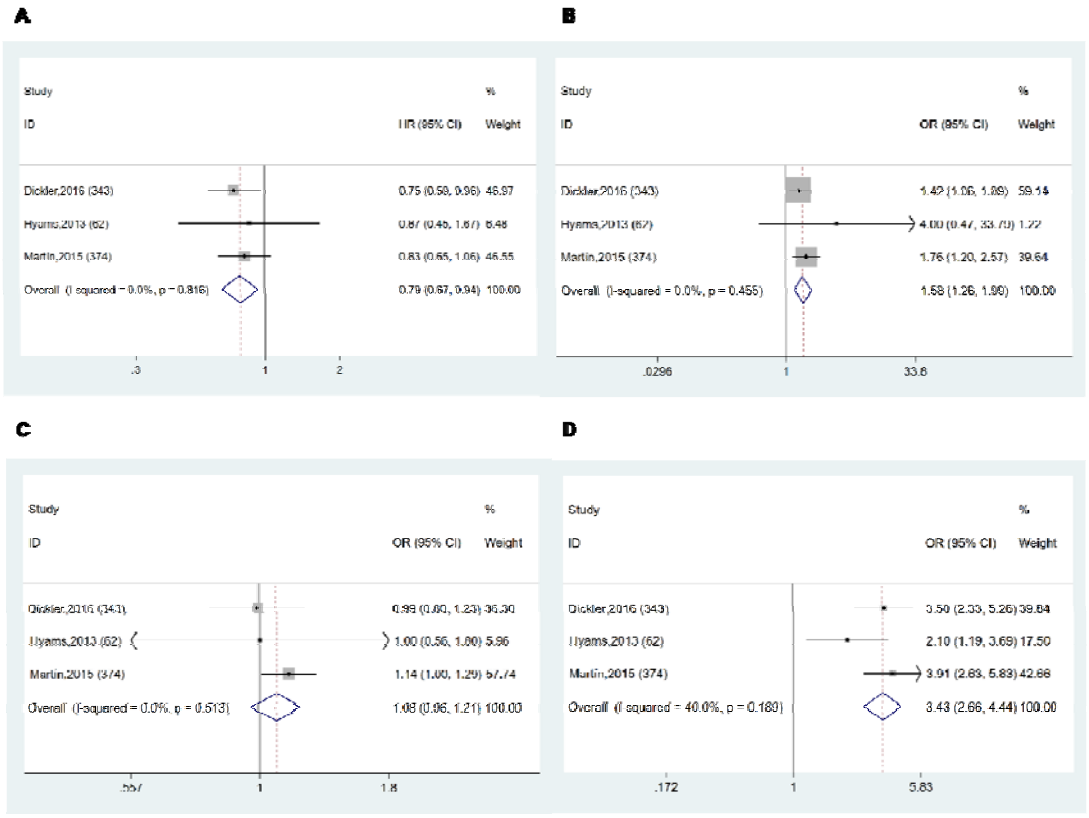

Figure S3 Forest plots of the analyses about efficacy of anti-angiogenesis agents plus endocrine therapy (ET) compared with ET alone, in terms of progression-free survival (PFS, A), objective response rate (ORR, B), clinical benefit rate (CBR, C) and toxicity (D). Fixed effect model was used as the pooling method.