## NEN PRECEPTORSHIP LA PRATICA CLINICA NELLE NEOPLASIE NEUROENDOCRINE

5/6 Aprile 2018 | IEO, Istituto Europeo di Oncologia - Milano

# Criteri di scelta della terapia chirurgica

Stefano Partelli, MD, PhD
Assistant Professor of Surgery
Pancreas Translational & Research Institute
University Vita-Salute,
IRCCS San Raffaele Hospital, Milan



### Criteria for Surgery: the two pillars

Disease-related factors

Stage

**Diameter** 

**Symptoms** 

**Aims** 

To cure

To control disease



### **Criteria for Surgery: Stage**

Stage I-III

To cure

To control disease

Stage IV

To cure (?)

To control disease



### Stage I-III

**Criteria for surgery:** 

**Tumor size** 

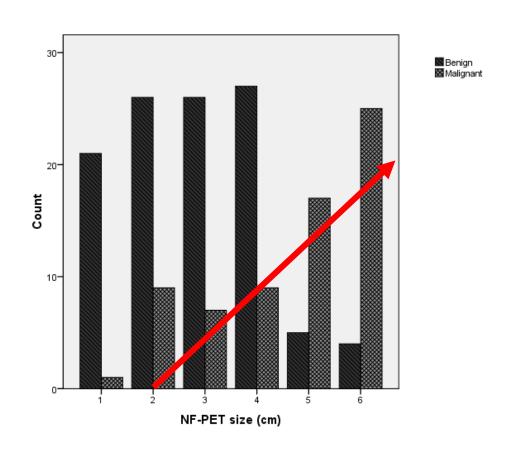
**Presence of syndrome** 

Vascular involvement



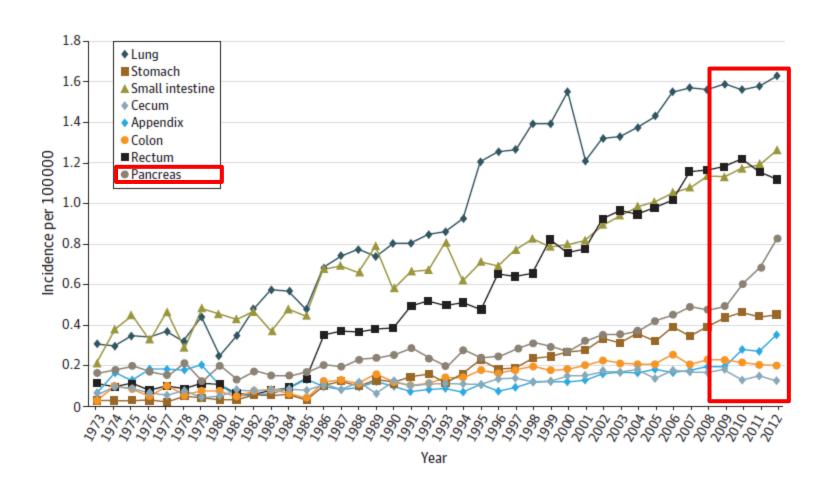
### Pancreatic NET: value of diameter

Tumor diameter is one of the most important prognostic factor for PanNET





### The "Tsunami" of PanNET

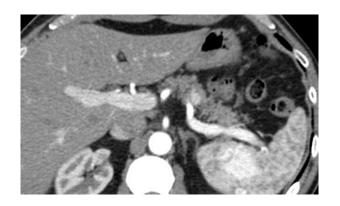




### A common finding





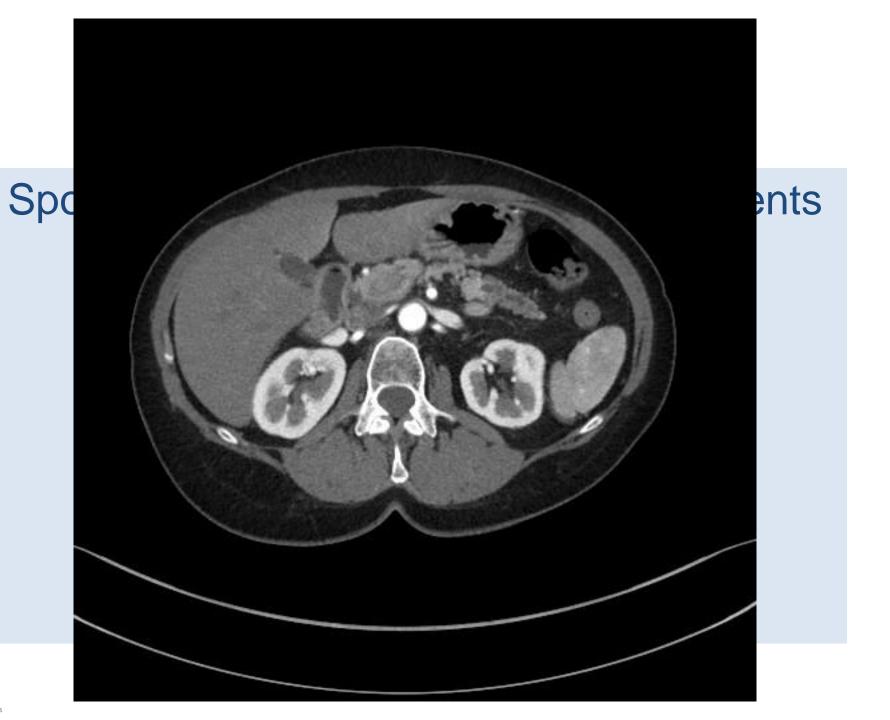




### PanNET<2 cm: follow-up is safe...

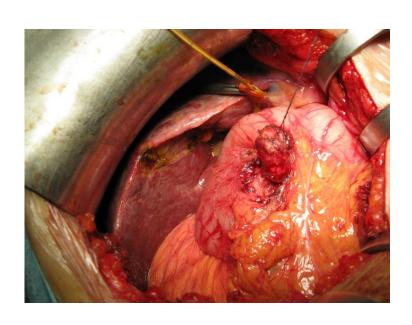
Authors	Median follow-up (months)	No change in tumor size n (%)	Growth > 20% n (%)	Surgery during follow-up n (%)
Lee et al.	45	77 (100)	0 (0)	0
Gaujoux et al.	34	40 (87)	6 (13)	8 (17)
Kishi et al.	45		3 (16)	0
Rosenberg et al.	28	NR	NR	0
Jung et al.	NR	70 (82)	3 (4)	12 (14)
Sadot et al.	44	51 (49)	NR	26 (25)
	28-45	49-100%	0-16%	14-25%

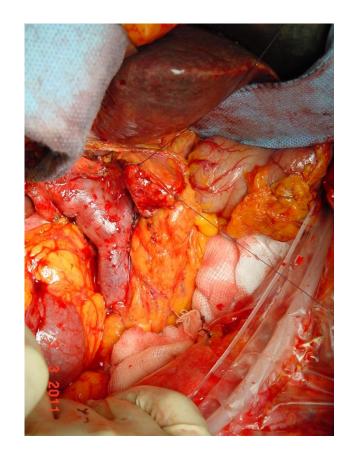




OSPEDALE SAN RAFFAELE Chirurgia del Pancreas

### Which type of surgery for PanNET<2 cm? Enucleation vs standard resection







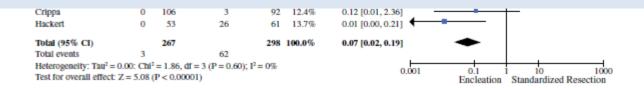
### **Enucleation vs resection**

#### (e) Endocrine Insufficiency

	Enuclea	ation	Standardized Res	ection		Odds Ratio	Od	1s Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Rar	dom, 95% Cl	

#### **WARNING**

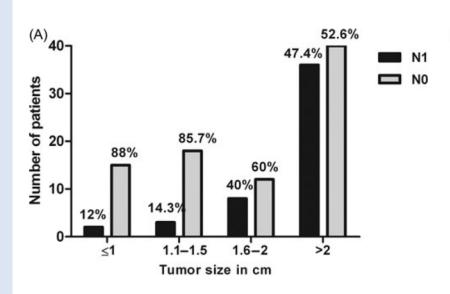
## Enucleation is not associated with a proper lymphadenectomy





## Risk of N+ is high for PanNET > 2 cm

Pancreatic resection + lymphadenectomy for PanNET > 2 cm





### Stage I-III

**Criteria for surgery:** 

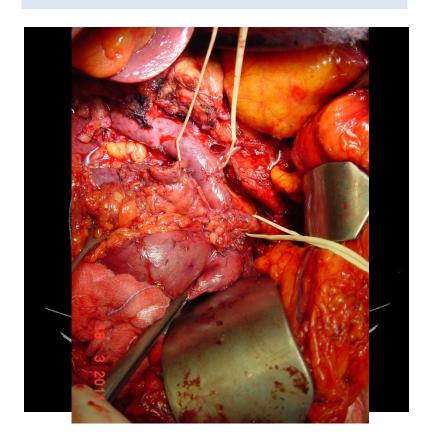
**Tumor size** 

**Presence of syndrome** 

Vascular involvement

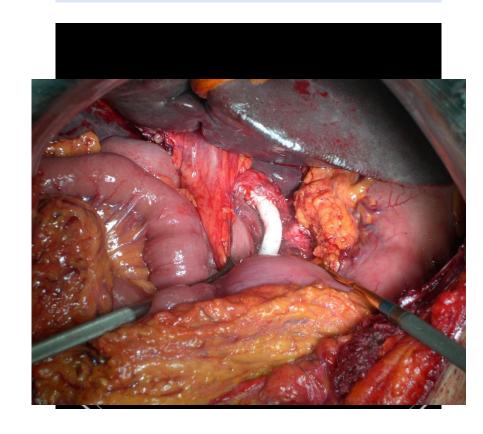


### Superior/Portal Vein



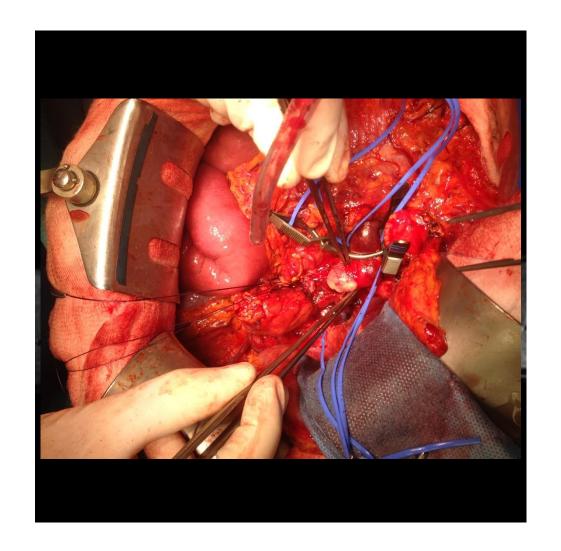
**Borderline resectable** 

## Superior Mesenteric Artery



Locally advanced

### Portal vein thrombosis







"My fellow Americans, ask not what your country can do for you; ask what you can do for your country."



"My fellow ONCOLOGISTS, ask not what your SURGEON can do for you; ask what you can do for your SURGEON"

### Morphology vs biology

#### **Consider neoadjuvant treatment:**

**PRRT** 

Chemotherapy







### **Criteria for Surgery: Stage**

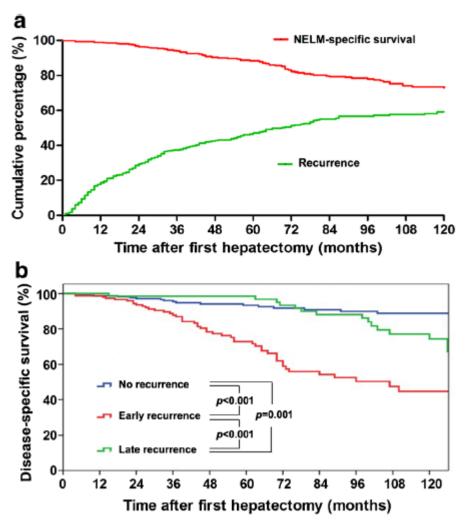
**Stage IV** 

To cure (?)

To control disease



### Recurrence after curative resection





# Oligometastatic disease: an illusion

No. LM Pre								Preoperatively Identified on Imaging				
			Pathologic	athologic Findings		Ultrasound Examination			Somatostatin			
Patient	Primary Tumor	Type of Hepatectomy	No. LM	Size cm (min-max)	Normal	Contrast Enhanced	CT-Scan	MRI	Receptor Scintigraphy	Intraoperative Findings		
1	Not identified	Right	13	(0.6-7)	8	8	6	7	0	9		
2	Stomach	Left	5	(0.25-1.2)	4	4	4	3	2	5		
3	Insulinoma	Right	22	(0.1-2.5)	7	8	5	10	3	10		
4	Glucagonoma	Left	59	(0.1-3.5)	4	7	6	13	3	18		
5	Insulinoma	Left	9	(0.7-5.5)	4	NA	5	9	0	6		
6	Small bowel	Right	16	(0.5-3.5)	7	7	4	7	3	4		
7	Small bowel	Right	13	(0.5-5)	6	NA	7	7	10	10		
8	Small bowel	Left	12	(0.1-1.4)	2	3	3	2	0	3		
9	Lung carcinoma	Right	8	(0.2-5)	3	NA	4	5	3	5		
10	Zollinger-Ellison	Left	88	(0.1-5)	0	8	2	6	3	8		
11	Glucagonoma	Right	28	(0.2-5)	15	NA	12	20	7	17		
Total			273		60	45	58	89	34	95		
Mean			24.8 ± 25.7		5.4 ± 3.9	6.4 ± 2.1	$5.3 \pm 2.7$	$8.1 \pm 5.0$	$3.1 \pm 3.0$	$8.6 \pm 5.0$		
Median			13		4	7	5	7	3	8		



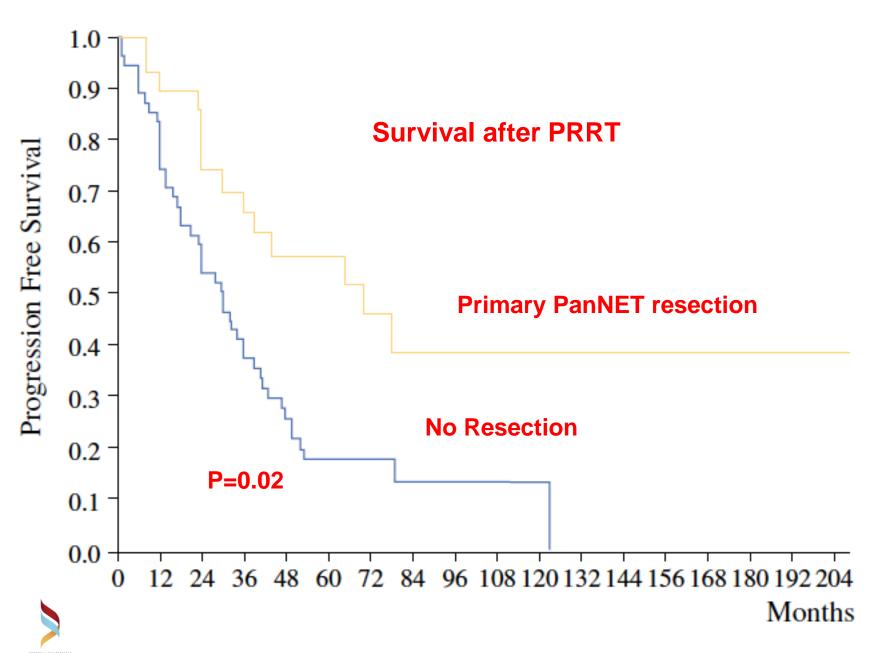
### The real aim: To kick the can



## Role of palliative pancreatic resection Overall survival

	Surge	ry	Non operative manage	ment		Odds Ratio	Odds Ratio	
Study or Subgroup	<b>Events</b>	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	
Bertani 2016	17	30	23	31	13.8%	0.45 [0.15, 1.34]		
Bettini 2009	13	19	18	32	12.3%	1.69 [0.51, 5.56]	+-	
Citterio 2017	7	18	16	18	7.1%	0.08 [0.01, 0.46]	<del></del>	
Hüttner 2015	39	75	290	367	24.8%	0.29 [0.17, 0.48]	-	
Nguyen 2013	15	20	29	31	7.1%	0.21 [0.04, 1.20]		
Partelli 2015	30	73	52	75	21.2%	0.31 [0.16, 0.61]		
Solorzano 2001	9	16	54	80	13.6%	0.62 [0.21, 1.85]		
Total (95% CI)		251		634	100.0%	0.38 [0.23, 0.65]	•	
Total events	130		482					
Heterogeneity: $Tau^2 = 0.22$ ; $Chi^2 = 11.72$ , $df = 6$ (P = 0.07); $I^2 = 49\%$								
Test for overall effect:	0.01 0.1 1 10 100 Favours Surgery Favours NOM							

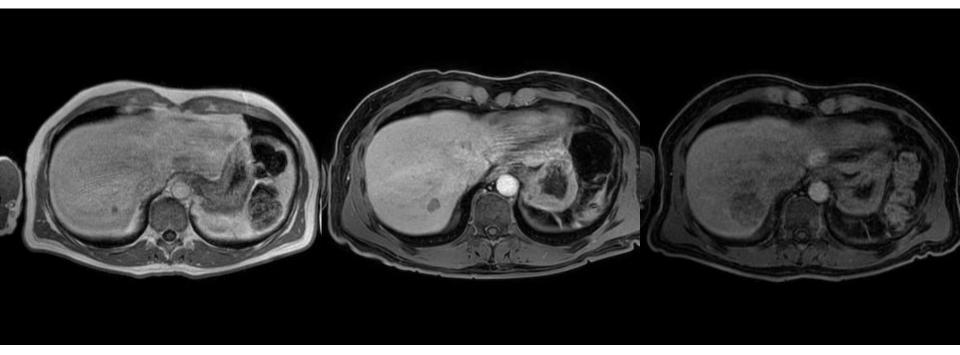




Bertani E, et al. Ann Surg Oncol 2016

### Single metastasis progression

2015 2016 2018



Somatostatin Analogs **Everolimus** 

Surgery



### Single metastasis progression

Local treatment can control discrete sites of progression

To allow patients to continue their existing therapy



### Outcomes of Locoregional Treatment for Unifocal Progression in Widespread Metastatic Gastroenteropancreatic Neuroendocrine Tumors

Taymeyah E. Al-Toubah, Mauro Cives, Daniel A. Anaya, Heloisa P. Soares, Jonathan R. Strosberg

H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida

#### **Patient Population:**

- 59 patients seen between 1/2014 and 5/2017 with metastatic GEP-NETs who underwent a local treatment for focal progression.
- Patients undergoing lobar HAE or cytoreductive hepatic surgery were not included.

