Table SI. Comparison of patient demographics and clinical characteristics between patients with and without grade 3 or 4 neutropenia within the first cycle of treatment.

Characteristic	Patients with grade 3 or 4 neutropenia (n=26)	Patients without grade 3 or 4 neutropenia (n=68)	P-value
Median age at enrollment, years (range)	61 (36-80)	61 (32-82)	
Sex			0.91
Male	10 (38.5)	27 (39.7)	
Female	16 (61.5)	41 (60.3)	
ECOG PS			0.91
0	18 (69.2)	46 (67.6)	
1	6 (23.1)	18 (26.5)	
2	2 (7.7)	4 (5.9)	
Primary site			0.26
Right-sided colon	5 (19.2)	21 (31.0)	
Left-sided colon	21 (80.8)	47 (69.1)	
Metastatic site			
Liver	15 (57.7)	41 (60.3)	0.82
Lung	19 (73.1)	50 (73.5)	0.96
Peritoneal	10 (38.5)	30 (44.1)	0.19
Lymph node	11 (42.3)	35 (51.5)	0.43
Other	5 (19.2)	21 (30.9)	0.26
RAS status in tissue			0.13
Wild-type	7 (26.9)	30 (44.1)	
Mutant	19 (73.1)	38 (55.9)	
Time from the start of first-line chemotherapy, months			0.08
<18	10 (38.5)	12 (17.6)	
≥18	16 (61.5)	54 (79.4)	
Unknown	0 (0.0)	2 (3.0)	
Number of prior regimens			
1	0 (0.0)	0 (0.0)	
2	19 (73.1)	49 (72.1)	
3	7 (26.9)	15 (22.1)	
4	0 (0.0)	4 (5.9)	
Previous chemotherapy			
Fluoropyrimidine	26 (100.0)	68 (100.0)	
Irinotecan	26 (100.0)	68 (100.0)	
Oxaliplatin	25 (96.2)	68 (100.0)	
Angiogenesis inhibitor	26 (100.0)	68 (100.0)	
Anti-EGFR antibodies	3 (11.5)	13 (19.1)	
Number of metastasis			0.09
1	5 (19.2)	5 (7.4)	
>1	21 (80.8)	63 (92.6)	

ECOG PS, Eastern Cooperative Oncology Group Performance Status; *RAS*, rat sarcoma viral oncogene homolog; EGFR, epidermal growth factor receptor.

Table SII. Comparison of incidence of adverse events between patients with and without grade 3 or 4 neutropenia within the first cycle of treatment.

Adverse event, n (%)	Total number of patients (n=94)	Patients with grade 3 or 4 neutropenia (n=26)	Patients without grade 3 or 4 neutropenia (n=68)	P-value
Leucopenia	68 (72.3)	25 (96.2)	33 (48.5)	0.00005[b]
Anemia	45 (47.9)	17 (65.4)	28 (41.2)	0.03560[a]
Thrombocytopenia	18 (19.1)	11 (42.3)	7 (10.3)	0.00040[b]
Anorexia	4 (4.3)	0 (0.0)	4 (5.9)	0.20600
Vomiting	2 (2.1)	0 (0.0)	2 (2.9)	0.37700
Nausea	17 (18.1)	1 (3.8)	16 (23.5)	0.02660[a]
Diarrhea	7 (7.4)	3 (11.5)	4 (5.9)	0.35000
Febrile neutropenia	1 (1.1)	0 (0.0)	1 (1.5)	0.53400
Hypertension	12 (12.8)	7 (27.0)	5 (7.4)	0.01100[a]
Proteinuria	33 (35.1)	10 (38.5)	23 (33.8)	0.67300

[a]P<0.05; [b]P<0.001.

Table SIII. Previous reports of clinical outcomes in patients with metastatic colorectal cancer treated with trifluridine/tipiracil monotherapy as a late-line treatment.

Author, year (ref.)	Number of patients	RR, %	DCR, %	PFS, months	OS, months	Grade 3 or 4 neutropenia, %
Yoshino *et al*, 2012 (21)	112	1.0	43.0	2.0	9.0	50.0
Mayer *et al*, 2016 (5)	534	1.6	44.0	2.0	7.1	38.0
Arita *et al*, 2016 (22)	43	3.0	33.0	2.5	7.6	44.0
Masuishi *et al*, 2016 (23)	54	0	39.0	2.1	6.5	37.0
Kotani *et al*, 2016 (24)	55	3.7	37.0	2.0	5.3	41.8
Sueda *et al*, 2016 (25)	14	0	28.4	2.1	6.3	14.3
Xu *et al*, 2018 (6)	271	1.1	44.1	2.0	7.8	33.2
Kwakman *et al*, 2018 (26)	136	2.0	28.0	2.1	5.4	32.0
Cremolini *et al*, 2018 (27)	341	2.0	29.0	2.4	6.2	36.4
Moriwaki *et al*, 2018 (28)	327	1.0	29.6	-	7.4	33.0

RR, response rate; DCR, disease control rate; PFS, progression-free survival; OS, overall survival.