Supplemental Tables for:
Development and validation of a prognostic nomogram to guide decision-making for high-grade digestive neuroendocrine neoplasms
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Supplementary Table S1. Univariate and multivariable analysis of prognostic factors in the Training Cohort

Prognostic Factors Training Cohort	Univariate Cox Regression		MAXIMUM REGRESSION MODEL Multivariable Cox Regression		FINAL REGRESSION MODEL Multivariable Cox Regression	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Age, continuous variable	1.001 (0.98-1.02)	0.884	Not included	--	Not included	--
Gender			Not included	--	Not included	--
Female	1					
Male	0.77(0.52-1.14)	0.185				
Ki.67, continuous variable	2.07(0.81-5.33)	0.138	4.93(1.56-15.55)	0.007	5.47(1.72-17.34)	0.004
Neutrophil-to-lymphocyte ratio	1.16 (1.08-1.24)	<0.001	1.07(0.98-1.18)	0.147	Not included	
Platelet,10^9/L	1.001 (0.99-1.003)	0.435	Not included	--	Not included	
Alkaline phosphatase, UNL	1.22(1.05-1.43)	0.011	1.12(0.91-1.37)	0.280	Not included	
Lactate dehydrogenase, UNL	1.32(1.19-1.47)	<0.001	1.14(1.06-1.22)	<0.001	1.15(1.07-1.23)	<0.001
Performance status						
0-1	1		1		1	
2-3	2.38(1.46-3.87)	<0.001	2.51(1.45-4.33)	<0.001	2.71(1.60-4.60)	<0.001
MANEC, Yes	0.62(0.32-1.19)	0.149	Not included	--		
Stage						
Localized	1		1		1	
Regional	1.56(0.65-3.71)	0.317	2.70 (0.62-11.68)	0.184	2.96(0.69-12.79)	0.145
Distant	4.41(1.91-10.19)	<0.001	6.11(1.30-28.74)	0.022	7.42(1.73-31.85)	0.007
Presence of liver metastases, yes	2.59(1.76-3.81)	<0.001	1.09(0.59- 1.999)	0.786		
Site of primary tumor						
Gastrointestinal tract	1		1		1	
Hepato-biliary-pancreatic system	2.65(1.80-3.90)	<0.001	1.69(1.01-2.82)	0.044	1.76(1.06-2.92)	0.028

Unknown primary	0.86(0.34-2.16)	0.749	0.70(0.23-2.12)	0.527	0.67(0.23-1.98)	0.468

HR=hazard ratio; CI= Confidence interval ; UNL, upper normal limit; MANEC, mixed adenoneuroendocrine carcinoma.

Supplemental Table S2. Overall survival nomogram scoring system

Performance Status	Points	Stage	Points	Ki67	Points	Site of primary tumor	Points	Lactate dehydrogenase, upper normal limit	Points
0-1	0	Localized	0	0.20	0	Gastrointestinal tract	12	0	0
2-3	31	Regional	33	0.30	5	Hepato-biliary-pancreatic system	30	2	8
		Distant	61	0.40	10	Unknown primary	0	4	17
				0.50	16			6	25
				0.60	21			8	33
				0.70	26			10	42
				0.80	31			12	50
				0.90	36			14	58
				1.0	42			16	67
								18	75
								20	83
								22	92
								24	100

Total Points	1-year Overall Survival	Total Points	2-year Overall Survival
137	0.1	113	0.1
126	0.2	102	0.2
117	0.3	93	0.3
109	0.4	84	0.4
100	0.5	76	0.5
91	0.6	67	0.6
80	0.7	56	0.7
65	0.8	41	0.8
42	0.9	18	0.9

Supplementary Table S3. Distribution of the total score within the study population

Score	Training cohort N=172	Validation Cohort N=90	All Cohorts N=262
as a discrete variable			
Median [Min, Max]	98.0 [19.0, 215]	98.0 [25.0, 164]	98.0 [19.0, 215]
Median [IQR]	98.0 [78.0, 119]	98.0 [74.0, 110]	98.0 [78.0, 114]
as a dichotomised variable			
Group A	94 (54.7%)	47 (52.2%)	141 (53.8%)
Group B	78 (45.3%)	43 (47.8%)	121 (46.2%)

Group A, low-risk group; Group B, high-risk group.

Supplementary Table S4. The AUC for the OS nomogram and published prognostic score and regression model

Prediction Period	AUC		
	Our final regression model	Published prognostic score	Published regression model
Training cohort			
6 months	0.78(0.69- 0.87)	0.64(0.53- 0.74)	0.60(0.48-0.72)
12 months	0.86(0.78-0.93)	0.69(0.60-0.79)	0.66(0.55-0.77)
24months	0.82(0.73- 0.91)	0.75(0.65-0.85)	0.76(0.65-0.88)
Validation cohort			
6 months	0.76(0.63-0.90)	0.80(0.69-0.92)	0.76(0.61-0.90)
12 months	0.82(0.70-0.93)	0.78(0.66-0.90)	0.71(0.56-0.87)
24 months	0.81(0.67-0.95)	0.74(0.60-0.88)	0.72(0.57-0.87)

AUC, area under the time-dependent receiver operating characteristic curve; OS, overall survival.