

Supplementary Table 3: Univariate and multivariable analysis (based on selected variables) of overall survival of patients with High-grade Neuroendocrine Neoplasms

Variable	Univariate HR (95% CI)	P-value	Adjusted for Site HR (95% CI)	P-value	Multivariable HR (95% CI)	P-value
Gender (Male vs Female)	0.83 (0.44-1.57)	0.57				
Years (Increase of 10-years)	1.27 (0.91-1.78)	0.17				
Site						
Colon-rectum	1.00				1.00	
Stomach	0.64 (0.23-1.77)	0.39			0.94 (0.33-2.67)	0.91
Ileum	0.26 (0.10-0.69)	0.007			0.37 (0.13-1.04)	0.06
Pancreas	0.28 (0.13-0.62)	0.002			0.51 (0.21-1.23)	0.13
Stage (IV vs I-II-III)	1.18 (0.59-2.36)	0.63				
Ki-67 (>55 vs <55)	13.30 (4.40-40.23)	<0.0001	10.7 (3.34-34.26)	<0.0001	8.60 (2.61-28.33)	<0.0001
Cluster (1 vs 2)	0.36 (0.18-0.73)	0.005	0.30 (0.14-0.63)	0.001	0.43 (0.20-0.93)	0.03
Arginase S (4-12 vs 0-3)	0.34 (0.16-0.73)	0.006	0.40 (0.18-0.91)	0.03		
CD33 S (3-12 vs 0-2)	0.64 (0.33-1.24)	0.19				
CD163 S (4-12 vs 0-3)	1.45 (0.66-3.20)	0.36				
CD66 S (1-12 vs 0)	0.76 (0.39-1.45)	0.40				
CD3 S (3-12 vs 1-2)	0.33 (0.16-0.65)	0.002	0.31 (0.15-0.64)	0.001		
CD4 S (1-12 vs 0)	0.65 (0.31-1.40)	0.27				
CD8 S (2-12 vs 0-1)	0.49 (0.25-0.96)	0.04	0.45 (0.22-0.92)	0.03		
PD-L1 S (1-12 vs 0)	1.00 (0.53-1.90)	0.99				
PD-1 S (2-12 vs 0-1)	0.52 (0.28-0.98)	0.04	0.33 (0.15-0.71)	0.005		
HLA-1 S (1-12 vs 0)	0.78 (0.41-1.48)	0.45				
HLA-DR S (12 vs 0-9)	0.74 (0.35-1.55)	0.43				
NGFR S (1-12 vs 0)	0.99 (0.49-1.99)	0.98				
COX2 S (1-12 vs 0)	0.87 (0.45-1.70)	0.68				
S6 S (1-12 vs 0)	0.91 (0.45-1.82)	0.79				
CD31 S (Present vs Absent)	1.86 (0.97-3.58)	0.06				
COX2T (12 vs 0-9)	0.71 (0.38-1.35)	0.30				
S6 T (1-12 vs 0)	0.49 (0.26-0.94)	0.03				
Beta-Cat T (12 vs 0-9)	1.27 (0.66-2.44)	0.48				
HLA-1 T (6-12 vs 0-4)	0.93 (0.50-1.80)	0.83				
PD-L1 T (1-12 vs 0)	2.47 (0.57-10.81)	0.23				
CD31 T (Present vs Absent)	1.82 (0.94-3.52)	0.08				
Beta-Cat T						
Absent	1.00					
Cytoplasmic and/or membrane	0.37 (0.08-1.64)	0.19				
Nuclear	0.68 (0.16-2.99)	0.61				