

Table SI. Characteristics of patients.

Baseline Characteristics	Total count	First-line n=23 (%)	Second-line n=164 (%)	Third-/later-line n=18 (%)
Sex:				
Male	123	12 (52.17%)	97 (59.15%)	14 (77.78%)
Female	82	11 (47.83%)	67 (40.85%)	4 (22.22%)
Age:				
<40	19	2 (8.70%)	16 (9.76%)	1 (5.56%)
40-70	176	19 (82.60%)	140 (85.37%)	17 (94.44%)
>70	10	2 (8.70%)	8 (4.87%)	0 (0.00%)
Primary tumor Location:				
Colon	108	16 (69.57%)	82 (50.00%)	10 (55.56%)
Rectum	97	7 (30.43%)	82 (50.00%)	8 (44.44%)
T Stage:				
T1	2	2 (8.70%)	0 (0.00%)	0 (0.00%)
T2	5	0 (0.00%)	4 (2.44%)	1 (5.56%)
T3	144	16 (69.57%)	113 (68.90%)	15 (83.33%)
T4	29	5 (21.73%)	22 (13.41%)	2 (11.11%)
Unknown	25	0 (0.00%)	25 (15.25%)	0 (0.00%)
N Stage:				
N0	41	5 (21.74%)	29 (17.68%)	7 (38.89%)
N1	92	12 (52.17%)	74 (45.12%)	6 (33.33%)
N2	43	5 (21.74%)	34 (20.73%)	4 (22.22%)
Unknown	29	1 (4.35%)	27 (16.47%)	1 (5.56%)
M Stage:				
M0	130	21 (91.12%)	94 (57.32%)	15 (83.33%)
M1	75	2 (8.78%)	70 (42.68%)	3 (16.67%)
pTNM:				
I	2	1 (4.35%)	0 (0%)	1 (5.56%)
II	33	4 (17.39%)	23 (14.02%)	6 (33.33%)
III	95	16 (69.56%)	71 (43.29%)	8 (44.44%)
IV	75	2 (8.70%)	70 (42.69%)	3 (16.67%)
Genetic status:				
KRAS/NRAS Mut		3 (13.04%)	19 (11.59%)	2 (11.11%)
KRAS/NRAS Wild	38	1 (4.35%)	36 (21.95%)	1 (5.56%)
BRAF Mut	4	0 (0.00%)	4 (2.44%)	0 (0.00%)
BRAF Wild	43	4 (17.39%)	36 (21.95%)	3 (16.67%)
Unknown	143	19 (82.61%)	109 (66.46%)	15 (83.33%)
MSI status:				
MSS	53	6 (26.09%)	43 (26.22%)	4 (22.22%)
MSI-H	6	0 (0.00%)	5 (29.27%)	1 (5.56%)
Unknown	146	17 (73.91%)	116 (70.73%)	13 (72.22%)
CA19-9:				
<37(u/ml)	119	18 (78.26%)	92 (56.10%)	9 (50.00%)
≥37(u/ml)	86	5 (21.74%)	72 (43.90%)	9 (50.00%)
CEA:				
<5(ng/ml)	63	7 (30.43%)	50 (30.49%)	6 (33.33%)
≥5(ng/ml)	142	16 (69.57%)	114 (69.51%)	12 (66.67%)

Abbreviations: n, number; MSS, Microsatellite stability; MSI-H, Microsatellite instability-High.

Table SII. Characteristics of second-line group concerning prior therapies.

Characteristics	N (%)
Previous surgery:	
Radical	87 (53.0%)
Local radical	15 (9.1%)
Palliative	36 (22.0%)
No	26 (15.9%)
Prior adjuvant CT:	
Yes	27 (16.5%)
No	137 (83.5%)
Chemotherapy regimen of first-line:	
CAPEOX	133 (81.1%)
FOLFOX	19 (11.6%)
Others	12 (7.3%)
Tumor response to first-line CT:	
CR	1 (0.6%)
PR	15 (9.1%)
SD	112 (68.3%)
PD	36 (22.0%)
PFS≤7 months	85 (51.8%)
PFS>7 months	79 (48.2%)
Prior targeted therapy:	
Bevacizumab	12 (7.3%)
Cetuximab	8 (4.9%)
No	144 (87.8%)

Abbreviations: CT, chemotherapy; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; PFS, progression-free survival.

Table SIII. Relative treatment data of second-line group.

Characteristic	All Patients (n=164)
Tumor response	
CR	0 (0%)
PR	22 (13.4%)
SD	112 (68.3%)
PD	30 (18.3%)
ORR	13.4%
DCR	81.7%
Median PFS (range)	7 (2-48) months
Median OS (range)	41 (8-109) months
Treatment interval	
two-weekly	18
three-weekly	146
Dosage	
Irinotecan (two-weekly)	140-340 mg (103.6mg/m ² -264.5mg/m ²)
Irinotecan (three-weekly)	180-500 mg (82.1mg/m ² -196.5mg/m ²)
Raltitrexed (two-weekly)	3-6 mg (1.5mg/m ² -3mg/m ²)
Raltitrexed (three-weekly)	3-6 mg (1.5mg/m ² -3.1mg/m ²)
Cycles:	
Median (range)	4 (2-27)
>4	75 (45.7%)
Local treatment of metastasis:	
Yes	18 (11.0%)
No	146 (89.0%)
Treatment regimen of third-line:	
FOLFIRI	6 (3.6%)
Regorafenib	19 (11.6%)
Others	38 (23.2%)
Unknown	101 (61.6%)

Abbreviations: n, number; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; ORR, overall response rate; DCR, disease control rate; PFS, progression-free survival; OS, overall survival. Local treatments for metastases include: surgery, radiotherapy, and radiofrequency ablation.

Table SIV. Occurrence of individual adverse events.

AEs	First-line patients (n=23)	Second-line patients (n=164)	Third-/later-line patients (n=18)	Total (n=205)
Neutropenia				
G1/2	2(8.7%)	22(13.4%)	1(5.6%)	25(12.2%)
G3/4	0(0%)	5(3.1%)	0(0%)	5(2.4%)
Thrombocytopenia				
G1/2	2(8.7%)	18(11.0%)	1(5.6%)	21(10.2%)
G3/4	0(0%)	2(1.2%)	0(0%)	2(1.0%)
Anemia				
G1/2	6(26.1%)	43(26.2%)	7(38.9%)	56(27.3%)
G3/4	1(4.4%)	2(1.2%)	0(0%)	3(1.5%)
Elevated blood glucose	7(30.4%)	34(20.7%)	5(27.8%)	46(22.4%)
Proteinuria				
G1/2	9(39.1%)	61(37.2%)	8(44.4%)	78(38.1%)
G3/4	0(0%)	1(0.6%)	0(0%)	1(0.5%)
Hematuria				
G1/2	8(34.8%)	29(17.7%)	6(33.3%)	43(21.0%)
G3/4	0(0%)	0(0%)	0(0%)	0(0%)
Creatinine				
G1/2	1(4.4%)	5(3.1%)	1(5.6%)	7(3.4%)
G3/4	0(0%)	0(0%)	0(0%)	0(0%)
Hepatic dysfunction				
G1/2	11(47.8%)	92(56.1%)	10(55.6%)	113(55.1%)
G3/4	2(8.7%)	12(7.3%)	1(5.6%)	15(7.3%)

Abbreviations: AE, adverse event; G, grade; n, number.