

Supplementary material 3: Multivariable analysis of overall and progression free survival with the number of methylated CIMP loci as a continuous variable

Covariates in the final model	Overall survival		Covariates in the final model	Progression free survival	
	Adjusted HR (95% CI)	P		Adjusted HR (95% CI)	P
Overall population (N = 153)					
Age	1.02 (0.998-1.04)	0.085			
Female (N = 49)	1.56 (1.01-2.42)	0.044			
ECOG ≥ 1 (N = 119)	1.81 (1.02-3.22)	0.042			
Metastatic organ ≥ 3 (N = 11)	4.54 (2.23-9.22)	< 0.001			
CEA > 5.0 ng/mL (N = 94)	1.56 (1.00-2.41)	0.049			
N. methylated CIMP loci	1.44 (1.24-1.66)	< 0.001			
Fluoropyrimidine and oxaliplatin first-line chemotherapy (N = 128)					
ECOG ≥ 1 (N = 96)	1.62 (0.897-2.91)	0.11	ECOG ≥ 1 (N = 96)	1.81 (1.08-3.03)	0.024
Metastatic organ ≥ 3 (N = 9)	4.25 (2.02-8.95)	< 0.001	Metastatic organ ≥ 3 (N = 9)	2.51 (1.13-5.60)	0.024
Poor differentiation (N = 12)	1.97 (0.991-3.92)	0.053	N. methylated CIMP loci	1.26 (1.09-1.44)	0.001
N. methylated CIMP loci	1.38 (1.19-1.61)	< 0.001			
Fluoropyrimidine and irinotecan second-line chemotherapy (N = 86)					
Female (N = 30)	1.72 (0.955-3.11)	0.071	Female (N = 30)	2.00 (1.18-3.39)	0.01
Metastatic organ ≥ 3 (N = 6)	3.02 (1.13-8.10)	0.028	ECOG ≥ 1 (N = 66)	1.84 (1.03-3.29)	0.038
CEA ≥ 5.0 ng/mL (N = 54)	2.36 (1.29-4.31)	0.005	CEA ≥ 5.0 ng/mL (N = 54)	1.88 (1.11-3.17)	0.018
Distal location (N = 61)	2.36 (1.17-4.78)	0.017	MSS/MSI-low (N = 81)	4.89 (1.11-21.6)	0.036
N. methylated CIMP loci	1.72 (1.40-2.11)	< 0.001	N. methylated CIMP loci	1.28 (1.07-1.52)	0.006

Abbreviations: HR, hazard ratio; ECOG, eastern cooperative oncology group; CEA, carcinoembryonic antigen; CIMP, CpG island methylator phenotype; MSI, microsatellite instability; MSS, microsatellite stable.