

Table S1 Details of the regorafenib and TAS-102 combination regimen

Regimens	N (%)
Regorafenib combination	22 (100.0)
Regorafenib + anti-PD-1/PD-L1	17 (77.3)
Regorafenib + sintilimab	10 (45.5)
Regorafenib + camrelizumab	3 (13.6)
Regorafenib + toripalimab	2 (9.1)
Regorafenib + tislelizumab	2 (9.1)
Regorafenib + chemotherapeutic agents	5 (22.7)
Regorafenib + raltitrexed	2 (9.1)
Regorafenib + S-1	3 (13.6)
TAS-102 combination	19 (100)
TAS-102 + targeted therapeutic agents	12 (63.2)
TAS-102 + bevacizumab	11 (57.9)
TAS-102 + fruquintinib	1 (5.3)
TAS-102 + anti-PD-1/PD-L1	4 (21.1)
TAS-102 + sintilimab	3 (15.8)
TAS-102 + tislelizumab	1 (5.3)
TAS-102 + targeted therapeutic agents + anti-PD-1/PD-L1	3 (15.8)
TAS-102 + bevacizumab + sintilimab	2 (10.5)
TAS-102 + bevacizumab + toripalimab	1 (5.3)

PD-1/PD-L1, Programmed cell death protein 1/programmed cell death ligand 1.

Table S2 Univariate Cox analysis of OS₁

Characteristics	P value	HR (95% CI)
Gender		
Male	Ref	Ref
Female	0.75	0.798 (0.205–3.106)
Age		
<65 years	Ref	Ref
≥65 years	0.34	1.962 (0.499–7.719)
Site of primary disease	0.059	
Left-sided	Ref	Ref
Right-sided	0.10	4.902 (0.727–33.050)
Both left and right sided	#	#
Rectum	0.41	0.508 (0.101–2.545)
Number of metastatic sites, n (%)	0.042*	
1	Ref	Ref
2	0.04*	4.122 (1.075–15.810)
≥3	0.04*	3.805 (1.043–13.873)
Site of metastases		
Liver (no/yes)	0.28	2.026 (0.565–7.261)
Lung (no/yes)	0.55	0.658 (0.169–2.559)
Lymph node (no/yes)	0.08	3.270 (0.868–12.326)
Peritoneum (no/yes)	0.20	2.913 (0.574–14.792)
Other (no/yes)	0.86	0.883 (0.227–3.439)
Surgery	0.98	
No	Ref	Ref
Radical resection	0.83	1.263 (0.159–10.013)
Palliative surgery	>0.99	0.000 (0.000–NA)
Prior regimen		
Angiogenesis inhibitors (no/yes)	0.27	0.300 (0.035–2.580)
Anti-PD-1/PD-L1 (no/yes)	0.27	3.330 (0.388–28.613)
Treatment line of regorafenib	0.87	
Second-line	Ref	Ref
Third-line	0.61	0.555 (0.058–5.309)
Fourth line or later	0.63	0.574 (0.061–5.428)
Regorafenib regimen		
Regorafenib alone	Ref	Ref
Regorafenib combination	0.64	1.442 (0.305–6.812)
TAS-102 regimen		
TAS-102 alone	Ref	Ref
TAS-102 combination	0.53	0.664 (0.187–2.366)

*, P<0.05; #, failure to meet the study endpoint, resulting in missing data.