Neuroendocrine Tumors ESMO vis a vis NCCN Guidelines

Disclosure slide

- Advisory board and speaker:
  - Novartis
  - Ipsen
  - Pfizer

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- ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up are based on ENETS Guidelines (2012)
- NCCN Guidelines for NETs are based on UICC/AJCC Guidelines

TNM Staging of Neoplasms of the Endocrine Pancreas: Results From a Large International Cohort Study

G. Rindi, M. Falconi, C. Klersy, L. Albarello, L. Boninsegna, M. W. Buchler, C. Capella, M. Caplin, A. Couvelard, C. Doglioni, G. Delle Fave, L. Fischer, G. Fusai, W. W. de Herder, H. Jann, P. Komminoth, R. R. de Krijger, S. La Rosa, T. V. Luong, U. Pape, A. Perren, P. Ruszniewski, A. Scarpa, A. Schmitt, E. Solcia, B. Wiedenmann

T and stage definitions in the European Neuroendocrine Tumor Society (ENETS) and the International Union for Cancer Control/American Joint Cancer Committee/World Health Organization (UICC/AJCC/WHO) 2010 TNM staging systems (3-6)*

Definitions		ENETS TNM	UICC/AJCC/WHO 2010 TNM
T definition			
	T1	Limited to the pancreas, <2 cm	Limited to the pancreas, ≤2 cm in greatest dimension
	T2	Limited to the pancreas, 2–4 cm	Limited to the pancreas, >2 cm in greatest dimension
	T3	Limited to the pancreas, >4 cm or invading duodenum or bile duct	Beyond the pancreas but without involvement of the superior mesenteric artery
	T4	Tumor invading adjacent organs (stomach, spleen, colon, adrenal gland) or the wall of large vessels (celiac axis or the superior mesenteric artery)	Involvement of celiac axis or the superior mesenteric artery (unresectable tumor)
Stage definition			
	Stage I	T1, N0, M0	NA
	Stage IIa	T2, N0, M0	NA
	Stage IIb	T3, N0, M0	NA
	Stage IIIa	T4, N0, M0	NA
	Stage IIIb	Any T, N1, M0	NA
	Stage IV	Any T, any N, M1	NA
	Stage IA	NA	T1, N0, M0
	Stage IB	NA	T2, N0, M0
	Stage IIA	NA	T3, N0, M0
	Stage IIB	NA	T1–T3, N1, M0
	Stage III	NA	T4, any N, M0
	Stage IV	NA	Any T, any N, M1

* NA= not applicable

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Comparison of tumor-related death among 891 patients using the ENETS vs the UICC/AJCC/WHO 2010 TNM staging systems including four tumor stages for pancreatic neuroendocrine neoplasms

TNM staging system	Tumor-related death per No.	Death rate per 100 person-years (95% CI)	HR (95% CI)	P*	P†	Royston explained variation (95% CI)	Harrell C (95% CI)‡	Somer D (95% CI)‡
Complete TNM								
ENETS				<.001		0.59 (0.49 to 0.68)	0.80 (0.76 to 0.83)	0.69 (0.58 to 0.79)
I	1/248	0.1 (0.0 to 0.5)	1.0 (referent)					
IIA	7/134	0.8 (0.4 to 1.6)	11.1 (1.3 to 90.1)	.02	.02			
IIB	8/65	1.90 (0.9 to 3.8)	27.3 (3.4 to 218.3)	.002	.05			
IIIA	14/38	7.6 (4.5 to 13.0)	108.2 (14.2 to 23.8)	<.001	.002			
IIIB	25/156	2.9 (1.9 to 13.0)	40.5 (5.4 to 299.0)	<.001	.004			
IV	119/250	12.0 (9.8 to 14.0)	159.8 (22.3 to 1144.7)	<.001	<.001			
				<.001.		0.59 (0.48 to 0.69)	0.79 (0.75 to 0.83)	0.65 (0.54 to 0.76)
UICC/AJCC/WHO 2010								
IA	2/258	0.1 (0.0 to 0.5)	1.0 (referent)					
IB	7/141	0.7 (0.3 to 1.5)	5.2 (1.10 to 25.3)	.04	.04			
IIA	14/70	3.7 (2.2 to 6.2)	27.0 (6.13 to 118.9)	<.001	<.001			
IIB	23/125	3.4 (2.3 to 5.2)	25.2 (5.9 to 106.9)	<.001	.84			
III	9/47	3.4 (1.8 to 6.5)	25.1 (5.4 to 116.5)	<.001	1.0			
IV	119/250	12.0 (9.7 to 4.0)	83.1 (20.5 to 336.7)	<.001	.001			
Four-stage TNM								
ENETS				<.001		0.61 (0.54 to 0.71)	0.80 (0.76 to 0.84)	0.70 (0.58 to 0.82)
I	1/248	0.1 (0.0 to 0.5)	1.0 (referent)					
II	15/199	1.1 (0.7 to 1.9)	16.23 (2.14 to 123)	.007	.007			
III	39/194	3.7 (2.7 to 5.0)	51.81 (7.11 to 377)	<.001	<.001			
IV	119/250	12.0 (9.8 to 14.0)	160 (22.30 to 1143)	<.001	<.001			
				<.001		0.58 (0.48 to 0.65)	0.79 (0.76 to 0.83)	0.68 (0.56 to 0.80)
UICC/AJCC/WHO 2010								
I	9/399	0.4 (0.2 to 0.7)	1.0 (referent)					
II	37/195	3.5 (2.5 to 4.8)	9.57 (4.62 to 19.88)	<.001	<.001			
III	9/47	3.4 (1.8 to 6.5)	9.32 (3.69 to 23.52)	<.001	.94			
IV	119/250	10.2 (9.7 to 14.0)	30.84 (15.62 to 60.87)	<.001	.001			

* Cox models were used to calculate two-sided *P* values with stag I or IA as the reference for the ENETS and UICC/AJCC/WHO TNM classification systems, respectively. CI=confidence interval; HR=hazard ratio

† Cox models were used to calculate two-sided *P* values with the previous stage as the reference

‡ Comparison of model performance was done informally

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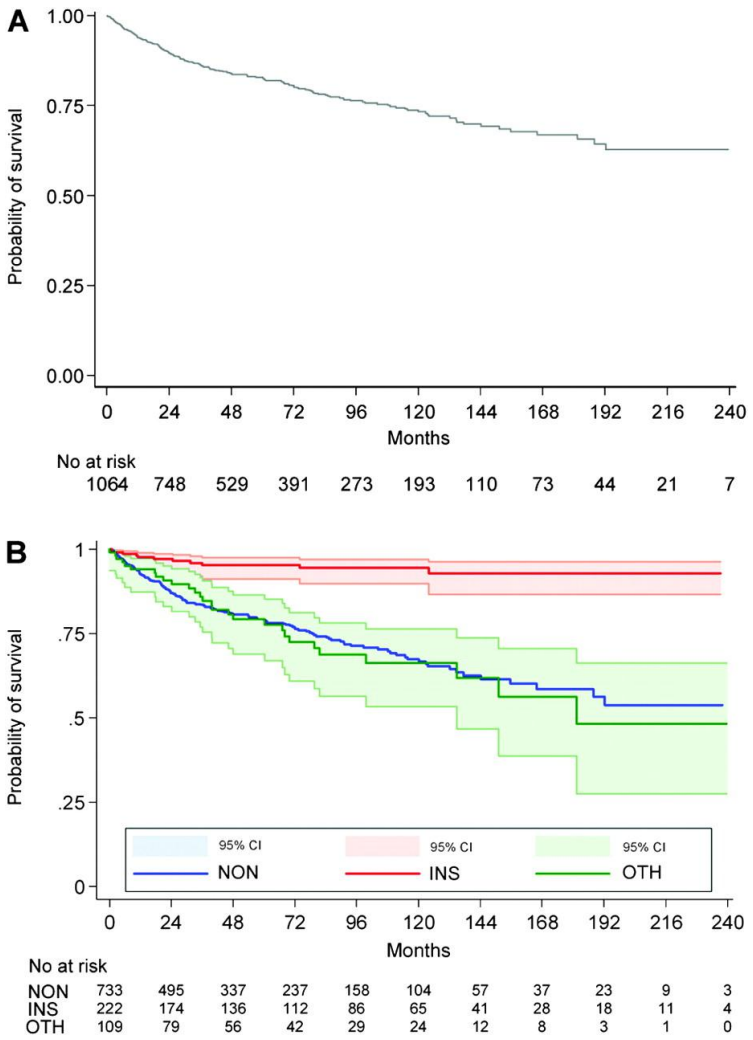
Kaplan–Meier survival curves for pancreatic neuroendocrine neoplasms (n = 1064) overall and by functioning status.



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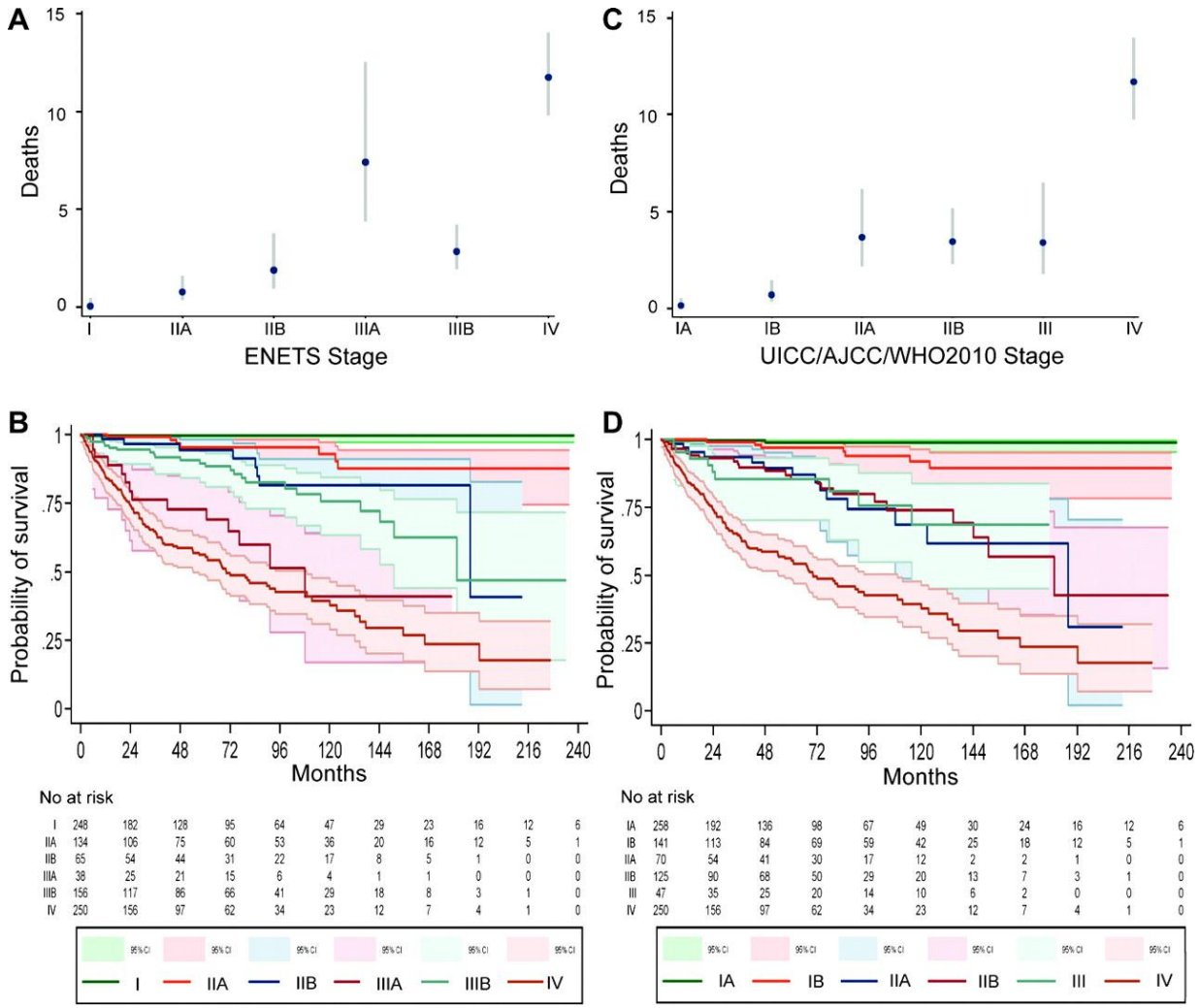
Death incidence and survival by European Neuroendocrine Tumor Society (ENETS) and the International Union for Cancer Control/American Joint Cancer Committee/World Health Organization (UICC/AJCC/WHO) 2010 TNM staging systems.



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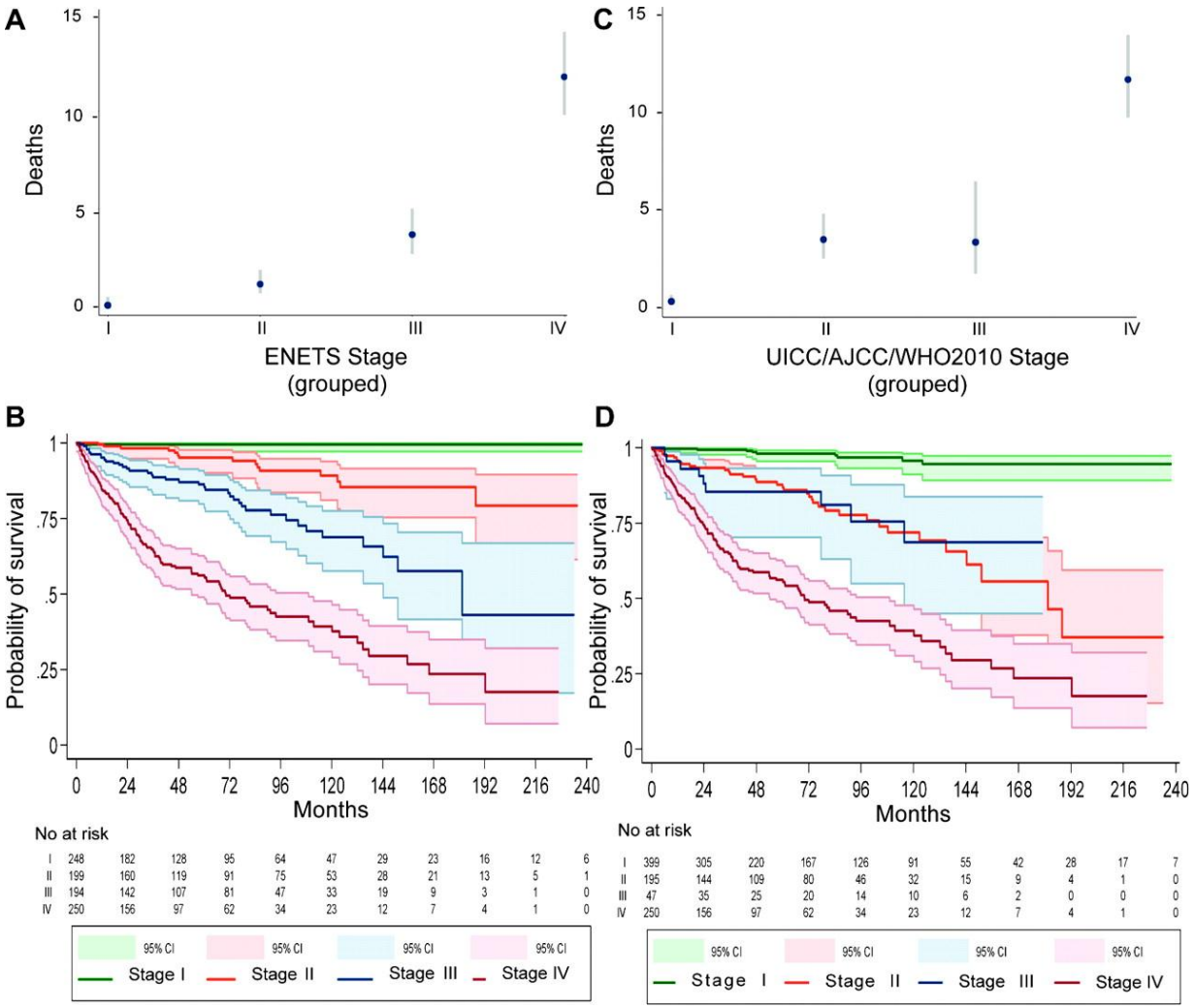
Death incidence and survival by European Neuroendocrine Tumor Society (ENETS) and the International Union for Cancer Control/American Joint Cancer Committee/World Health Organization (UICC/AJCC/WHO) 2010 TNM staging systems when stages were grouped into four classes.



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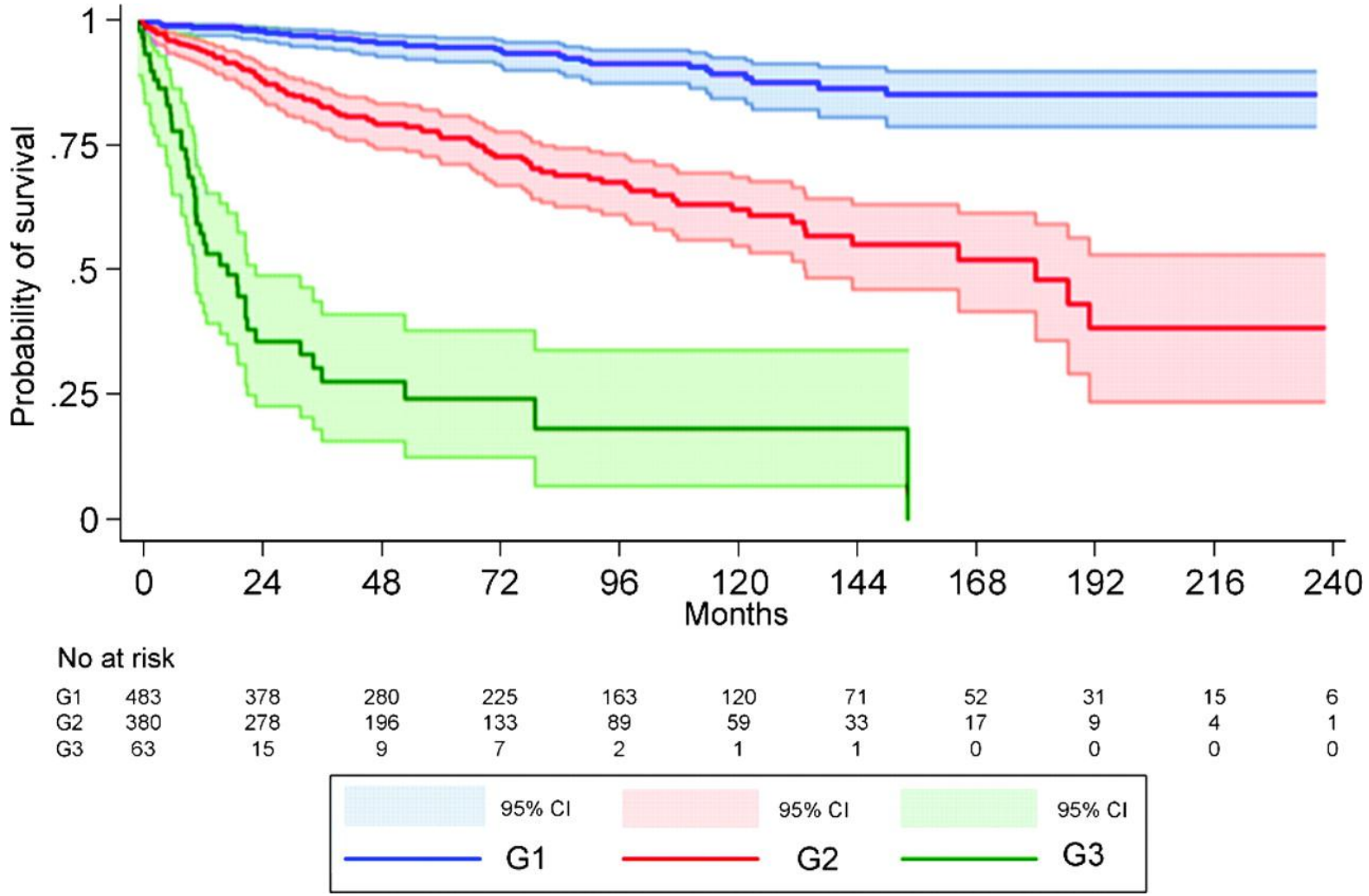
Kaplan–Meier survival curves of 926 neoplasms by the European Neuroendocrine Tumor Society /World Health Organization 2010 grade.



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Relapse-Free Survival in Patients With Nonmetastatic, Surgically Resected Pancreatic Neuroendocrine Tumors

An Analysis of the AJCC and ENETS Staging Classifications

Jonathan R. Strosberg, MD, Asima Cheema, MD,* Jill M. Weber, MPH,* Masoumeh Ghayouri, MD,† Gang Han, PhD,‡ Pamela J. Hodul, MD,* and Larry K. Kvols, MD**

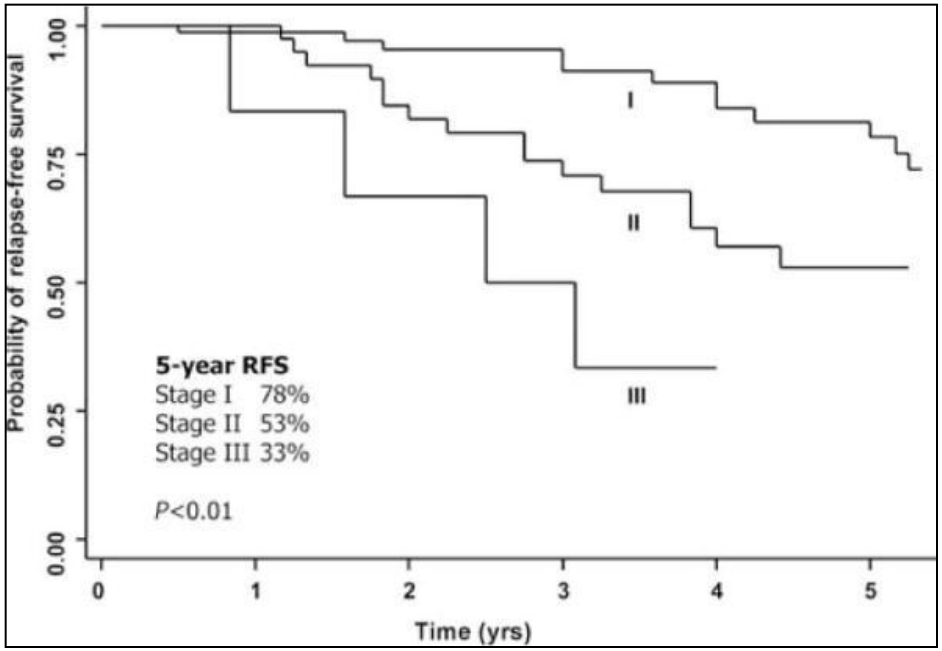


FIGURE 1 . Kaplan-Meier estimate of RFS, according to AJCC stage.

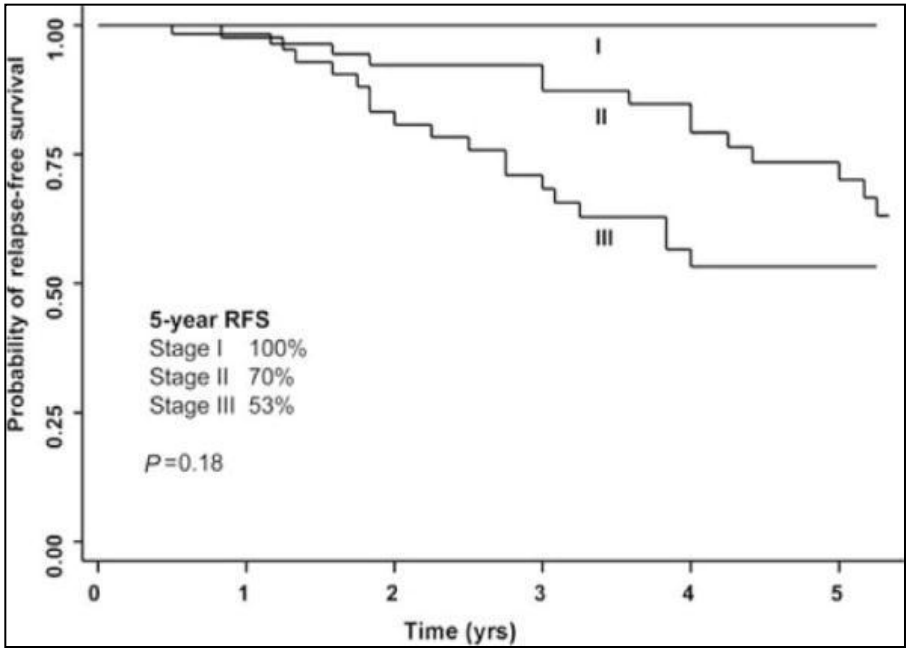
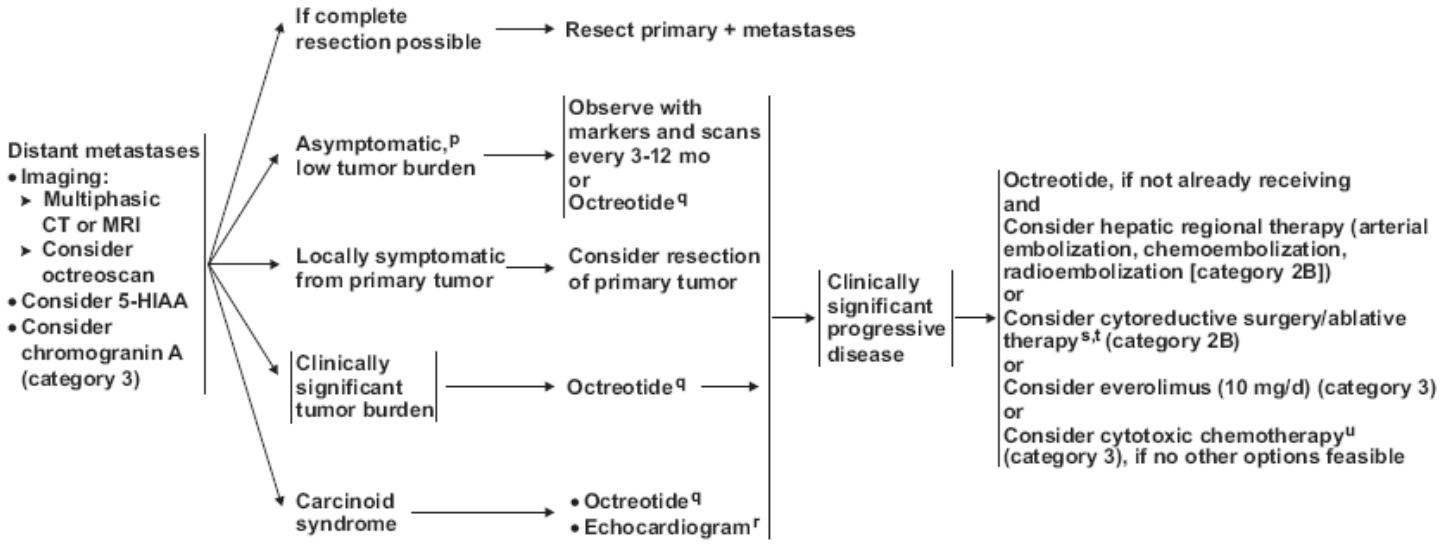


FIGURE 2 . Kaplan-Meier estimate of RFS, according ENETS stage.

Treatment of NET

MANAGEMENT OF LOCOREGIONAL UNRESECTABLE DISEASE AND/OR DISTANT METASTASES [c]



[c] See Surgical Principles for Management of Neuroendocrine Tumors (NE-C).

[p] Resection of a small asymptomatic (relatively stable) primary in the presence of unresectable metastatic disease is not indicated.

[q] Octreotide 150-250 mcg SC TID or octreotide LAR 20-30 mg IM every 4 weeks. Dose and frequency may be further increased for symptom control as needed. Therapeutic levels of octreotide would not be expected to be reached for 10-14 d after LAR injection. Short-acting octreotide can be added to octreotide LAR for rapid relief of symptoms or for breakthrough symptoms. See PROMID study: J Clin Oncol. 2009;27:4656-4663.

[r] If signs and symptoms of heart disease or planning major surgery.

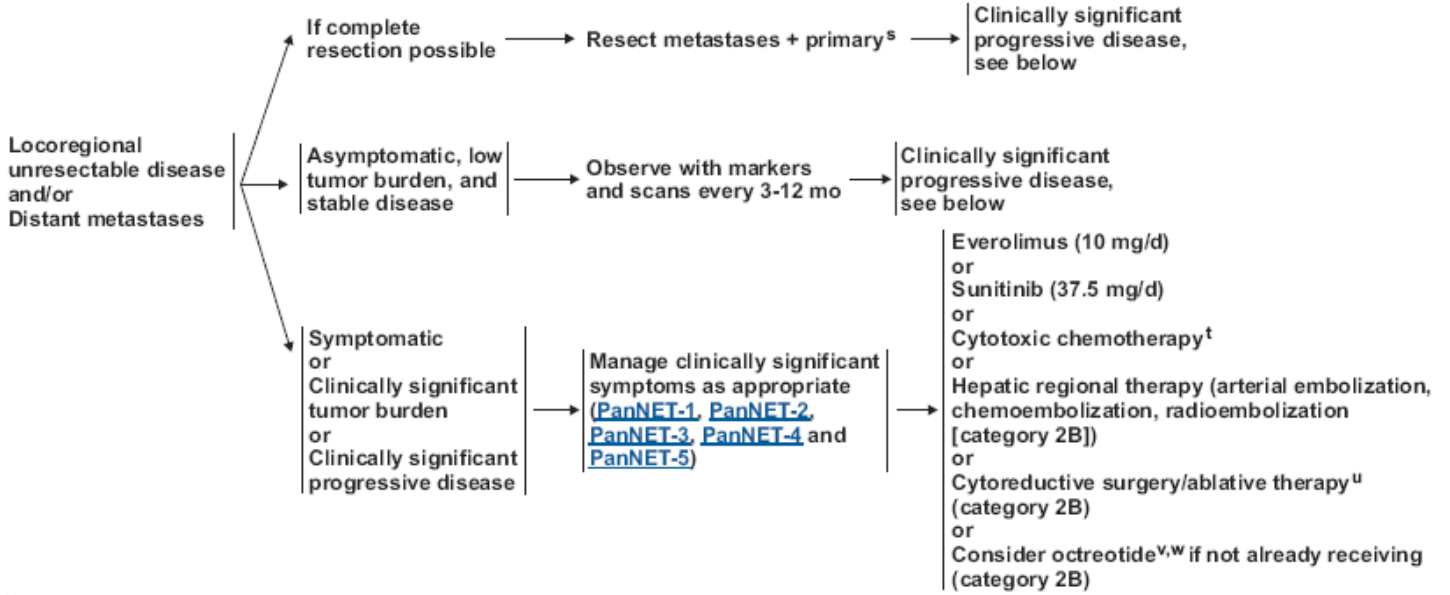
[s] Includes ablative techniques such as radiofrequency, microwave, and cryotherapy. There are no randomized clinical trials and prospective data for these interventions are limited. However, data on the use of these interventions are emerging.

[t] Only if near complete resection can be achieved.

[u] Anticancer agents such as, capecitabine, dacarbazine, 5-fluorouracil, interferon, and temozolomide can be used in patients with progressive metastases for whom there are no other treatment options.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

MANAGEMENT OF LOCOREGIONAL UNRESECTABLE DISEASE AND/OR DISTANT METASTASES[f]



[f] See Surgical Principles for Management of Neuroendocrine Tumors (NE-C).

[s] Staged or synchronous resection when possible. When performing staged pancreatoduodenectomy and liver resection, consider hepatectomy prior to pancreatic resection in order to reduce risk of perihepatic sepsis. De Jong MC, Farnell MB, Sclabas G, et al. Liver-directed therapy for hepatic metastases in patients undergoing pancreaticoduodenectomy: A dual-center analysis. Ann Surg 2010;252:142-148.

[t] The following agents have been used: capecitabine, dacarbazine, doxorubicin, 5-FU, streptozocin, and temozolomide.

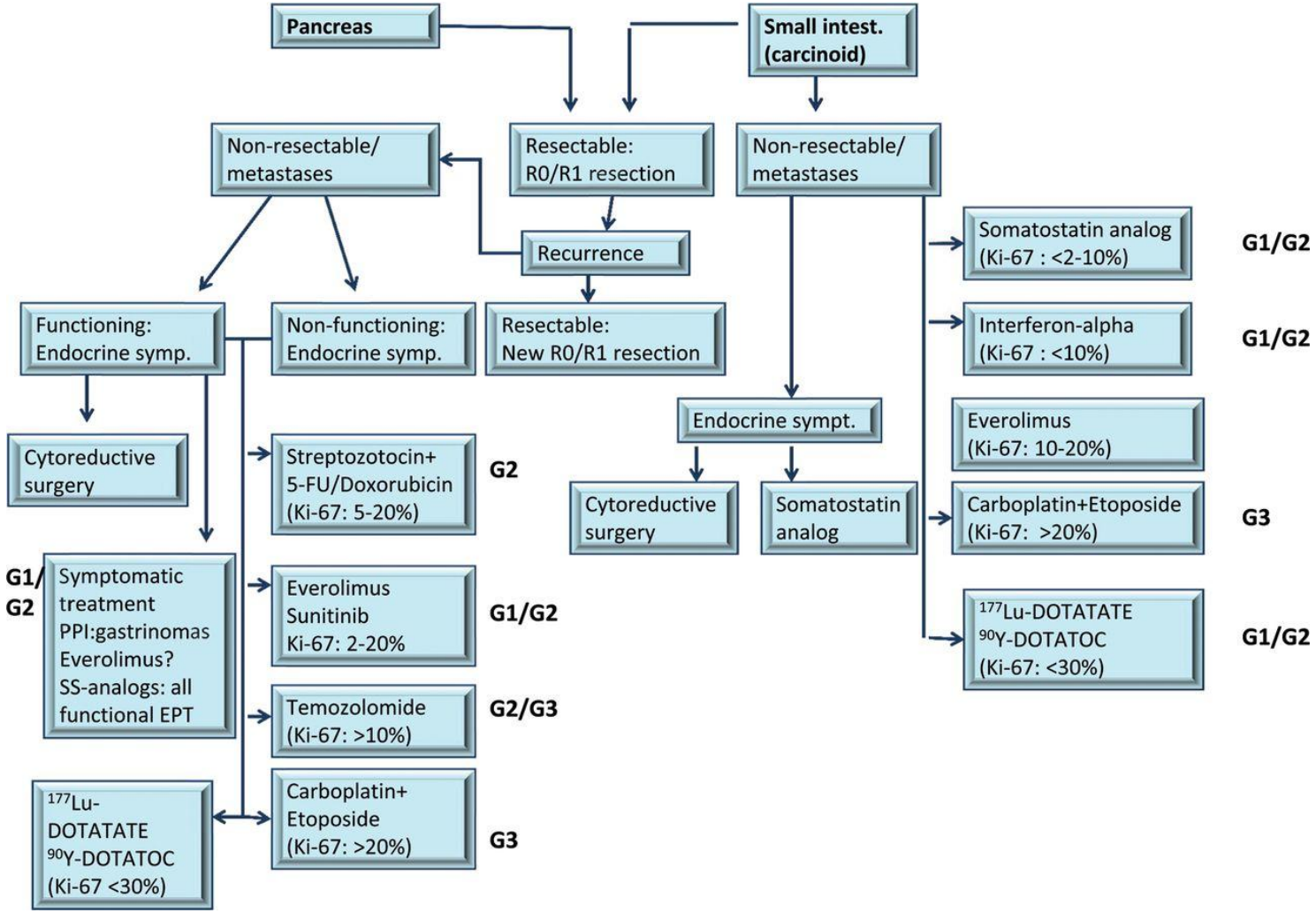
[u] Includes ablative techniques such as radiofrequency, microwave, and cryotherapy. There are no randomized clinical trials and prospective data for these interventions are limited, but data on their use are emerging.

[v] Octreotide should be used with caution in patients with insulinoma as it may transiently worsen hypoglycemia (see discussion).

[w] Octreotide 150-250 mcg SC TID or octreotide LAR 20-30 mg IM every 4 weeks. Dose and frequency may be further increased for symptom control as needed. Therapeutic levels of octreotide would not be expected to be reached for 10-14 d after LAR injection. Short-acting octreotide can be added to octreotide LAR for rapid relief of symptoms or for breakthrough symptoms. Octreotide can be used alone or in combination with other agents.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Treatment algorithm.



Öberg K et al. Ann Oncol 2012;23:vii124-vii130

Thank you!

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http://www.endocrinetumors.org/