

Table SI. General information of patients with colorectal neuroendocrine carcinoma.

Parameters	Group	N	%
Total	-	157	100
Sex	Male	102	65.0
	Female	55	35.0
Body mass index, kg/m ²	≤24.49	77	49.0
	>24.49	80	51.0
Age, years	≤55	75	47.8
	>55	82	52.2
Surgical history	No	125	79.6
	Yes	32	20.4
Hypertension	No	131	83.4
	Yes	26	16.6
Diabetes	No	141	89.8
	Yes	16	10.2
Primary site	Colon	32	20.4
	Rectum	125	79.6
Gross type	Elevated type	72	45.9
	Ulcerative type	22	14.0
	Infiltrative type	63	40.1
Tumor size, cm	≤2	81	51.6
	>2	41	26.1
	Unknown	35	22.3
Treatment modality	Surgery	128	81.5
	Non-surgery	29	18.5
Histological type	NET-G1	82	52.2
	NET-G2	13	8.3
	NEC-G3	54	34.4
	MANEC	8	5.1
Differentiation	Low-grade (G1)	83	52.9
	Intermediate-grade (G2)	16	10.2
	High-grade (G3)	58	36.9
Distant metastasis	No	118	75.2
	Yes	39	24.8
Total number of lymph node	≤18	37	23.6
	>18	22	14.0
	Unknown	98	62.4
Positive number of lymph node	≤5	40	25.5

	>5	19	12.1
	Unknown	98	62.4
TNM stage	Tis	4	2.5
	I	63	40.1
	II	5	3.2
	III	28	17.8
	IV	43	27.4
	Unknown	14	8.9
Perineural invasion	No	145	92.4
	Yes	12	7.6
Vascular tumor thrombus	No	134	85.4
	Yes	23	14.6
AE1/AE3	Negative	86	54.8
	Positive	71	45.2
Postoperative chemotherapy	No	119	75.8
	Yes	38	24.2
Postoperative radiotherapy	No	150	95.5
	Yes	7	4.5

TNM, tumor-node-metastasis; NET, neuroendocrine tumor; NEC, neuroendocrine carcinoma; MANEC, mixed adenoendocrine carcinoma.

Table SII. Univariate and multivariate Cox proportional hazards regression model for disease-free survival in colorectal neuroendocrine carcinoma.

Parameter	Group	Univariate				Multivariate			
		P-value	HR	95% CI		P-value	HR	95% CI	
				Low	High			Low	High
Sex	Male	0.056	1 (Ref.)						
	Female		2.542	0.975	6.626				
Body mass index, kg/m ²	≤24.49	0.034	1 (Ref.)			0.044	1 (Ref.)		
	>24.49		2.848	1.082	7.494		2.002	1.018	3.939
Age, years	≤55	0.013	1 (Ref.)			0.001	1 (Ref.)		
	>55		3.308	1.289	8.485		3.438	1.615	7.319
Hypertension	No	0.735	1 (Ref.)						
	Yes		1.286	0.300	5.514				
Diabetes	No	0.056	1 (Ref.)						
	Yes		4.628	0.961	22.298				
Primary site	Colon	0.266	1 (Ref.)						
	Rectum		1.709	0.665	4.395				
Gross type	Elevated type	0.270	1 (Ref.)						
	Ulcerative type		3.183	0.783	12.939				
	Infiltrative type		2.026	0.548	7.494				
Tumor size, cm	≤2	0.715	1 (Ref.)						
	>2		1.785	0.432	7.375				
	Unknown		1.642	0.399	6.747				
Histological type	NET-G1	0.030	1 (Ref.)						
	NET-G2		0.865	0.040	18.635				
	NEC-G3		19.385	1.696	221.619				
	MANEC		3.961	0.289	54.309				
Differentiation	Low-grade (G1)	<0.001	1 (Ref.)			<0.001	1 (Ref.)		
	Intermediate-grade (G2)		5.732	1.598	20.556		5.947	1.654	21.381

	High-grade (G3)		10.705	4.475	25.608		10.524	4.363	25.385
Perineural invasion	No	0.512	1 (Ref.)						
	Yes		1.793	0.313	10.278				
Vascular tumor thrombus	No	0.841	1 (Ref.)						
	Yes		0.862	0.201	3.701				
AE1/AE3	Negative	0.244	1 (Ref.)						
	Positive		2.243	0.577	8.728				
Postoperative chemotherapy	No	0.623	1 (Ref.)						
	Yes		0.762	0.258	2.253				
Postoperative radiotherapy	No	0.479	1 (Ref.)						
	Yes		1.929	0.313	11.870				

CI, confidence interval; HR, hazard ratios; NET, neuroendocrine tumor; NEC, neuroendocrine carcinoma; MANEC, mixed adenoendocrine carcinoma.

Table SIII. Univariate and multivariate Cox proportional hazards regression model for overall survival in colorectal neuroendocrine carcinoma.

Parameter	Group	Univariate				Multivariate			
		P-value	HR	95% CI		P-value	HR	95% CI	
				Low	High			Low	High
Sex	Male	0.032	1 (Ref.)			0.029	1 (Ref.)		
	Female		2.857	1.097	7.442		2.890	1.111	7.513
Body mass index, kg/m ²	≤24.49	0.059	1 (Ref.)						
	>24.49		2.531	0.966	6.628				
Age, years	≤55	0.019	1 (Ref.)			0.008	1 (Ref.)		
	>55		3.095	1.205	7.950		2.512	1.276	4.945
Hypertension	No	0.748	1 (Ref.)						
	Yes		1.267	0.300	5.349				
Diabetes	No	0.018	1 (Ref.)						
	Yes		6.990	1.397	34.983				
Primary site	Colon	0.625	1 (Ref.)						
	Rectum		1.264	0.494	3.235				
Gross type	Elevated type	0.091	1 (Ref.)						
	Ulcerative type		4.957	1.178	20.861				
	Infiltrative type		2.827	0.745	10.723				
Tumor size, cm	≤2	0.834	1 (Ref.)						
	>2	0.587		0.354	6.281				
	Unknown	0.568		0.378	5.878				
Histological type	NET-G1	0.099	1 (Ref.)						
	NET-G2		1.896	0.073	49.562				
	NEC-G3		12.340	0.978	155.721				
	MANEC		2.926	0.174	49.321				
Differentiation	Low-grade (G1)	<0.001	1 (Ref.)			<0.001	1 (Ref.)		
	Intermediate-grade (G2)		4.877	1.363	17.443		4.791	1.326	17.303
	High-grade (G3)		10.299	4.307	24.624		7.377	2.995	18.168

Perineural invasion	No	0.492	1 (Ref.)						
	Yes		1.819	0.330	10.040				
Vascular tumor thrombus	No	0.560	1 (Ref.)						
	Yes		0.665	0.168	2.629				
AE1/AE3	Negative	0.293	1 (Ref.)						
	Positive		2.071	0.534	8.034				
Postoperative chemotherapy	No	0.404	1 (Ref.)						
	Yes		0.628	0.211	1.874				
Postoperative radiotherapy	No	0.797	1 (Ref.)						
	Yes		1.301	0.175	9.655				

CI, confidence interval; HR, hazard ratios; NET, neuroendocrine tumor; NEC, neuroendocrine carcinoma; MANEC, mixed adenoendocrine carcinoma.

Table SIV. Clinicopathological characteristics of patients with colorectal neuroendocrine carcinoma of AE1/AE3 expression.

Parameters	Group	N	AE1/AE3(-)	AE1/AE3(+)	P-value
Total	-	157	86	71	
Sex	Male	102 (65.0)	62 (72.1)	40 (56.3)	0.059
	Female	55 (35.0)	24 (27.9)	31 (43.7)	
Body mass index, kg/m ²	≤24.49	77 (49.0)	41 (47.7)	36 (50.7)	0.828
	>24.49	80 (51.0)	45 (52.3)	35 (49.3)	
Age, years	≤55	75 (47.8)	38 (44.2)	37 (52.1)	0.407
	>55	82 (52.2)	48 (55.8)	34 (47.9)	
Surgical history	No	125 (79.6)	70 (81.4)	55 (77.5)	0.682
	Yes	32 (20.4)	16 (18.6)	16 (22.5)	
Hypertension	No	131 (83.4)	75 (87.2)	56 (78.9)	0.237
	Yes	26 (16.6)	11 (12.8)	15 (21.1)	
Diabetes	No	141 (89.8)	81 (94.2)	60 (84.5)	0.084
	Yes	16 (10.2)	5 (5.8)	11 (15.5)	
Primary site	Colon	32 (20.4)	22 (25.6)	10 (14.1)	0.114
	Rectum	125 (79.6)	64 (74.4)	61 (85.9)	
Gross type	Elevated type	72 (45.9)	30 (34.9)	42 (59.2)	0.002 ^a
	Ulcerative type	22 (14.0)	18 (20.9)	4 (5.6)	
	Infiltrative type	63 (40.1)	38 (44.2)	25 (35.2)	
Tumor size, cm	≤2	81 (51.6)	32 (37.2)	49 (69.0)	<0.001
	>2	41 (26.1)	27 (31.4)	14 (19.7)	
	Unknown	35 (22.3)	27 (31.4)	8 (11.3)	
Histological type	NET-G1	82 (52.2)	29 (33.7)	53 (74.6)	<0.001 ^a
	NET-G2	13 (8.3)	6 (7.0)	7 (9.9)	
	NEC-G3	54 (34.4)	47 (54.7)	7 (9.9)	
	MANEC	8 (5.1)	4 (4.7)	4 (5.6)	
Differentiation	Low-grade (G1)	83 (52.9)	30 (34.9)	53 (74.6)	<0.001
	Intermediate-grade (G2)	16 (10.2)	7 (8.1)	9 (12.7)	

	High-grade (G3)	58 (36.9)	49 (57.0)	9 (12.7)	
Total number of lymph node	≤18	37 (23.6)	20 (23.3)	17 (23.9)	0.994
	>18	22 (14.0)	12 (14.0)	10 (14.1)	
	Unknown	98 (62.4)	54 (62.8)	44 (62.0)	
Positive number of lymph node	≤5	40 (25.5)	19 (22.1)	21 (29.6)	0.319
	>5	19 (12.1)	13 (15.1)	6 (8.5)	
	Unknown	98 (62.4)	54 (62.8)	44 (62.0)	
TNM stage	Tis	4 (2.5)	3 (3.5)	1 (1.4)	0.027 ^a
	I	63 (40.1)	24 (27.9)	39 (54.9)	
	II	5 (3.2)	3 (3.5)	2 (2.8)	
	III	28 (17.8)	17 (19.8)	11 (15.5)	
	IV	43 (27.4)	30 (34.9)	13 (18.3)	
	Unknown	14 (8.9)	9 (10.5)	5 (7.0)	
Perineural invasion	No	145 (92.4)	82 (95.3)	63 (88.7)	0.106 ^a
	Yes	12 (7.6)	4 (4.7)	8 (11.3)	
Vascular tumor thrombus	No	134 (85.4)	72 (83.7)	62 (87.3)	0.683
	Yes	23 (14.6)	14 (16.3)	9 (12.7)	
Postoperative chemotherapy	No	119 (75.8)	59 (68.6)	60 (84.5)	0.033
	Yes	38 (24.2)	27 (31.4)	11 (15.5)	
Postoperative radiotherapy	No	150 (95.5)	81 (94.2)	69 (97.2)	0.308 ^a
	Yes	7 (4.5)	5 (5.8)	2 (2.8)	

^aData were analyzed using Fisher's exact test. NET, neuroendocrine tumor; NEC, neuroendocrine carcinoma; MANEC, mixed adenoendocrine carcinoma; TNM, tumor-node-metastasis.