

Supplementary Table 1. Baseline characteristics of patients with NEN at sNRP2^(Q0-Q3/Q3-Q4) and CgA assessments.

	Number of available data	NEN patients, N=229	sNRP2 levels		p-value
			sNRP2 ^{Q0-Q3} n=171	sNRP2 ^{Q3-Q4} n=58	
Women, n (%)	229	107 (47)	81 (47)	26 (45)	0.738
Age in years, median (IQR Q1-Q3)	229	65 (55-73)	66 (56-73)	64 (52-72)	0.239
Chronic congestive heart failure, n (%)	229	0 (0)	0 (0)	0 (0)	
Liver failure, n (%)	229	0 (0)	0 (0)	0 (0)	
Renal deficiency, n (%)	229	38 (17)	30 (18)	8 (14)	0.463
Chronic gastritis, n (%)	229	3 (1)	3 (2)	0 (0)	0.462
Inflammatory syndrome, n (%)	147	57 (39) ^a	30 (29)	27 (63)	0.05
Time (months) from diagnosis to NRP2 assay, median (IQR Q1-Q3)	229	49 (20-90)	47 (22-93)	52 (14-83)	0.945
Primary tumour site, jejunum-ileum vs other, n (%)	229				0.103
Jejunum-ileum		108 (47)	86 (50)	22 (38)	
Duodenum-pancreas		78 (34)	54 (32)	24 (41)	
Bronchus-Lung		27 (12)	20 (12)	7 (12)	
Unknown primary		8 (3.5)	6 (3)	2 (3)	
Other		8 (3) ^b	5 (3)	3 (5)	
Functioning tumour, n (%)	229	109 (48) ^c	84 (49)	25 (43)	0.406
Genetic syndrome, n (%)	229	16 (7) ^d	12 (7)	4 (7)	0.927
Number of metastatic sites, 1 vs ≥ 2 , n (%)	229				0.393
0		26 (11)	18 (11)	8 (14)	
1		92 (40)	73 (43)	19 (33)	
≥ 2		111 (49)	80 (47)	31 (53)	
Localisation of metastases, n (%)	229				
Liver		181 (79)	137 (80)	44 (76)	0.491
Distant lymph nodes		67 (29)	53 (31)	14 (24)	0.321
Bone		48 (21)	33 (19)	15 (26)	0.289
Peritoneum		41 (18)	25 (15)	16 (28)	0.026
Lung		15 (7)	13 (8)	2 (3)	0.269

Other		15 (7) ^e	10 (6)	5 (9)	0.531
Patients with uptake on SSTR imaging, n (%)	190	174 (92) ^f	130 (91)	44 (94)	0.562
WHO classifications, n (%)	229				0.939
NET G1 or typical carcinoid		77 (34)	58 (34)	19 (33)	
NET G2 or atypical carcinoid		119 (52)	91 (53)	28 (48)	
NET G3		10 (4)	6 (4)	4 (7)	
Undefined NET or carcinoid		15 (7)	11 (6)	4 (7)	
Neuroendocrine carcinoma (poorly differentiated)		8 (3)	5 (3)	3 (5)	
Ki67 index in %, median (IQR Q1-Q3)	214	4 (2-10) ^g	4 (2-9)	5 (2-10)	0.368
Grade 1-2		193 (90)	146 (91)	47 (87)	
Grade 3		21 (10)	14 (9)	7 (13)	
Prior locoregional treatment, n (%)	229				
Surgery of primary tumour		141 (62)	106 (62)	35 (60)	0.824
Surgery of metastases		53 (23)	42 (25)	11 (19)	0.383
Liver embolisation		37 (16)	31 (18)	6 (10)	0.164
Radiological ablation		14 (6)	10 (6)	4 (7)	0.773
Endoscopic treatment		1 (<1)	1 (<1)	0 (0)	0.559
Prior systemic treatment, n (%)	229				
SSA		164 (72)	127 (74)	37 (64)	0.126
Chemotherapy		95 (41)	67 (39)	28 (48)	0.224
PRRT		53 (23)	41 (24)	12 (21)	0.608
Everolimus		35 (15)	25 (15)	10 (17)	0.632
Sunitinib		14 (6)	10 (6)	4 (7)	0.773
Interferon		3 (1)	2 (1)	1 (<1)	0.748
Concurrent proton pump inhibitors, n (%)	229	44 (19)	36 (21)	8 (14)	0.225
Concurrent SSA, n (%)	229	123 (54)	96 (56)	27 (47)	0.206
sNRP2 in ng/mL, median (IQR Q1-Q3)	229	2.1 (1.4-3.4)	1.7 (1.2-2.3)	4.6 (3.9-5.8)	<0.0001
CgA in ng/mL, median (IQR Q1-Q3)	229	176.3 (61.6-808.7)	203.9 (64-819.7)	95.6 (55.4-739)	0.049
CgA ^{Abn} , n (%)	229	140 (61)	110 (64)	26 (45)	0.009

Abbreviations: NEN, neuroendocrine neoplasm; Nor, normal values; Abn, abnormal values; IQR, interquartile range; NRP2, neuropilin-2; SSTR, somatostatin receptor; WHO, World Health Organization; NET, neuroendocrine tumour; SSA, somatostatin analogues; PRRT, peptide receptor radionuclide therapy; sNRP2, soluble neuropilin-2; CgA, chromogranin A.

^a Rectum (n=3), biliary tract (n=2), stomach (n=2), colon (n=1).

^b Carcinoid syndrome (n=88), Zollinger-Ellison (n=7), Insulinoma (n=6), Vipoma (n=3), Parathyroid hormone-related protein (n=3), Cushing (n=2).

^c Multiple endocrine neoplasia type (n=14), Tuberous Sclerosis Complex (n=1), von Hippel-Lindau Disease (n=1).

^d Pancreas (n=3), ovary (n=3), adrenal gland (n=3), brain (n=2), thymus (n=1), heart (n=1), skin (n=1), kidney (n=1), breast (n=1).