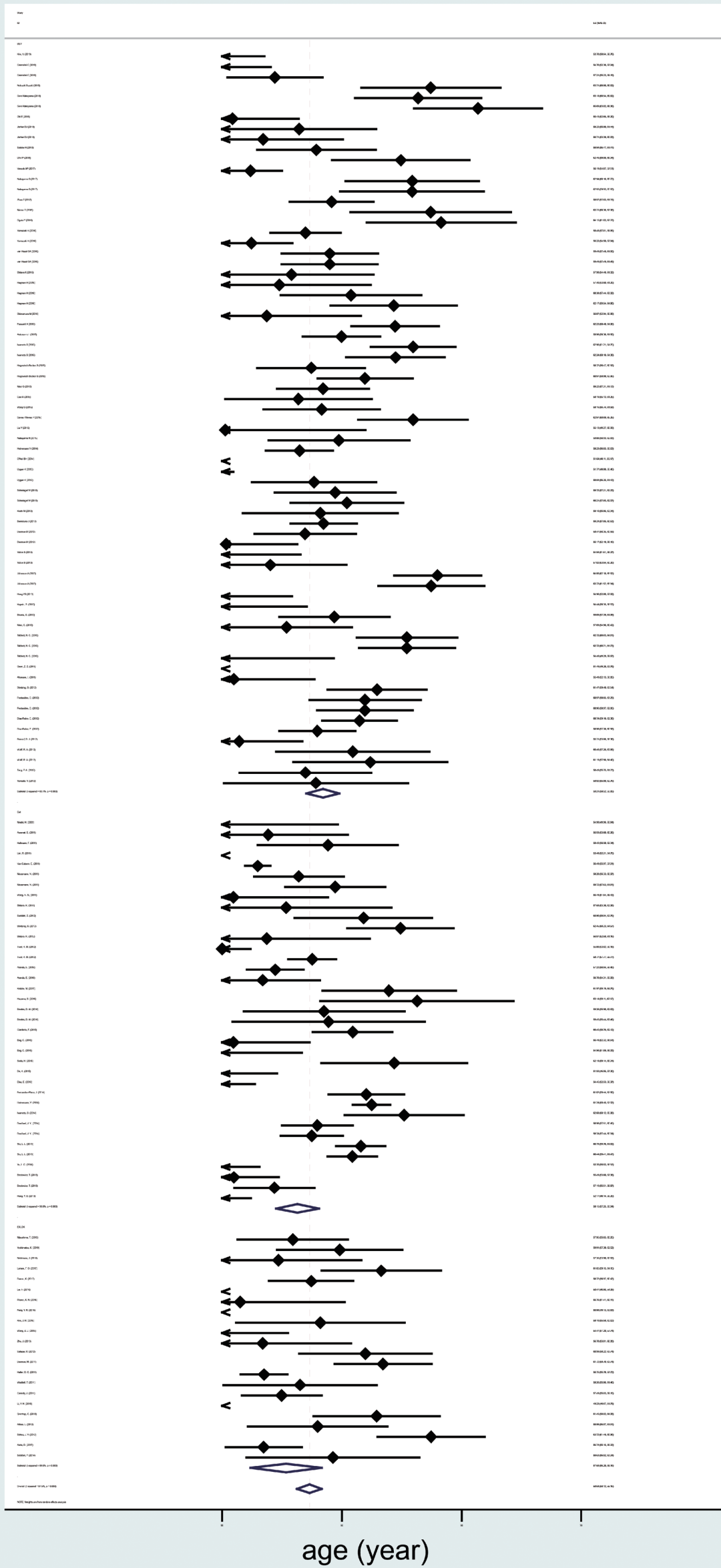


**Supplementary**

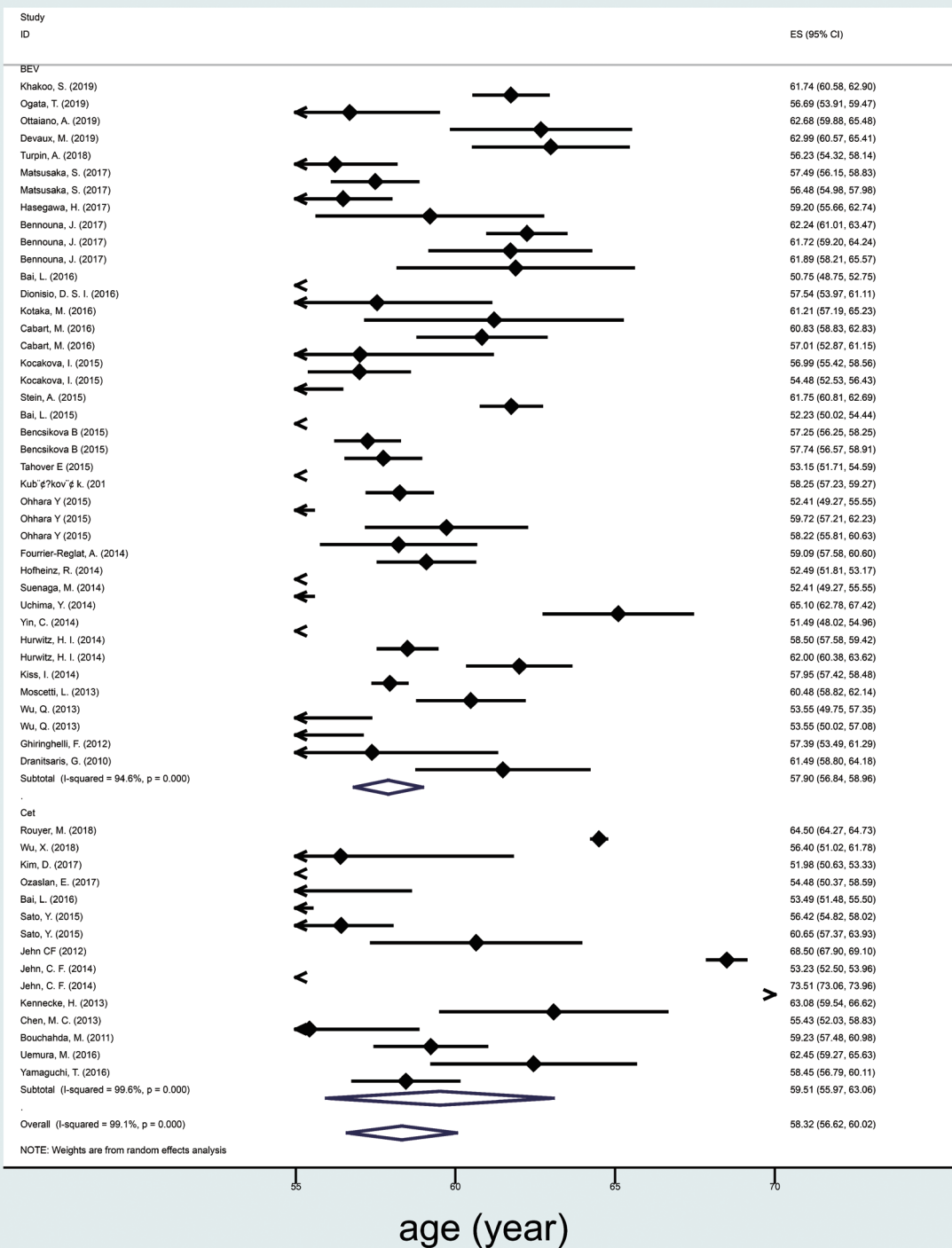
**Table S1** Meta-analyses result of patient characteristics

Drug	Study type	Age				Gender				ECOG				Treat-line			
		Study	Sample	ES	P	Study	Sample	ES	P	Study	Sample	ES	P	Study	Sample	ES	P
All	RCTs	130	14,854	58.641	0.932	146	17,196	0.613	0.004	121	14,660	0.005	0.000	117	13,681	0.274	0.708
	RWS	69	20,219	58.752		102	27,170	0.581		56	16,162	0.09		74	24,085	0.297	
BEV	RCTs	71	7,662	59.205	0.043	79	8,900	0.601	0.106	70	7,955	0.006	0.000	78	9,246	0.282	0.186
	RWS	40	16,893	57.901		55	21,543	0.584		32	13,004	0.081		53	21,516	0.189	
CET	RCTs	37	4,089	58.148	0.464	43	4,831	0.632	0.351	34	4,181	0.006	0.000	32	3,374	0.281	0.012
	RWS	15	1,995	59.513		26	3,576	0.598		15	2,247	0.181		19	2,416	0.631	
XELOX	RCTs	22	3,103	57.68	0.567	24	3,465	0.622	0.038	17	2,524	0.002	0.125	7	1,061	0.143	0.173
	RWS	14	1,331	58.706		21	2,051	0.562		9	911	0.009		2	153	0.001	

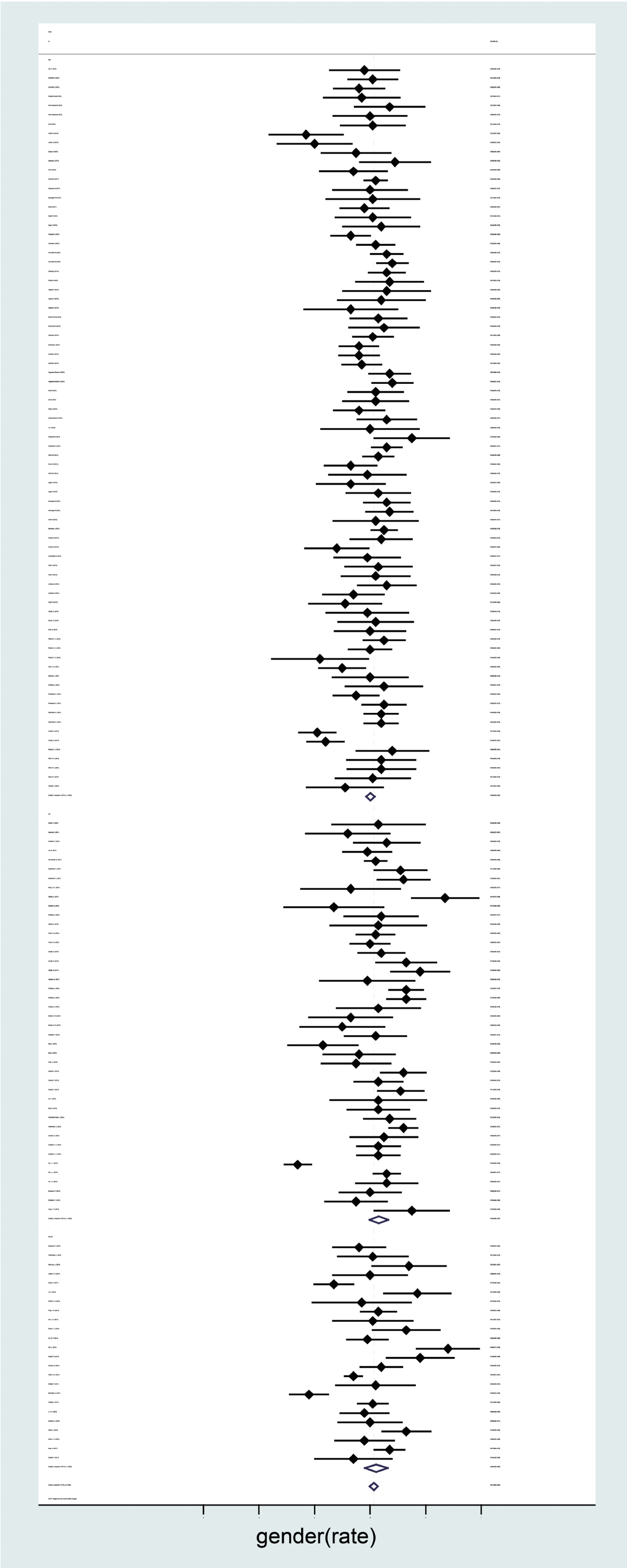
RCT, randomized controlled trial; RWS, real-world studies; BEV, bevacizumab; CET, cetuximab; XELOX, oxaliplatin combined with capecitabine; ECOG, Eastern Cooperative Oncology Group.



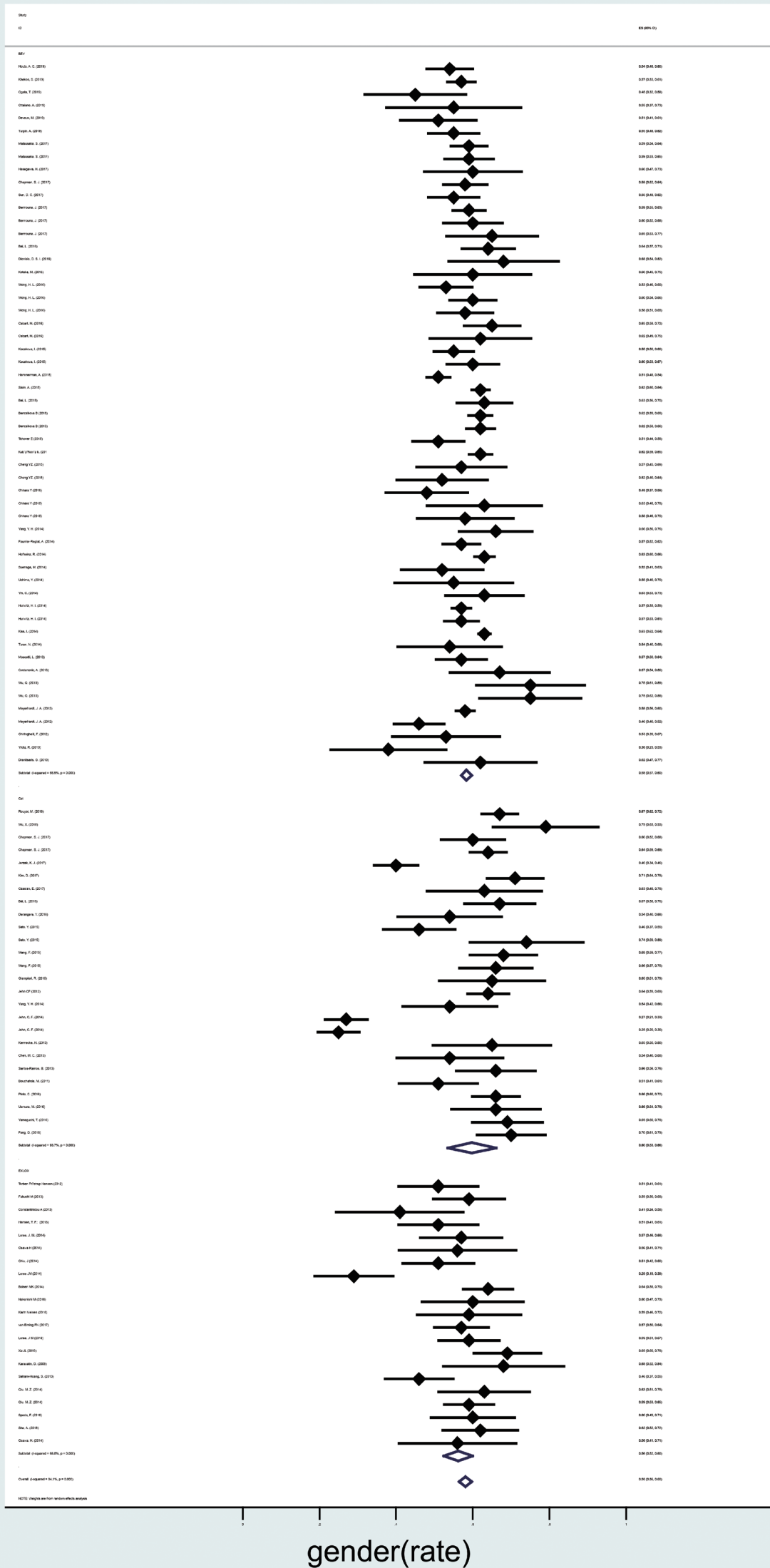
**Figure S1** Age of patients in RCT. RCT, randomized controlled trial; BEV, bevacizumab; CET, cetuximab; XELOX, oxaliplatin combined with capecitabine.



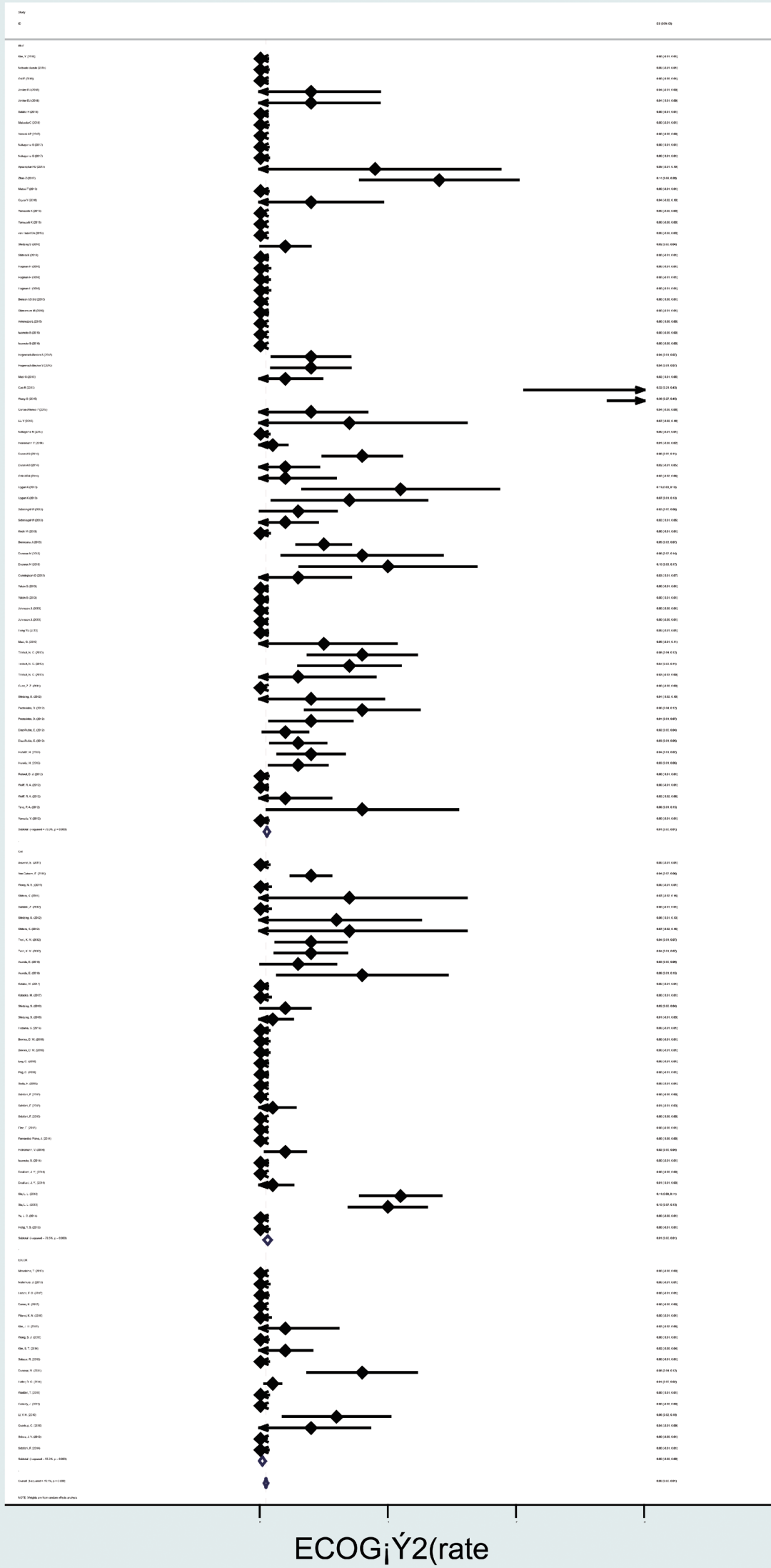
**Figure S2** Age of patients in RWS. RWS, real-world studies; BEV, bevacizumab; CET, cetuximab; XELOX, oxaliplatin combined with capecitabine.



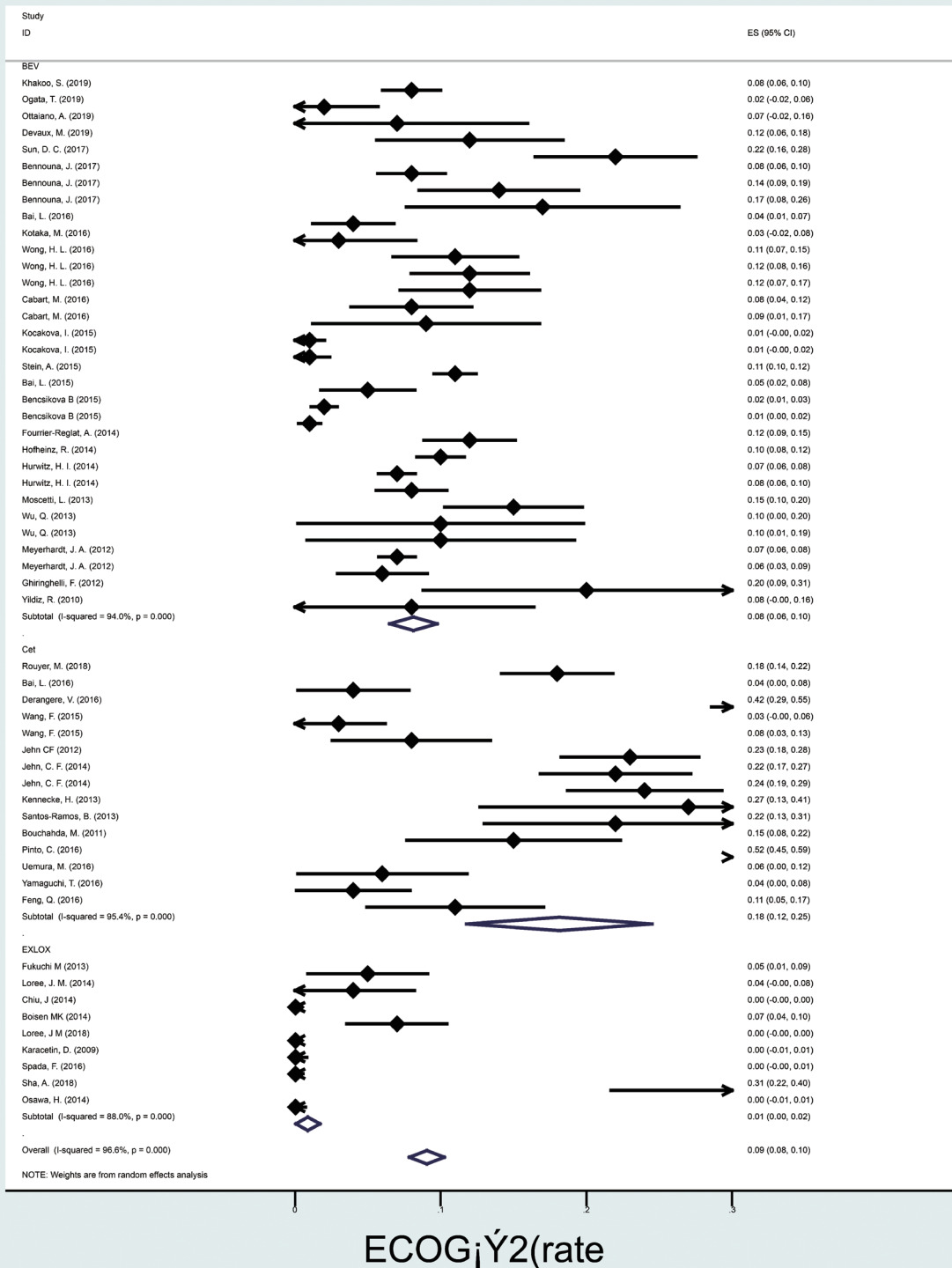
**Figure S3** Proportion of male patients in RCT. RCT, randomized controlled trial; BEV, bevacizumab; CET, cetuximab; XELOX, oxaliplatin combined with capecitabine.



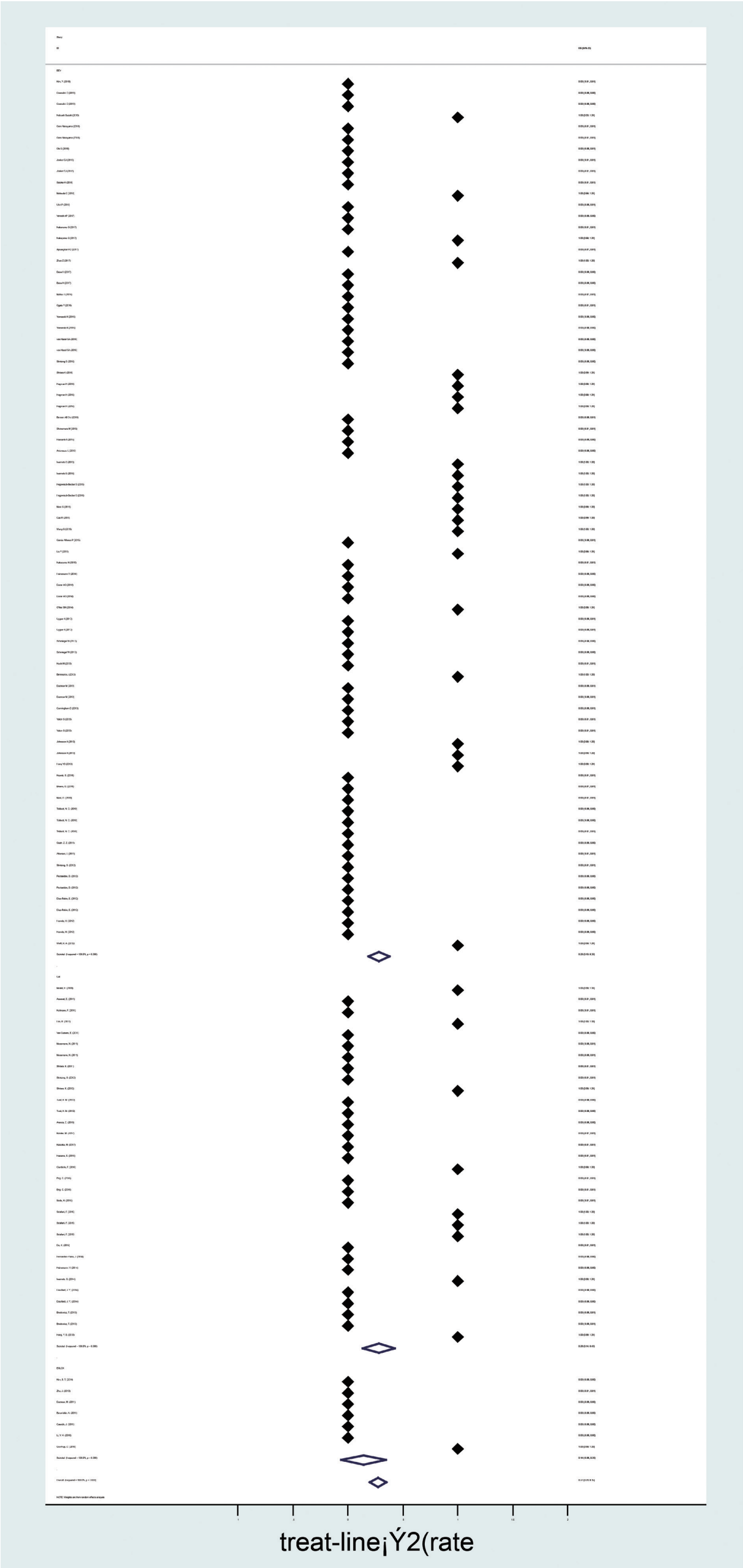
**Figure S4** Proportion of male patients in RWS. RWS, real-world studies; BEV, bevacizumab; CET, cetuximab; XELOX, oxaliplatin combined with capecitabine.



**Figure S5** Proportion of patients with ECOG  $\geq 2$  in RCT. ECOG, Eastern Cooperative Oncology Group; RCT, randomized controlled trial; BEV, bevacizumab; CET, cetuximab; XELOX, oxaliplatin combined with capecitabine.

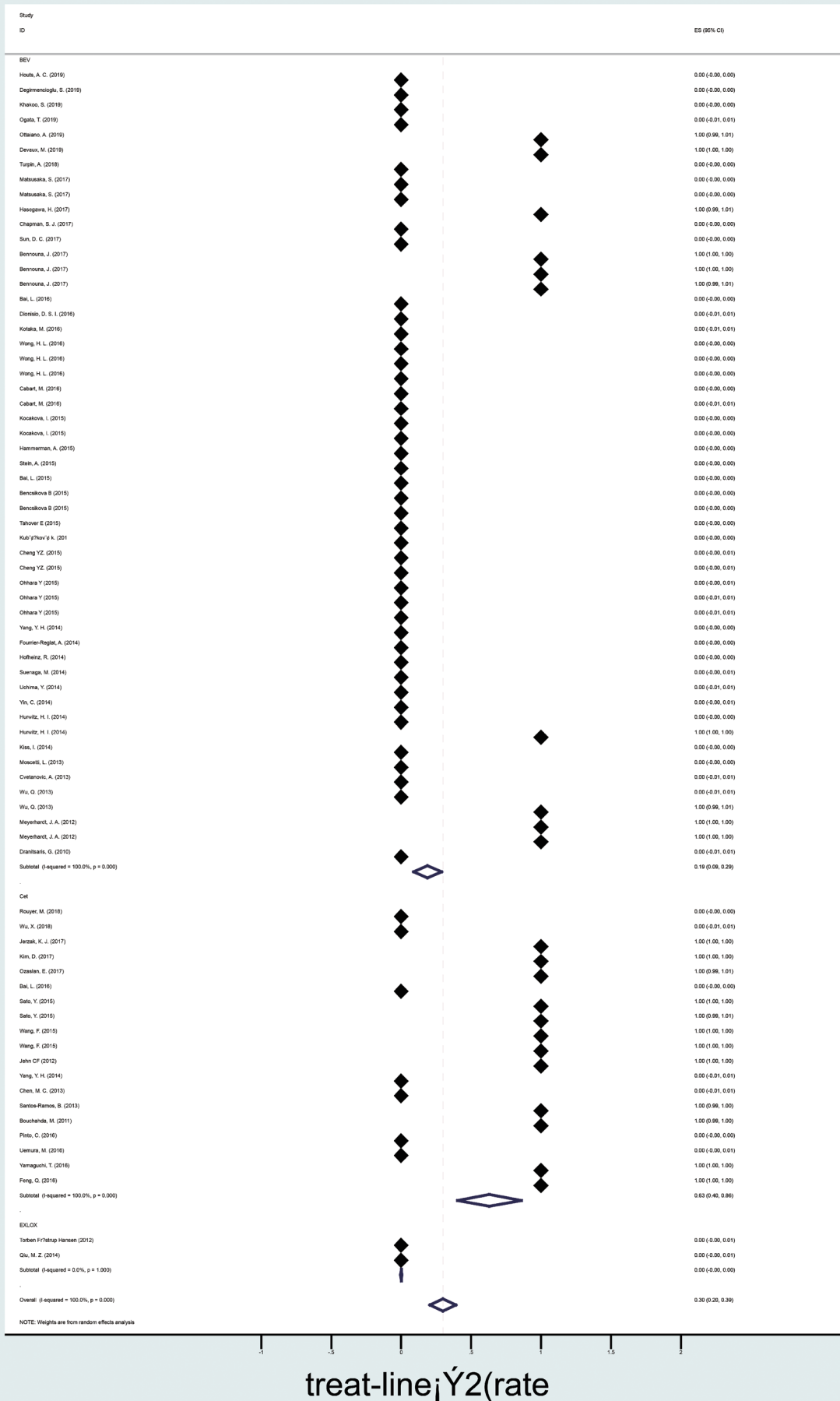


**Figure S6** Proportion of patients with ECOG  $\geq 2$  in RWS. ECOG, Eastern Cooperative Oncology Group; RWS, real-world studies; BEV, bevacizumab; CET, cetuximab; XELOX, oxaliplatin combined with capecitabine.



**Figure S7** Second-line and above-second-line treatments in RCT. RCT, randomized controlled trial; BEV, bevacizumab; CET, cetuximab; XELOX, oxaliplatin combined with capecitabine.



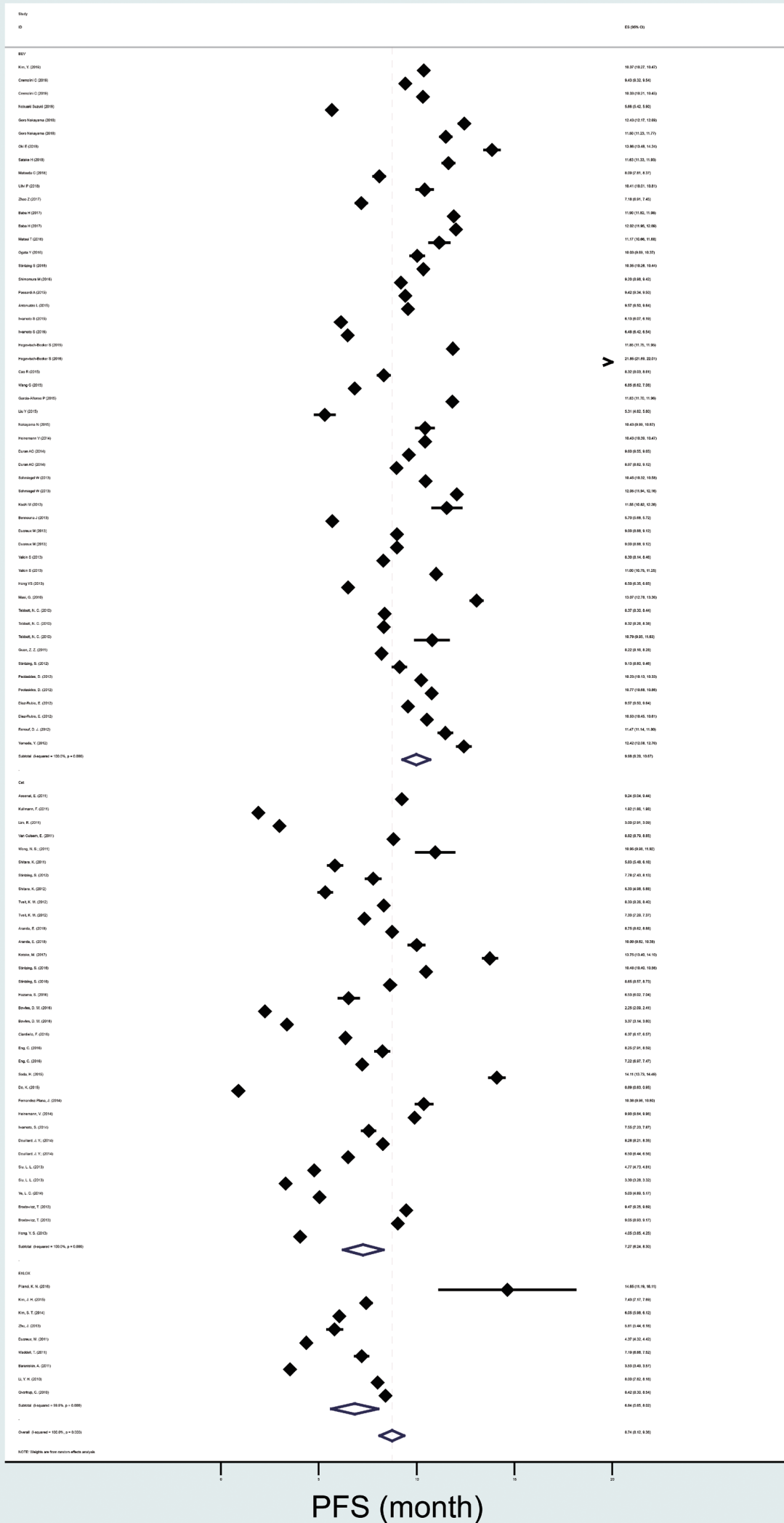


**Figure S8** Second-line and above-second-line treatments in RWS. RWS, real-world studies; BEV, bevacizumab; CET, cetuximab; XELOX, oxaliplatin combined with capecitabine.

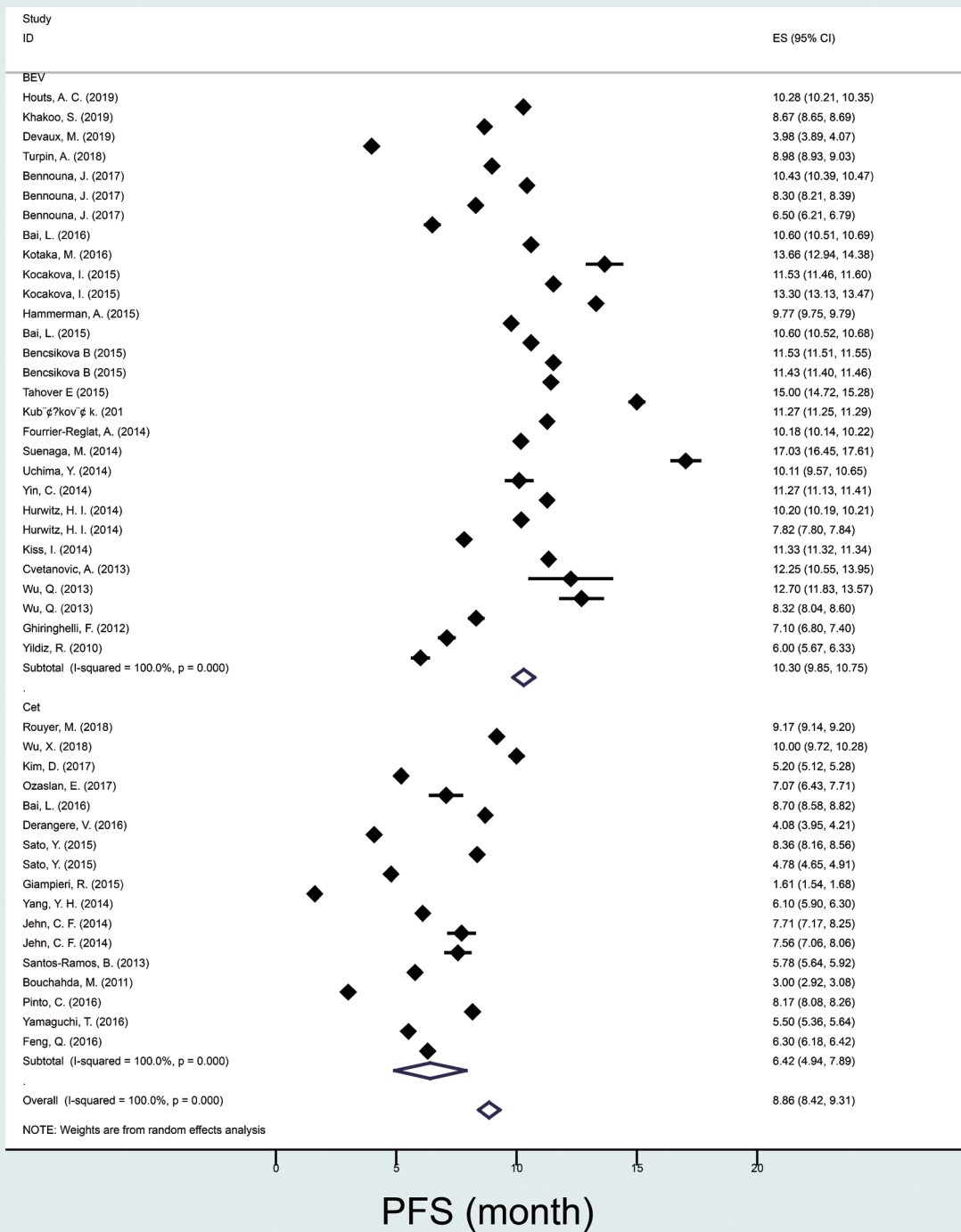
**Table S2** Meta-analyses result of treatment effects

Drug	Study type	OS				PFS				ORR				DCR			
		Study	Sample	ES	P	Study	Sample	ES	P	Study	Sample	ES	P	Study	Sample	ES	P
All	RCT	104	12,869	17.696	0.685	95	11,343	8.74	0.456	109	12,435	0.416	0.384	58	5,217	0.806	0.762
	RWS	69	22,314	17.143		53	16,765	8.444		45	13,258	0.46		33	6,239	0.798	
BEV	RCT	65	7,838	18.358	0.478	52	6,245	9.986	0.453	59	6,926	0.484	0.548	22	1,343	0.883	0.402
	RWS	42	18,938	19.457		29	13,724	10.3		28	11,456	0.507		19	4,703	0.863	
CET	RCT	29	3,851	17.432	0.023	34	4,134	7.273	0.350	41	4,638	0.409	0.715	33	3,737	0.748	0.335
	RWS	17	2,321	13.248		17	2,108	6.415		15	1,616	0.39		13	1,428	0.7	
XELOX	RCT	10	1,180	14.014	0.997	9	863	6.837	0.374	9	871	0.563	0.001	3	137	0.936	0.001
	RWS	10	1,055	14.018		7	633	5.667		2	186	0.312		1	108	0.73	

PFS, progression-free survival; OS, overall survival; ORR, objective response rate; DCR, disease control rate; RCT, randomized controlled trial; RWS, real-world studies; BEV, bevacizumab; CET, cetuximab; XELOX, oxaliplatin combined with capecitabine.



**Figure S9** PFS of patients in RCT. PFS, progression-free survival; RCT, randomized controlled trial; BEV, bevacizumab; CET, cetuximab; XELOX, oxaliplatin combined with capecitabine.



**Figure S10** PFS of patients in RWS. PFS, progression-free survival; RWS, real-world studies; BEV, bevacizumab; CET, cetuximab; XELOX, oxaliplatin combined with capecitabine.

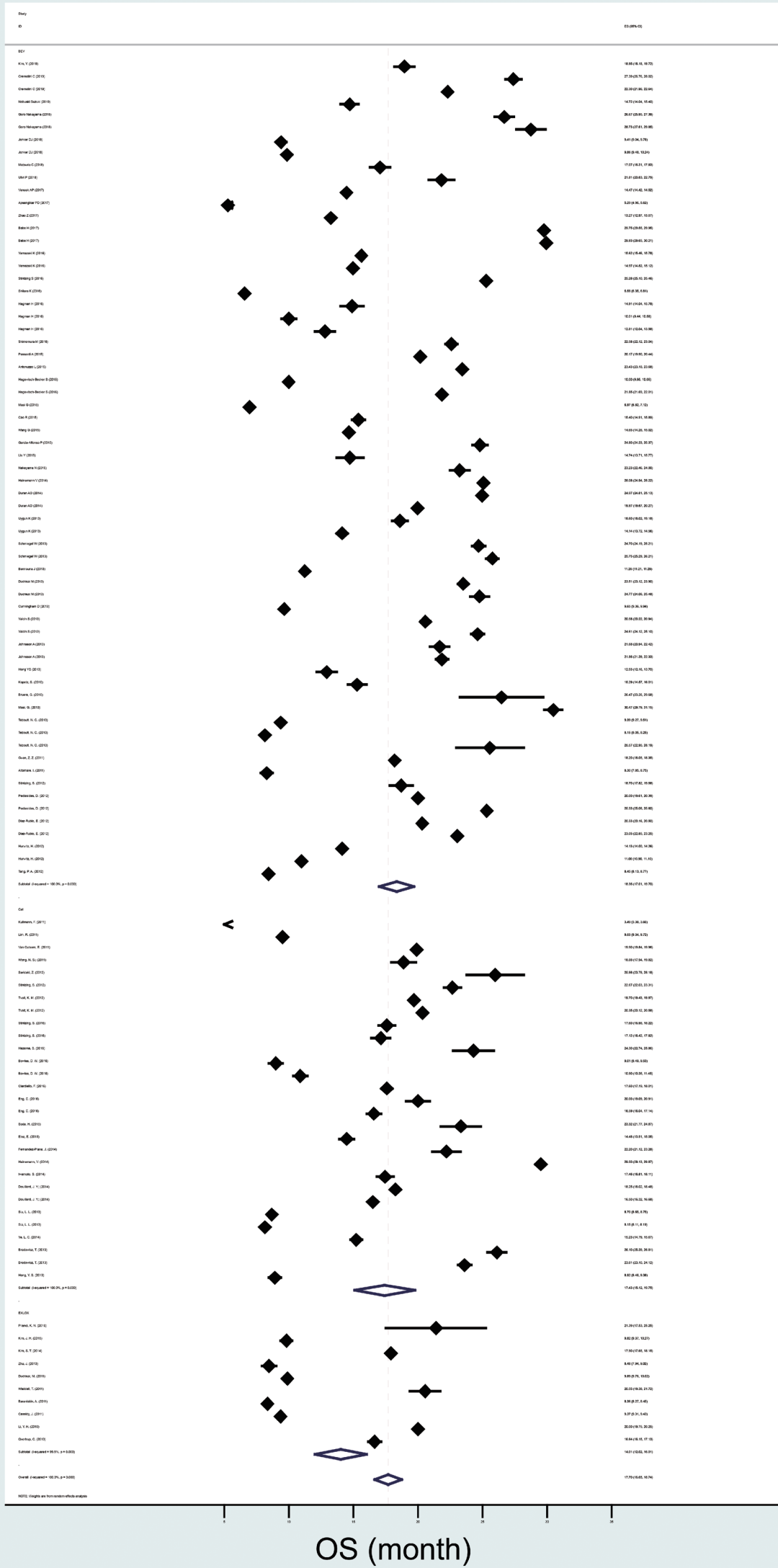
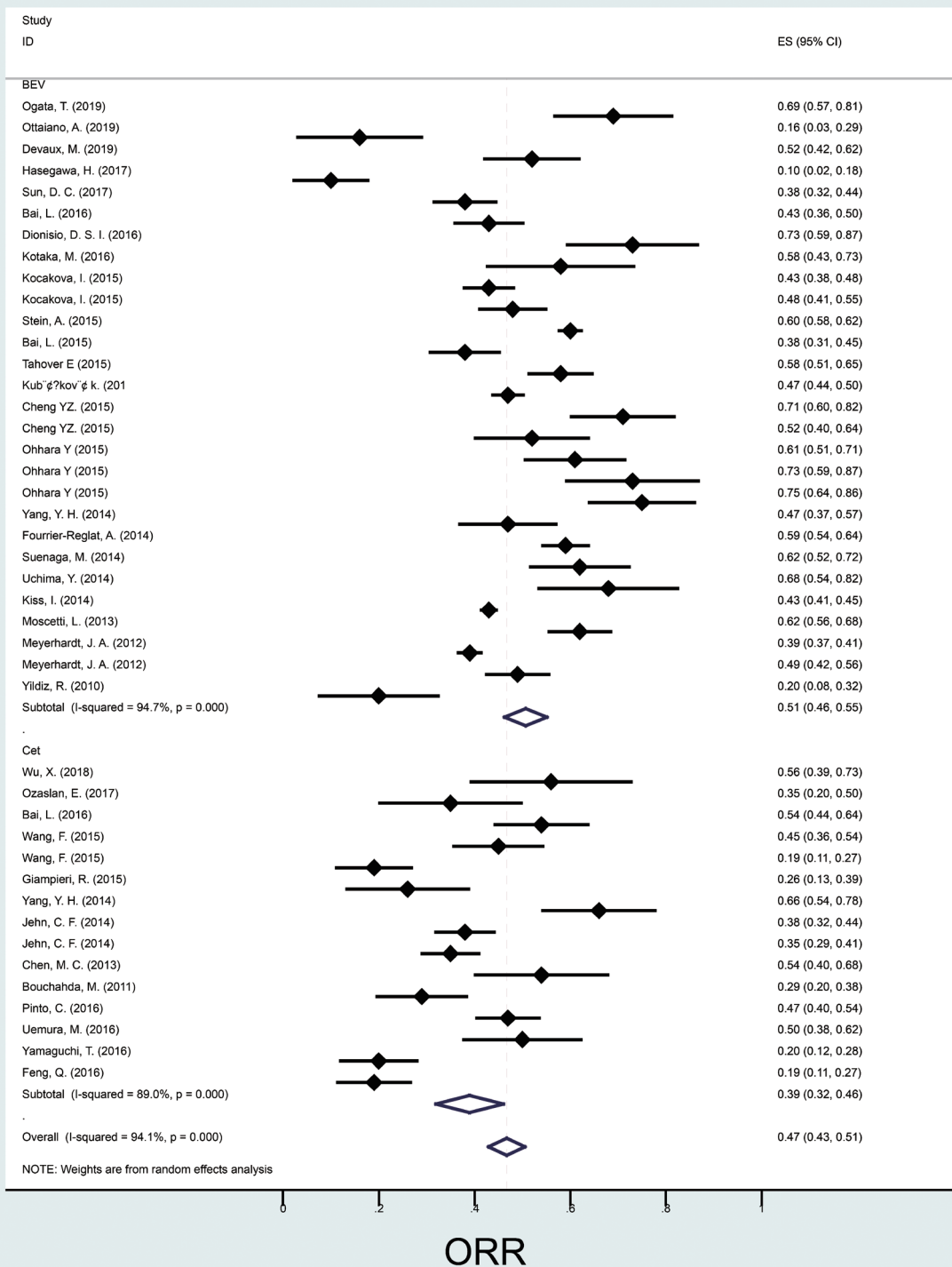
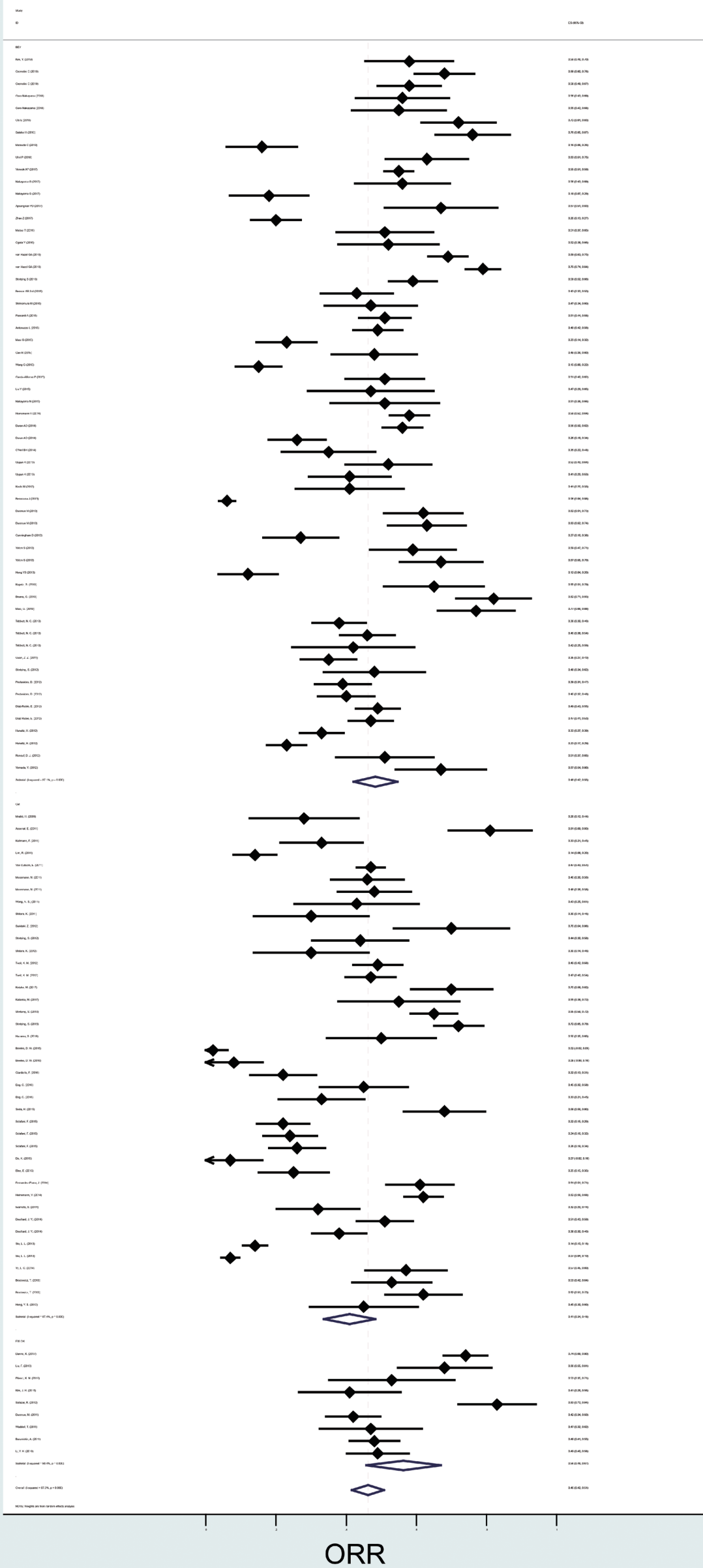


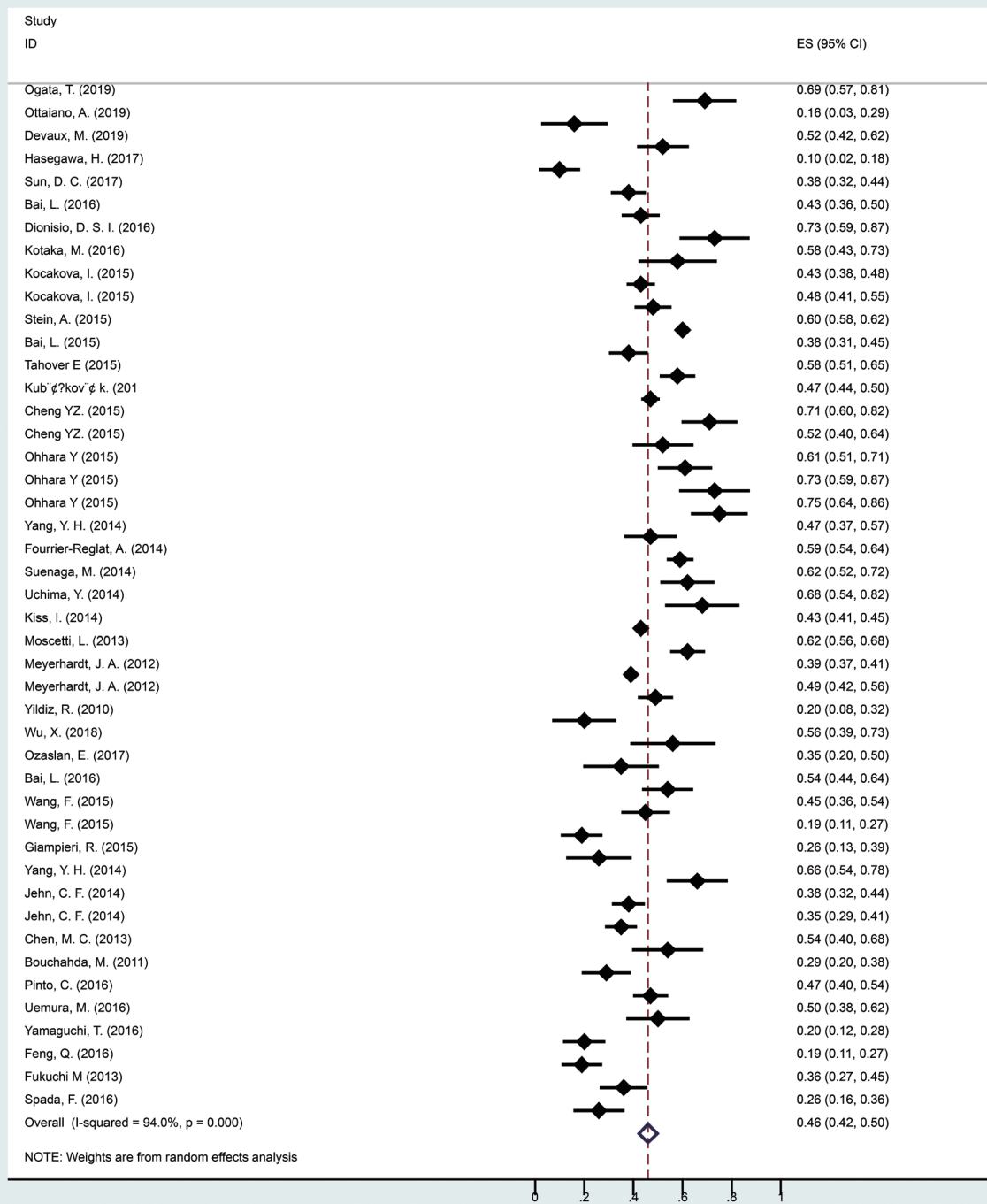
Figure S11 OS of patients in RCT. OS, overall survival; RCT, randomized controlled trial; BEV, bevacizumab; CET, cetuximab; XELOX, oxaliplatin combined with capecitabine.



**Figure S12** OS of patients in RWS. OS, overall survival; RWS, real-world studies; BEV, bevacizumab; CET, cetuximab; XELOX, oxaliplatin combined with capecitabine.

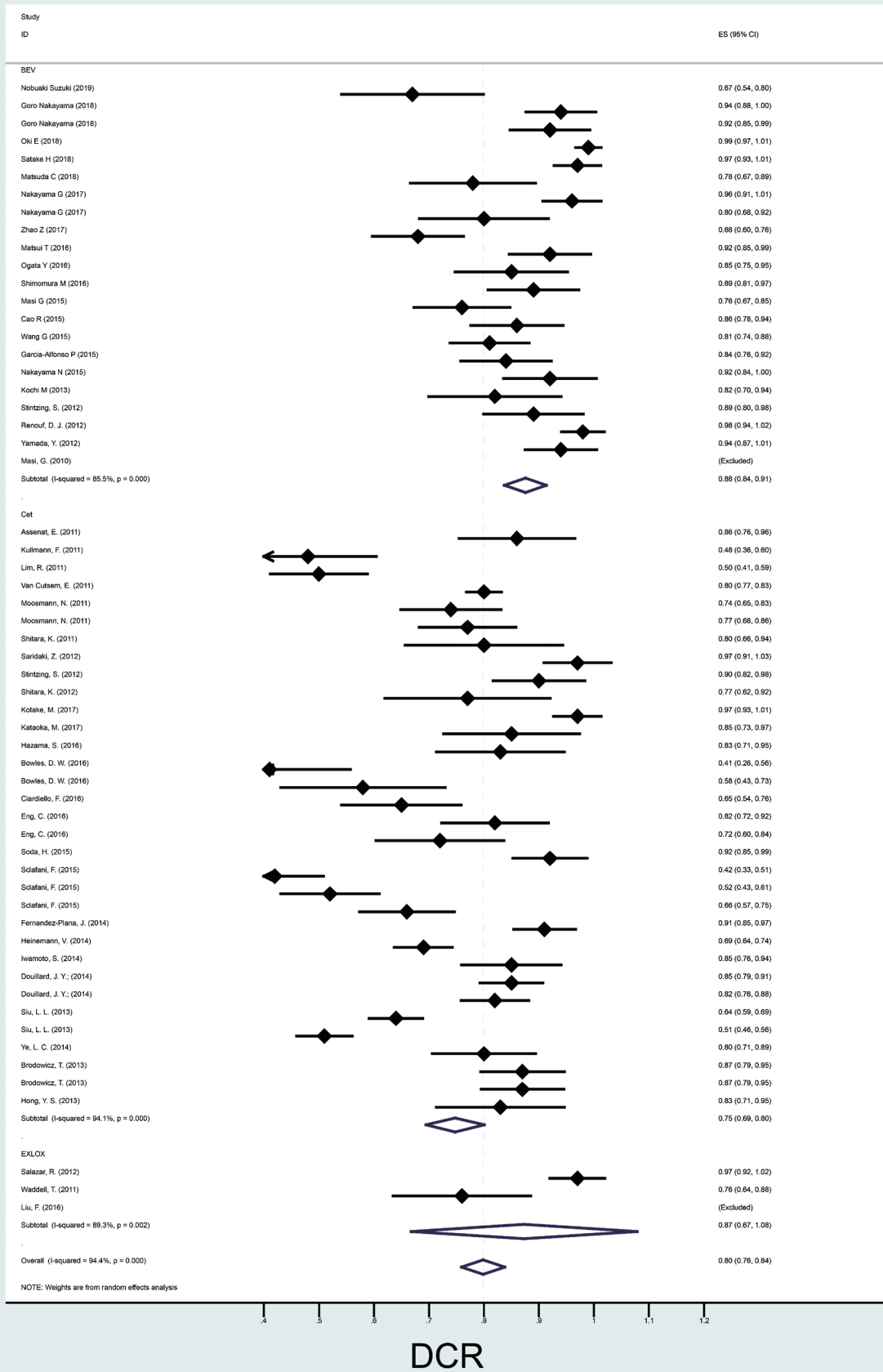


**Figure S13** ORR of patients in RCT. ORR, objective response rate; RCT, randomized controlled trial; BEV, bevacizumab; CET, cetuximab; XELOX, oxaliplatin combined with capecitabine.

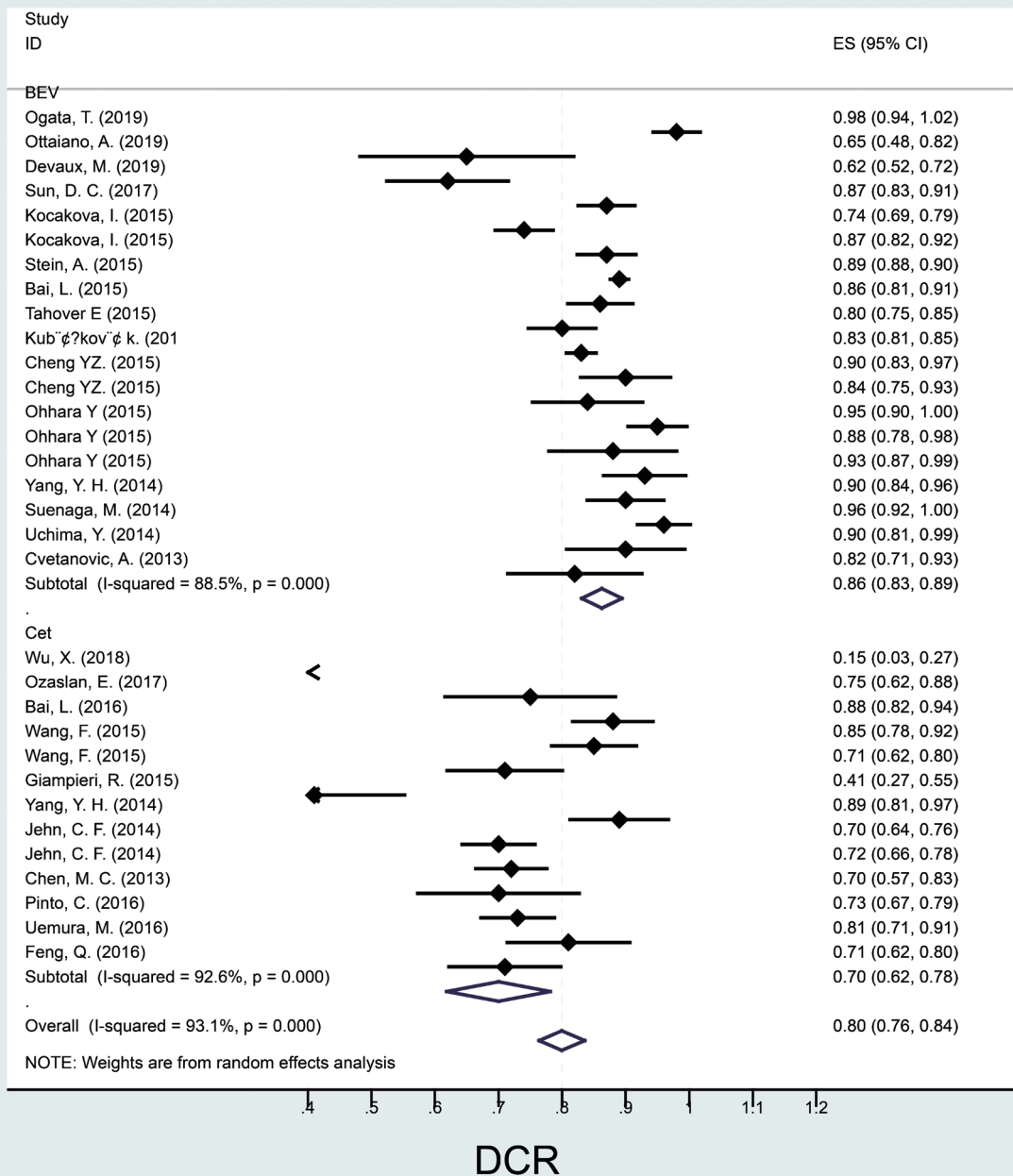


**Figure S14** ORR of patients in RWS. ORR, objective response rate; RWS, real-world studies; BEV, bevacizumab; CET, cetuximab; XELOX, oxaliplatin combined with capecitabine.





**Figure S15** DCR of patients in RCT. DCR, disease control rate; RCT, randomized controlled trial; BEV, bevacizumab; CET, cetuximab; XELOX, oxaliplatin combined with capecitabine.



**Figure S16** DCR of patients in RWS. DCR, disease control rate; RWS, real-world studies; BEV, bevacizumab; CET, cetuximab; XELOX, oxaliplatin combined with capecitabine.