66° SIGG CONGRESSO NAZIONALE
ROMA, 1-4 DICEMBRE 2021
Geriatria e Rinascita
SOCIETÀ ITALIANA DI GERONTOLOGIA E GERIATRIA

17:40–18:00 Lettura

TUMORI NEUROENDOCRINI NELL'ANZIANO

Multidisciplinary Group for Neuroendocrine Tumors NAPLES
ENETS Center of Excellence

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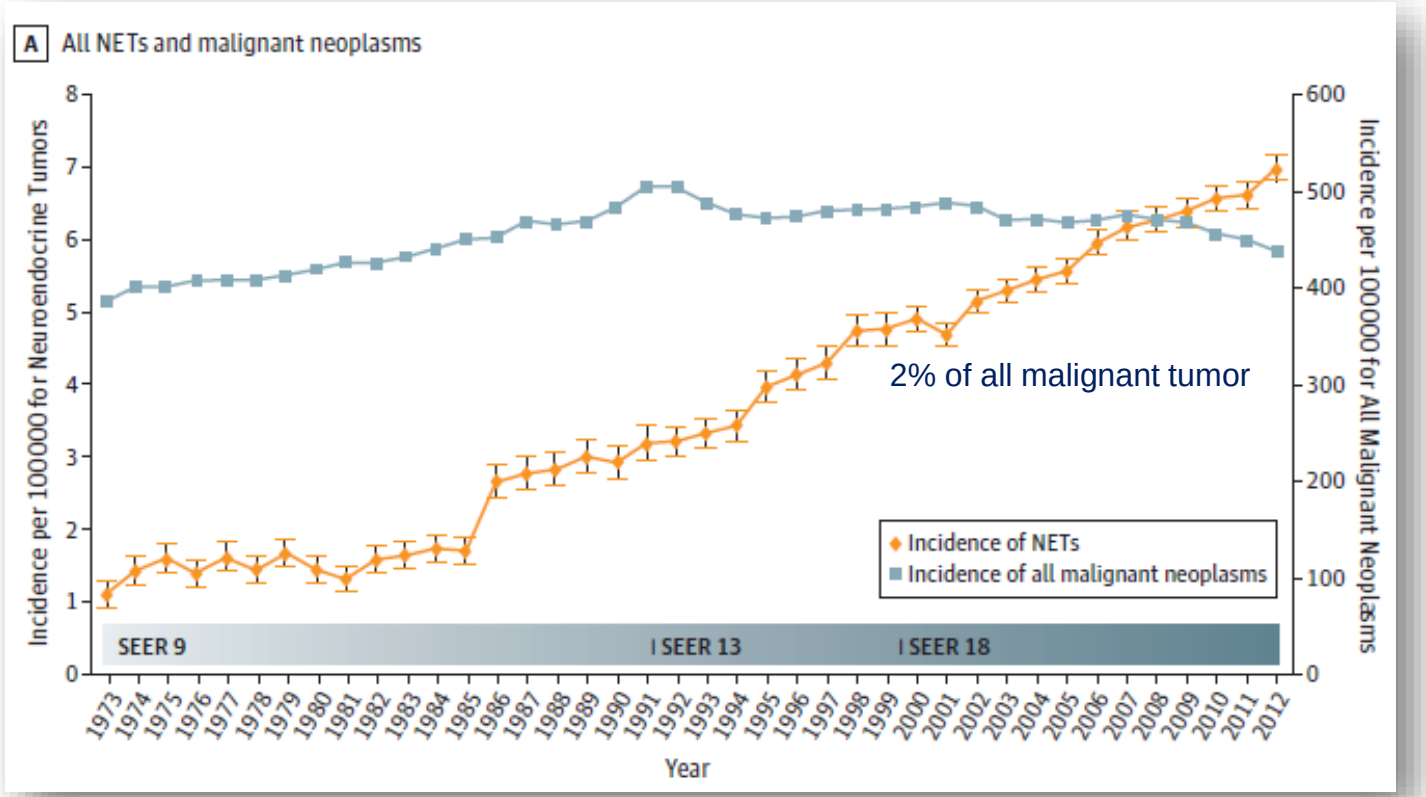
FINANCIAL DISCOLSURE

Ipsen travel grant

NEUROENDOCRINE NEOPLASMS (NEN): EPIDEMIOLOGY

NEN incidence is increasing 6.4-fold from 1973 (1.09 per 100 000) to 2012 (6.98 per 100 000)

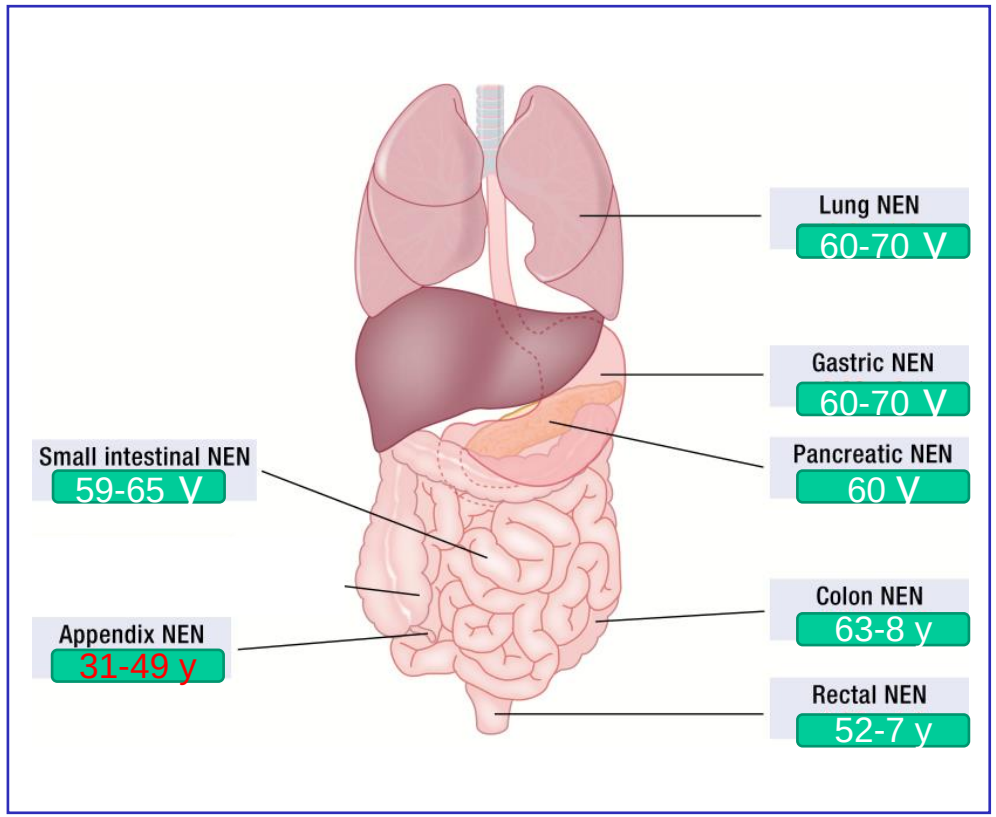
Most dramatic rise in incidence in patients **65 years or older** with a more than 8-fold rise

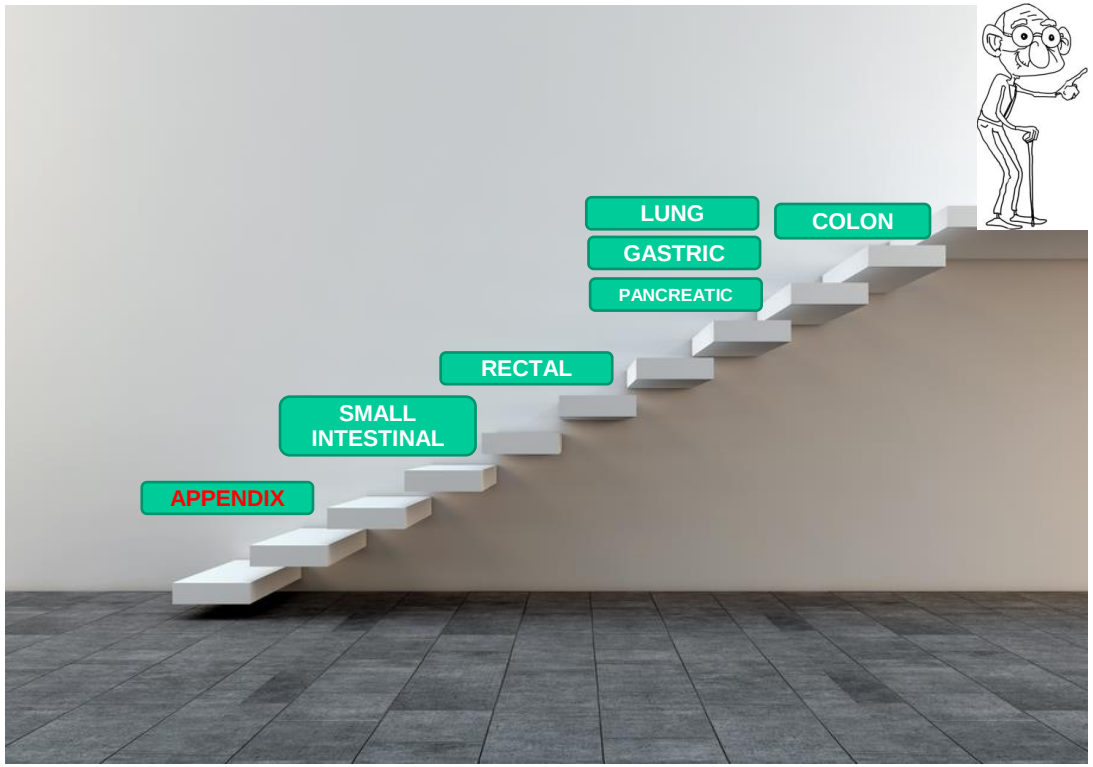


Jao et al. *JCO*, 2008

NEN: SITE OF PRIMARY AND AGE

NEN mostly arise in the gastroenteropancreatic tract (GEP) (67%) and lung (25%)

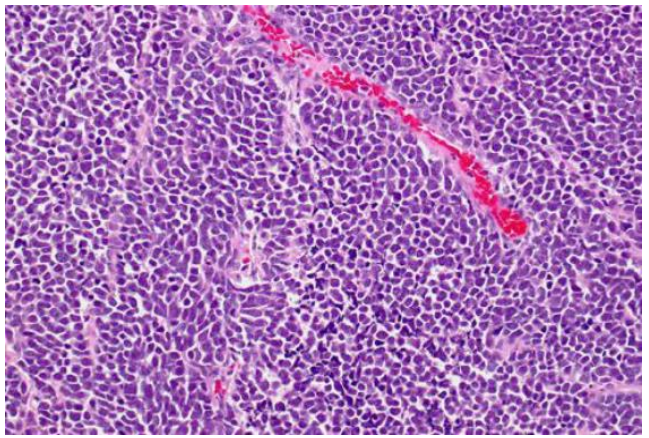


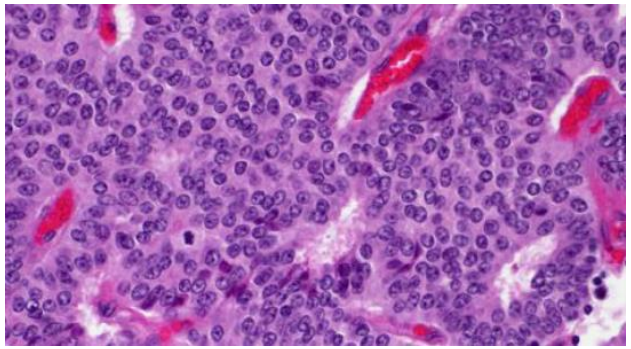


FRONT HORM RES. 2015;44:1-23. DOI: 10.1159/000381970. EPUB 2015 AUG 14. EPIDEMIOLOGY OF NEUROENDOCRINE TUMORS. MERAV FRAENKEL , ANTONGIULIO FAGGIANO, GERLOF D VALK

NEN: UPDATED PATHOLOGICAL CLASSIFICATIONS

WELL DIFFERENTIATED GEP NEN	KI 67 (%)	MITOTIC INDEX
NEUROENDOCRINE TUMOR (NET) G1	<3	<2/10 HPF
NEUROENDOCRINE TUMOR (NET) G2	3-20	2-20/10 HPF
NEUROENDOCRINE TUMOR (NET) G3	>20	>20/10 HPF
POORLY DIFFERENTIATED GEP NEN		
NEUROENDOCRINE CARCINOMA (NEC) G3	>20	>20/10 HPF

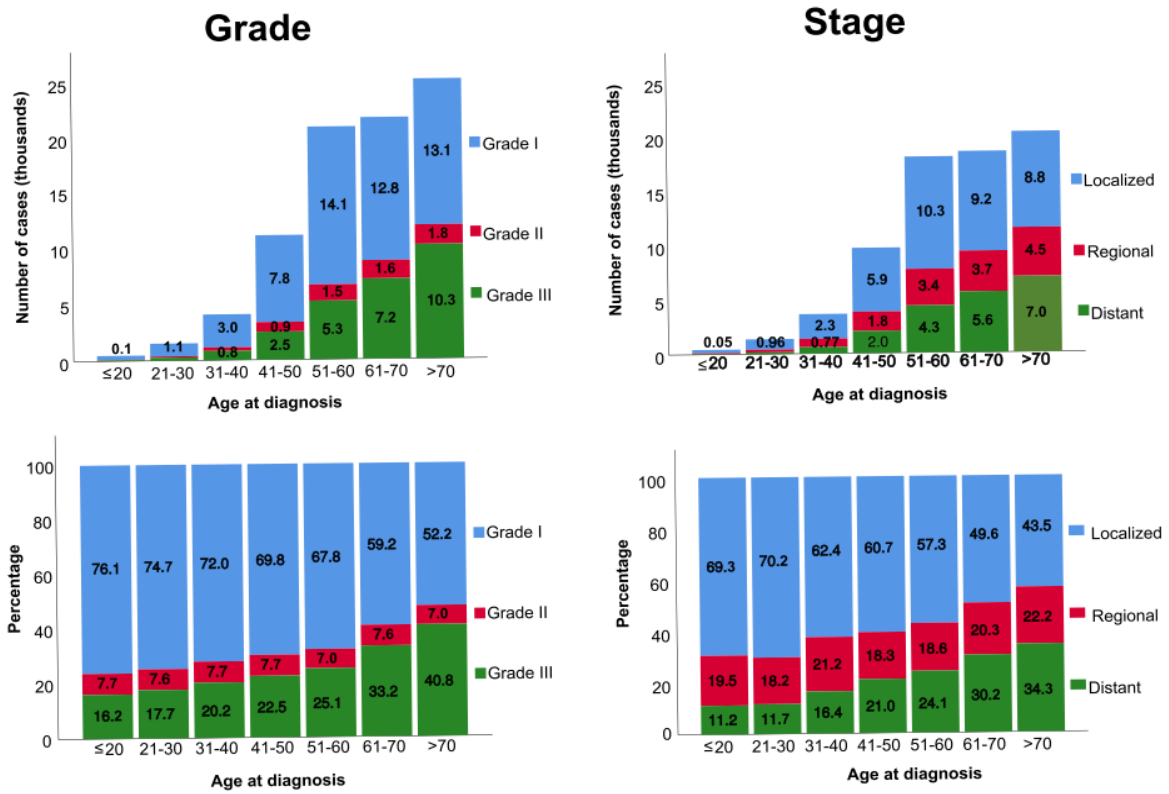




LUNG	Typical Carcinoid	Atypical Carcinoid	Large Cell Neuroendocrine Carcinoma	Small Cell Carcinoma
Mitoses per 2 mm^2	0-1	2-10	>20 (median 70)	>10 (median 80)
Necrosis	No	Focal, if any	Yes	Yes

WHO Classification of Tumours Editorial Board. Digestive system tumours. Lyon (France): International Agency Research on cancer; 2019; The 2015 WHO classification of lung tumors

NEN: AGE IMPACTS ON SURVIVAL



85,133 NET patients (1995 – 2014)

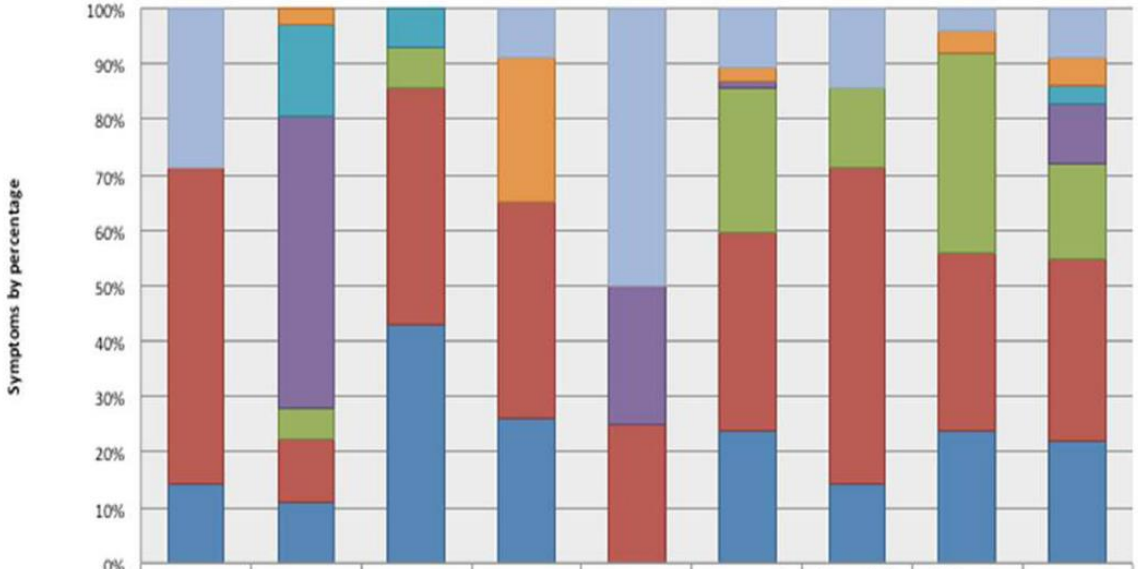
Median overall survival decreased with age across the entire spectrum of ages

- patients >70 years particularly poor prognosis (28 months)
- Patients >70 years old often had distant (34.3%) or grade 3 disease (40.8%)
- **Elderly patients** with lower grade and/or stage disease had **worse OS** compared with younger subjects

Age appears to be associated with a worse prognosis independent of NET stage and grade at the time of diagnosis

Sackstein PE et al. *Seminars in Oncology*, 2018

NEN: CLINICAL PRESENTATION AND DELAYED DIAGNOSIS



	Appendix	Lung	Not sure	Pancreas	Rectal	Small Bowel	Stomach / gastric	Unknown Primary	Grand Total
Other	29%	0%	0%	9%	50%	11%	14%	4%	9%
Fatigue / Tired	0%	3%	0%	26%	0%	2%	0%	4%	5%
Wheeze	0%	17%	7%	0%	0%	0%	0%	0%	3%
Cough	0%	53%	0%	0%	25%	1%	0%	0%	10%
Flushing	0%	6%	7%	0%	0%	26%	14%	36%	17%
Pain	57%	11%	43%	39%	25%	36%	57%	32%	33%
Diarrhoea	14%	11%	43%	26%	0%	24%	14%	24%	22%

- **Median time from first symptom to diagnosis 53.8 months**
- Most frequent initial symptoms pain, change in bowel habit and fatigue
- 31% noted weight loss prior to diagnosis. 80% of respondents visited their GP regarding the symptoms a median of 11 times
- 58% were referred to secondary care where they were seen a median 3 times
- 30% presented acutely and this led to their diagnosis

Basuroy et al. *BMC Cancer* 2018

Limited Diagnostic Utility of Chromogranin A Measurements in Workup of Neuroendocrine Tumors

Jonas Baekdal [1,2], Jesper Krogh [1,2], Marianne Klose [1,2], Pernille Holmager [1,2], Seppo W Langer [1,3], Peter Oturai [1,4,5], Andreas Kjaer [1,4,5], Birgitte Federspiel [1,6], Linda Hilsted [1,7], Jens F Rehfeld [1,7], Ulrich Knigge [1,2,8], Mikkel Andreassen [1,2]

197

167
CgA

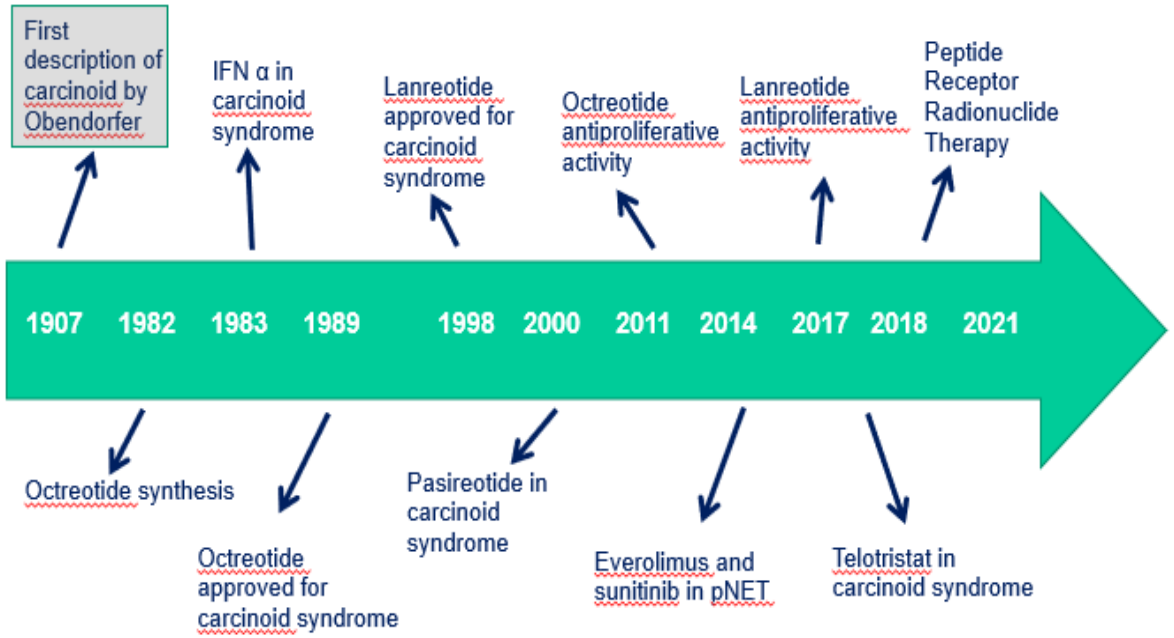
19 NEN

The o[illegible]rall p[illegible] [illegible]edictive value [illegible] pa[illegible] [illegible]Pi were [illegible]cluded

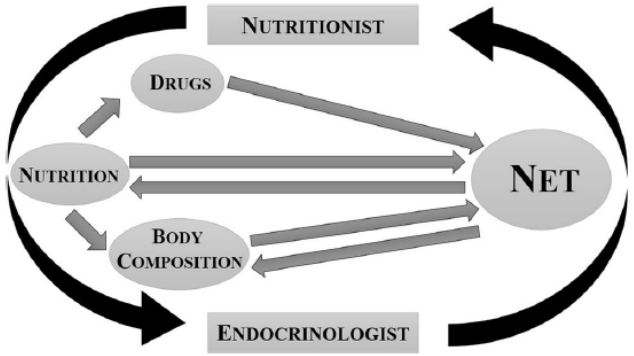
NO CGA

Diagnostics **2020**, *10*, 881; doi:10.3390/diagnostics10110881

NEN: THERAPEUTIC OPTIONS AND TOXICITIES



TREATMENT	POTENTIAL SIDE EFFECTS
Surgery	Steatorrhea, nutrient malabsorption, diarrhea, hyperglycemia, short gut syndrome, bacterial overgrowth, dehydration
Somatostatin analogs (SSA)	Abdominal pain/cramps, diarrhea, steatorrhea, fat malabsorption, gallstones, nausea, constipation, pancreatic insufficiency, fatigue, hyperglycemia, hypothyroidism
Everolimus	Stomatitis, rash, diarrhea, fatigue, mucositis, hypothyroidism, nausea, hyerglycemia
Sunitinib	Hypertension, diarrhea, fatigue, nausea, hypothyroidism, mucositis
PRRT	Neutropenia, thrombocytopenia, lymphopenia, renal toxicity, nausea, vomiting, pain, carcinoid syndrome flare
Chemotherapy	Fatigue, nausea, vomiting, low appetite, diarrhea, constipation, mucositis



MALNUTRITION

- 14-25% GEP-NET
- Negative prognostic factor, higher risk of complications and mortality
- Need for an individualized approach
- Nutritional assessment, based on body composition and lifestyle modifications, to avoid 'food-drug interaction'

TREATMENT	POTENTIAL SIDE EFFECTS
Surgery	Steatorrhea, nutrient malabsorption, diarrhea, hyperglycemia, short gut syndrome, bacterial overgrowth, dehydration
Somatostatin analogs (SSA)	Abdominal pain/cramps, diarrhea, steatorrhea, fat malabsorption, gallstones, nausea, constipation, pancreatic insufficiency, fatigue, hyperglycemia, hypothyroidism
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Chemotherapy	Fatigue, nausea, vomiting, low appetite, diarrhea, constipation, mucositis

Altieri B et al. *Reviews in Endocrine and Metabolic Disorders*, 2018

NEN & DIABETES

- Estimates suggest that 8-18% of cancer patients have co-existent DM

Cardio-Metabolic Indices and Metabolic Syndrome as Predictors of Clinical Severity of Gastroenteropancreatic Neuroendocrine Tumors

Luigi Barrea[1,2†], Giovanna Muscogiuri[2,3†], Roberta Modica[3], Barbara Altieri[4], Gabriella Pugliese[2,3], Roberto Minotta[3], Antongiulio Faggiano[5], Annamaria Colao[2,3,6] and Silvia Savastano[2,3]*

WHY?

- ❑ Mass effect on the pacreas
- ❑ Paraneoplastic syndromes
- ❑ Surgery (total or partial pancreatectomy)
- ❑ Medical therapies

→

- **DIAZOXIDE**
- **SSA**
- **TIROSYNE KINASE INHIBITORS**
- **EVEROLIMUS**

MEDITERRANEAN DIET

2018 Jun;67:1-9. doi: 10.1016/j.ctrv.2018.04.013.

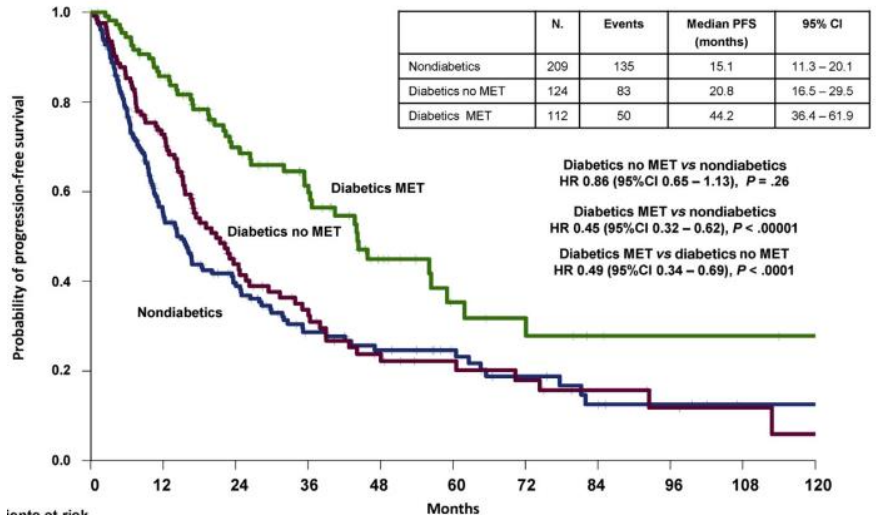
2019;59(7):1046-1057. doi: 10.1080/10408398.2017.1390729

Metformin Use Is Associated With Longer Progression-Free Survival of Patients With Diabetes and Pancreatic Neuroendocrine Tumors Receiving Everolimus and/or Somatostatin Analogues

Retrospective study
- 445 patients with advanced pNET
- 24 medical centers in Italy 1999-2015

Progression free survival (PFS) was significantly longer in patients with diabetes (median 32 months) than without diabetes (median 15.1 months)

Metformin was associated with increased PFS of patients receiving somatostatin analogues and in those receiving everolimus, with or without somatostatin analogues



	N.	Events	Median PFS (months)	95% CI
Nondiabetics	209	135	15.1	11.3 – 20.1
Diabetics no MET	124	83	20.8	16.5 – 29.5
Diabetics MET	112	50	44.2	36.4 – 61.9

Kaplan-Meier plot of PFS among nondiabetic patients, diabetics treated with metformin (MET), and diabetics not receiving metformin but treated with insulin or diet

Pusceddu S et al. *Gastroenterology*, 2018

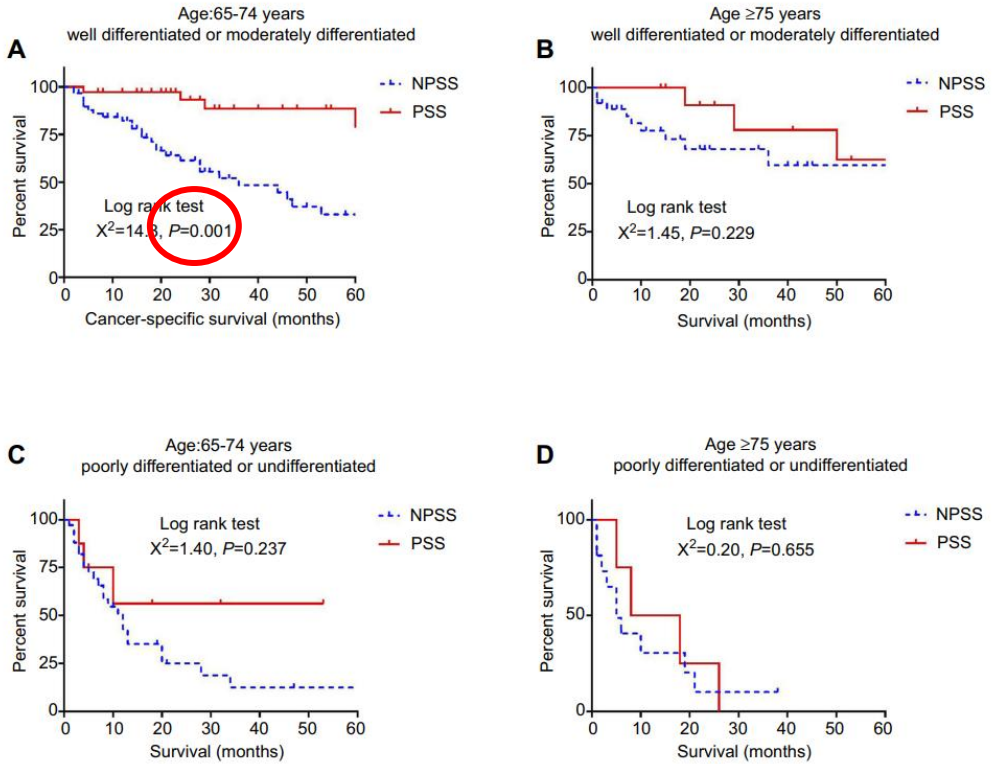
Primary site surgery for elderly patients with distant metastatic pancreatic neuroendocrine tumor: to do or not to do?

Jing Zhang [1], Chao-Sheng Peng [# 2], Yu-Hong Tian [# 3] 2019 Aug 6;14:1419-1432. doi: 10.2147/CIA.S209428

- Elderly patients (≥65 years) account for 40.7% of all pNET patients (1973-2015 in SEER database)
- In the distant metastatic cases, elderly patients account for 41.4%

Primary Site Surgery (PSS) was an independent protective factor only in cases with age of 65–74 years and well or moderately differentiated tumors (P< 0.001)

Patients aged 65–74 years with well or moderately differentiated disease may benefit from PSS but should be evaluated carefully



Survival Benefit of Primary Tumor Resection Among Elderly Patients with Pancreatic Neuroendocrine Tumors

Junya Toyoda[1] · Kota Sahara[1,2] · Diamantis I. Tsilimigras[2] · Kentaro Miyake[1] · Yasuhiro Yabushita[1] · Yuki Homma[1] · Takafumi Kumamoto[1] · Ryusei Matsuyama[1] · Timothy M. Pawlik[2]

2,319 elderly patients
942 (40.6%) primary site surgery (PSS)
1,377 (59.4%) no PSS

PSS was generally associated with **prolonged** overall survival (**OS**) and cancer specific survival (**CSS**) among **older patients**

PSS was **not** associated with improved CSS among a subset of patients **aged 80 or older**, as well as among patients **age ≥ 70 years with NF-pNET less than 2 cm**

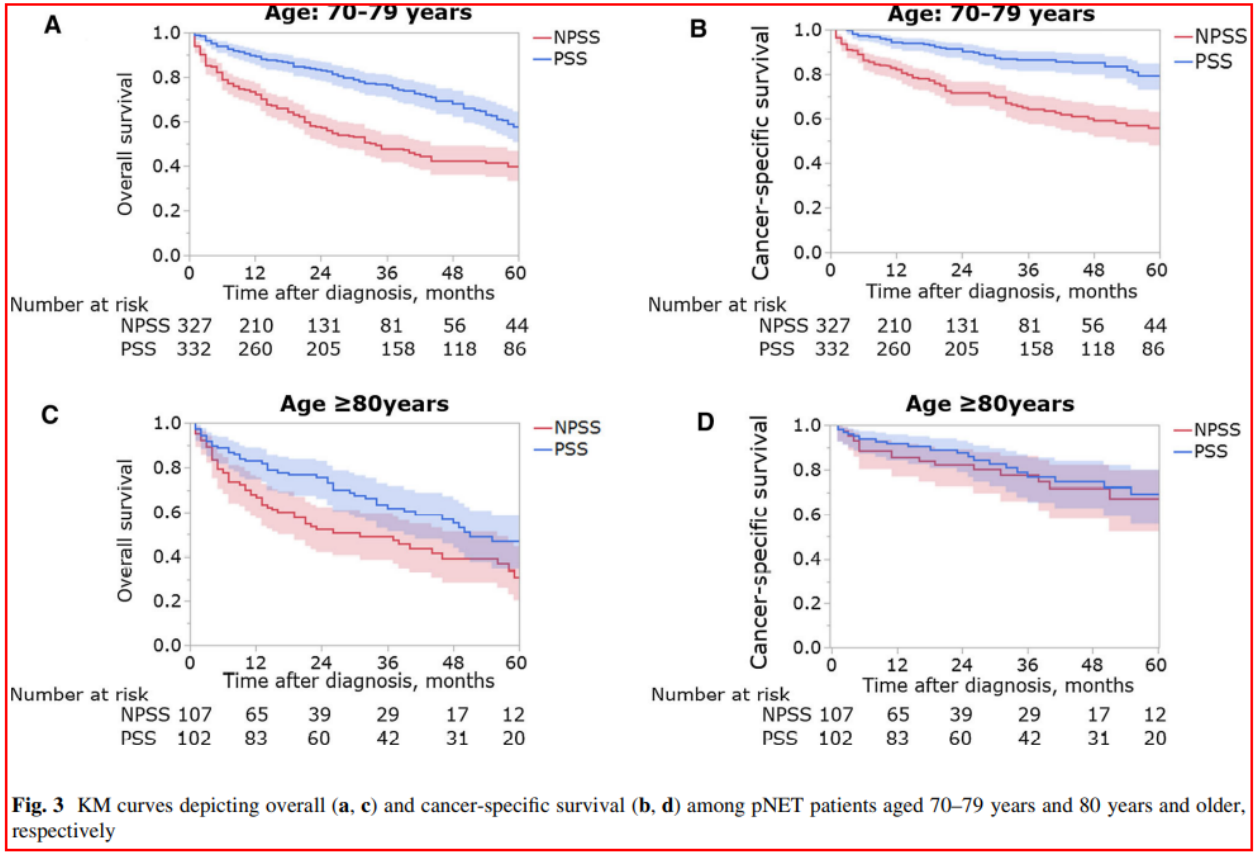
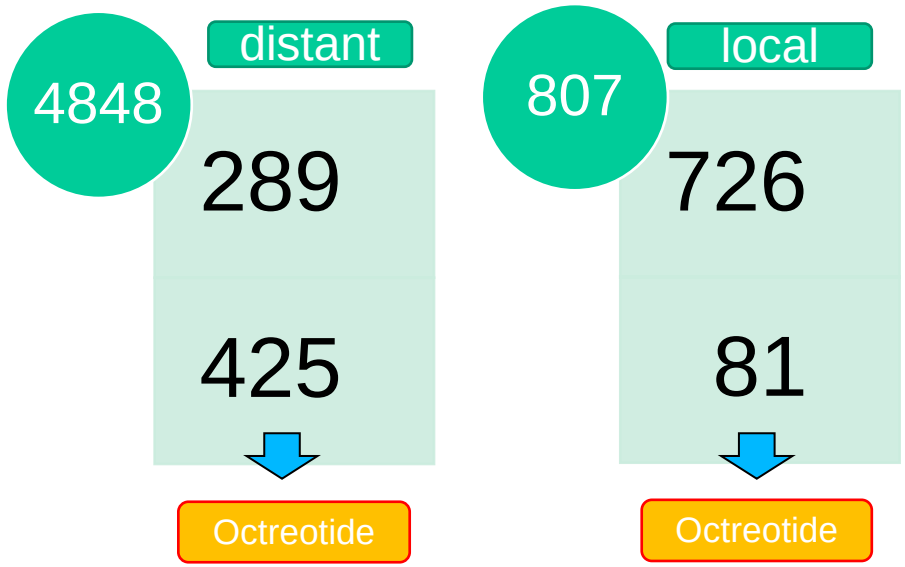


Fig. 3 KM curves depicting overall (**a**, **c**) and cancer-specific survival (**b**, **d**) among pNET patients aged 70–79 years and 80 years and older, respectively

Toyoda J al. *World J Surg*, 2021

Octreotide long-acting repeatable use among elderly patients with carcinoid syndrome and survival outcomes: a population-based analysis

Chan Shen [1], Ya-Chen Tina Shih, Ying Xu, James C Yao



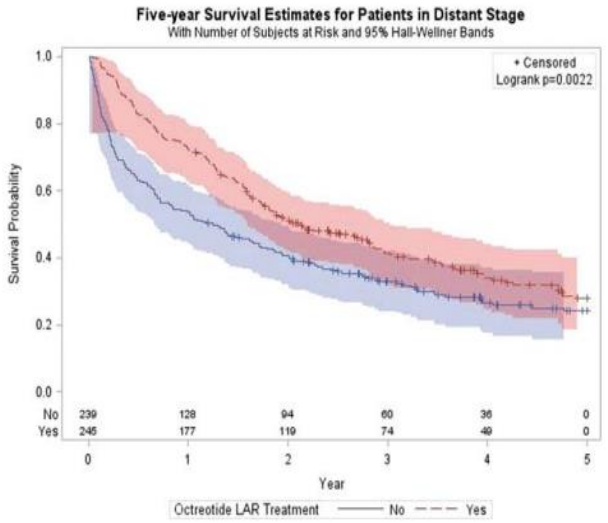


Figure 1. Unadjusted Kaplan-Meier curves for patients in distant stage.

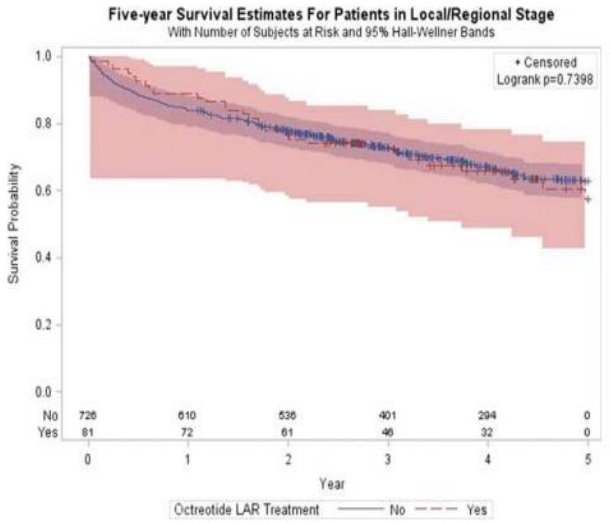


Figure 2. Unadjusted Kaplan-Meier curves for patients in local/regional stage.

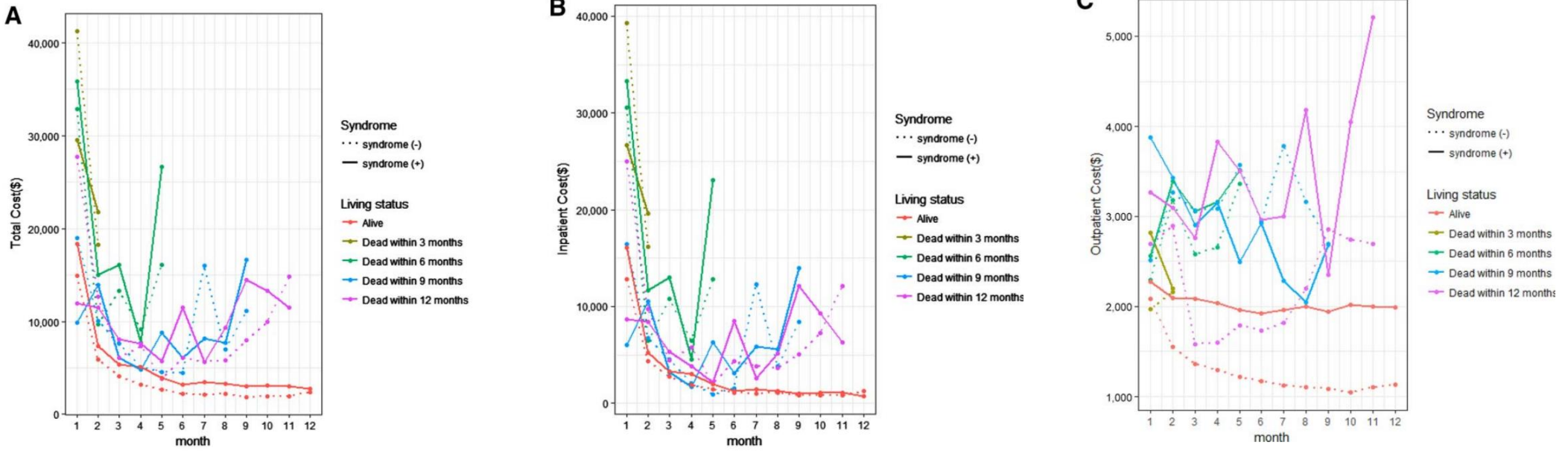
Octreotide LAR provided a significant 5-year survival benefit for patients with distant-stage disease (P .001)

CANCER. 2014 JUL 1;120(13):2039-49. DOI: 10.1002/CNCR.28653. EPUB 2014 MAR 26

Carcinoid Syndrome and Costs of Care During the First Year After Diagnosis of Neuroendocrine Tumors Among Elderly Patients

Chan Shen [1 2], Yiyi Chu [3], Daniel M Halperin [4], Arvind Dasari [4], Shouhao Zhou [2], Ying Xu [3], James C Yao [4], Ya-Chen Tina Shih [3]

Carcinoid syndrome was significantly associated with higher health care costs including overall, inpatient and outpatient costs in patients with NET and > 65y during the first year of disease



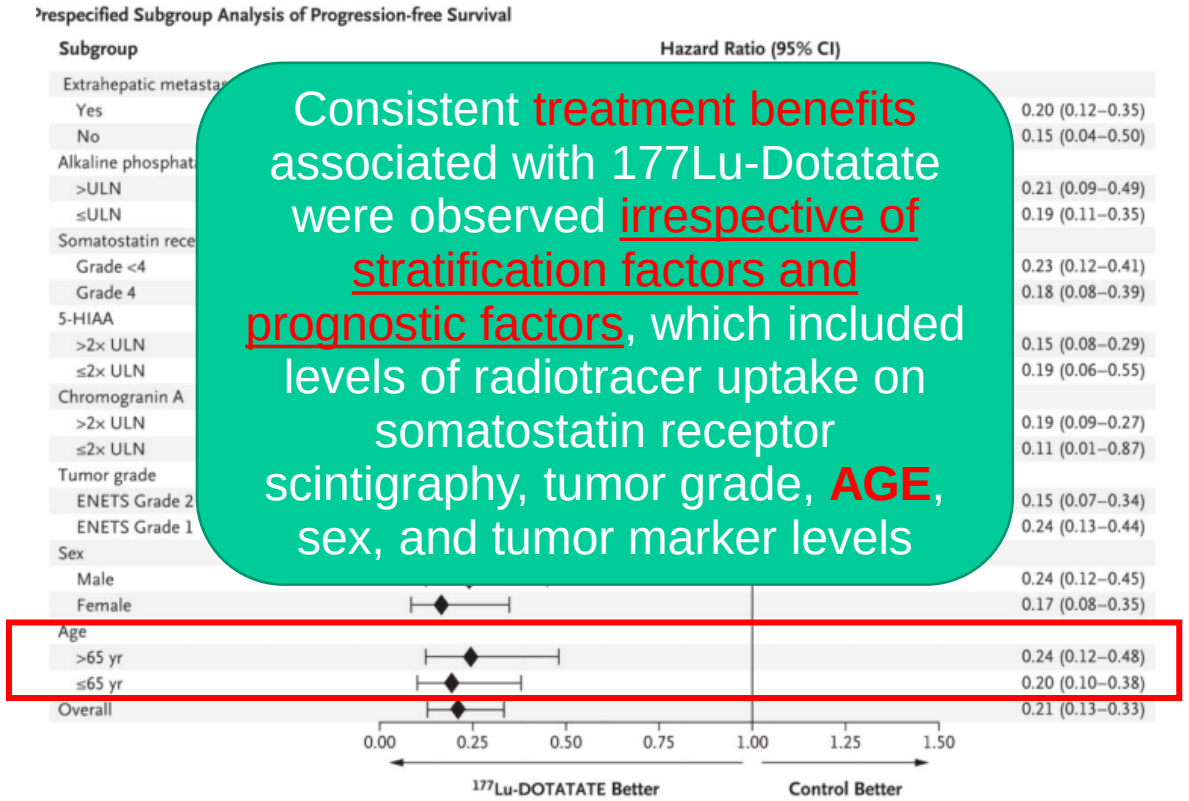
Oncologist. 2017 Dec;22(12):1451-1462. doi: 10.1634/theoncologist.2017-0149. Epub 2017 Jun 22.

Phase 3 Trial of ^{177}Lu-Dotatate for Midgut Neuroendocrine Tumors

Jonathan Strosberg [1], Ghassan El-Haddad [1], Edward Wolin [1], Andrew Hendifar [1], James Yao [1], Beth Chasen [1], Erik Mittra [1], Pamela L Kunz [1], Matthew H Kulke [1], Heather Jacene [1], David Bushnell [1], Thomas M O'Dorisio [1], Richard P Baum [1], Harshad R Kulkarni [1], Martyn Caplin [1], Rachida Lebtahi [1], Timothy Hobday [1], Ebrahim Delpassand [1], Eric Van Cutsem [1], Al Benson [1], Rajaventhan Srirajaskanthan [1], Marianne Pavel [1], Jaime Mora [1], Jordan Berlin [1], Enrique Grande [1], Nicholas Reed [1], Ettore Seregni [1], Kjell Öberg [1], Maribel Lopera Sierra [1], Paola Santoro [1], Thomas Thevenet [1], Jack L Erion [1], Philippe Ruszniewski [1], Dik Kwekkeboom [1], Eric Krenning [1], NETTER-1 Trial Investigators

111 177Lu-Dotatate + octreotide LAR

110 Octreotide LAR



Consistent treatment benefits associated with 177Lu-Dotatate were observed irrespective of stratification factors and prognostic factors, which included levels of radiotracer uptake on somatostatin receptor scintigraphy, tumor grade, **AGE**, sex, and tumor marker levels

N Engl J Med. 2017 Jan 12;376(2):125-135. doi: 10.1056/NEJMoa1607427.

CANCER BIOTHERAPY AND RADIOPHARMACEUTICALS
Volume 31, Number 6, 2016
© Mary Ann Liebert, Inc.
DOI: 10.1089/cbr.2016.2035

Review Article

Myelotoxicity of Peptide Receptor Radionuclide Therapy of Neuroendocrine Tumors: A Decade of Experience

Murali Kesavan and J. Harvey Turner

16 articles involving primary research
2225 patients

Factors associated with development of significant short and long-term myelotoxicity included:

- **age >70 years**
- impaired renal function,
- baseline cytopenias
- prior number of therapies
- prior chemotherapy
- prior radiation therapy

Author	*Number of patients included in analysis*	*Average age (years)*	*Prior therapy*	*PRRT treatment*	*G 3/4 hematologic toxicity (%)*	*Median f/up (m)*	*MDS/AL (%)*
PRRT monotherapy							
Kwekkeboom et al.,	504	59	Surgery/SSA/chemo/radio	177-LuDOTATATE	48 (9.5%)	19	4
Bodei et al.[19]	51	57 (median)	SSA	177-LuDOTATATE	1 (1.9%)	29	Nil
Pfeifer et al.[14]	69	58	SSA/chemotherapy/IFN		17 (25%)	—	1 (1.4%)
			$n=53$	90-YDOTATOC			
			$n=12$	90-YDOTATOC +177-LuDOTATATE			
			$n=4$	177-LuDOTATATE			
Sansovini et al.[20]	52	61	SSA/90-Y/chemo/radio	177-LuDOTATATE	0	29	Nil
Sabet et al.[21]	33	61	PRRT with initial response	177-LuDOTATAE	7 (21%)	37	Nil
Delpassand et al.[23]	32	63.4	SSA/chemo	177-LuDOTATATE	4 (12.5%)	14 (mean)	Nil
Paganelli et al.[22]	43	64 (median)	SSA/surgery/chemo	177-LuDOTATATE	0	38	Nil
Sabet et al.[24]	61	62	SSA/chemo/surg/radio	177-LuDOTATATE	5 (8%)	62	Nil
Bodei et al.[15]	807	53	SSA/chemo/surg/radio		77 (9.5%)	30	21 (2.6%; 13 MDS, 6 MDS t/f to AL, 2 AL)
			$n=360$	90-YDOTATOC	51 (14.2%)		
			$n=157$	90-YDOTATOC +177-LuDOTATATE	17 (10.8%)		
			$n=290$	177-LuDOTATATE	9 (3.1%)		
Bergsma et al.[25]	320	—	Chemo/radio (22%)	177-LuDOTATATE	34 (11%)	—	Incidence not reported
Mariniello et al.[16]	112	60.3	Not specified		7 (6.25%)	45.1	0
			44	90-YDOTATOC	5 (11.4%)		
			21	90-YDOTATOC +177-LuDOTATATE	2 (9.5%)		
			47	177-LuDOTATATE	0		
Brieau et al.[26]	20		PRRT/chemo/radio	177-LuDOTATATE	6 (30%)	37	4 (20%)
PRRT in combination							
van Essen et al.[30]	7	62 (median)	No prior chemo/PRRT	177-LuDOTATATE+capecitabine	2 (28%)	—	0
Claringbold et al.[5]	33	60	SSA/surgery/chemo	177-LuDOTATATE+capecitabine	1 (3%)	16	0
Kesavan et al.[32]	65	60	SSA/chemo/surg/radio		9 (13.8%; 1 ST, 8 LT)		2 (5.4%)
			$n=28$	177-LuDOTATATE+capecitabine	3 (10.7%; 1ST, 2 LT)	60	0
			37	177-LuDOTATATE+capecitabine+ temozolomide	6 (16.2%; 0 ST, 6 LT)	36	2 (5.4%)
Claringbold et al.[5]	16	63 (median)	SSA/chemo/surg/PRRT		3 (18.75%)	6	0
			$n=4$	177-LuDOTATATE+everolimus 5 mg			
			$n=9$	177-LuDOTATATE+everolimus 7.5 mg			
			$n=3$	177-LuDOTATATE+everolimus 10 mg			

Clinicopathological features and prognosis factors for survival in elderly patients with pancreatic neuroendocrine tumor: A STROBE-compliant article

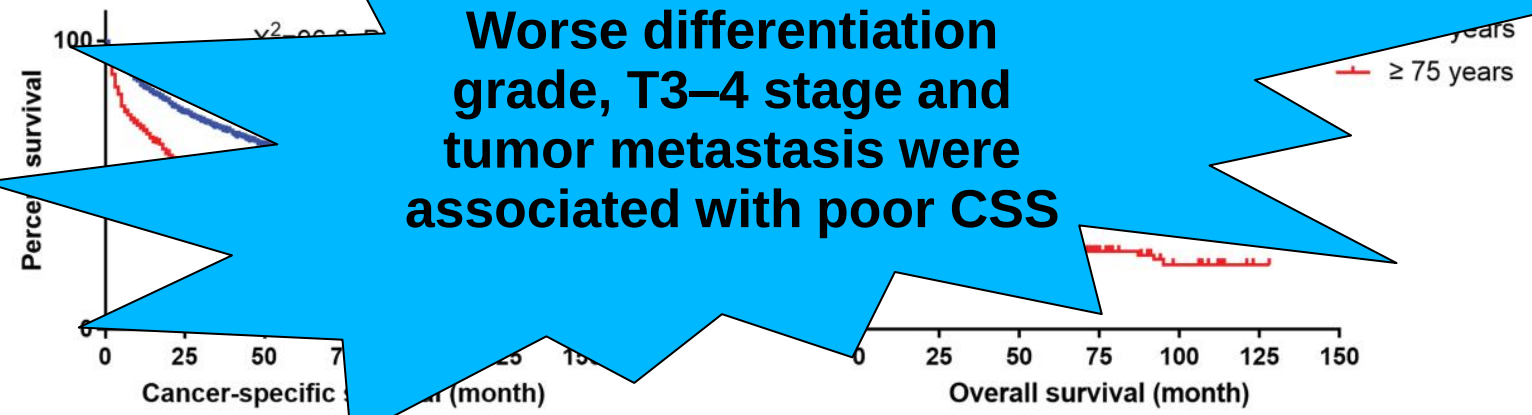
Gang Li [1], Mao-Lin Tian, Yun-Tao Bing, Lian-Yuan Tao, Hang-Yan Wang, Bin Jiang, Chun-Hui Yuan, Dian-Rong Xiu

4608 patients (2004-2014) from SEER, with "one primary only" histologically pNETs were confirmed and 653 were **older than 75 years**

- Elderly patients (≥75 years) have disadvantage in cancer sp[illegible]c survival (CSS) and overall survival (OS) compared with younger cohort

The 3 and 5-year CSS rates were 67.3% and 58.0% in the younger cohort, and 44.6% and 35.7% in the elderly respectively

Worse differentiation grade, T3–4 stage and tumor metastasis were associated with poor CSS



The 3 and 5-year OS rates were 64.5% and 37.7% in the younger cohort, and 54.0% and 27.7% in the elderly, respectively

Medicine (Baltimore). 2019 Mar;98(11):e14576. doi: 10.1097/MD.0000000000014576.

Elderly Patients with Metastatic Neuroendocrine Tumors Are Undertreated and Have Shorter Survival: The LyREMeNET Study

Annie Lemelin [1], Delphine Maucort-Boulch [2 3], Elisabeth Castel-Kremer [4], Julien Forestier [1], Valérie Hervieu [5 3], Marianne Lorcet [1], Florent Boutitie [2], Aurélie Theillaumas [1], Philip Robinson [6], Antoine Duclos [7 3], Catherine Lombard-Bohas [1], Thomas Walter [8 9]

- Elderly patients presented significantly more frequently with **synchronous metastases** compared to younger patients, and a **shorter median interval between initial diagnosis of NET and metachronous metastasis**

866

198, >70y

NEN database of the Hospices Civils de Lyon (France)

1990-2017

	Total population (n = 866)	≥70 years old (n = 198)	<70 years old (n = 668)	p value
Median age (range), years	60 (11–91)	75 (70–91)	56 (11–69)	
Female, n (%)	408 (47.1)	96 (48.5)	312 (46.7)	0.66
Primary site, n (%)				0.20
Small intestine	383 (44.2)	92 (46.5)	291 (43.6)	
Pancreas	289 (33.4)	57 (28.8)	232 (34.7)	
Lung	100 (11.6)	23 (11.6)	77 (11.5)	
Other	52 (6.0)	11 (5.6)	41 (6.1)	
Unknown	42 (4.8)	15 (7.6)	27 (4.0)	
Functioning status, n (%)				0.53
Nonfunctioning	436 (50.4)	104 (52.5)	332 (49.7)	
Carcinoid syndrome	338 (39.0)	76 (38.4)	262 (39.2)	
Zollinger-Ellison	32 (3.7)	4 (2.0)	28 (4.2)	
Other hormone release[a]	60 (6.7)	14 (7.1)	46 (6.9)	
Genetic syndrome[b], n (%)	18 (2.1)	1 (0.5)	17 (2.6)	0.09
Type of metastasis, n (%)				0.02
Synchronous metastasis	660 (76.2)	158 (79.8)	502 (75.2)	
Metachronous metastasis	199 (23.0)	36 (18.2)	163 (24.4)	
Locally advanced	7 (0.8)	4 (2.0)	3 (0.5)	
Median time between metachronous metastasis and initial diagnosis (range), months	37.5 (1.8–439.3)	26.4 (7.5–146.1)	43.6 (1.8–439.3)	0.01

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Elderly Patients with Metastatic Neuroendocrine Tumors Are Undertreated and Have Shorter Survival: The LyREMeNET Study

Annie Lemelin [1], Delphine Maucort-Boulch [2 3], Elisabeth Castel-Kremer [4], Julien Forestier [1], Valérie Hervieu [5 3], Marianne Lorcet [1], Florent Boutitie [2], Aurélie Theillaumas [1], Philip Robinson [6], Antoine Duclos [7 3], Catherine Lombard-Bohas [1], Thomas Walter [8 9]

- Elderly patients were significantly less frequently treated by: chemotherapy (p< 0.0001), PRRT (p < 0.0001), targeted therapy (p= 0.001), surgery of the primary tumor (p< 0.0001), surgery of metastases (p< 0.0001), hepatic embolization (p= 0.0006)
  radiological ablation (p= 0.01)

- **≥70 yo received significantly fewer lines of treatment (2 lines vs 3 in younger, p <0.0001) for both systemic and locoregional treatments**

- ≥70 yo received **more frequently SSA as first-line** (77%) vs <70 yo (58%), but less frequently chemo

	Total population (n = 856)	≥70 years old (n = 196)	<70 years old (n = 660)	p value
Number of lines of treatment (locoregional and systemic) received per patient, median (range)	2.0 (0–19.0)	2.0 (0–9.0)	3.0 (0–19.0)	<0.0001
Number of systemic lines of treatment per patient, median (range)	2.00 (0–12.0)	1.00 (0–9.0)	2.00 (0–12.0)	<0.0001
Number of locoregional lines of treatment per patient, median (range)	0.0 (0–7.0)	0.0 (0–2.0)	1.0 (0–7.0)	<0.0001
First-line treatment patterns				
Total number of first-line systemic treatments received	636	154	482	
Type of first-line systemic treatments, n (%)				<0.0001
Somatostatin analog	398 (62.6)	119 (77.3)	279 (57.9)	
Chemotherapy	206 (32.4)	28 (18.2)	178 (36.9)	
Peptide receptor radionuclide therapy	4 (0.6)	–	4 (0.8)	
Targeted therapies	9 (1.4)	–	9 (1.9)	
Interferon	19 (3.0)	7 (4.6)	12 (2.5)	
Total number of locoregional first-line treatments received	173	21	152	
Type of first-line locoregional treatment received, n (%)				0.19
Liver embolization	22 (12.7)	3 (14.3)	19 (12.5)	
Surgery of metastases	138 (79.8)	15 (71.4)	123 (80.9)	
Radiological ablation	6 (3.5)	1 (4.8)	5 (3.3)	
Endoscopic treatment	3 (1.7)	–	3 (2.0)	
Other surgery	4 (2.3)	2 (9.5)	2 (1.3)	
Number of patients receiving at least one line of these locoregional or systemic treatments during follow-up				
Systemic treatments during follow-up, n (%)				
Somatostatin analog	635 (74.2)	148 (75.5)	487 (73.8)	0.6285
Chemotherapy	421 (49.2)	62 (31.6)	359 (54.4)	<0.0001
Peptide receptor radionuclide therapy	115 (13.4)	10 (5.1)	105 (15.9)	<0.0001
Targeted therapies	230 (26.9)	32 (16.3)	198 (30.0)	0.0001
Interferon	129 (15.1)	24 (12.2)	105 (15.9)	0.2080
Locoregional treatments during follow-up, n (%)				
Surgery of the primary	571 (66.7)	99 (50.5)	472 (71.5)	<0.0001
Surgery of metastases	245 (28.6)	25 (12.8)	220 (33.3)	<0.0001
Liver embolization	200 (23.4)	28 (14.3)	172 (26.1)	0.0006
Radiologic ablation	42 (4.9)	3 (1.5)	39 (5.9)	0.0127
Cardiac valve replacement for carcinoid heart disease	16 (1.9)	7 (3.6)	9 (1.4)	0.0658

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The Oncologist®
Symptom Management and Supportive Care

Patterns of Symptoms Burden in Neuroendocrine Tumors: A Population-Based Analysis of Prospective Patient-Reported Outcomes

Julie Hallet,[a,b,f,g,h] Laura E. Davis,[g] Alyson L. Mahar,[i] Calvin H.L. Law,[a,b,f,g,j] Elie Isenberg-Grzeda,[a,c] Lev D. Bubis,[f,g] Simron Singh,[a,d,g,h,j] Sten Myrehaug,[a,e,g] Haoyu Zhao,[h] Kaitlyn Beyfuss,[g] Lesley Moody,[j] Natalie G. Coburn[b,f,g,h]

Older patients presented a lower risk of anxiety, nausea, and overall well-being

		Anxiety		Depression		Drowsiness		Lack of appetite		Nausea	
Variable	Value	Relative risk	95% CI	Relative risk	95% CI	Relative risk	95% CI	Relative risk	95% CI	Relative risk	95% CI
Age, years; Ref: 18–39	40–59	0.90	0.74–1.10	1.11	0.83–1.49	1.16	0.88–1.52	1.12	0.84–1.50	0.96	0.63–1.46
	60–79	**0.70**	**0.57–0.85**	0.80	0.60–1.08	0.92	0.70–1.21	1.11	0.84–1.48	**0.59**	**0.38–0.90**
	80–99	**0.55**	**0.40–0.75**	0.68	0.44–1.05	1.00	0.69–1.44	1.40	0.99–1.98	**0.43**	**0.22–0.82**

		Pain		Shortness of breath		Tiredness		Overall well-being	
Variable	Value	Relative Risk	95% CI	Relative Risk	95% CI	Relative Risk	95% CI	Relative Risk	95% CI
Age, years; Ref: 18–39	40–59	1.02	0.76–1.37	1.35	0.92–1.99	1.02	0.85–1.22	0.91	0.76–1.10
	60–79	0.83	0.62–1.11	1.31	0.89–1.92	0.89	0.74–1.06	**0.83**	**0.69–0.99**
	80–99	0.86	0.58–1.27	**1.63**	**1.03–2.59**	0.90	0.70–1.16	0.86	0.68–1.10

The Oncologist 2019;24:1384–1394

J Clin Endocrinol Metab. 2020 Dec 1;105(12):e4661-e4670. doi: 10.1210/clinem/dgaa608.

Predicting Metastatic Potential in Pheochromocytoma and Paraganglioma: A Comparison of PASS and GAPP Scoring Systems

Heather Wachtel [1 2 3], Troy Hutchens [4], Ezra Baraban [4], Lauren E Schwartz [3 4], Kathleen Montone [3 4], Zubair Baloch [3 4], Virginia LiVolsi [3 4], Lauren Krumeich [1], Douglas L Fraker [1 2 3], Katherine L Nathanson [2 3 5], Debbie L Cohen [3 6], Lauren Fishbein [7]

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PCC106

PGL 37

Older age is associated with longer recurrent free survival

Univariate logistic regression analysis of predictors of recurrent pheochromocytoma/paraganglioma (PCC/PGL)

Characteristics	Odds Ratio	95% Confidence Interval	*P* value
Age	0.969	0.945-0.994	**.0170**
Female sex	1.601	0.744-3.445	.2292
Race			
African-American	3.819	0.947-15.393	.0596
Caucasian	2.966	0.811-10.848	.1004
Other	Reference	—	—
Germline susceptibility gene mutation			
No mutation	Reference	—	—
Not tested	0.128	0.027-0.602	**.0092**
NF1	<0.001	<0.001-999.999	.9665
RET	1.538	0.252-9.392	.6407
SDHB	8.205	1.892-35.581	**.0049**
SDHD	>999.9999	<0.001-999.999	.9758
Variant of undetermined significance	3.077	0.179-52.746	.4382
VHL	4.103	0.810-20.782	.0881
Dominant secreted catecholamine			
Epinephrine	Reference	—	—
Norepinephrine	2.516	0.946-6.691	.0645
Unknown	1.500	0.254-8.843	.6542
Tumor type			
Pheochromocytoma	Reference	—	—
Paraganglioma	6.357	2.736-14.767	**<.0001**
Tumor size, cm	1.005	0.883-1.143	.9410
Ki-67 index (%)			
<1	Reference	—	—
1-3	4.810	1.016-22.759	**.0477**
>3	<0.001	<0.001-999.999	.9891
PASS score	1.128	0.947-1.343	.1779
GAPP score	1.537	1.141-2.070	**.0047**

OUR EXPERIENCE

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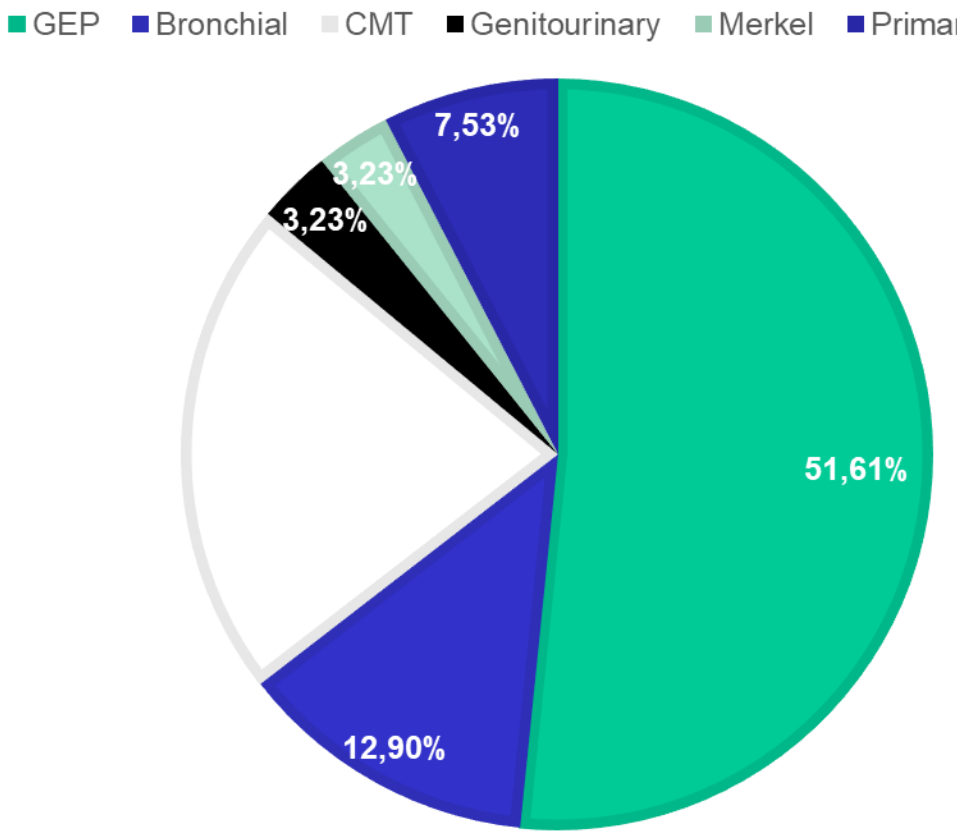

PATIENTS >65yo	93 (46♂/47 ♀)
mean age at diagnosis	**71 ± 5.4**
Ki 67% (± DS)	16.3 ± 26%

G1	G2	G3
42%	**33%**	**25%**

CONCLUSIONS

- Elderly patients are **more frequently** affected by NEN, compared to younger patients
- Advanced age is associated with **lower survival rates**, even in low grade and stage disease
- **CgA** should **not** be used as a **biomarker** for diagnosis, especially in elderly patients
- Caution in the timing and choice of treatment should be used in elderly patients due to potential **side effects and comorbidities**
- **Somatostatin analogues are preferred** over surgical approach, chemotherapy and peptide receptor radionuclide therapy, but **undertreatment should be avoided**
- The diagnostic and therapeutic approach of NEN in elderly must be individualized, favoring a **multidisciplinary evaluation** to improve outcomes

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