

Long-term Survival Outcomes After Minimally Invasive Surgery for Ileal Neuroendocrine Tumors

Akitada Yogo^{1,2}, Alan Paciorek^{2,3}, Yosuke Kasai⁴, Farhana Moon², Kenzo Hirose^{1,2}, Carlos U. Corvera^{1,2}, Emily K. Bergsland^{2,5} ,Eric K. Nakakura^{1,2}

1: Division of Surgical Oncology, Section of Hepatopancreaticobiliary Surgery, Department of Surgery, University of California, San Francisco, San Francisco, California, USA.

2: Helen Diller Family Comprehensive Cancer Center, San Francisco, California, USA.

3: Department of Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, California, USA.

4: Department of Surgery, Kyoto University, Kyoto, Japan

5: Division of Hematology and Oncology, Department of Medicine, University of California, San Francisco, San Francisco, California, USA.

Surgical resection of primary ileal neuroendocrine tumors



single-institution retrospective cohort study



Open surgery: 39 cases
vs
Minimally Invasive Surgery with hand-access port (MIS): 129 cases



Overall survival (OS) with median follow-up time 49 mos (IQR = 23, 87 mos)

Propensity-score matching (PSM)



-higher tumor grade
-more mesenteric mass extension
-more frequent mesenteric mass > 2cm
-more frequent liver surgery in Open surgery

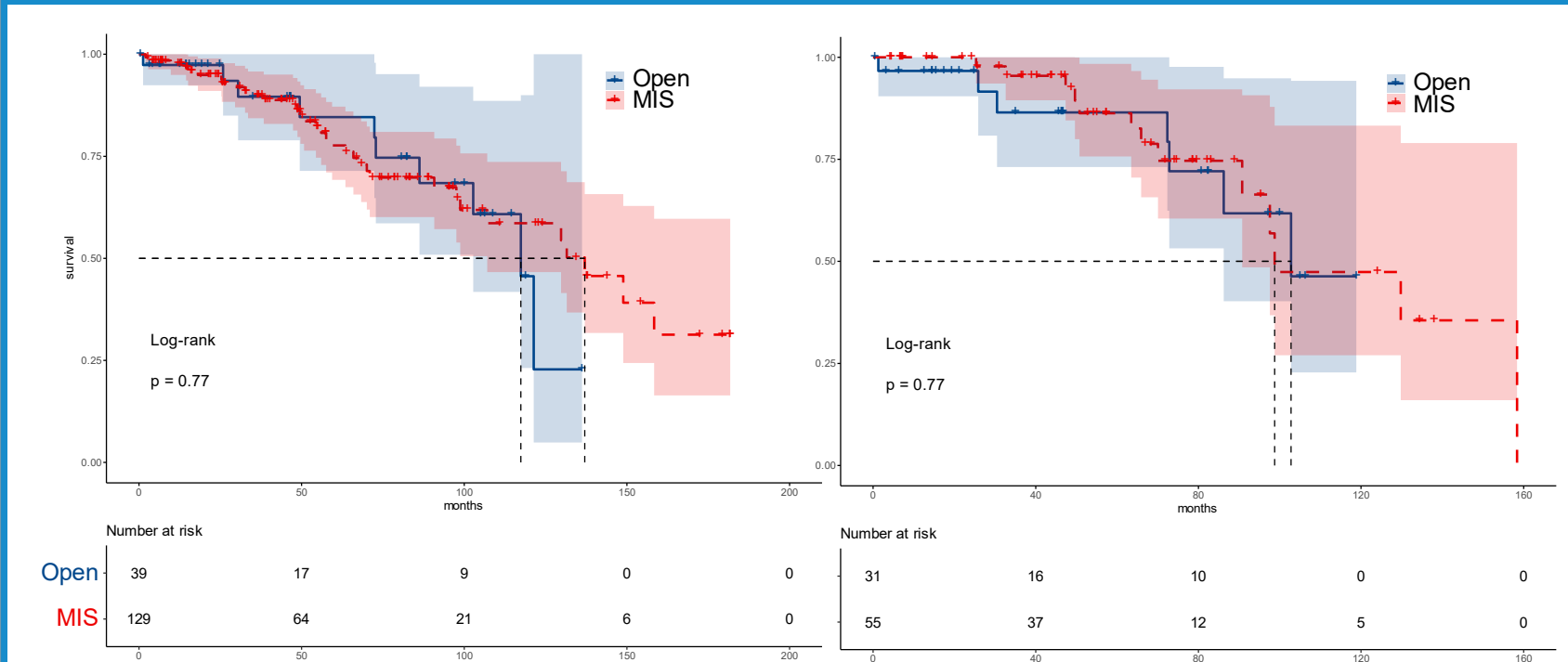


PSM based on age, history of small bowel obstruction, tumor grade, T, N, M, Stage, mesenteric mass extension, mesenteric mass > 2cm, liver surgery



31 cases from Open surgery
55 cases from MIS

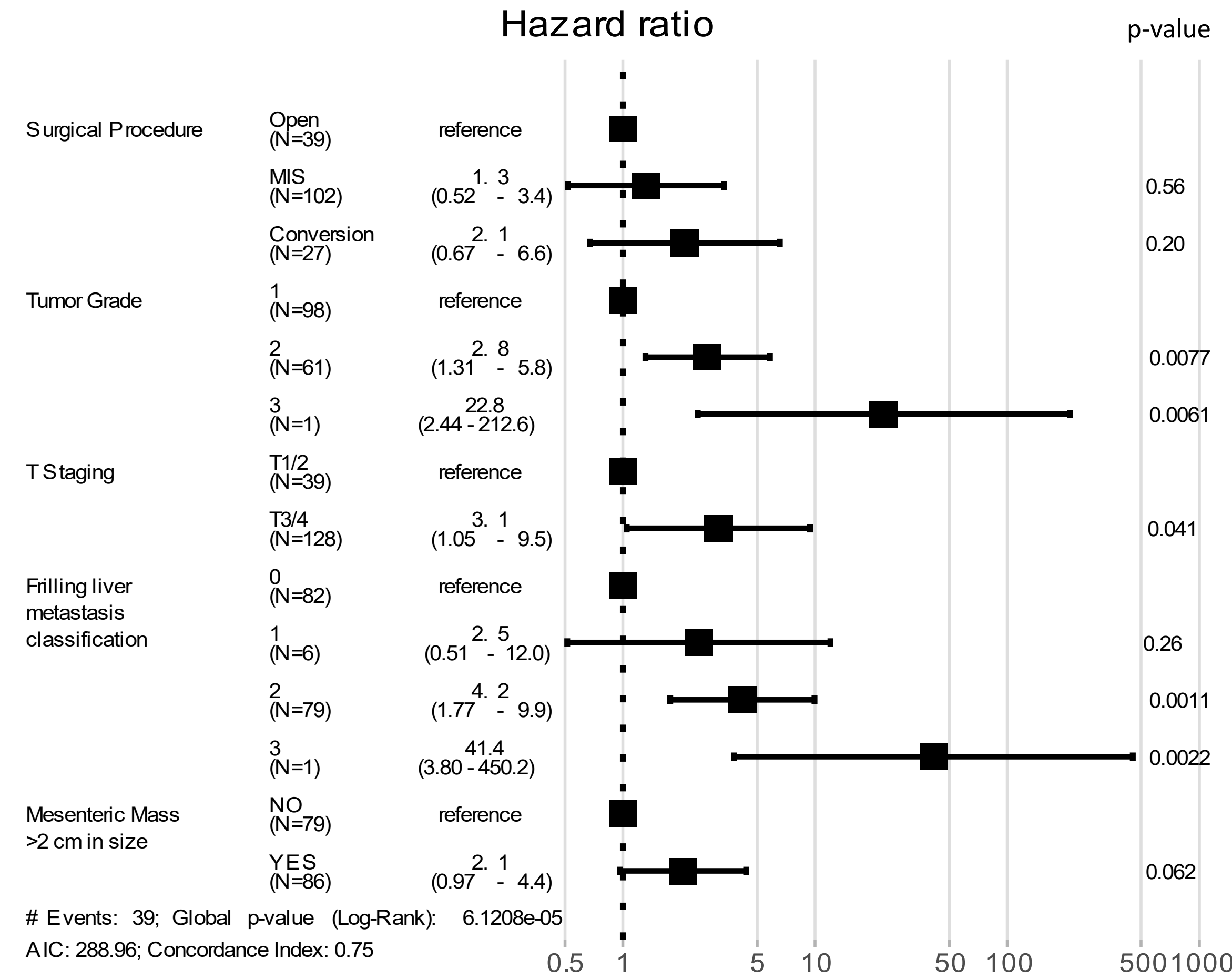
No clear difference in OS



unmatched matched

MIS: 99 mos [95% CI 91–NA]
Open: 103 mos [86–NA]; p = 0.77
HR 0.87 [0.33–2.2]; p = 0.77

Multivariable analysis for overall mortality



Background

Ileal neuroendocrine tumors (i-NETs) are characterized by their multifocality and bulky mesenteric mass. Although various guidelines mention possible benefits of using minimally invasive surgery (MIS) for i-NETs, none offer recommendations regarding specific techniques or established criteria for patient selection.

Having shown that MIS utilizing a hand-access port device has favorable short-term outcomes and achieves the goals of surgery for i-NETs, we sought to analyze long-term survival outcomes of MIS.

Material and Methods

One hundred sixty-eight patients who underwent resection of primary i-NETs at a single institution between January 2007 and February 2023 were retrospectively studied.

Patients were categorized into the MIS or open surgery cohort on an intention-to-treat basis. Open surgery was selected mainly based on the need for hepatectomy or bulky mesenteric mass resection.

Overall survival was analyzed using log-rank tests with propensity-score matching (PSM) and Cox proportional hazards regression. PSM was performed to reduce standardized mean differences of the variables to less than 0.2.

Table 1. Demographics and patient backgrounds

Characteristic	N	Unmatched		p-value	N	Matched		p-value
		Open, N = 39	MIS, N = 129			Open, N = 31	MIS, N = 55	
Surgical Procedure	168				86			
Open		39 (100)	0 (0)			31 (100)	0 (0)	
MIS without conversion		0 (0)	102 (79)			0 (0)	43 (78)	
MIS converted to Open		0 (0)	27 (21)			0 (0)	12 (22)	
Age, Median (IQR)	168	61 (53, 67)	60 (53, 67)	0.62	86	61 (53, 68)	62 (56, 68)	0.90
Gender Female	168	20 (51)	62 (48)	0.86	86	15 (48)	30 (55)	0.66
BMI (kg/m ²), Median (IQR)	167	27.0 (24.2, 29)	26.5 (22.6, 31)	0.98	86	27.1 (24.2, 29)	25.4 (22.2, 31)	0.65
Race White	165	29 (76)	97 (76)	1	86	24 (77)	45 (82)	0.78
Carcinoid syndrome	165	20 (53)	69 (54)	0.86	84	14 (47)	24 (44)	1
SSA before resection	168	14 (36)	38 (29)	0.44	86	11 (35)	13 (24)	0.32
History of small bowel obstruction	168	29 (74)	88 (68)	0.55	86	8 (26)	13 (24)	1

SSA, Somatostatin analogue; BMI, Body mass index

Table 2. Tumor characteristics

Characteristic	N	Unmatched		p-value	N	Matched		p-value
		Open, N = 39	MIS, N = 129			Open, N = 31	MIS, N = 55	
Size of primary tumor (cm), Median (IQR)	166	1.9 (1.3, 3)	1.9 (1.3, 3)	0.91	85	2.0 (1.4, 3)	1.8 (1.5, 3)	0.82
Number of primary tumor(s), Median (IQR)	167	1 (1, 4)	1 (1, 2)	0.37	86	1.0 (1.0, 4)	1.0 (1.0, 3)	0.84
Multiple tumors	167	17 (45)	49 (38)	0.46	86	13 (42)	26 (47)	0.66
Mesenteric mass involvement to the root of the mesentery	168	9 (23)	13 (10)	0.055	86	5 (16)	8 (15)	1
Size of mesenteric mass (cm), Median (IQR)	165	2.6 (1.1, 3.5)	1.8 (1.0, 3.2)	0.21	86	2.4 (1.1, 3.6)	2.5 (1.4, 3.9)	0.48
Mesenteric mass > 2 cm in size	165	25 (66)	61 (48)	0.065	86	20 (65)	38 (69)	0.81
Tumor Grade	160			0.14	86			1
1		18 (49)	80 (65)			17 (55)	30 (55)	
2		19 (51)	42 (34)			14 (45)	25 (45)	
3		0 (0)	1 (0.8)			0 (0)	0 (0)	
T Staging	167			0.35	86			0.68
T1		2 (5.3)	10 (7.8)			1 (3.2)	3 (5.5)	
T2		3 (7.9)	24 (19)			1 (3.2)	3 (5.5)	
T3		19 (50)	60 (47)			16 (52)	33 (60)	
T4		14 (37)	35 (27)			13 (42)	16 (29)	
N +	166	36 (95)	122 (97)	0.62	86	1 (3.2)	2 (3.6)	1
M Staging	168			0.25	86			0.46
M0		13 (33)	59 (46)			12 (39)	24 (44)	
M1a		13 (33)	45 (35)			9 (29)	21 (38)	
M1b		4 (10)	6 (4.7)			3 (9.7)	4 (7.3)	
M1c		9 (23)	19 (15)			7 (23)	6 (11)	
Stage	168			0.23	86			0.49
I		0 (0)	4 (3.1)			0 (0)	2 (3.6)	
II		1 (2.6)	1 (0.8)			1 (3.2)	0 (0)	
III		12 (31)	54 (42)			11 (35)	22 (40)	
IV		26 (67)	70 (54)			19 (61)	31 (56)	
Frilling Liver Metastasis Classification	168			0.34	86			0.68
0		17 (44)	65 (50)			15 (48)	28 (51)	
1		1 (2.6)	5 (3.9)			1 (3.2)	3 (5.5)	
2		20 (51)	59 (46)			14 (45)	24 (44)	
3		1 (2.6)	0 (0)			1 (3.2)	0 (0)	
Concurrent liver surgery	168	10 (26)	9 (7.0)	0.0029	86	6 (19)	8 (15)	0.6

Results

One hundred twenty-nine (77%) patients underwent MIS and thirty-nine (23%) underwent open surgery. Twenty-seven MIS patients were converted to an open procedure. The median follow-up time was 49 mos (IQR = 23, 87 mos). In the PSM cohorts, overall survival did not differ significantly between the MIS and open surgery cohorts (median 99 mos [95% CI 91–NA] vs. 103 mos [86–NA]; p = 0.77, HR 0.87 [95% CI 0.33–2.2]; p = 0.77).

Conclusion

MIS is an alternative to open surgery for i-NETs, achieving similar short- and long-term oncological outcomes with less blood loss and possible shorter length of stay. Bulky mesenteric mass and plan for concurrent liver resection are potential criteria for open surgery. An accompanying editorial by Dr. Gustafson and Dr. Sadowski of the NIH found our study mitigated the major arguments against a minimally invasive approach for SB-NETs by using a hand-access port. (Ann Surg Oncol. 2024;31(9):5487- 5488.)

Table 3. Surgical outcomes

Characteristic	N	Unmatched		p-value	N	Matched		p-value
		Open, N = 39	MIS, N = 129			Open, N = 31	MIS, N = 55	
Incomplete mesenteric lymph node dissection	167	9 (23)	18 (14)	0.21	86	6 (19)	10 (18)	1
Microscopically positive mesenteric margin	168	7 (18)	20 (16)	0.80	86	5 (16)	11 (20)	0.77
Complete mesenteric lymph node dissection	167	23 (59)	90 (70)	0.24	86	20 (65)	34 (62)	1
Estimated blood loss (ml), median (IQR)	161	100 (30, 150)	50 (20, 100)	0.0082	82	100 (35, 150)	50 (20, 100)	0.0071
Postoperative complications >= G3	168	4 (10)	4 (3.1)	0.085	86	2 (6.5)	2 (3.6)	0.9
Length of stay (days), Median (IQR)	168	6 (5, 7)	5 (4, 7)	0.063	86	6 (5, 7)	5 (4, 7)	0.098
Postoperative treatment	168				86			
SSA or telotristat		19 (49)	61 (47)	1		13 (42)	26 (47)	0.66
Liver directed therapy		10 (26)	30 (23)	0.83		13 (42)	26 (47)	0.66
Surgical resection		5 (13)	13 (10)	0.57		4 (13)	4 (7.3)	0.45
PRRT		6 (15)	19 (15)	1		6 (19)	10 (18)	1
Systemic medication		8 (21)	14 (11)	0.17		6 (19)	9 (16)	0.77
Survival status Dead	168	10 (26)	34 (27)	1	86	7 (23)	13 (24)	1
Follow-up months, Median (IQR)	168	46 (16, 99)	50 (25, 83)	0.62	86	46 (16, 82)	53 (33, 79)	0.31

SSA, Somatostatin analogue; PRRT, Peptide receptor radionuclide therapy