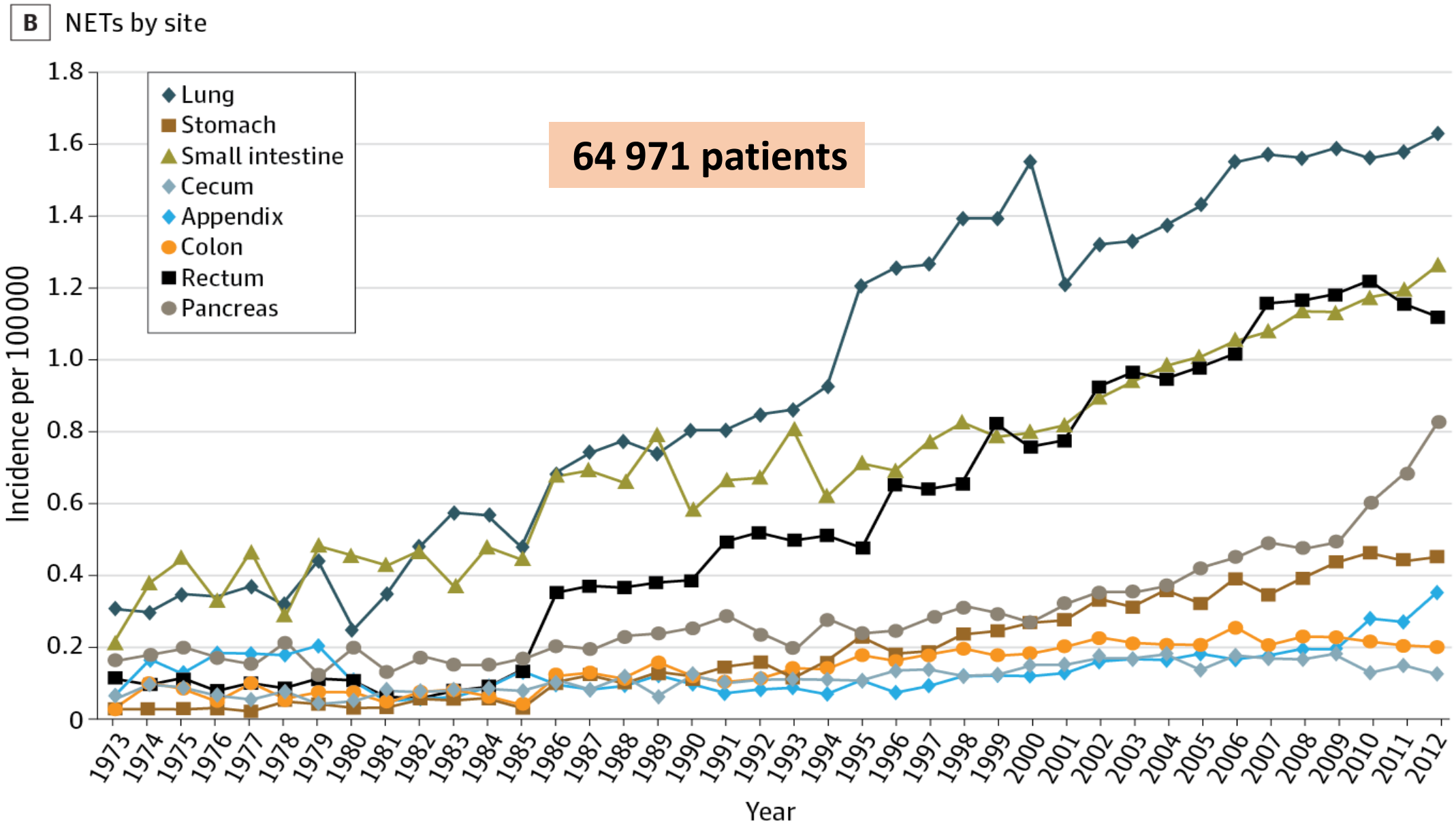
Κλινικό Φροντιστήριο Νευροενδοκρινών Νεοπλασμάτων - ΙΙ
Άτυπο Καρκινοειδές Πνεύμονα

Γιώργος Ευαγγέλου



JAMA Oncol. 2017;3(10):1335-1342. doi:10.1001/jamaoncol.2017.0589

eTable 3. Median Survival of Distant Stage G1/G2 NETs Diagnosed From 2000-2012

Primary Tumor Site	Median Survival (months)	Survival Rate (%)	
		3-year	5-year
Appendix	NA	NA	NA
Cecum	98	70	61
Colon	14	33	29
Lung	24	39	32
Pancreas	60	62	50
Rectum	33	48	28
Small Intestine	103	80	69
Stomach	29	45	32

	Octreotide[1] (PROMID)	Lanreotide[2] (CLARINET)	^{177}Lu-Dotatate[4] (NETTER-1)	Sunitinib[5] (Raymond)	Everolimus[6] (RADIANT 4)
Ki 67%	≤ 2%	< 10%	≤ 20%	78% ≤ 10%	63% G1
Primary End Point	PFS	PFS	PFS	PFS	PFS
ORR	2%	-	18%	9%	2%
Lung					+
Stomach		+			+
Pancreas		+		+	RADIANT3
Small bowel	+	+	+		+
Appendix	+	+	+		+
Colon		+	+		+
Rectum		+			+
Unknown		+			+

1. DOI: 10.1200/JCO.2009.22.8510
2. DOI: 10.1056/NEJMoa1316158
3. https://doi.org/10.1093/annonc/mdw369.36
4. DOI: 10.1056/NEJMoa1607427
5. DOI: 10.1056/NEJMoa1003825
6. DOI:https://doi.org/10.1016/S0140-6736(15)00817-X

	Everolimus plus Pasireotide[1] (LUNA)	Capecitabine Temozolomide[2] (ACRIN)	A-interferon[3,4]	Streptozocin (Moertel)
Ki 67%	69% atypical	56%G1	-	-
Primary End Point	PFS at 9 mo	PFS	DOR, PFS	PFS
ORR	1%	33,3%	6 - 20%	6 – 36%
Lung	+			
Stomach				
Pancreas		+	+	+
Small bowel			+	
Appendix				
Colon				
Rectum				
Unknown			+	

1. https://doi.org/10.1016/S1470-2045(17)30681-2
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8.. DOI: 10.1097/01.coc.0000135343.06038.eb

Limited role of Ki-67 proliferative index in predicting overall short-term survival in patients with typical and atypical pulmonary carcinoid tumors

Ann E Walts, Delma Ines & Alberto M Marchevsky

Modern Pathology **25**, 1258–1264 (2012) | Download Citation

Ariol® SL50 Image Analyzer system to measure ki67 index

N = 101 pulmonary carcinoid tumors (78 typical and 23 atypical)

correlated the Ki-67 index and the histological diagnoses in univariate and multivariable analysis with overall survival

mean Ki-67 indices for the typical carcinoids (3.7 s.d.±4.0)

mean Ki-67 indices for the atypical carcinoids (18.8 s.d.±17.1) were significantly different (P<0.001)

DOI https://doi.org/10.1038/modpathol.2012.81

Efficacy of different drugs in **atypical** bronchial NETs

	Octreotide[1] (PROMID)	Lanreotide[2] (CLARINET)	^{177}Lu-Dotatate[4] (NETTER-1)	Sunitinib[5] (Raymond)	Everolimus[6] (RADIANT 4)
Ki 67%	≤ 2%	< 10%	≤ 20%	78% ≤ 10%	63% G1
Primary End Point	PFS	PFS	PFS	PFS	PFS
ORR	2%	-	18%	9%	2%
Lung					
Stomach		+			
Pancreas		+			
Small bowel	+	+	+		
Appendix	+	+	+		+
Colon		+	+		+
Rectum		+			+
Unknown		+			+

- Bronchial NETs not included
- We have to decide based on Ki67%
- PROMID recruited only G1

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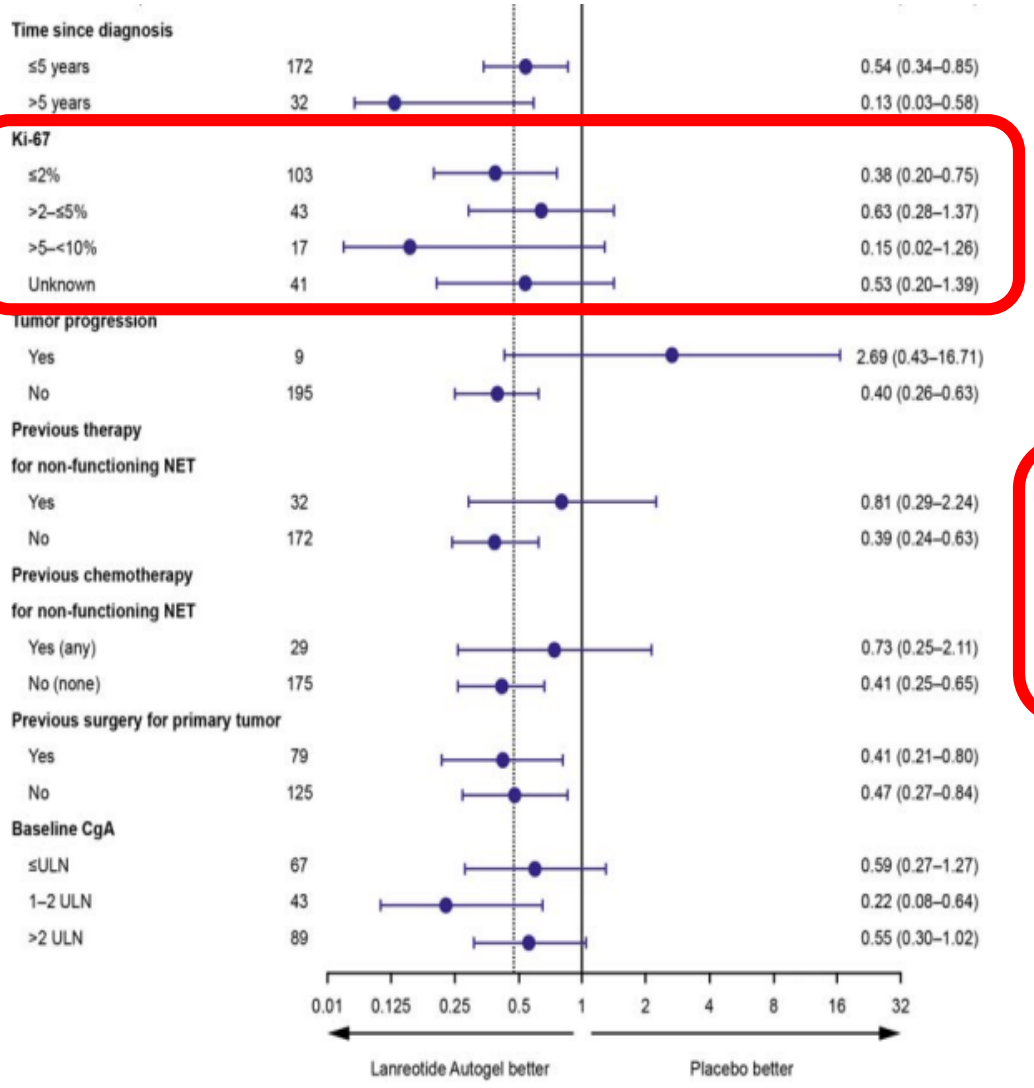
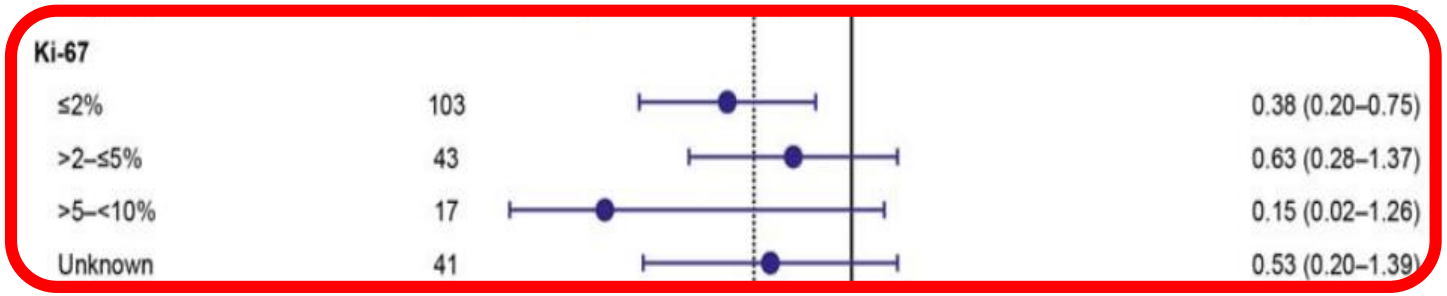
6. DOI:https://doi.org/10.1016/S0140-6736(15)00817-X

Lanreotide in Metastatic Enteropancreatic Neuroendocrine Tumors

Martyn E. Caplin, D.M., Marianne Pavel, M.D., Jarosław B. Ćwikła, M.D., Ph.D., Alexandria T. Phan, M.D., Markus Raderer, M.D., Eva Sedláčková, M.D., Guillaume Cadiot, M.D., Ph.D., Edward M. Wolin, M.D., Jaume Capdevila, M.D., Lucy Wall, M.D., Guido Rindi, M.D., Ph.D., Alison Langley, M.Sc., et al., for the CLARINET Investigators*



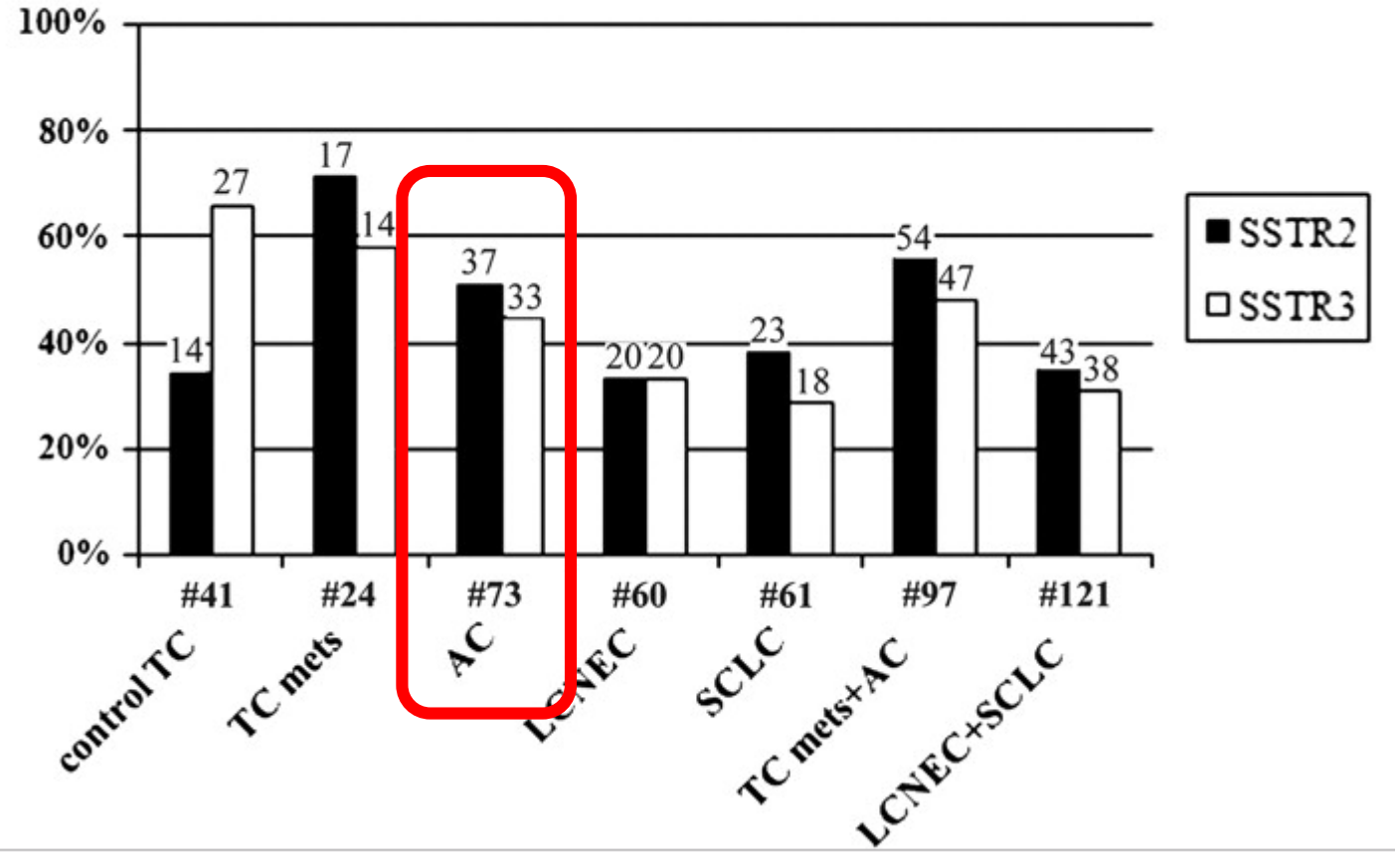


DOI: 10.1056/NEJMoa1316158

Somatostatin receptor tissue distribution in lung neuroendocrine tumours: a clinicopathologic and immunohistochemical study of 218 'clinically aggressive' cases FREE

L. Righi ✉, M. Volante, V. Tavaglione, A. Billè, L. Daniele, T. Angusti, F. Inzani, G. Pelosi, G. Rindi, M. Papotti

Annals of Oncology, Volume 21, Issue 3, March 2010, Pages 548–555,
https://doi.org/10.1093/annonc/mdp334
Published: 16 September 2009 **Article history** ▾



ENETS Consensus Guidelines Update for the Management of Distant Metastatic Disease of Intestinal, Pancreatic, Bronchial Neuroendocrine Neoplasms (NEN) and NEN of Unknown Primary Site

M. Pavel[a] D. O'Toole[b] F. Costa[c] J. Capdevila[d] D. Gross[e] R. Kianmanesh[f]
E. Krenning[g] U. Knigge[h] R. Salazar[i] U.-F. Pape[a] K. Öberg[j]
all other Vienna Consensus Conference participants

SSA may also be used in NET of other sites (e.g. rectal or bronchial NET),

- **when the SSTR status is positive (on somatostatin imaging or histology)**,
- if the tumor is slowly growing, G1 or G2 and preferably with **Ki-67 <10%**

Although comprehensive clinical data are lacking for the use of SSA in lung NET, it is expected that the clinical behavior of typical carcinoids (mitotic count <2/10 HPF; G1 NET) is similar to G1 NET of other sites.

https://doi.org/10.1159/000443167

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Ki 67%	≤ 2%	< 10%	≤ 20%	78% ≤ 10%	63% G1
Primary End Point	PFS	PFS	PFS	PFS	PFS
ORR	2%	-	18%	9%	2%
Lung					+
Stomach		+			+
Pancreas		+			
Small bowel	+	+	+		
Appendix	+	+	+		+
Colon		+	+		+
Rectum		+			+
Unknown		+			+

- Result depends **mostly** on tumor uptake score on somatostatin receptor scintigraphy (grade 2, 3, or

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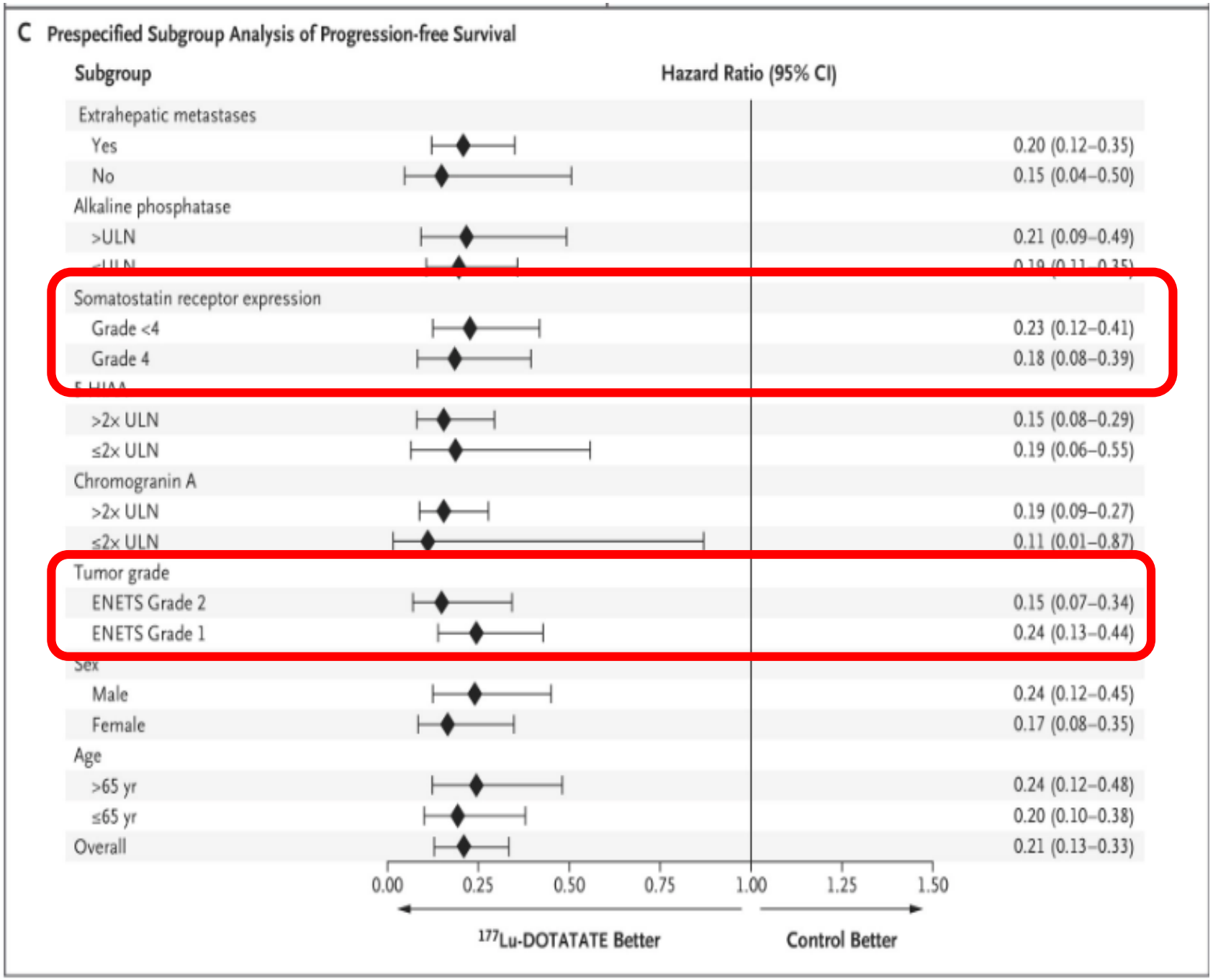

Somatostatin receptor scintigraphy, Krenning scale Grade 3 (29%), Grade 4 (61%)

ENETs guidelines

A strong SSTR expression **on imaging** is necessary to achieve better results with PRRT, while extensive hepatic and/or bone disease as well as decreased kidney function may limit its use

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Rectum		+			+
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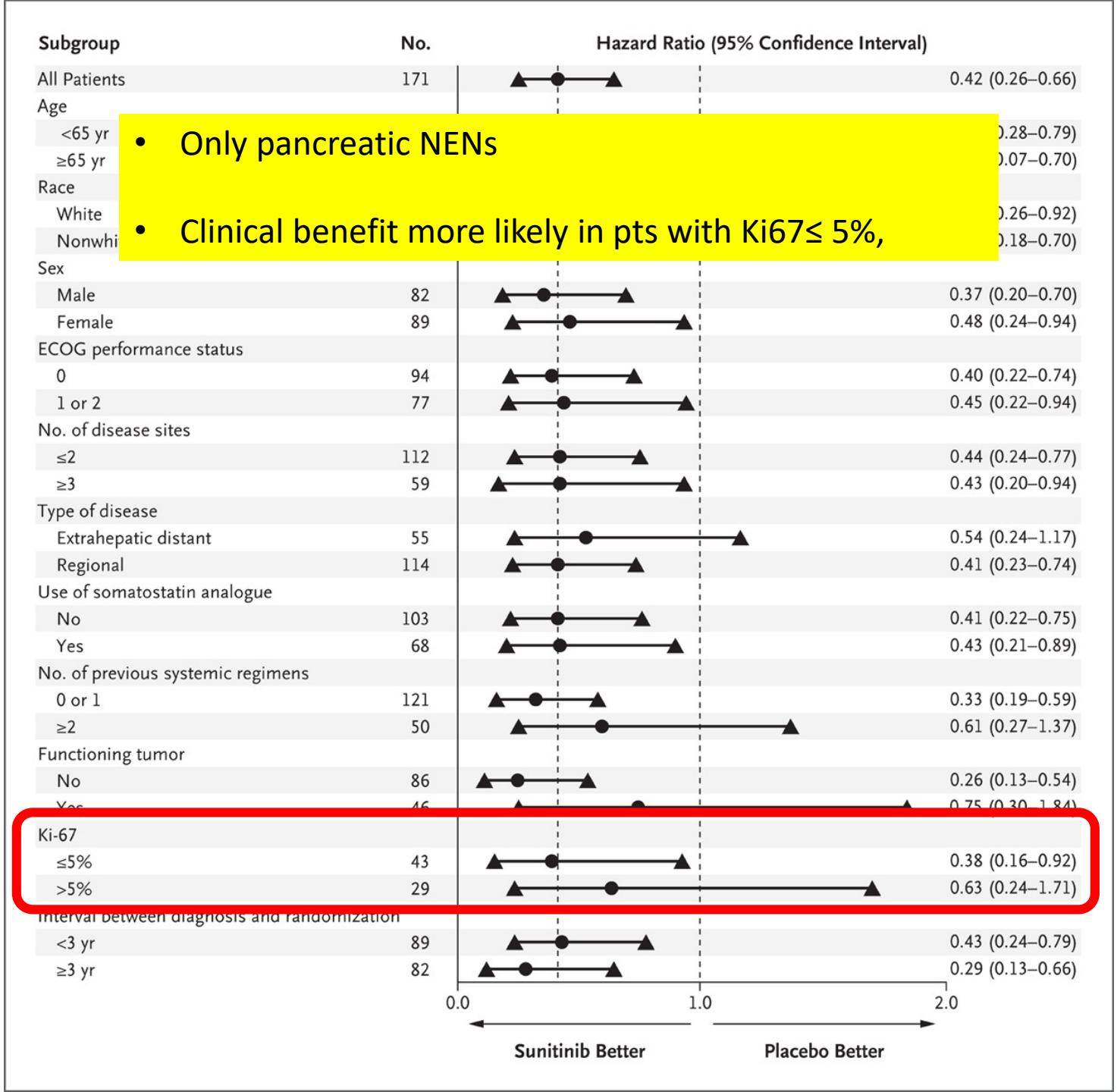
ENETs guidelines

Antiangiogenic drugs including sunitinib are not recommended in non-pancreatic NEN outside of clinical trials.



- Only pancreatic NENs
- Clinical benefit more likely in pts with Ki67≤ 5%,

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Pancreas		+		+	RADIANT3
Small bowel	+	+	+		+
Appendix	+	+	+		+
Colon		+	+		+
Rectum		+			+
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ORIGINAL ARTICLE | Open Access

Everolimus in advanced, progressive, well-differentiated, non-functional neuroendocrine tumors: RADIANT-4 lung subgroup analysis

Nicola Fazio, Roberto Buzzoni, Gianfranco Delle Fave, Margot E. Tesselaar, Edward Wolin, Eric Van Cutsem, Paola Tomassetti, Jonathan Strosberg, Maurizio Voi ... See all authors

First published: 21 October 2017 | https://doi.org/10.1111/cas.13427 | Cited by: 9

In the patients in whom Ki-67 percentage was reported (n=63), it varied from 0% to 60% (median, 8%)

Characteristics	Patients with lung NET (n = 90)	
	Everolimus n = 63	Placebo n = 27
Prior antineoplastic therapy		
Yes	56 (85.7)	24 (88.9)
No[d]	9 (14.3)	3 (11.1)
Prior treatments, n (%)		
Surgery	33 (52.4)	18 (66.7)
Somatostatin analogs	27 (42.9)	11 (40.7)
Chemotherapy	25 (39.7)	13 (48.1)
Radiotherapy including peptide receptor radionuclide therapy	25 (39.7)	13 (48.1)

Post-hoc analysis

Characteristics	with lung NET (n = 90)	
	Everolimus n = 63	Placebo n = 27
Age, years, median (range)	67.0 (34-86)	61.0 (24-80)
Male, n (%)	32 (50.8)	15 (55.6)
WHO performance status, n (%)[a]		
0	46 (73.0)	18 (66.7)
1	16 (25.4)	9 (33.3)
Race, n (%)		
Caucasian	53 (84.1)	24 (88.9)
Asian	7 (11.1)	2 (7.4)
Others[b]	3 (4.8)	1 (3.7)
Stage IV at initial diagnosis, n (%)	38 (60.3)	9 (33.3)
Median time from initial diagnosis to randomization, months (range)	25.8 (2.2-258.4)	37.5 (3.7-303.3)
Liver tumor burden		
None	14 (22.2)	5 (18.5)
>0%-10%	33 (52.4)	17 (63.0)
>10%-25%	10 (15.9)	2 (7.4)
>25%	6 (9.5)	3 (11.1)
Metastatic extent of disease, n (%)		
Hepatic (with or without other organ) involvement[c]	43 (68.3)	20 (74.1)
Extrahepatic	20 (31.7)	7 (25.9)

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Post-hoc analysis

Partial response was observed in one patient in each treatment arm; no patients in either arm showed complete response

- Everolimus ORR 1 out of 63
- Placebo ORR 1 out of 27

The median PFS, by central review, was 9.2 months (95% CI, 6.8-10.9) for patients receiving everolimus compared with 3.6 months (95% CI, 1.9-5.1) for those receiving placebo.

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Prior therapy	Median PFS, months (95% CI)	
	Everolimus (n = 63)	Placebo (n = 27)
Overall lung subgroup (n = 90)	9.2 (6.8-10.9)	3.6 (1.9-5.1)
Prior chemotherapy (n = 38)	8.5 (5.6-11.7)	2.9 (1.8-3.7)
No prior chemotherapy (n = 52)	9.2 (6.0-NE)	3.7 (1.7-NE)
Prior SSA (n = 38)	9.5 (6.0-11.7)	3.7 (1.0-11.2)
No prior SSA (n = 52)	9.2 (5.6-11.0)	3.6 (1.9-5.6)
Prior radiotherapy[a] (n = 38)	9.2 (5.7-NE)	3.0 (1.9-5.1)
No prior radiotherapy (n = 52)	9.2 (6.0-9.9)	3.7 (1.7-NE)
Any prior therapy (n = 78)	9.2 (6.0-11.0)	3.4 (1.9-5.1)

Post-hoc analysis

ENETs guidelines

In the absence of approved drugs in **metastatic lung NET,** everolimus may be recommended as a **first-line therapy** in progressive disease. However, in patients with low proliferative activity (G1, typical carcinoid) with strong SSTR expression on imaging, SSA may be considered as a first-line therapy.

	Everolimus plus Pasireotide[1] (LUNA)	Capecitabine Temozolomide[2] (ACRIN)	A-interferon[34]	Streptozocin (Moertel)
Ki 67%	69% atypical	56%G1	-	-
Primary End Point	PFS at 9 mo	PFS	DOR, PFS	PFS
ORR	1%	33,3%	6 - 20%	6 – 36%
Lung	+			
Stomach				
Pancreas		+	+	+
Small bowel			+	
Appendix				
Colon				
Rectum				
Unknown			+	

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8.. DOI: 10.1097/01.coc.0000135343.06038.eb

Efficacy and safety of long-acting pasireotide or everolimus alone or in combination in patients with advanced carcinoids of the lung and thymus (LUNA): an open-label, multicentre, randomised, phase 2 trial

Piero Ferolla, Maria Pia Brizzi, Tim Meyer, Wasat Mansoor, Julien Mazieres, Christine Do Cao, Hervé Léna, Alfredo Berruti, Vincenzo Damiano, Wieneke Buikhuisen, Henning Grønbæk, Catherine Lombard-Bohas, Christian Grohé, Vincenzo Minotti, Marcello Tiseo, Javier De Castro, Nicholas Reed, Gabriella Gislimberti, Neha Singh, Miona Stankovic, Kjell Öberg, Eric Baudin

- Around two-thirds (69%) of patients presented with **atypical carcinoid**

	Pasireotide group (n=41)	Everolimus group (n=42)	Combination group (n=41)
Overall lesion response at month 9*			
Complete response	0 (0%, 0·0–8·6)	0 (0%, 0·0–8·4)	0 (0%, 0·0–8·6)
Partial response	1 (2·4%, 0·1–12·9)	1 (2·4%, 0·1–12·6)	1 (2·4%, 0·1–12·9)

Median PFS

- 8·5 months in the pasireotide group,
- 12·5 months in the everolimus group, and
- 11·8 months in the combination group

DOI:https://doi.org/10.1016/S1470-2045(17)30681-2

	Pasireotide group (n=41)	Everolimus group (n=42)	Combination group (n=41)
Age (years)			
<65	21 (51%)	18 (43%)	24 (59%)
≥65	20 (49%)	24 (57%)	17 (41%)
Median (IQR)	64 (51–69)	66 (61–73)	61 (56–69)
Sex			
Female	15 (37%)	19 (45%)	13 (32%)
Male	26 (63%)	23 (55%)	28 (68%)
Race			
White	40 (98%)	42 (100%)	40 (98%)
Black African American	1 (2%)	0	0
Asian	0	0	1 (2%)
Other	0	0	0
ECOG performance status			
0	28 (68%)	24 (57%)	27 (66%)
1	11 (27%)	17 (40%)	14 (34%)
2	2 (5%)	1 (2%)	0
Histological grade*			
Typical	14 (34%)	12 (29%)	13 (32%)
Atypical	27 (66%)	30 (71%)	28 (68%)
Primary site of cancer			
Lung	38 (93%)	39 (93%)	39 (95%)
Thymus	3 (7%)	3 (7%)	2 (5%)
Functional status of tumour			
Functional	12 (29%)	7 (17%)	9 (22%)
Non-functional	29 (71%)	35 (83%)	32 (78%)
Current metastatic extent†			
Liver	30 (73%)	34 (81%)	31 (76%)
Bone	32 (78%)	15 (36%)	22 (54%)
Lung	15 (37%)	13 (31%)	20 (49%)
Cervical or thoracic lymph nodes	14 (34%)	15 (36%)	9 (22%)
Pleura	2 (5%)	2 (5%)	6 (15%)
Other‡	28 (68%)	24 (57%)	27 (66%)

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E. Krenning[g] U. Knigge[h] R. Salazar[i] U.-F. Pape[a] K. Öberg[j]
all other Vienna Consensus Conference participants

The upfront combination therapy of targeted drugs with SSA **cannot be recommended**.

Furthermore, data are lacking to support the use of SSA beyond progression in combination with targeted drugs

	Everolimus plus Pasireotide[1] (LUNA)	Capecitabine Temozolomide[2] (ACRIN)	A-interferon[34]	Streptozocin (Moertel)
Ki 67%	69% atypical	56%G1	-	-
Primary End Point	PFS at 9 mo	PFS	DOR, PFS	PFS
ORR	1%	33,3%	6 - 20%	6 – 36%
Lung	+			
Stomach				
Pancreas		+	+	+
Small bowel			+	
Appendix				
Colon				
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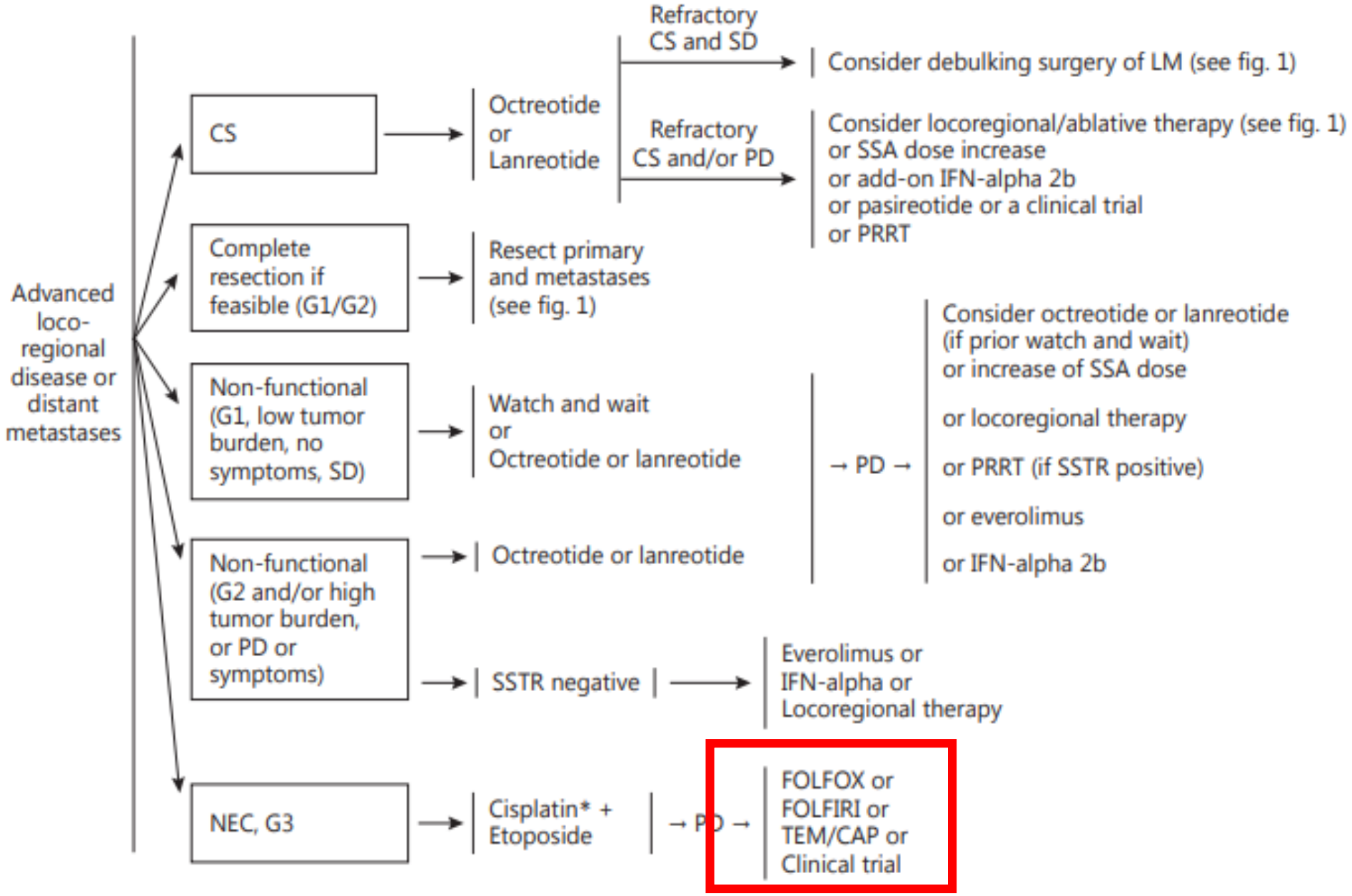
ENETS Consensus Guidelines Update for the Management of Distant Metastatic Disease of Intestinal, Pancreatic, Bronchial Neuroendocrine Neoplasms (NEN) and NEN of Unknown Primary Site

Therapeutic options and conditions for preferential use as first-line therapy in advanced NEN

TEM/CAP	+/–	G2	pancreas	progressive in short-term* or high tumor burden or symptomatic; if STZ is contraindicated or not available

There is no established Ki-67 cut-off value for the recommendation of chemotherapy.

Patients with pan creatic NET with Ki-67 of 5–20% can be treated with chemotherapy



https://doi.org/10.1159/000443167

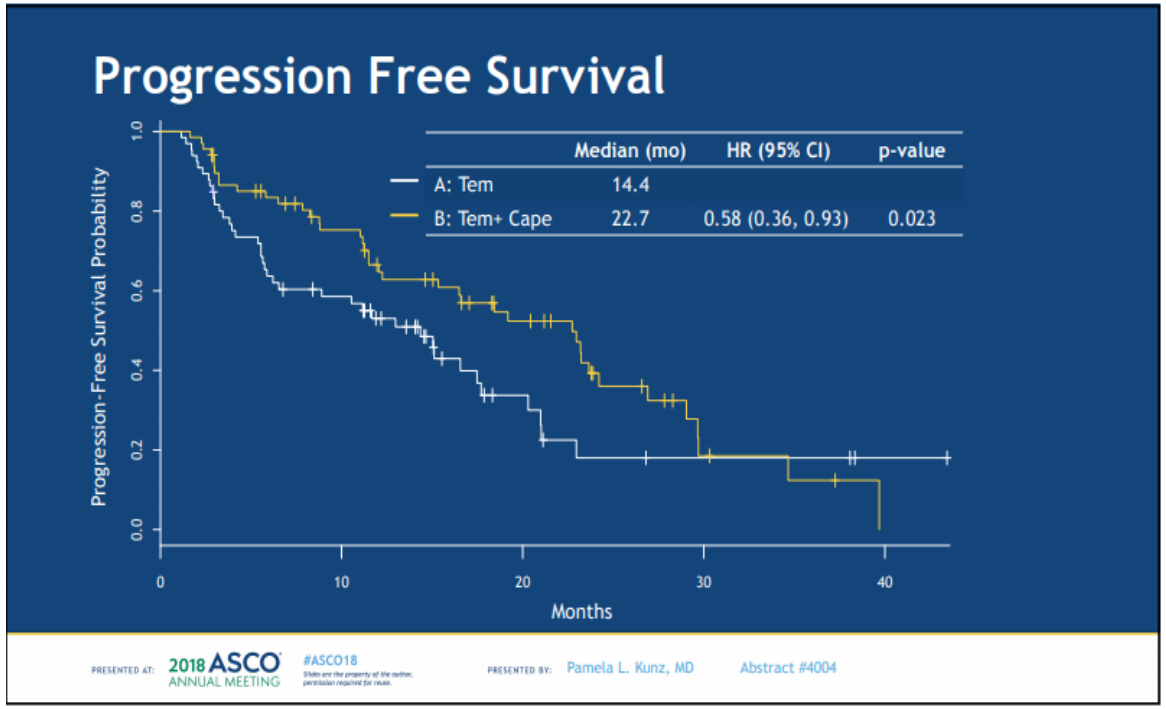
A randomized study of temozolomide or temozolomide and capecitabine in patients with advanced pancreatic neuroendocrine tumors: A trial of the ECOG-ACRIN Cancer Research Group (E2211).

Pamela L. Kunz, Paul J. Catalano, Halla Nimeiri, George A. Fisher, Teri A. Longacre, Carlos J. Suarez, ...

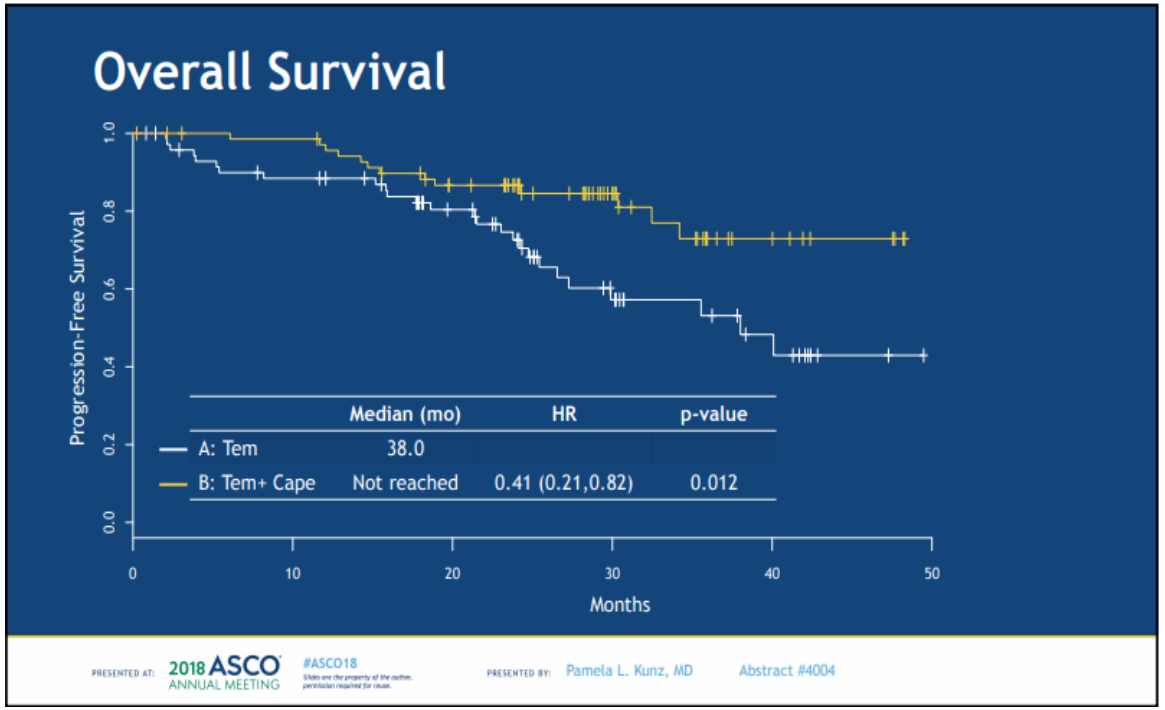
	Temozolomide (N=72)	Temozolomide + Capecitabine (N=72)	p-value
Complete response	2.8%	0	
Partial response	25.0%	33.3%	
Stable disease	40.3%	48.6%	
Progressive disease	19.4%	13.9%	
Unevaluable	12.5%	4.2%	
Objective Response Rate (CR+PR)	27.8%	33.3%	0.47
Disease Control Rate (CR+PR+SD)	68.1%	81.9%	
Response Duration (median)	9.7 mo	12.1 mo	

- **56% G1**
- 53% concurrent SSA
- 35% prior everolimus
- 12% prior sunitinib

PFS HR = 0.58, p = 0.023



OS HR = 0.41, p = 0.012



	Everolimus plus Pasireotide[1] (LUNA)	Capecitabine Temozolomide[2] (ACRIN)	A-interferon[45]	Streptozocin[5678] (Moertel)
Ki 67%	69% atypical	56%G1	-	-
Primary End Point	PFS at 9 mo	PFS	DOR, PFS	PFS
ORR	1%	33,3%	6 - 20%	6 – 36%
Lung	+			
Stomach				
Pancreas		+	+	+
Small bowel			+	
Appendix				
Colon				
Rectum				
Unknown			+	

1. https://doi.org/10.1016/S1470-2045(17)30681-2
2. DOI: 10.1200/JCO.2018.36.15_suppl.4004
3. DOI: 10.1002/1097-0142(19900501)65:9<1883::aid-cncr2820650902>3.0.co;2-3
4. M. CAPLIN ANTICANCER RESEARCH 34: 6601-6608 (2014)
5. DOI: 10.1056/NEJM199202203260804
6. DOI: 10.1056/NEJM198011203032101
7. https://doi.org/10.1002/(SICI)1097-0142(19990915)86:6<944::AID-CNCR8>3.0.CO;2-P
8. DOI: 10.1097/01.coc.0000135343.06038.eb

Interferon-α and somatostatin analog in patients with gastroenteropancreatic neuroendocrine carcinoma: single agent or combination? FREE

N Fazio ✉, F de Braud, G Delle Fave, K Öberg

Annals of Oncology, Volume 18, Issue 1, January 2007, Pages 13–19,
https://doi.org/10.1093/annonc/mdl144
Published: 23 June 2006 **Article history** ▾

ENETs guidelines

IFN-alpha is a **second-line** therapy in NEN that are **functionally active**. It is recommended to use IFN-alpha **as add-on therapy** to SSA therapy in functional tumors.

IFN-α/sst-analog combination therapy: published randomized trials

Author	No. pts	Arms	Results
			5-year-survey (%)
Kölby 2003	68	IFNα	36.6
	1991–98	OCT+IFNα	56.8
			HR 0.62 (CI 95% = 0.3–1.1) *P* = 0.132
			1-year PFS (%)
Faiss 2003	80	IFNα	44.4
	1995–98	LAN	44
		IFNα+LAN	5 *p* = 0.69
			Median survival (months)
Arnold 2005	109	OCT	35
	1995–98	OCT+IFNα	51
			HR 1.19 (CI 95% = 0.67–2.13 *P* = 0.55

	Everolimus plus Pasireotide[1] (LUNA)	Capecitabine Temozolomide[2] (ACRIN)	A-interferon[45]	Streptozocin[5678] (Moertel)
Ki 67%	69% atypical	56%G1	-	-
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Lung	+			
Stomach				
Pancreas		+	+	+
Small bowel			+	
Appendix				
Colon				
Rectum				
Unknown			+	

1. https://doi.org/10.1016/S1470-2045(17)30681-2
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8. DOI: 10.1097/01.coc.0000135343.06038.eb

Streptozocin Alone Compared with Streptozocin plus Fluorouracil in the Treatment of Advanced Islet-Cell Carcinoma

Charles G. Moertel, M.D., James A. Hanley, Ph.D., and Lewis A. Johnson, M.D.

1980

November 20, 1980

Lack of Efficacy of Streptozocin and Doxorubicin in Patients With Advanced Pancreatic Endocrine Tumors

Vilar, Eduardo, MD; Tabernero, Josep, MD; Casado, Esther, MD; Macarulla, Teresa, MD; Ramos, Francisco J., MD; Martinelli, Erika, MD; Saura, Cristina, MD

American Journal of Clinical Oncology: August 2005 - Volume 28 - Issue 4 - p 424
doi: 10.1097/01.coc.0000162426.79311.a5

2005

Streptozocin–Doxorubicin, Streptozocin–Fluorouracil, or Chlorozotocin in the Treatment of Advanced Islet-Cell Carcinoma

Charles G. Moertel, M.D., Myrto Lefkopoulo, Sc.D., Stuart Lipsitz, Sc.D., Richard G. Hahn, M.D., and David Klaassen, M.D.

Article Figures/Media

1992

Cancer

Original Article

Failure to confirm major objective antitumor activity for streptozocin and doxorubicin in the treatment of patients with advanced islet cell carcinoma

Paul N. M. Cheng M.D., Leonard B. Saltz M.D.

2000

First published: 20 November 2000 |
https://doi.org/10.1002/(SICI)1097-0142(19990915)86:6<944::AID-CNCR8>3.0.CO;2-P | Cited by: 125

- Controversial results – metanalysis needed
- Only pancreatic NENs
- Old trials, no information on Ki67%

Immunotherapy in bronchial NETs

DART trial (BASKET)

- Ipilimumab (1mg/kg q6 weeks) plus nivolumab (240mg intravenously every 2 weeks)
- Pancreatic neuroendocrine tumors not included
- **The primary endpoint was overall response rate (ORR) by RECIST v1.1**
- Secondary endpoints included progression-free (PFS) and, overall survival (OS), stable disease (SD) >6 months, and toxicity.

DOI: 10.1158/1538-7445.AM2019-CT039

DART trial (BASKET)

- n = 39 (GI = 15, **Bronchial = 6**)

Response Type	All Patients (n=33)	High grade (n=19)	Low/Intermediate grade (n=14)
Complete Response (CR)	1 (3%)	1 (5%)	0
Partial Response (PR)	7 (21%)	7 (37%)	0
Stable Disease (SD)>6months	2 (6%)	0	2 (14%)
SD	11 (33%)	3 (17%)	8 (57%)
Progressive Disease (PD)	12 (36%)	8 (42%)	4 (29%)
CR+PR	8 (24%)	8 (42%)	0
CR+PR+SD>6mo	10 (30%)	8 (42%)	2 (14%)

DOI: 10.1158/1538-7445.AM2019-CT039

DUNE Trial / GETNE 1601

Ongoing trial

Durvalumab plus Tremelimumab for the Treatment of Patients (pts) with Advanced Neuroendocrine Neoplasms (NENs) of Lung or Gastroenteropancreatic (GEP) Origin. A Phase II Multicohort Trial

Authors: Hernando-Cubero J, Manzano J L, Benavent M, Lopez C, Teulé R, Garcia-Carbonero R, Carmona-Bayonas A, Crespo G, Cubillo A, Jimenez-Fonseca P, LaCasta A, Capdevila J

Pts included in the trial must have progressed to all standard therapies in each setting for **lung and GEP** grade 1-2 NENs up to 4 prior lines.

All pts will receive durvalumab 1500 mg every 28 days for 12 months, and tremelimumab 75 mg Q4W up to 4 doses/cycles.

The primary endpoint is disease control rate at 9 months, or stable disease according to RECIST v1.1

15th Annual ENETS conference (2018)

CANCERS OF THE PANCREAS, SMALL BOWEL, AND HEPATOBILIARY TRACT

Pembrolizumab treatment of advanced neuroendocrine tumors: Results from the phase II KEYNOTE-158 study.

Jonathan R. Strosberg, Nobumasa Mizuno, Toshihiko Doi, Enrique Grande, Jean-Pierre Delord, Ronnie Shapira-Frommer, ...

- n = 107 pts
- Well- and moderately-differentiated NET of the **lung**, appendix, small intestine, colon, rectum, or pancreas;
- ≥ 1 line of standard therapy
- Primary endpoint was ORR assessed per RECIST v1.1
- median follow-up duration was 18.6

DOI: 10.1200/JCO.2019.37.4_suppl.190

CANCERS OF THE PANCREAS, SMALL BOWEL, AND HEPATOBILIARY TRACT

Pembrolizumab treatment of advanced neuroendocrine tumors: Results from the phase II KEYNOTE-158 study.

Jonathan R. Strosberg, Nobumasa Mizuno, Toshihiko Doi, Enrique Grande, Jean-Pierre Delord, Ronnie Shapira-Frommer, ...

- ORR was 3.7% (95% CI, 1.0-9.3), with 0 CR and 4 PR (3 pancreatic and 1 gastrointestinal [unknown primary]). All responders had PD-L1 negative tumors

- Median (95% CI) PFS was 4.1 (3.5-5.4) mo

- **Conclusions:** Pembrolizumab monotherapy **showed limited antitumor activity** and manageable safety in pts with previously treated advanced NET

DOI: 10.1200/JCO.2019.37.4_suppl.190

Activity & safety of spartalizumab (PDR001) in patients (pts) with advanced neuroendocrine tumors (NET) of pancreatic (Pan), gastrointestinal (GI), or thoracic (T) origin, & gastroenteropancreatic neuroendocrine carcinoma (GEP NEC) who have progressed on prior treatment (Tx) FREE

J C Yao, J Strosberg, N Fazio, M E Pavel, P Ruszniewski, E Bergsland, D Li, S Tafuto, N Raj, D Campana ... Show more

n = 116 pts enrolled (33 panNET, 32 GI NET, **30 T NET**, & 21 GEP NEC)

median follow-up of 7.6 mo

ORR was 7.4% in well-diff NET (pooled) & 4.8% in poorly-diff GEP NEC

https://doi.org/10.1093/annonc/mdy293.001

Activity & safety of spartalizumab (PDR001) in patients (pts) with advanced neuroendocrine tumors (NET) of pancreatic (Pan), gastrointestinal (GI), or thoracic (T) origin, & gastroenteropancreatic neuroendocrine carcinoma (GEP NEC) who have progressed on prior treatment (Tx) FREE

J C Yao, J Strosberg, N Fazio, M E Pavel, P Ruszniewski, E Bergsland, D Li, S Tafuto, N Raj, D Campana ... Show more

	T*	P	GI	Overall NET (T+P+GI)	GEP NEC
Partial response, %	20.0	3.0	0	7.4	4.8
Stable disease, %	53.3	54.5	59.4	55.8	14.3
Unknown, %	10.0	3.0	6.3	6.3	14.3
Disease control rate, %	73.3	57.6	59.4	63.2	19.0

* All responses were observed in atypical carcinoid cohort.

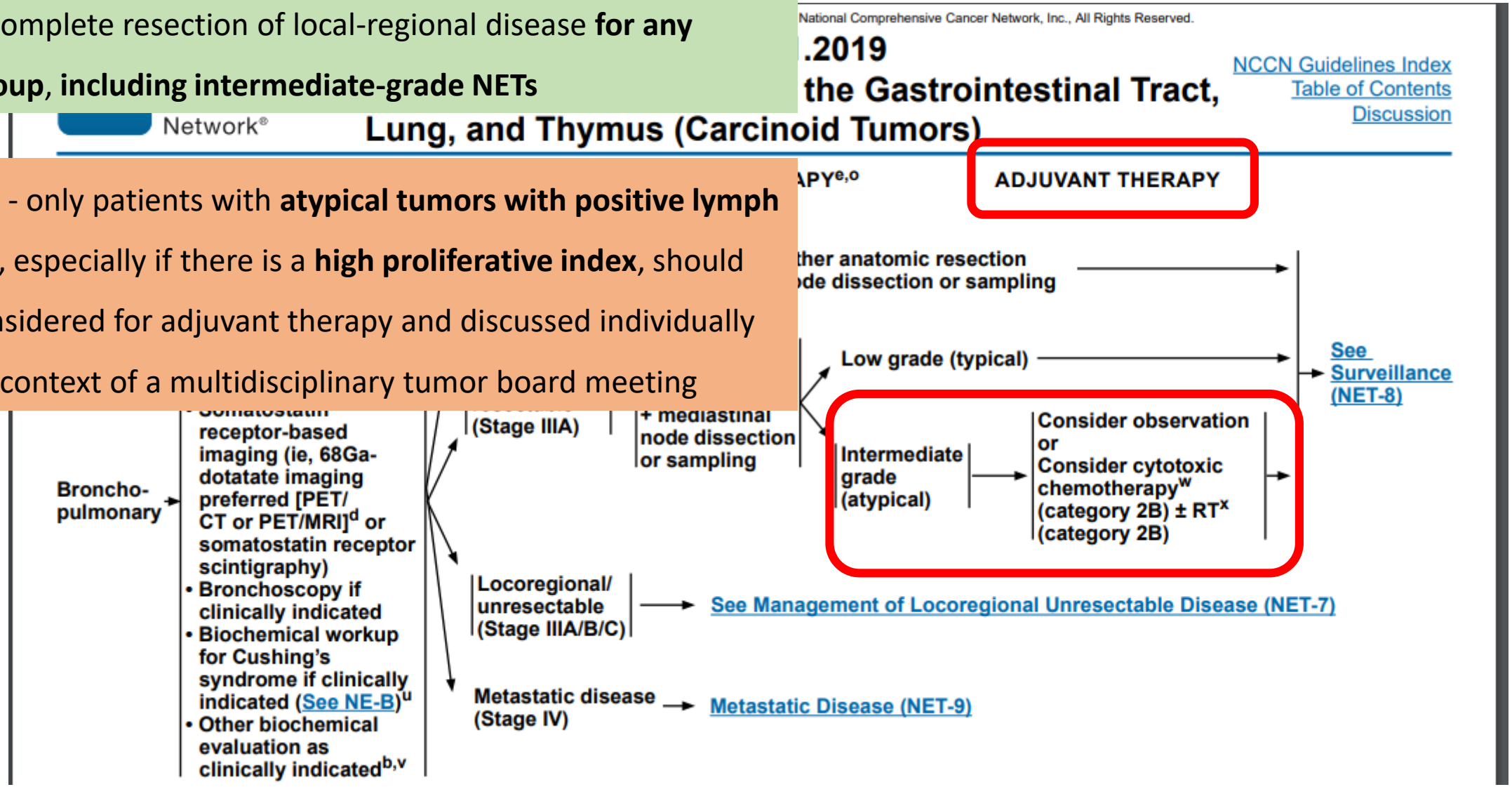
Conclusions: These preliminary results suggest clinical activity of spartalizumab in pts with well-diff nonfunctional NET of T origin. Further studies are needed to explore the role of immunotherapy combinations, identifying predictive biomarkers for immunoncology (IO) response or strategies to increase response to IO in this pt population

https://doi.org/10.1093/annonc/mdy293.001

Adjuvant Radiotherapy in atypical bronchial NETs

NANETS - insufficient data to recommend adjuvant therapy after complete resection of local-regional disease **for any subgroup**, **including intermediate-grade NETs**

ENETS - only patients with **atypical tumors with positive lymph nodes**, especially if there is a **high proliferative index**, should be considered for adjuvant therapy and discussed individually in the context of a multidisciplinary tumor board meeting



Outcome of patients with pulmonary carcinoid tumors receiving chemotherapy or chemoradiotherapy

Lori J. Wirth[a,b,c,*], Mark R. Carter[d], Pasi A. Jänne[a,b,c], Bruce E. Johnson[a,b,c]

PlumX Metrics

DOI: https://doi.org/10.1016/j.lungcan.2003.11.016

- Retrospective study
- Patients treated at a single institution
- N = 18 (typical = 8, atypical = 10)
- **4 received chemotherapy plus RT** – 14 chemotherapy only
- 2 PR, 8 SD

DOI: https://doi.org/10.1016/j.lungcan.2003.11.016

Chromogranin A as a biomarker in bronchial NETs

An Assessment of Circulating Chromogranin A as a Biomarker of Bronchopulmonary Neuroendocrine Neoplasia: A Systematic Review and Meta-Analysis

Anna Malczewska[a] Mark Kidd[b] Somer Matar[b] Beata Kos-Kudła[a] Lisa Bodei[c] Kjell Oberg[d] Irvin M. Modlin[e]

[a]Department of Endocrinology and Neuroendocrine Tumors, Medical University of Silesia, Katowice, Poland; [b]Wren Laboratories, Branford, CT, USA; [c]Memorial Sloan Kettering Cancer Centre, New York, NY, USA; [d]Department of Endocrine Oncology, University Hospital, Uppsala, Sweden; [e]Yale University School of Medicine, New Haven, CT, USA

- 33 original scientific papers and 3 case reports
- All studies, except 2, were retrospective
- Ten different CgA assay types were reported, **without consistency in the upper limit of normal (ULN)**
- Sensitivity 34.5 ± 2.7% **(TC and AC)** **Vs** 59.9 ± 6.8% **(SCLC)**
- Specificity 93.8 ± 4.7% **(TC and AC)** **Vs** 79.4 ± 3.1 **(SCLC)**
- CgA metrics were not available separately for typical or atypical carcinoids

DOI: 10.1159/000500525

An Assessment of Circulating Chromogranin A as a Biomarker of Bronchopulmonary Neuroendocrine Neoplasia: A Systematic Review and Meta-Analysis

Anna Malczewska[a] Mark Kidd[b] Somer Matar[b] Beata Kos-Kudła[a] Lisa Bodei[c] Kjell Oberg[d]
Irvin M. Modlin[e]

- Management of the patients with bronchopulmonary neuroendocrine neoplasia (NEN) is difficult since there is a **paucity of biomarkers to facilitate diagnosis and follow-up**.

- No evidence was presented for predicting treatment response or identifying post-surgery residual disease

- The clinical value of CgA remains to be determined. This requires validated, well-constructed, multicenter, prospective, randomized studies

DOI: 10.1159/000500525

Ευχαριστώ!

Ερωτήσεις;