IMAGERIE MOLECULAIRE
TEP AU GALLIUM

TEP AU 68GaDOTATOC

Modalités pratiques, performances diagnostiques, indications, impacts dans la prise en charge

Dr L Dierickx, Dr L Vija, Pr F Courbon

Hôtel Vatel 19 septembre 2019 Bordeaux

Liens d'intérêt:

Financements recherche

Covidien /Mallinkrodt, IBA, Roche, GEHC

Expertise

Covidien/Mallinkrodt, Ipsen, Novartis, Norgine, Bayer, GEHC, Cyclopharma, AAA

Pr F COURBON

Biophysique & Médecine Nucléaire : UFR MédecineToulouse Rangueil

Centre de recherche en cancérologie de Toulouse UMR 1037 Equipe n°12 « Métabolisme des Stérols et Innovations thérapeutiques en Oncologie »

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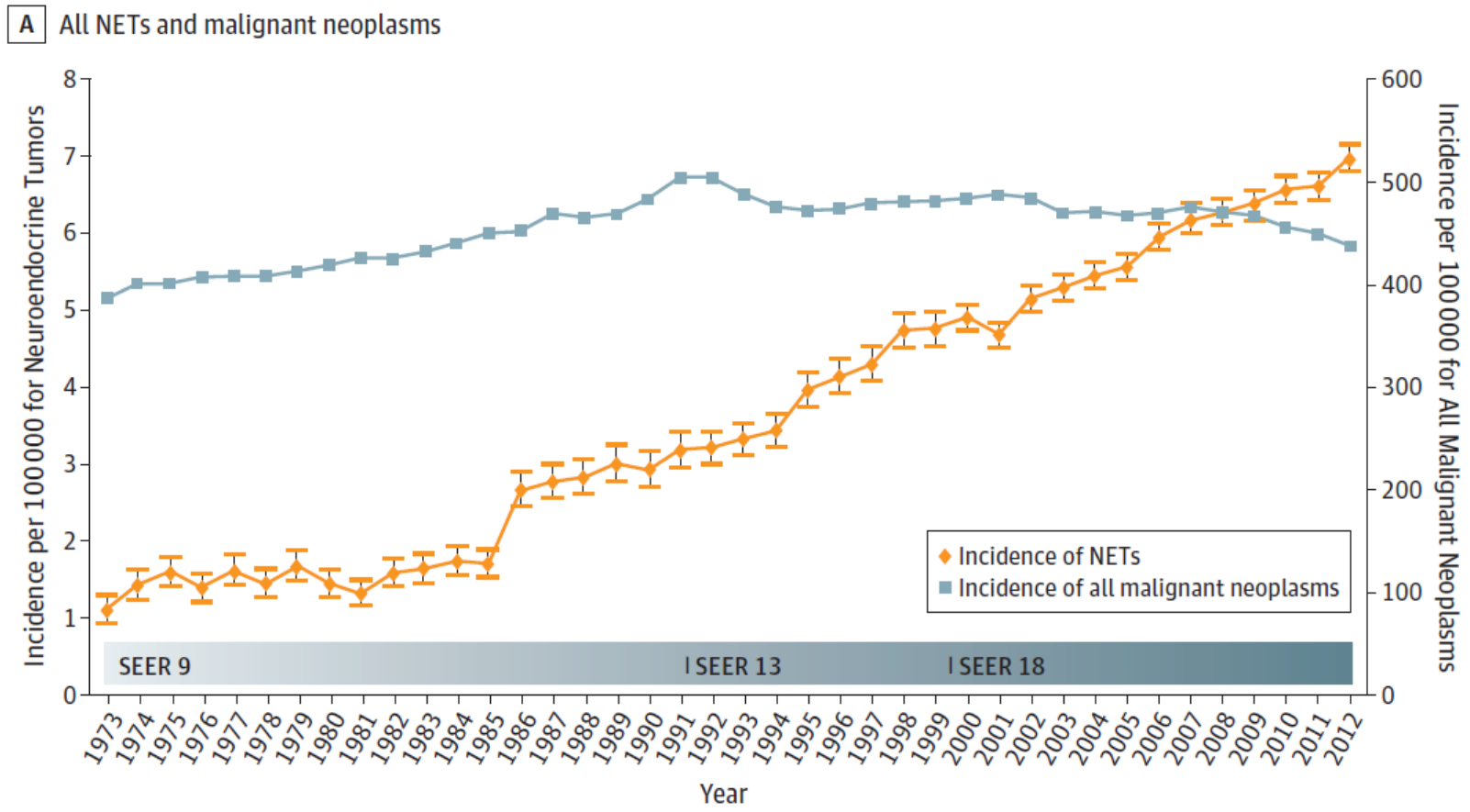
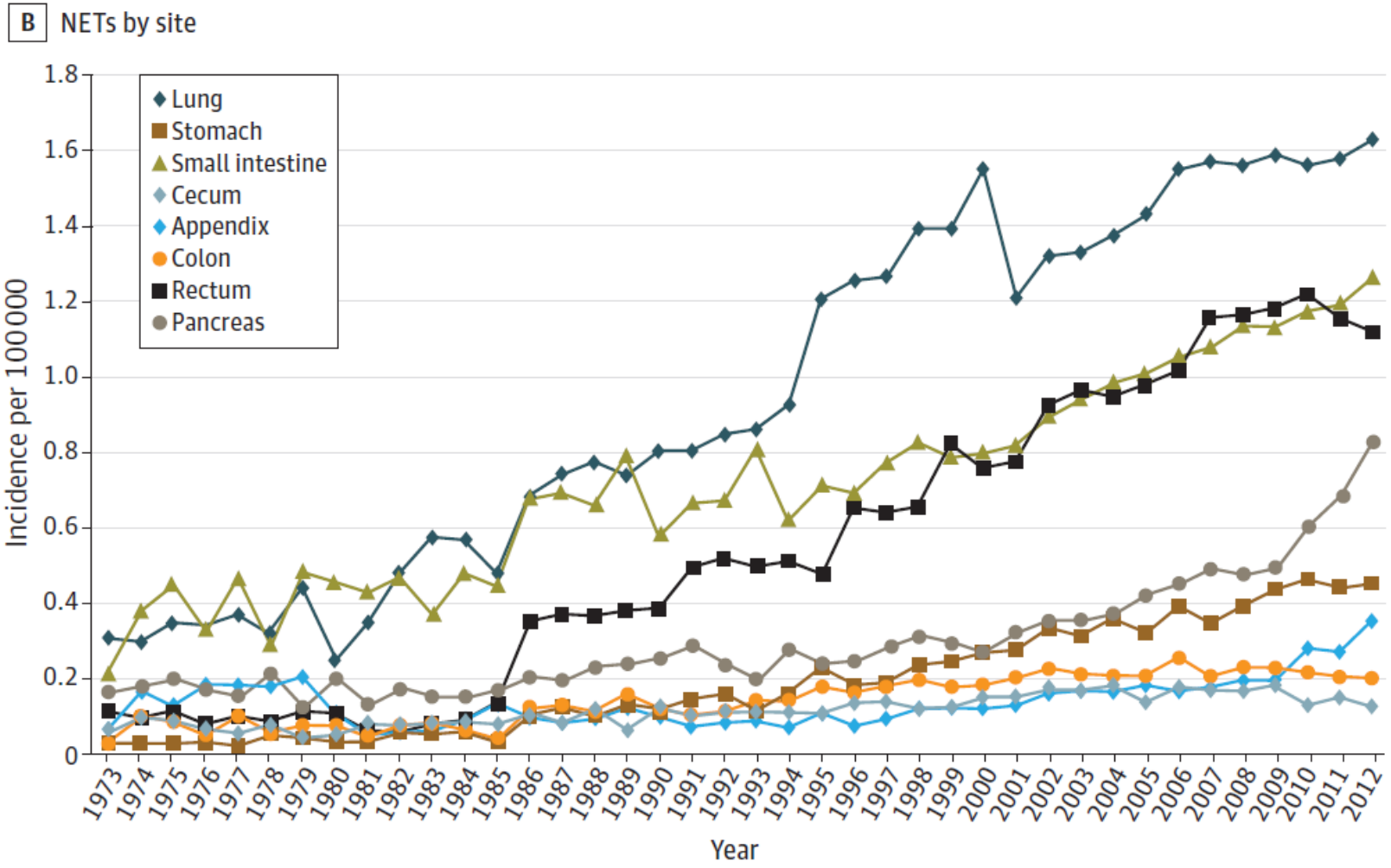
Tél : 05 31 15 56 27

NETs : Increasing incidence



In France (2004) NE en 2004 1% of Digestive system malignancies


B
NETs by site
Lung
Stomach
Small intestine
Cecum
Appendix
Colon
Rectum
Pancreas
Incidence per 100 000
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0
1973 1974 1975 1976 1977 1978 1979 1980 1981 1982 1983 1984 1985 1986 1987 1988 1989 1990 1991 1992 1993 1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012
Year

Yao, 2017

0163-769X/03/$20.00/0
Printed in U.S.A.

Endocrine Reviews 24(4):389–427

doi: 10.1210/er.2002-0007

Peptide Receptors as Molecular Targets for Cancer Diagnosis and Therapy

JEAN CLAUDE REUBI

Division of Cell Biology and Experimental Cancer Research, Institute of Pathology, University of Berne, CH-3010 Berne, Switzerland

TABLE 2. Regulatory peptides as targeting agents

Advantages	Disadvantages
• Small molecules	• Rapidly degraded by peptidases
• Excellent permeability	
• No antigenicity	
• Minimal side effects	
• Easy to synthesize and modify chemically	
• Easy to link to chelators	
• Easy to radiolabel	
• High-affinity receptor binding	
• Rapid clearance from the body	
	• No brain targeting due to inability to cross the blood-brain barrier

More or less !

Somatostatin Receptor Subtypes (RSST) expression in healthy tissues

Tissu	RSST-1	RSST-2	RSST-3	RSST-4	RSST-5
Pineal glands	+	+	+	+	+
Parathyroid	+	-	+	+	-
Thyroid	+	-	+	+	+
lung	+	-	-	+	
Heart	-	-	-	-	+
stomach	+	+	+	+	+
pancreas	+	+	+	+	+
liver	+	+	-	-	-
spleen	-	+	-	-	-
Adrenal glans	-	+	-	-	+
Colon	+	+	-	-	+

Nb Lymphocytes are rsst2+

Wild *et al*.

Reubi *et al*.

Peptide receptor expression in human tumors (Reubi et al)

TABLE 4. Peptide receptor expression at the protein level in human tumors

Tumor type	Somatostatin-R[a]	VIP/PACAP-R[a]	GRP/bombesin-R[a]	NTR1	CCK_1/CCK_2[a]	NK_1	NPY-R[a]
GH-producing pituitary adenoma	+ (sst_2, sst_5)	+ (PAC_1)		−	−		
Nonfunctioning pituitary adenoma	+ ($sst_3 > sst_2$)	+ (PAC_1)		−	−		
Gut carcinoid	+ ($sst_2 > sst_1$, sst_5)	+	+ (NMB-R)	−	+ (CCK_1)		
Gastrinoma	+ (sst_2)	+	+ (GRP-R)	−			
Insulinoma	+	+		−	+ (CCK_2)		
Paraganglioma	+ (sst_2)	+ (PAC_1)		−	−		
Pheochromocytoma	+ (sst_2)	+ (PAC_1)			−		
Medullary thyroid carcinoma	+	−		+	+ (CCK_2)	+	
Small cell lung cancer	+ (sst_2)	+	+ (BB_3)	+	+ (CCK_2)	+	
Non-small cell lung cancer	−	+ ($VPAC_1$)		−	−	−	−
Meningioma	+ (sst_2)	+		+	+ (CCK_1)		
Neuroblastoma	+ (sst_2)	+ (PAC_1)		−	+ (CCK_1)	−	
Medulloblastoma	+ (sst_2)	+		+			
Astrocytoma	+	+ (PAC_1)		+	+ (CCK_2)	+	
Glioblastoma	−	+ (PAC_1)				+	
Exocrine pancreatic tumor	−	+ ($VPAC_1$)	−	+	−	−	
Colorectal carcinoma	−	+ ($VPAC_1$)		−	−	−	−
Gastric carcinoma	+	+ ($VPAC_1$)		−	−		
Hepatocellular carcinoma	+	+ ($VPAC_1$)		−	−		
Esophageal carcinoma	−	+ ($VPAC_1$)					
Renal cell carcinoma	+	+ ($VPAC_1$)	+ (GRP-R)	−	−		
Prostate carcinoma	+ (sst_1)	+ ($VPAC_1$)	+ (GRP-R)	−	−		−
Urinary bladder carcinoma	−	+ ($VPAC_1$)					
Breast carcinoma	+	+ ($VPAC_1$)	+ (GRP-R)	−	−	+	+ (Y_1)
Endometrial carcinoma	−	+					
Ovarian carcinoma	+	+ ($VPAC_1$)		−	−		
Lymphoma	+	+		−	−	−	
Ewing sarcoma	−	−		+			
Leiomyoma	+	+ ($VPAC_2$)					

Bold +, receptors with particularly high density and incidence.

[a] Subtype preferentially expressed is listed in parentheses, only when compelling evidence is available (immunohistochemistry or autoradiography).

^{68}Ga-peptides PET for NETs

Eur J Nucl Med Mol Imaging (2010) 37:2004–2010
DOI 10.1007/s00259-010-1512-3

GUIDELINES

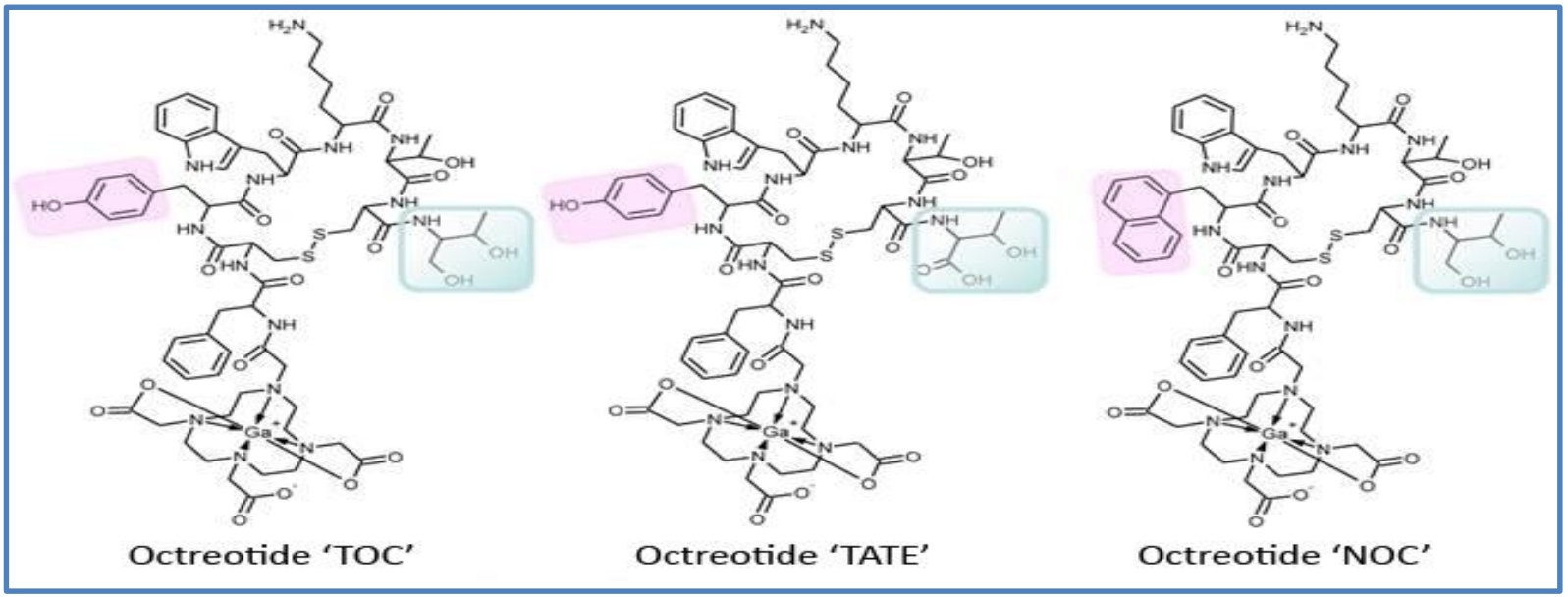
Procedure guidelines for PET/CT tumour imaging with ^{68}Ga-DOTA-conjugated peptides: ^{68}Ga-DOTA-TOC, ^{68}Ga-DOTA-NOC, ^{68}Ga-DOTA-TATE

Irene Virgolini · Valentina Ambrosini · Jamshed B. Bomanji · Richard P. Baum · Stefano Fanti · Michael Gabriel · Nikolaos D. Papathanasiou · Giovanna Pepe · Wim Oyen · Clemens De Cristoforo · Arturo Chiti

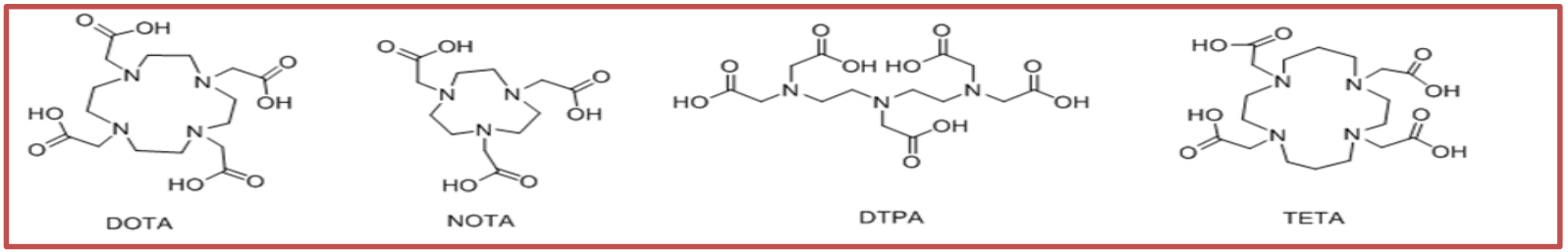
Author	Journal	Year	No Patients	Tumor	Lesions	Reference
Goel et al	IJNM	2014	30	All NET	Mets	[26]
Armbruster et al	JIR	2014	42	All NET	Liver Mets	[27]
Haug et al	Radiology	2013	63	All NET (Excluded MTC)	Mets	[19]
Schmid et al	EJNMMI	2013	18	Pancreatic NET	Panc lesions+mets	[25]
Haug et al	JNM	2012	104	All NET	Primary lesions+mets	[18]
Maurice et al	EJNMMI	2012	15	PCC, PGL	Primary lesions+mets	[23]
Hofman et al	JMIRO	2012	59	NET (GEP, Bronc, PCC, PGL)	Primary lesions+mets	[12]
Łapińska et al	NMRCEE	2011	97	NET (GEP, MCT)	Primary lesions+mets	[21]
Naji et al	MIAB Aug	2010	12	PCC, PGL	Primary lesions+mets	[24]
Srirajaskanthan et al	JNM June	2010	51	All NET	Primary lesions+mets	[20]
Conry et al	EJNMMI	2010	18	MTC	Primary lesions+mets	[28]
Kayani et al	JNM	2009	18	All NET	Primary lesions+mets	[30]
Kayani et al	Cancer	2008	38	All NET	Primary lesions+mets	[28]
Win et al	NMC	2007	5	PCC	Mets	[22]

NET: Neuroendocrine Tumor, MTC: Medullary Thyroid Cancer, PCC: Pheochromocytoma, PGL: Paraganglioma, GEP: Gastroenteropancreatic, Bronc: Bronchial.

Peptides

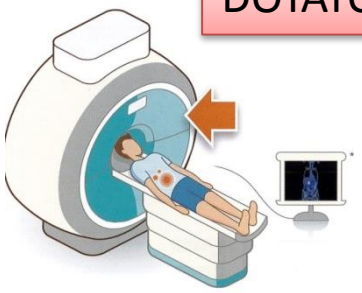


chelating agent



68Ga-DOTA0-Tyr3-Octreo**tate** (68Ga-DOTATATE) or
68Ga-DOTA0-Tyr3-Octreo**tide** (68Ga-DOTATOC),

DOTATOC



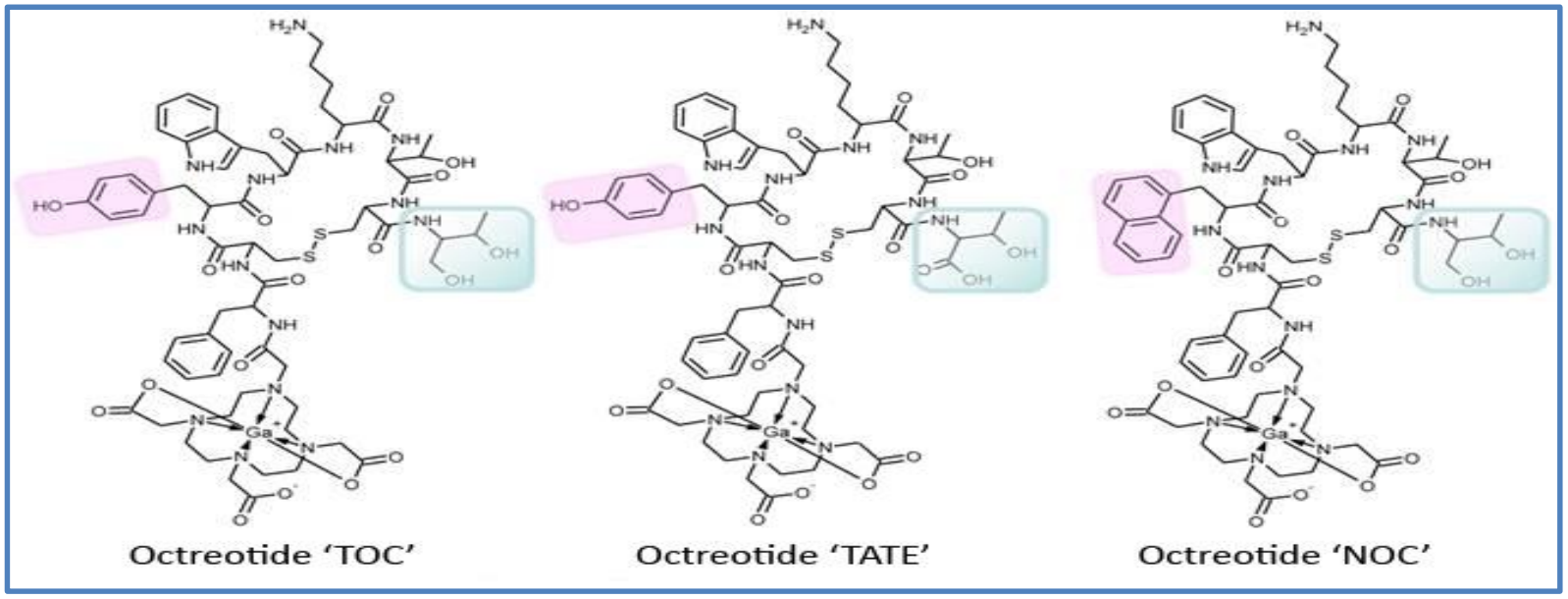
Szymanowski B, et al. Nuclear Med Rev. 2016; 19, 1: 54–57

^{68}Ga

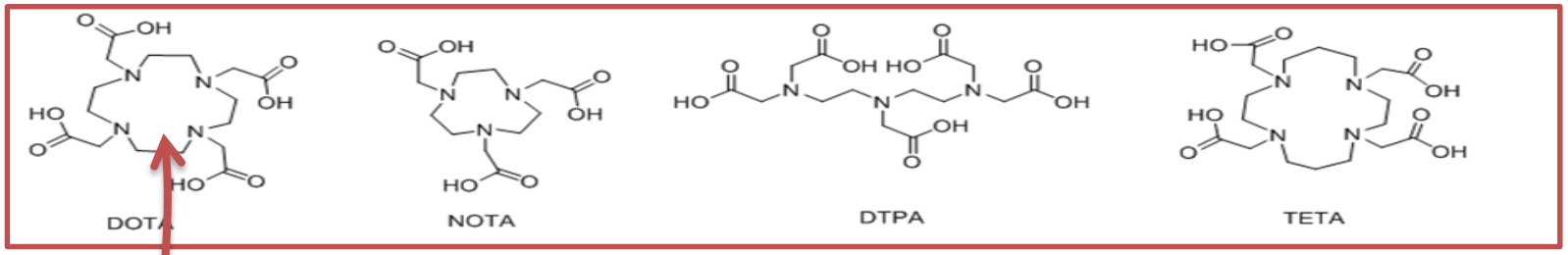
DOTATATE

^{177}Lu

Peptides



chelating agent



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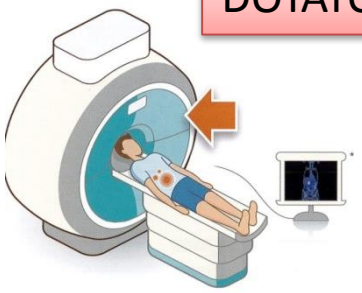
68Ga-DOTA0-Tyr3-Octreo**tide** (68Ga-DOTATOC),

DOTATOC

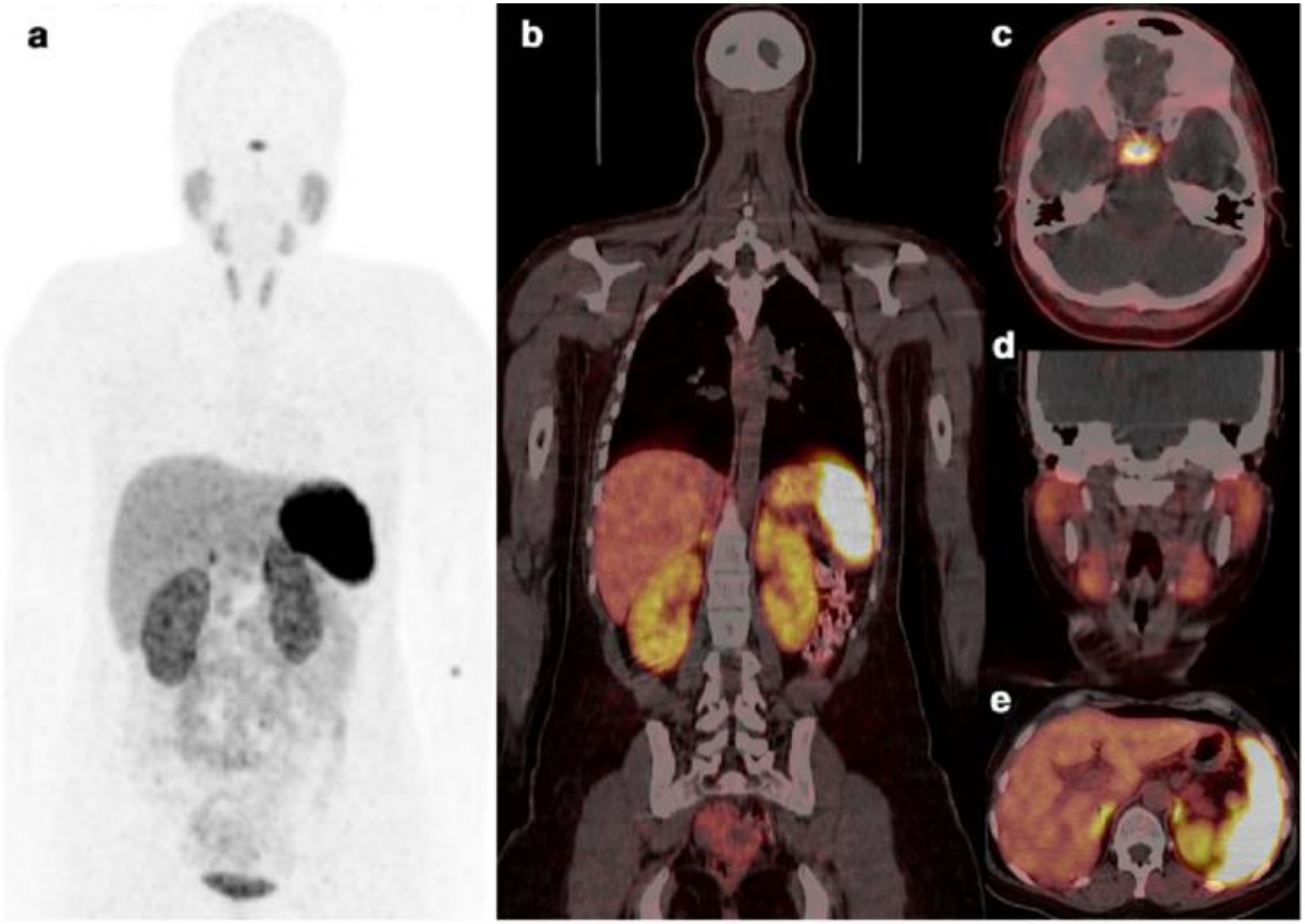


^{68}Ga

Szymanowski B, et al. Nuclear Med Rev. 2016; 19, 1: 54–57

DOTATATE

^{177}Lu



Kuyuncu, Annals of Nucl Med, 2013

^{68}Ga-DOTATOC Imaging of Neuroendocrine Tumors: A Systematic Review and Metaanalysis

Michael M. Graham[1], Xiaomei Gu[2], Timothy Ginader[3], Patrick Breheny[3], and John J. Sunderland[1]

[1]*Division of Nuclear Medicine, L*
Sciences, University of Iowa, Iow

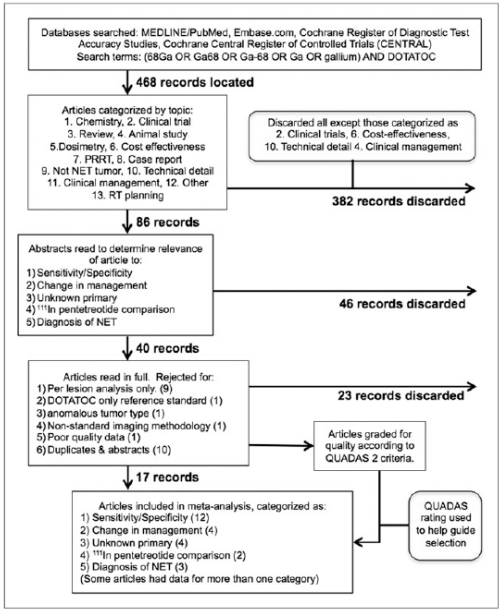


FIGURE 1. Study flow diagram.

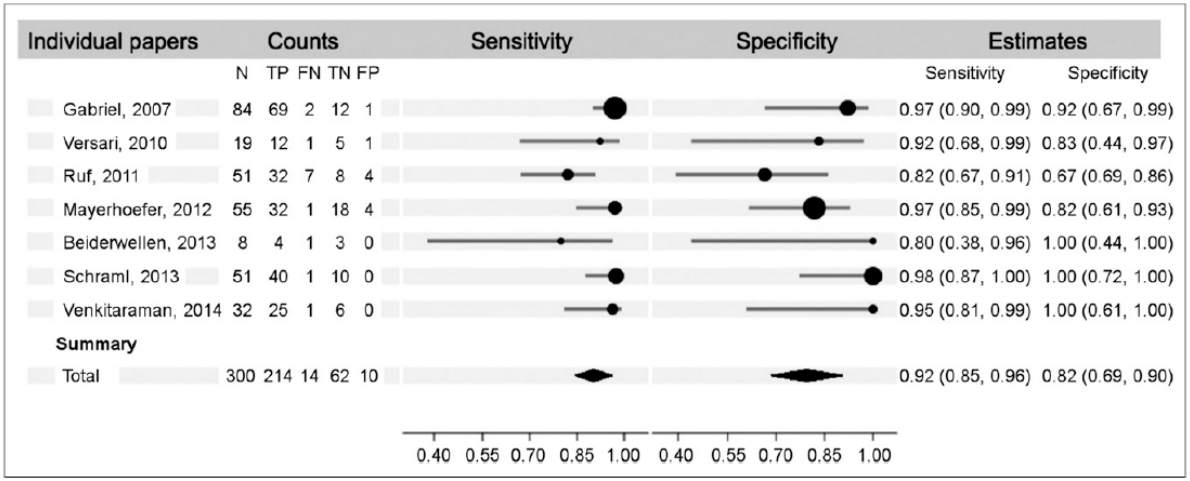


FIGURE 2. Sensitivity and specificity forest plot.

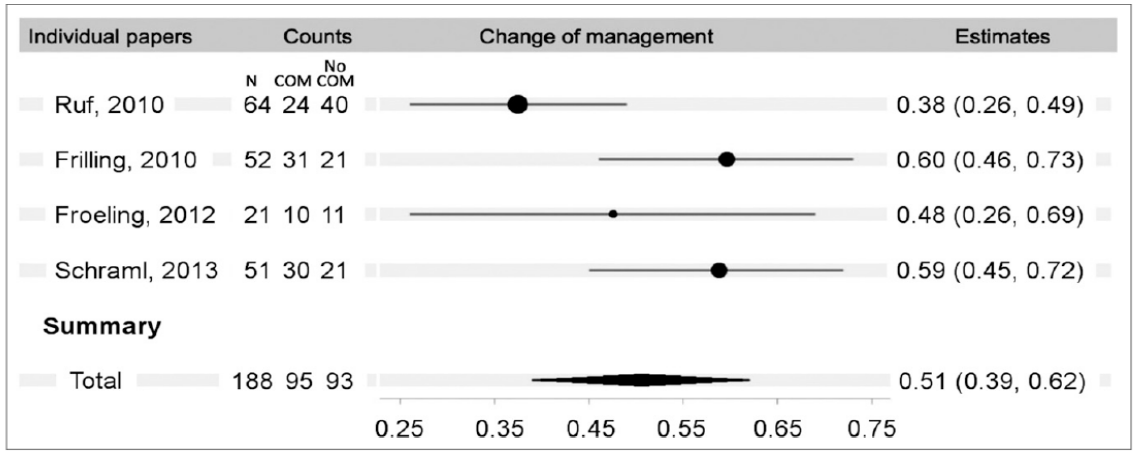


FIGURE 4. Change of management forest plot.

1. TNE iléale métastatique hépatique

^{68}Ga DOTANOC TEP/TDM

Mr CB Jean, 68 ans

Bilan douleurs abdominales

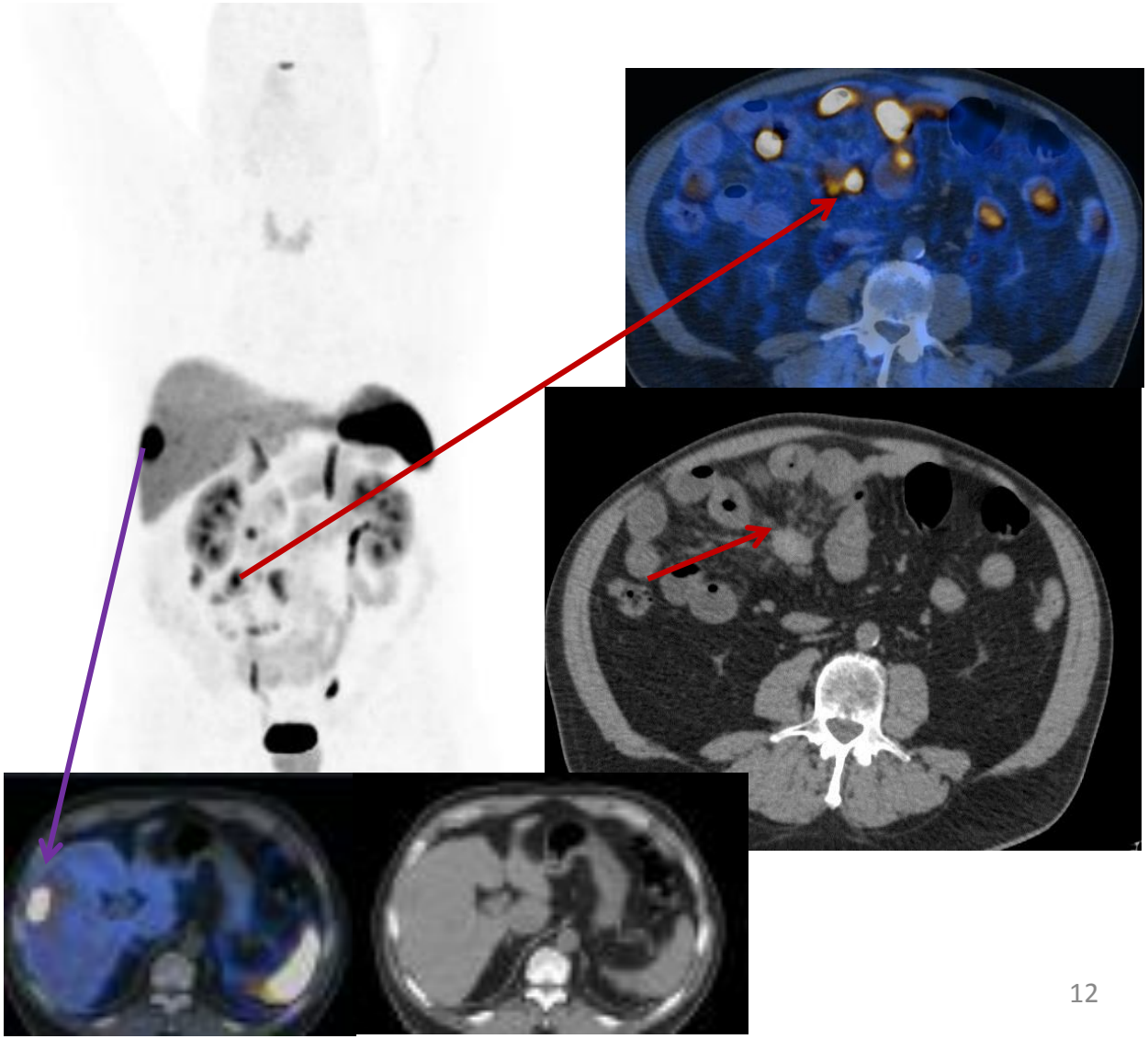
CgA x6 Normale

TEP-TDM ^{68}Ga DOTANOC:

-lésion rétractile mésentérique

-lésion hépatique secondaire

Intérêt du TDM



2. TNE pancréatique métastatique hépatique

Mr MC Kurt, 51 ans

Recherche primitif

Devant métastases hépatiques, splénique et thrombose veine splénique- biopsie TNE de grade 2 (Ki 67:5-10%).

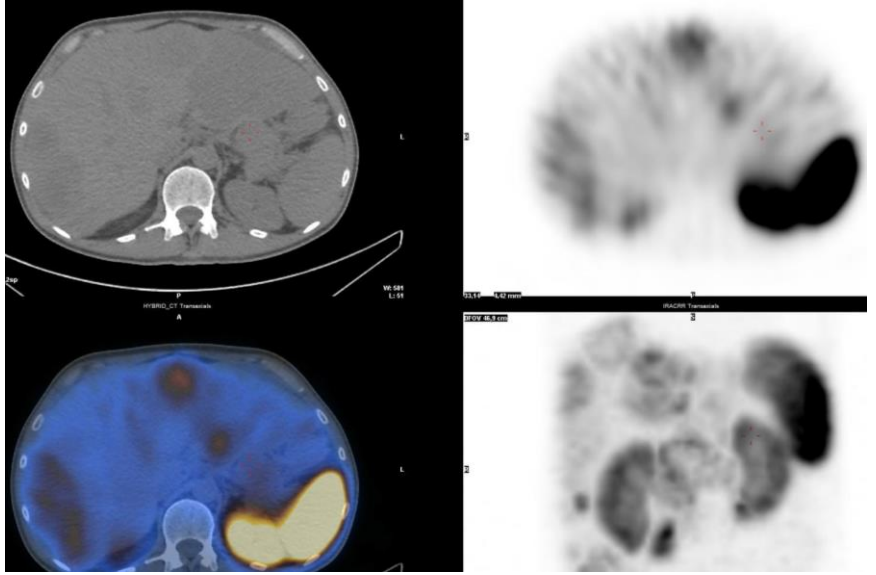
Octreoscan® foyers hépatiques, pas de primitif identifié

TEP TDM ^{68}Ga-DOTANOC:

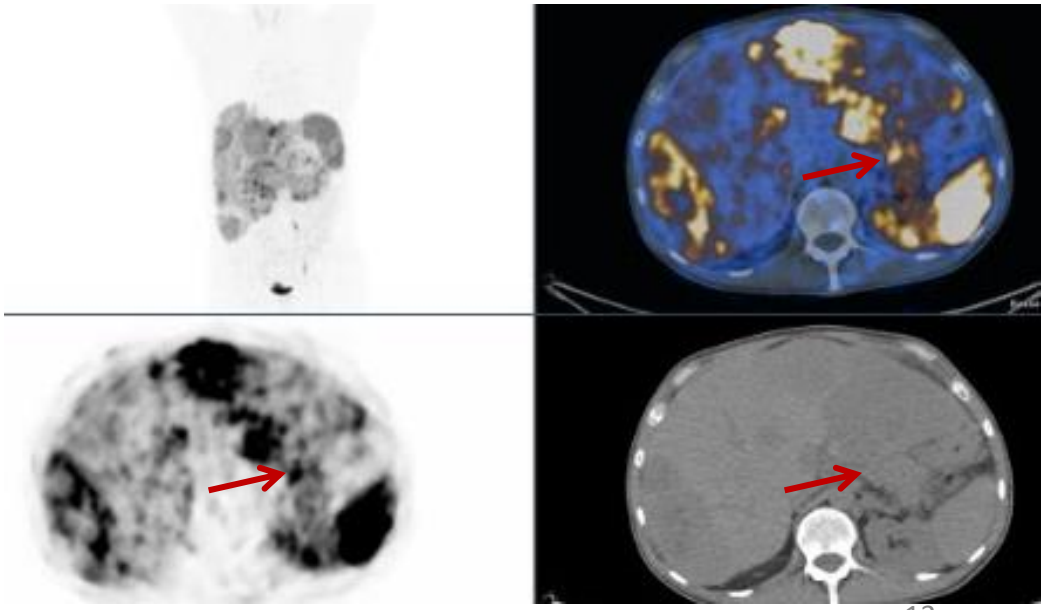
Primitif: queue du pancréas

foyers hépatiques, splénique et ADP mésentérique

Nb Hétérogénéité du « phénotype »



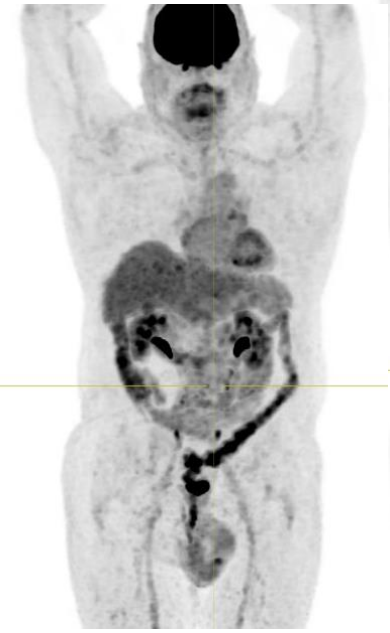
Octreoscan® TEMP/TDM



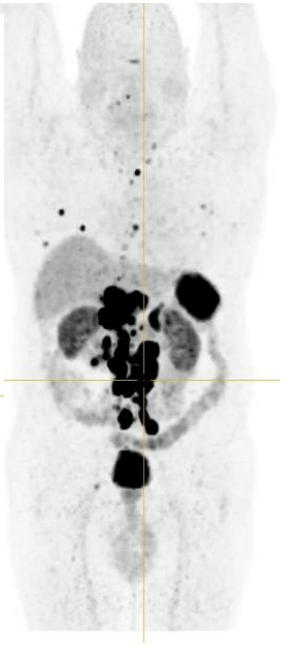
^{68}Ga DOTANOC TEP/TDM

Homme, 68 ans, TNE iléale G2, KI67 5%, M+ ggl et os

FDG -

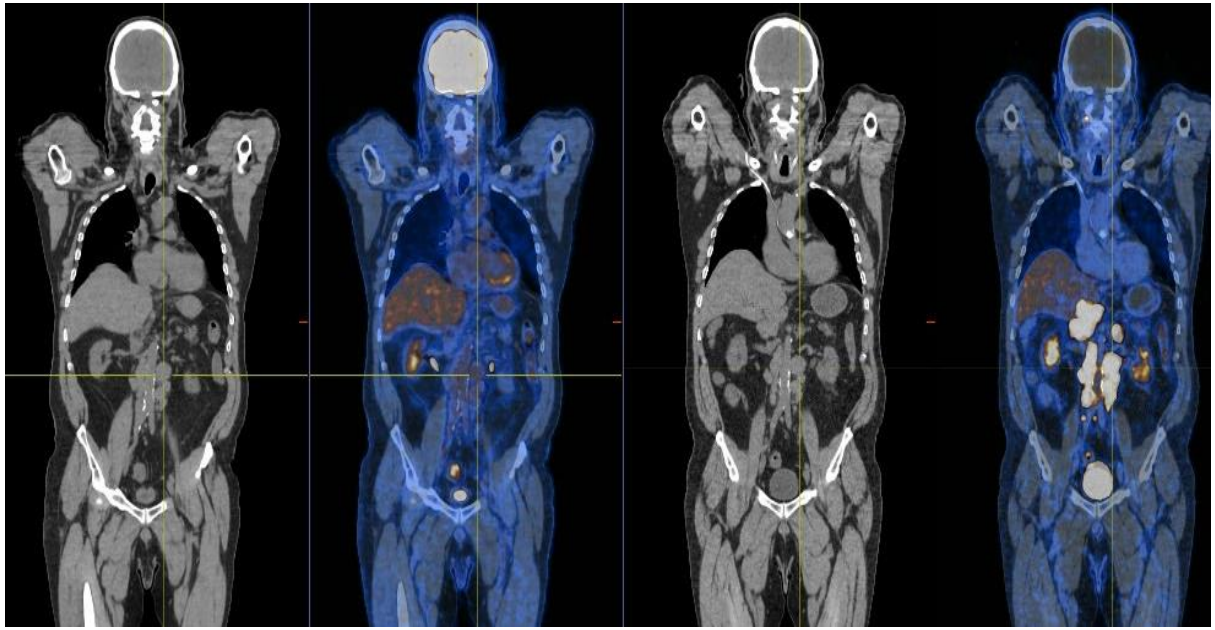


Ga-68 DOTA +++



FDG -

Ga-68 DOTA +++



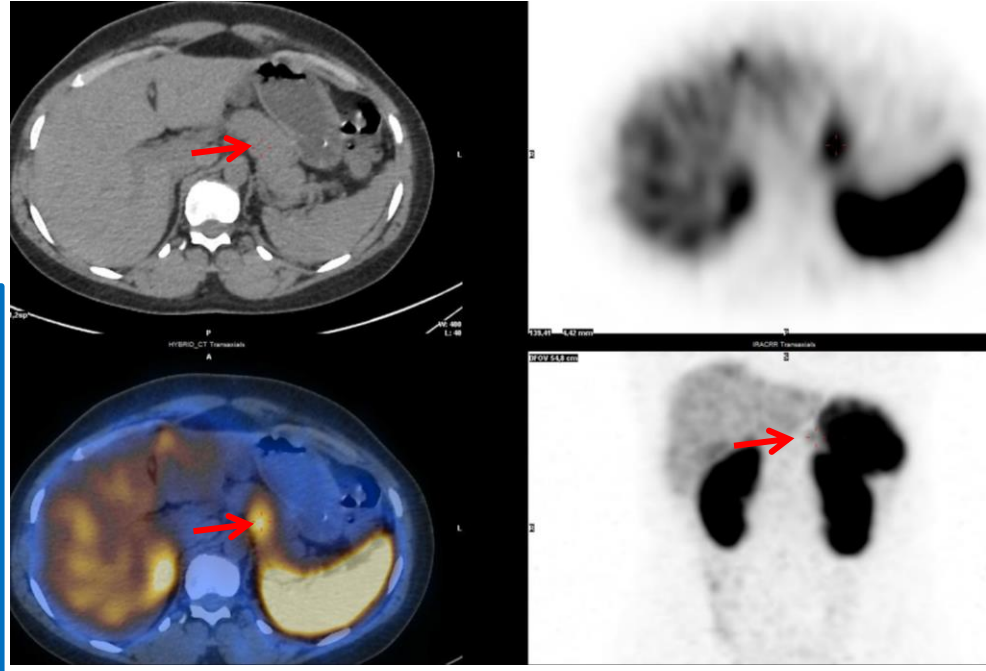
Stabilité biologique et RECIST après 2 injections Lu-177 PRRT

BJJ, IUCT-O

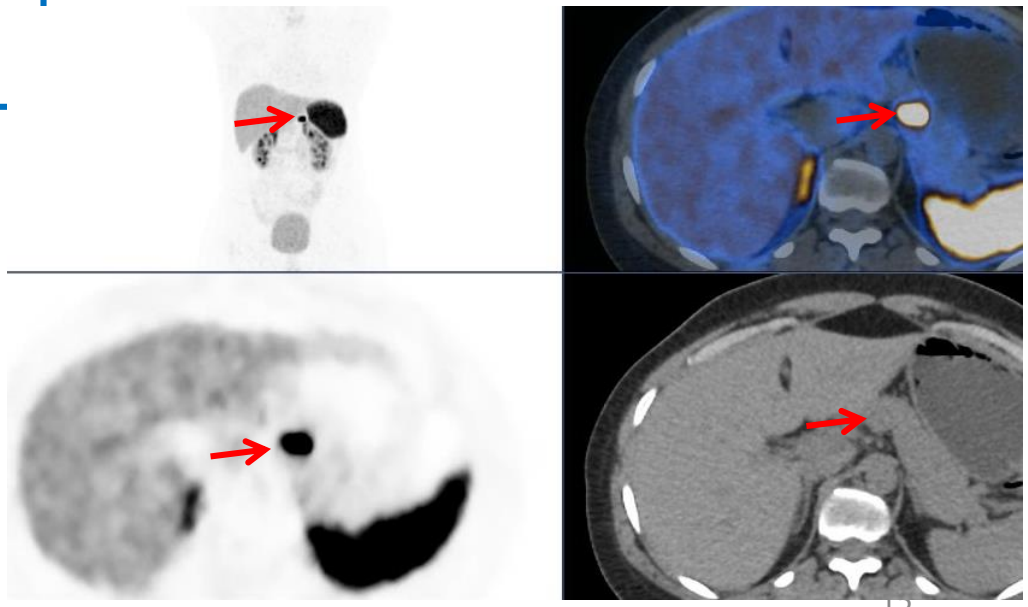
3. Insulinome

Patiente, 34 ans, B Nez,

- hypoglycémies fréquentes (0,3 g/L) depuis 6 mois au réveil,
- insulinémies hautes
- Pas de masse pancréatique visible à l'IRM
- Echo-endoscopie- lésion 8 mm de la partie postérieure du corps pancréatique
- **Octreoscan® + TEP TDM ^{68}Ga DOTANOC**: foyer unique de 8 mm du pancréas
- Traitement: pancréatectomie: TNE grade 2 (Ki67 de 4% IHC+ve pour l'insuline)



Octreoscan® TEMP/TDM



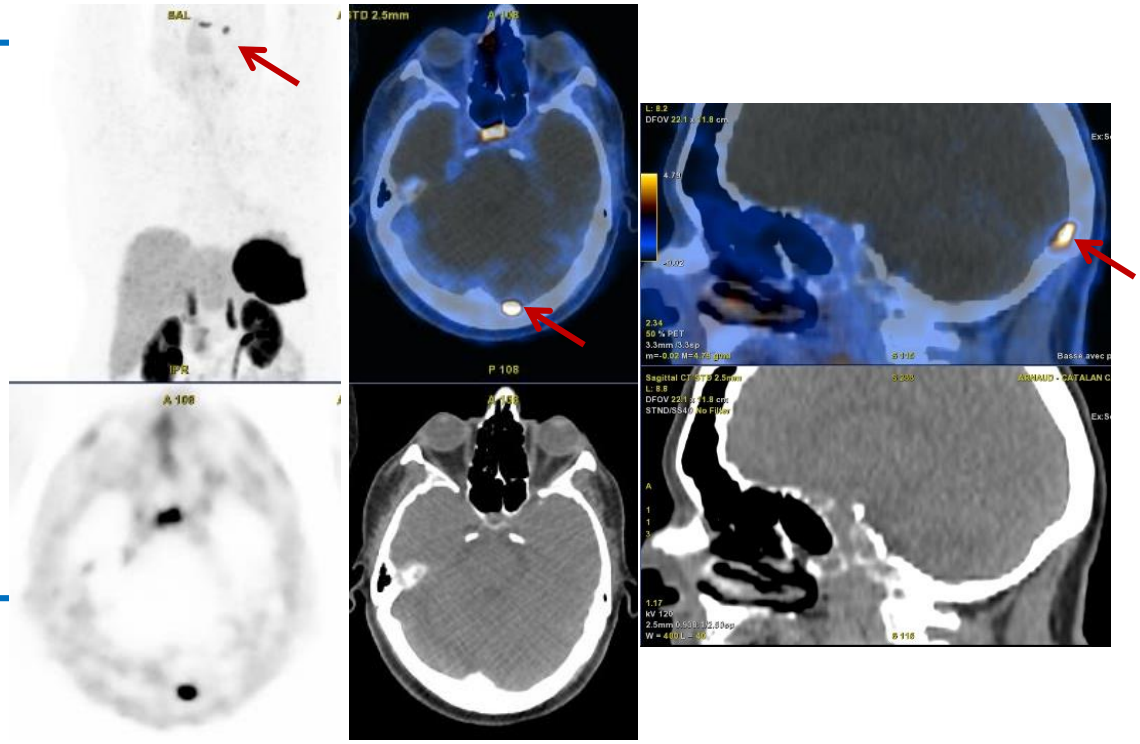
^{68}Ga DOTANOC TEP/TDM

Différence de « contraste »

4. Autre tumeurs détectées par le ^{68}Ga DOTANOC Méningiome

Patiente, 59 ans,

- bilan d'extension d'une tumeur carcinoïde pulmonaire opérée
- TEP/TDM ^{68}Ga DOTANOC:
- Pas de foyer de fixation suspecte pulmonaire ni à distance
- Fixation méningée occipitale isolée-méningiome??



^{68}Ga DOTANOC TEP/TDM

Tout ce qui fixe n'est pas une TNE !

^{68}Ga DOTANOC TEP/TDM : pourquoi faire ?

NCCN Guidelines® Insights
Neuroendocrine and Adrenal Tumors, Version 2.2018
Featured Updates to the NCCN Guidelines

7 « or »

Shah et al J Natl Compr Canc Netw 2018

If complete resection possible[e,ee] → Resect primary[e] + metastases[gg] → Refer to surveillance for appropriate primary disease sites (See NET-1 through NET-4)

Asymptomatic,[ff] low tumor burden → Observe with markers and abdominal/pelvic multiphasic[c] CT or MRI every 3–12 mo, and chest CT (± contrast) as clinically indicated
or
Octreotide[o,hh] or lanreotide[o,hh] →

Locally symptomatic from primary tumor → Consider resection of primary tumor[e] →

Clinically significant tumor burden → Octreotide[o,hh] or lanreotide[o,hh] →

Follow with abdominal/pelvic multiphasic CT or MRI every 3–12 mo, and chest CT (± contrast) as clinically indicated

If disease progression, Octreotide[o,hh] or lanreotide[o,hh] (if not already receiving) →

If disease progression[bb]:
Everolimus[o] (10 mg/d)
or
PRRT with ^{177}Lu-dotatate, if somatostatin receptor positive imaging (category 1 for mid-gut tumors)[o,aa]
or
Hepatic-directed therapy for hepatic-predominant disease:
- Arterial embolization, or
- Hepatic chemoembolization, or
- Hepatic radioembolization (category 2B), or
- Cytoreductive surgery/ablative therapy[gg,ii] (category 2B)

or
Interferon alfa-2b[o] (category 3)
or
Cytotoxic chemotherapy[o] (category 3), if no other options feasible

al Testing (NE-B).

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Rx Imaging

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Featured Updates to the NCCN Guidelines

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Shah et al J Natl Compr Canc Netw 2018

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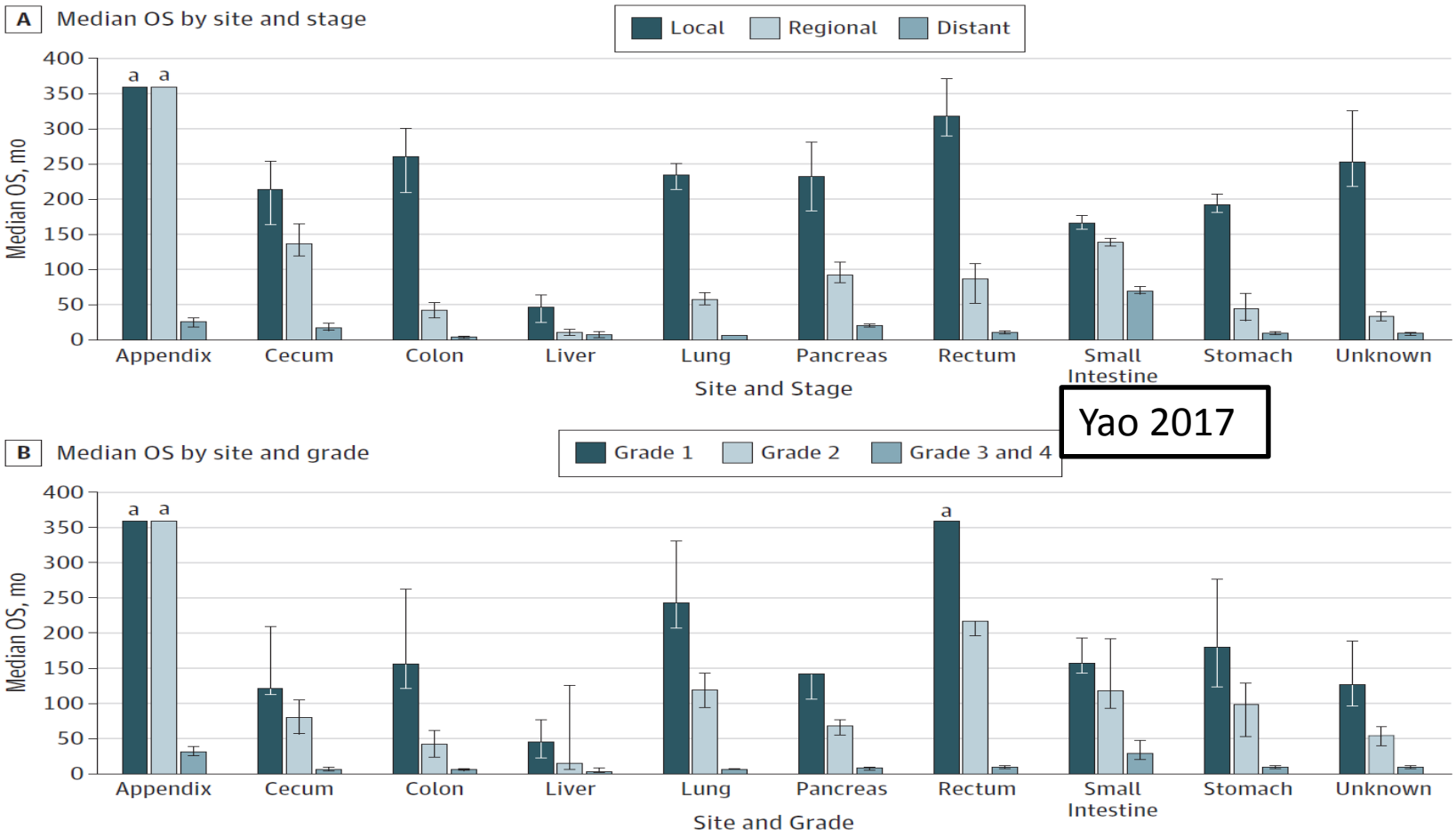
al Testing (NE-B).

Theranostic

Rx Imaging

Location – Stage - Differenciation - Proliferation (Ki67) - Grade

Figure 3. Median Overall Survival (OS) of Neuroendocrine Tumors



Yao 2017

Nb WHO 2017	Well Differentiated and Poorly Differentiated G3

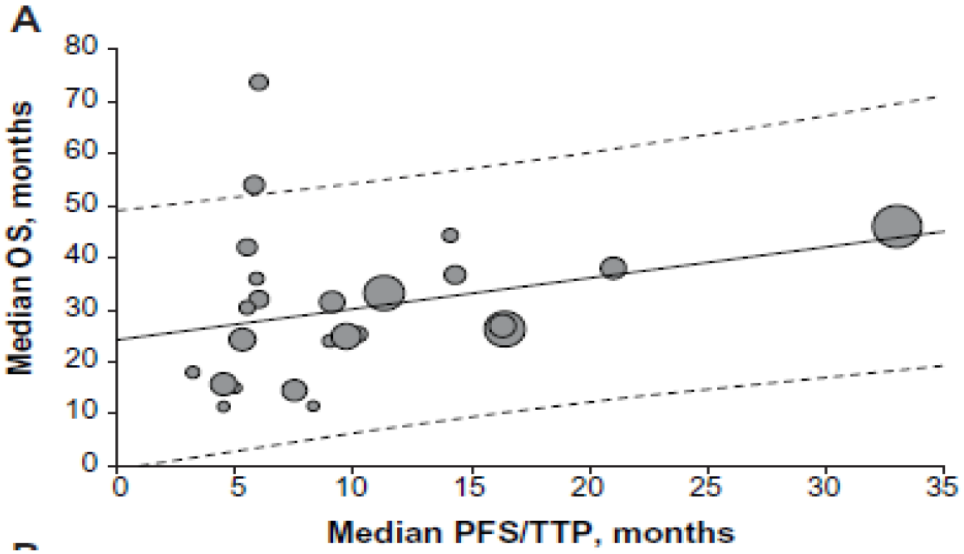
Medical Imaging : staging :

- T US CT, MRI (PET)
- N US CT, MRI(liver), **PET**
- M US CT, MRI(liver), **PET**

Medical Imaging : staging :

- T US CT, MRI (PET)
- N US CT, MRI(liver), **PET**
- M US CT, MRI(liver), **PET**

NB Progression rate !



Singh S et al 2014 : 22 essais , 2584 patients

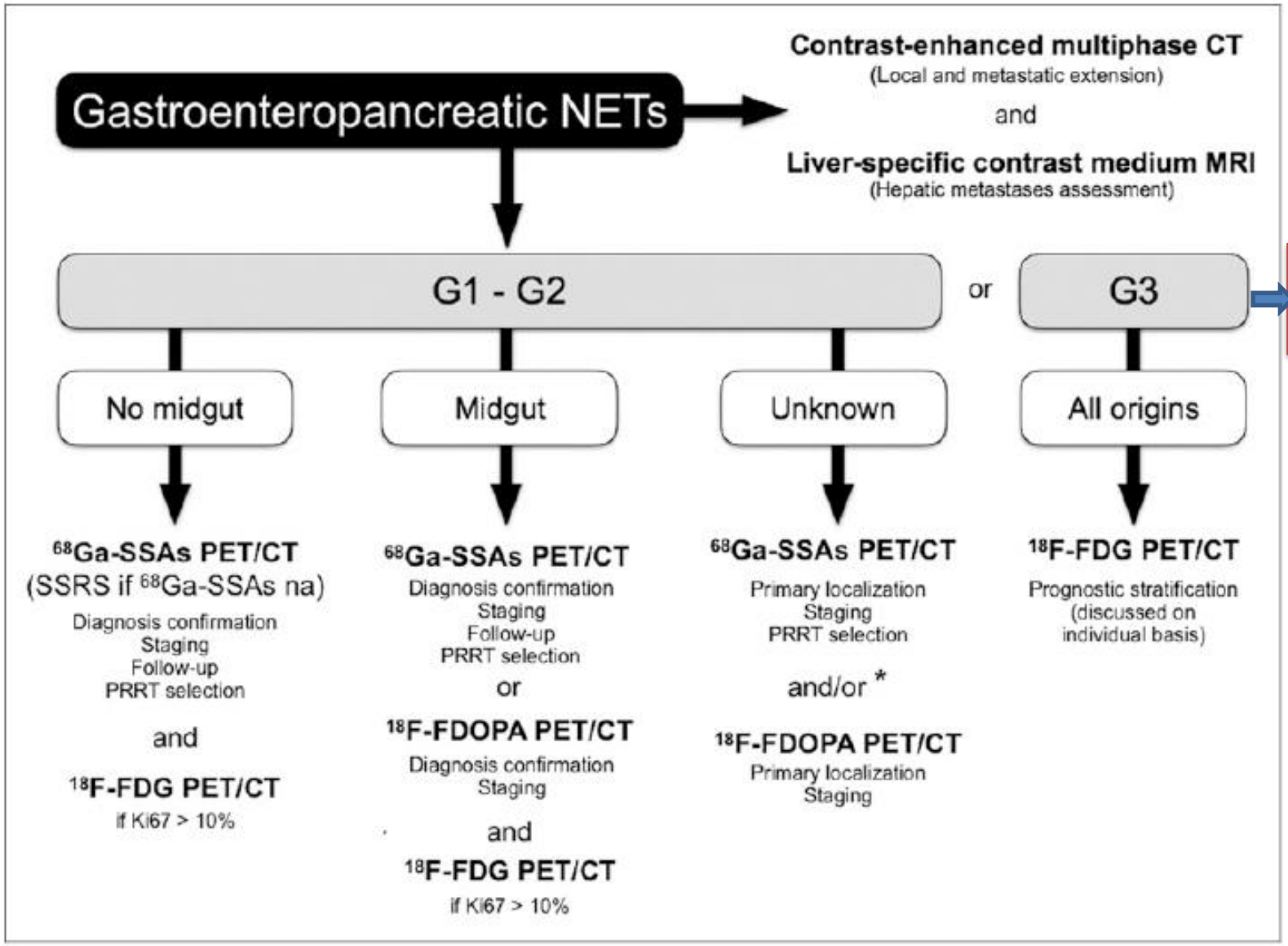
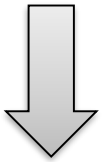


FIGURE 6. Proposed diagnostic imaging algorithm for patients with GEP NETs. na = not available; SSRS = SSTR scintigraphy. *Based on presumption of origin and hormonal secretion if present.

Adapted from Imperiale et al

From *in vitro* to *in vivo* whole body "grading"



Bosman FT, World Health Organization., International Agency for Research on Cancer. *WHO classification of tumours of the digestive system (page 211)*. 4th ed. Lyon: International Agency for Research on Cancer; 2010.

Velayoudom-Cephise et al. Are G3 ENETS neuroendocrine neoplasms heterogeneous? *Endocr Relat Cancer.* 2013;20:649-657.

Milione M, et al. The Clinicopathologic Heterogeneity of Grade 3 Gastroenteropancreatic Neuroendocrine Neoplasms: Morphological Differentiation and Proliferation Identify Different Prognostic Categories. *Neuroendocrinology.* 2017;104:85-93.

From *in vitro* to *in vivo* whole body "grading"

Table 1. 2010 WHO grading system for NENs

Differentiation	Grade	Proliferative Rate	
		Lung and Thymus NENs[6]	Gastroenteropancreatic NENs[6]
Well-differentiated	G1 (low grade)	< 2 mitoses/10 hpf AND no necrosis	< 2 mitoses/10 hpf AND < 3% Ki-67 index
	G2 (intermediate grade)	2-10 mitoses/10 hpf OR necrosis	2-20 mitoses/10 hpf OR 3-20% Ki-67 index
Poorly differentiated	G3 (high grade)	> 10 mitoses/10 hpf	> 20 mitoses/10 hpf OR > 20% Ki-67 index

Abbreviations: NEN, neuroendocrine neoplasm; G1, grade 1; G2, grade 2; G3, grade 3; hpf, high power field

Table 2. 2017 WHO grading system for pancreatic NENs

Differentiation	Grade	Mitotic Index	Proliferative Rate
Well-differentiated NET	G1 (low grade)	< 2 mitoses/10 hpf	< 3% Ki-67 index
	G2 (intermediate grade)	2-20 mitoses/10 hpf	3-20% Ki-67 index
	G3 (high grade)	> 20 mitoses/10 hpf	> 20% Ki-67 index
Poorly differentiated NEC Small cell type Large cell type	G3 (high grade)	> 20 mitoses/10 hpf	> 20% Ki-67 index

Abbreviations: NEN, neuroendocrine neoplasm; NET, neuroendocrine tumor; NEC, neuroendocrine carcinoma; G1, grade 1; G2, grade 2; G3, grade 3; hpf, high power field

Well D and Poorly D G3

Bosman FT, World Health Organization., International Agency for Research on Cancer. *WHO classification of tumours of the digestive system (page 211)*. 4th ed. Lyon: International Agency for Research on Cancer; 2010.

Velayoudom-Cephise et al. Are G3 ENETS neuroendocrine neoplasms heterogeneous? *Endocr Relat Cancer.* 2013;20:649-657.

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Well-differentiated grade 3 neuroendocrine tumours and poorly differentiated grade 3 neuroendocrine carcinomas: will dual tracer PET-computed tomography (^{68}Ga-DOTATATE and FDG) play a pivotal role in differentiation and guiding management strategies?

Sandip Basu[a,b] and Aadil Adnan[a,b] [a]Radiation Medicine Centre, Bhabha Atomic Research Centre, Tata Memorial Centre Annexe and [b]Homi Bhabha National Institute, Mumbai, India

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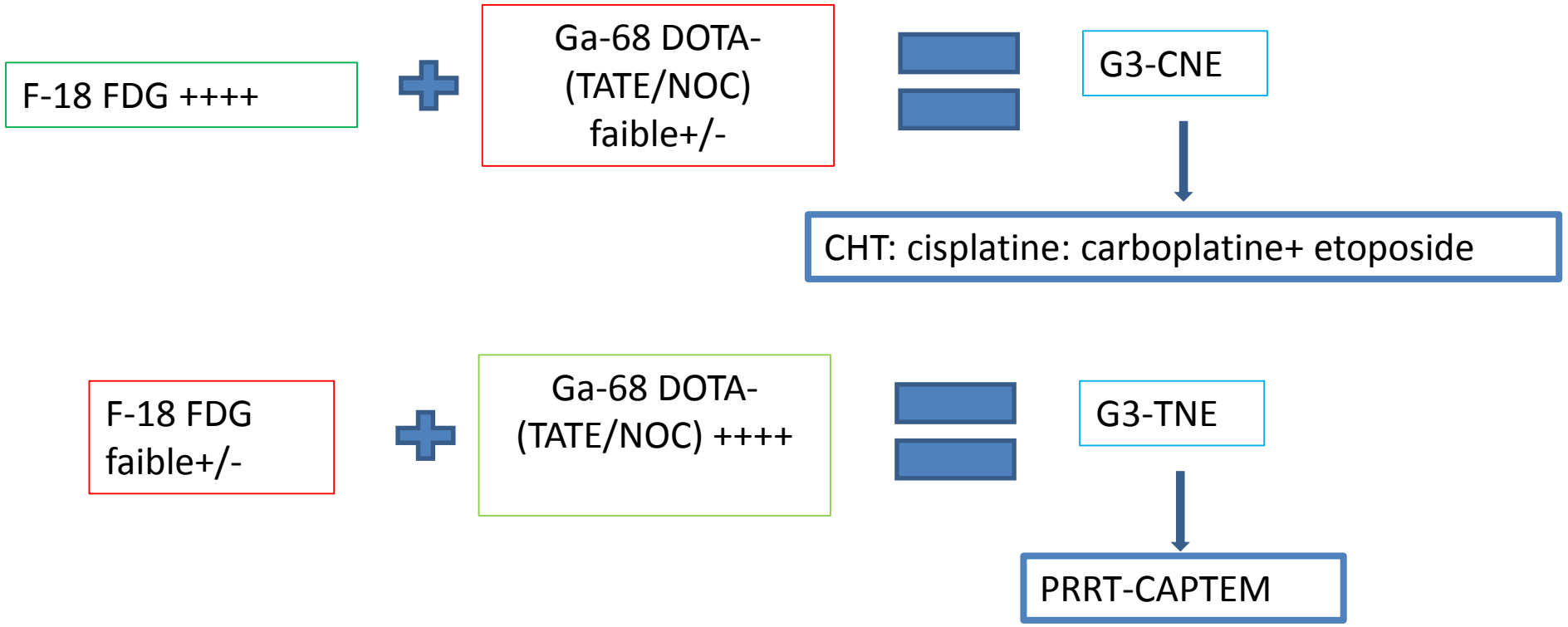
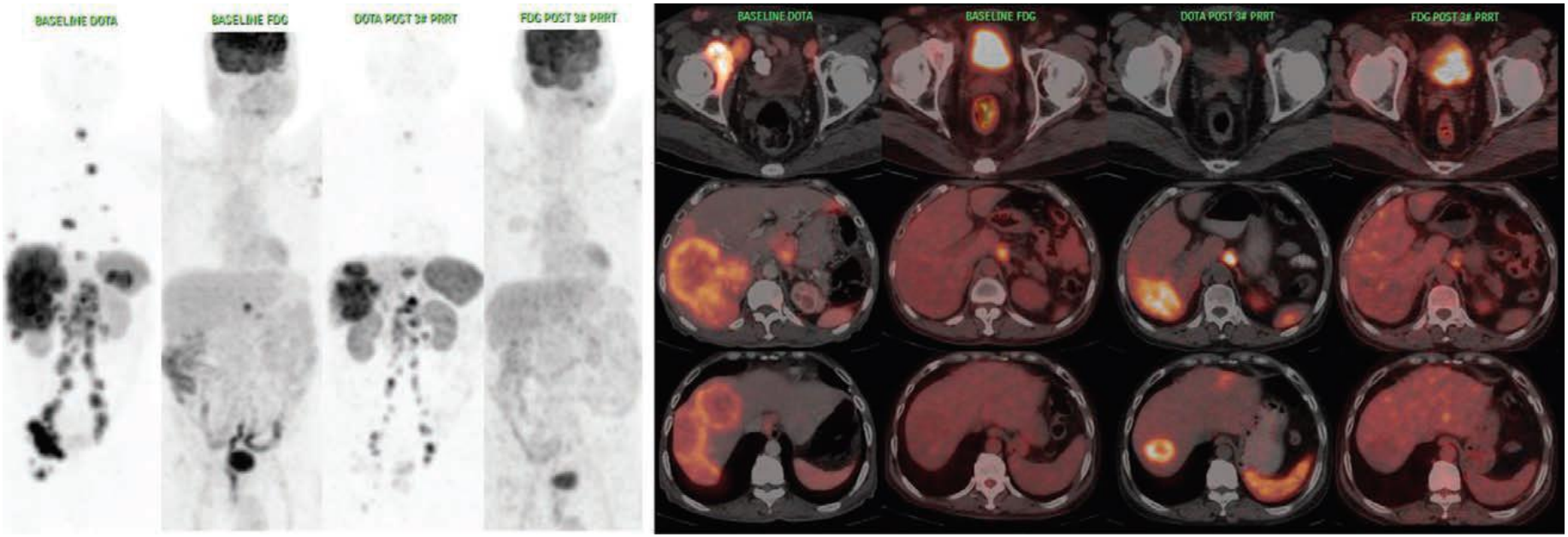
Received 8 June 2019 **Accepted** 27 June 2019

TEP et stratification des TNE G3
TNE G3 (bien diff) vs CNE G3 (peu diff)



Basu S, Nucl Med Comm, 2019

Homme, 61 ans
TNE occulte, G3 (MIB-1: 25%), M+ hépatique, ganglionnaire en sus et sous diaphragmatique et osseux
Avant et après 3 inj Lu-177 PRRT



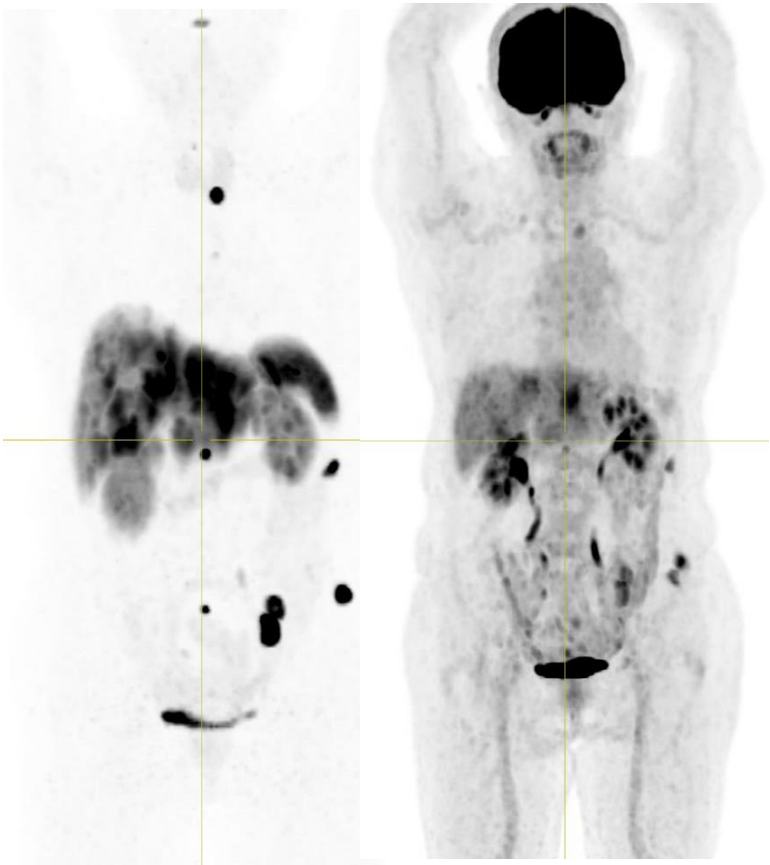
Biologie tumorale favorable: bonne réponse au traitement

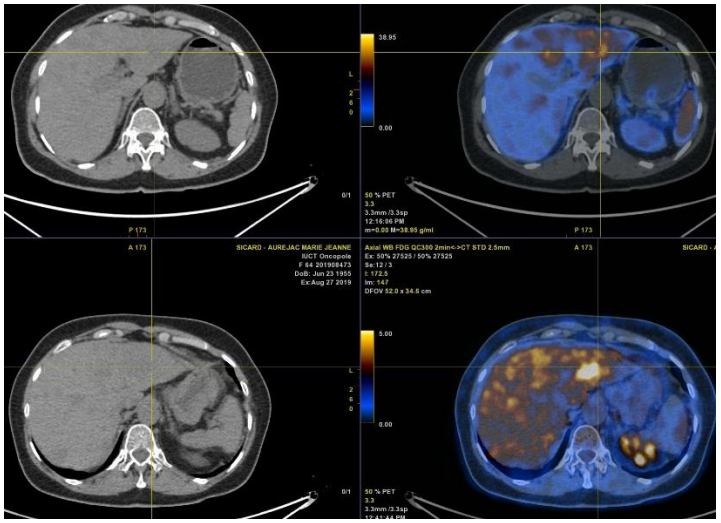
Basu S, Nucl Med Comm, 2019

Femme, 64 ans, TNE G3 pancréas ,M+ foie+os
ultérieurement relecture RENATEN Ki67 18% G2 ??

Ga-68 DOTA +++

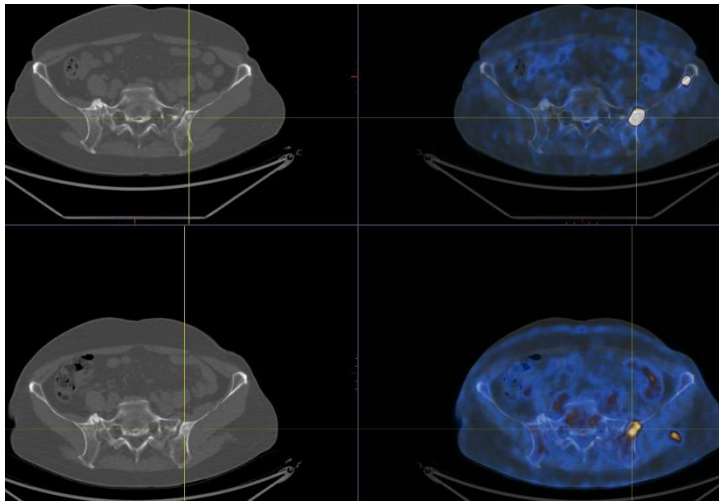
FDG +





FDG +

Ga-68 DOTA +++



Ga-68 DOTA +++

FDG +

SAMJ, IUCT-O

^{68}Ga DOTApeptides.. , ^{18}F DOPA, ^{18}FDG ?

^{18}F-FDOPA PET/CT should be included systematically in the preoperative work-up of Small Bowel NET. Imperiale et al 2018

See also

Montravers F, et al. Impact of fluorodihydroxyphenylalanine-18F positron emission tomography on management of adult patients with documented or occult digestive endocrine tumors. J Clin Endocrinol Metab. 2009;94:1295–1301.

Koopmans KP, et al. Staging of carcinoid tumours with 18FDOPA PET: a prospective, diagnostic accuracy study. Lancet Oncol. 2006;7:728–734.

Pape UF,. ENETS Consensus Guidelines for the management of patients with neuroendocrine neoplasms from the jejuno-ileum and the appendix including goblet cell carcinomas. *Neuroendocrinology.* 2012;95:135-156.

Hope TA, et al. Appropriate Use Criteria for Somatostatin Receptor PET Imaging in Neuroendocrine Tumors. *J Nucl Med.* 2018;59:66-74.

The Impact of Somatostatin Receptor–Directed PET/CT on the Management of Patients with Neuroendocrine Tumor: A Systematic Review and Meta-Analysis

JNM 2017

Martin Barrio[1], Johannes Czernin[1], Stefano Fanti[2], Valentina Ambrosini[2], Ina Binse[3], Lin Du[4], Matthias Eiber[1], Ken Herrmann[1,3], and Wolfgang P. Fendler[1,5]

1561 pts

- TT changes 44% (range, 16%–71%)

TABLE 2
Change in Management in Patients with Prior Octreoscan

Study	Radioligand	No. of patients	Change in management
Srirajaskanthan et al. (*21*)	^{68}Ga-DOTATATE	51	36 (71%)
Krausz et al. (*12*)	^{68}Ga-DOTANOC	19	3 (16%)
Sadowski et al. (*20*)	^{68}Ga-DOTATATE	130	43 (33%)
Deppen et al. (*22*)	^{68}Ga-DOTATATE	78	28 (36%)

SRS imaging = In vivo whole body "R SST2 expression assay"

^{111}In DTPA OCTREOTIDE SCINTIGRAPHY

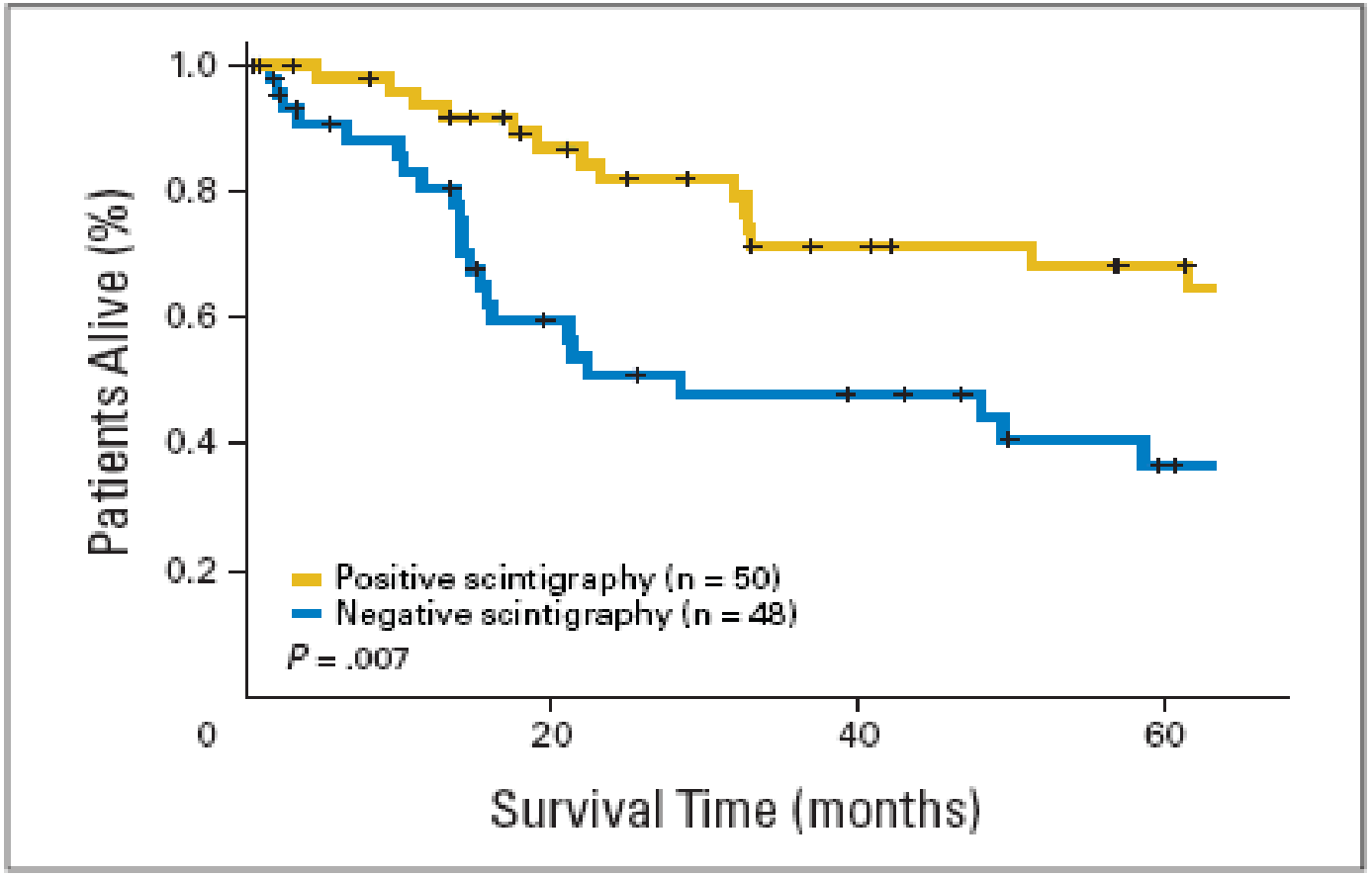


Fig 2. Survival analysis of the two groups of patients with well-differentiated endocrine carcinoma using Kaplan-Meier method.

Asnacios et al JCO 2008

FDG : In vivo whole body "proliferation assay"

^{18}F Deoxy Glucose PET

SRS Neg FDG Pos

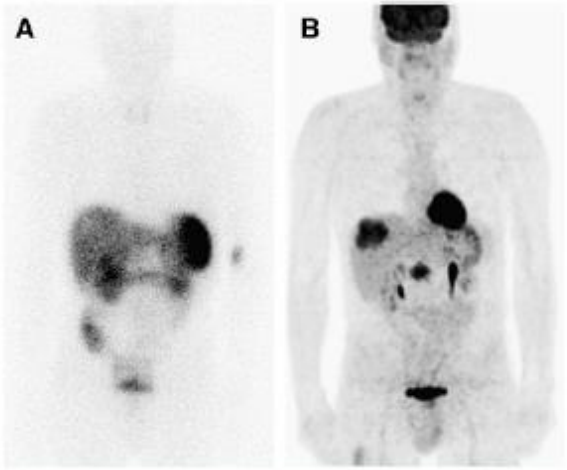
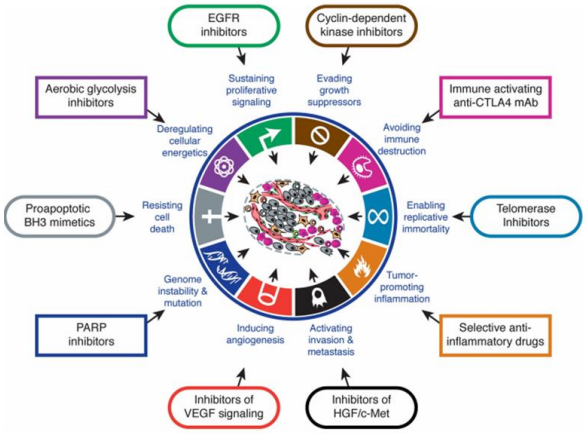


FIGURE 1. A 63-y-old patient who has liver metastases of pancreatic low-grade endocrine tumor. (A) SRS shows no uptake. (B) PET shows intense uptake in pancreatic tumor (SUV, 14.6; tumor-to-nontumor ratio, 6.3) and in liver metastases (SUV, 9.9; tumor-to-nontumor ratio, 4.3). Ki67 immunostaining was less than 2%; p53 immunostaining was 18%. Disease progressed at 3 mo.



Hanahan D, Cell, 2011; 144:646-74

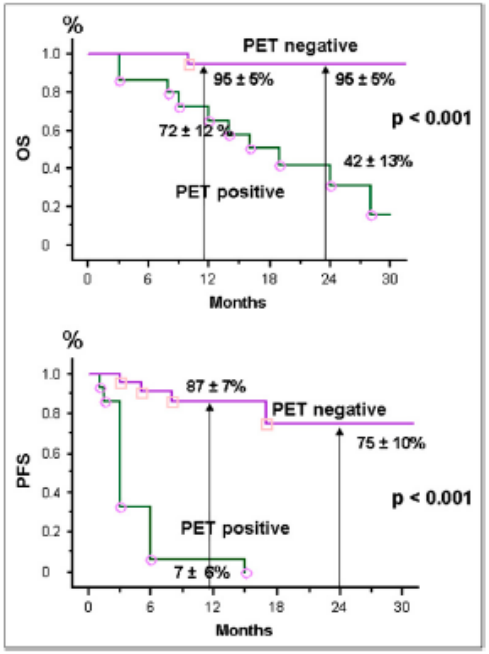


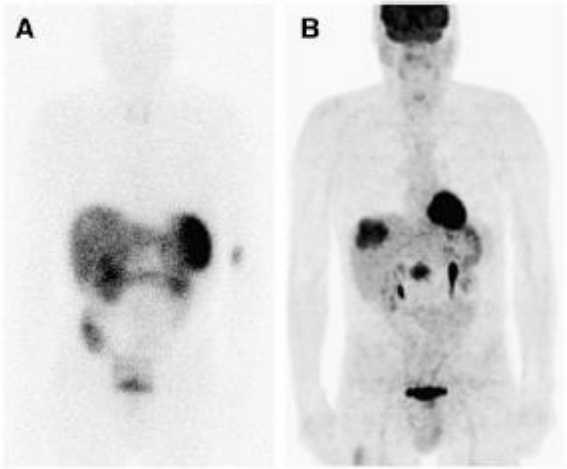
FIGURE 3. Progression-free survival (PFS) and overall survival (OS) are significantly ($P < 0.001$) better in PET-negative patients than in PET-positive patients; $n = 38$.

Garin et al

FDG : In vivo whole body "proliferation assay"

^{18}F Deoxy Glucose PET

SRS Neg FDG Pos



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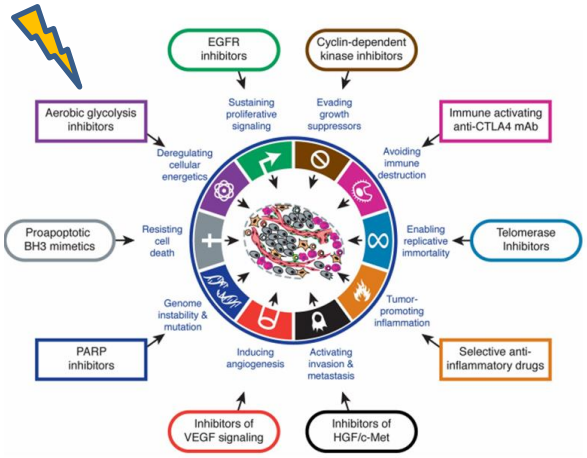

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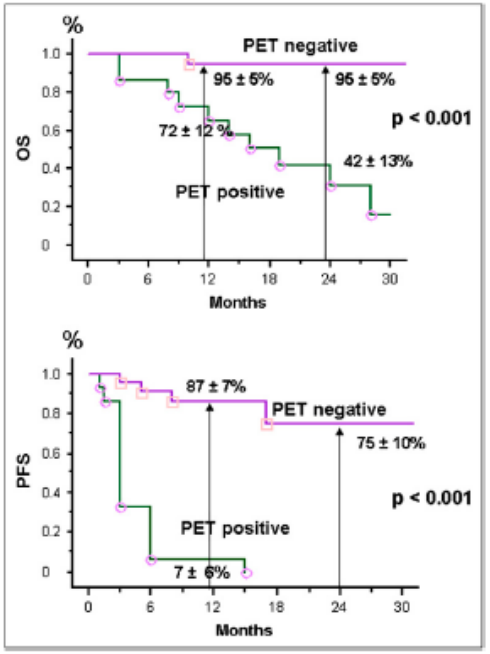

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Garin et al

Theranostics 2017, Vol. 7, Issue 5 1159

IVYSPRING INTERNATIONAL PUBLISHER

Theranostics

2017; 7(5): 1159-1163. doi: 10.7150/thno.19588

Editorial

The NETPET Score: Combining FDG and Somatostatin Receptor Imaging for Optimal Management of Patients with Metastatic Well-Differentiated Neuroendocrine Tumors

Elif Hindié

Metastatic disease heterogeneity

Whole Body « grading »

Eur J Nucl Med Mol Imaging (2014) 41:2194–2202
DOI 10.1007/s00259-014-2850-3

ORIGINAL ARTICLE

Comparison of the prognostic values of ^{68}Ga-DOTANOC PET/CT and ^{18}F-FDG PET/CT in patients with well-differentiated neuroendocrine tumor

Punit Sharma · Niraj Naswa · Sudhir Suman KC · Luis Andres Alvarado · Alok Kumar Dwivedi · Yashwant Yadav · Rakesh Kumar · Ariachery C. Ammini · Chandrasekhar Bal

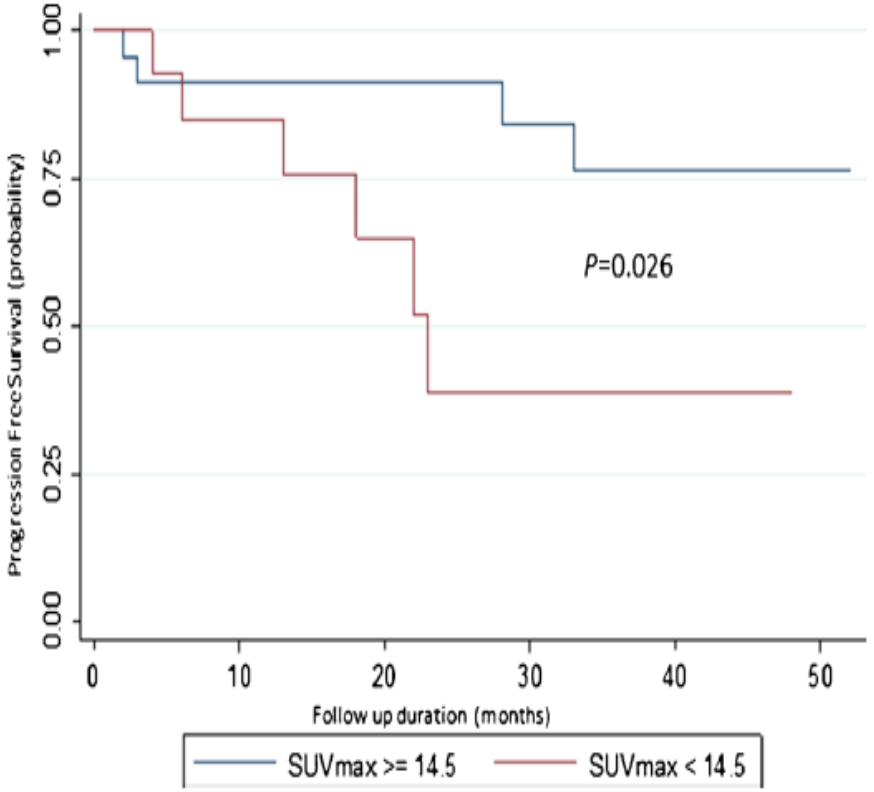


Fig. 4 Kaplan-Meier survival curve for PFS stratified on the basis of ^{68}Ga-DOTANOC SUVmax cut-off derived from the ROC analysis

^{68}Ga-DOTATATE SUVmax G1 > G3 (P = 0.012).
^{68}FDG SUV vs Grade NS !
NEG . Ki-67 vs ^{68}Ga-DOTATATE SUVmax (Spearman r = 20.374, P = 0.001).
POS. Ki-67 vs ^{18}F-FDG SUVmax (r = 20.345, P = 0.002)

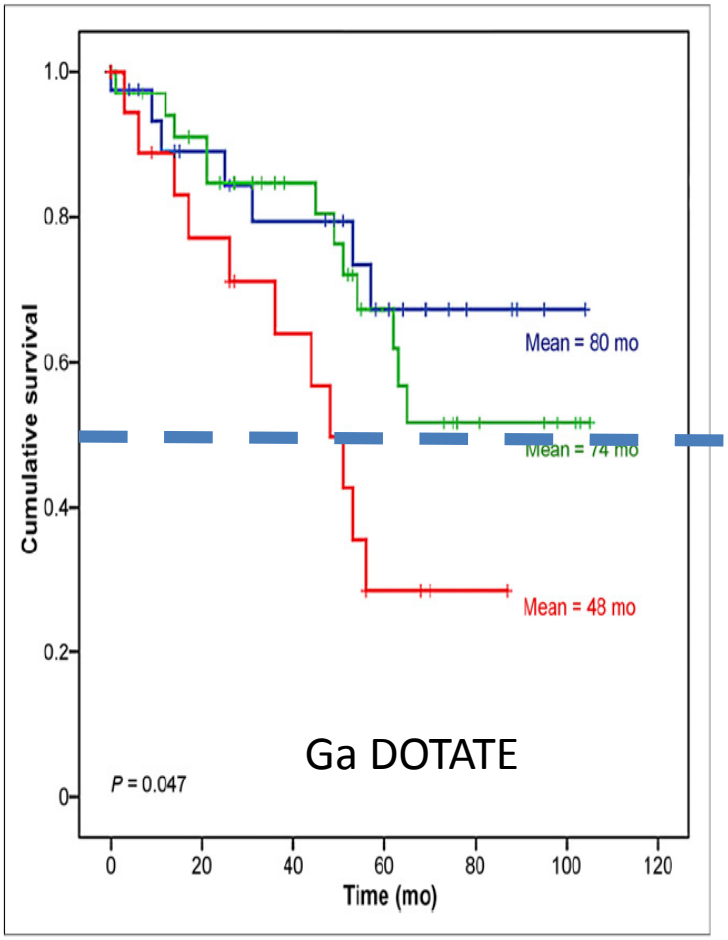


FIGURE 2. Survival curves for patients with bone metastasis (red) vs. soft-tissue metastasis (green) or no metastasis (blue) detected using ^{68}Ga-DOTATATE.

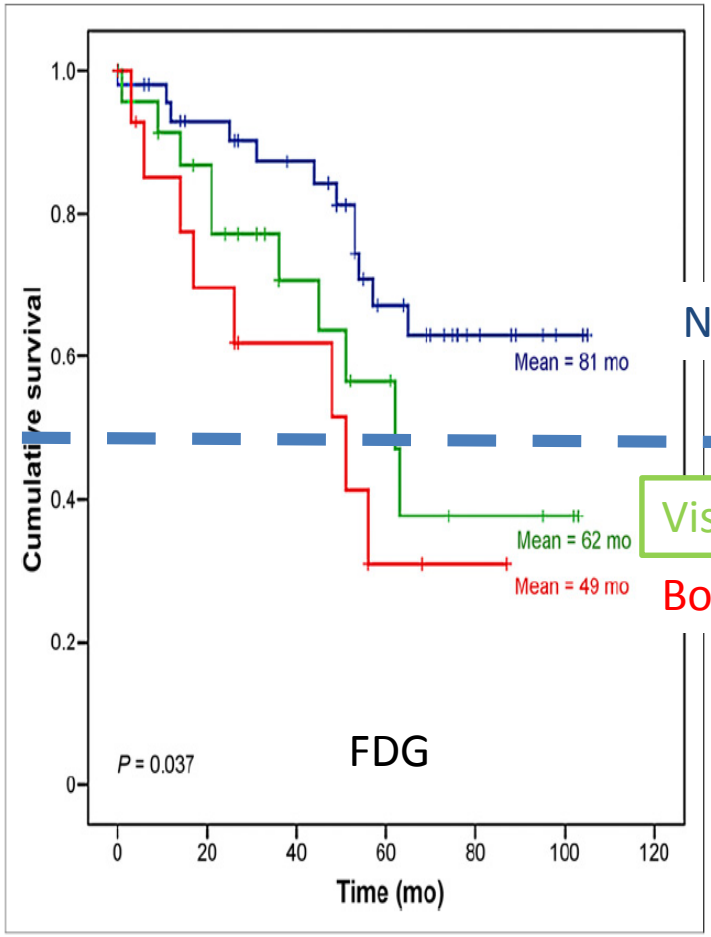
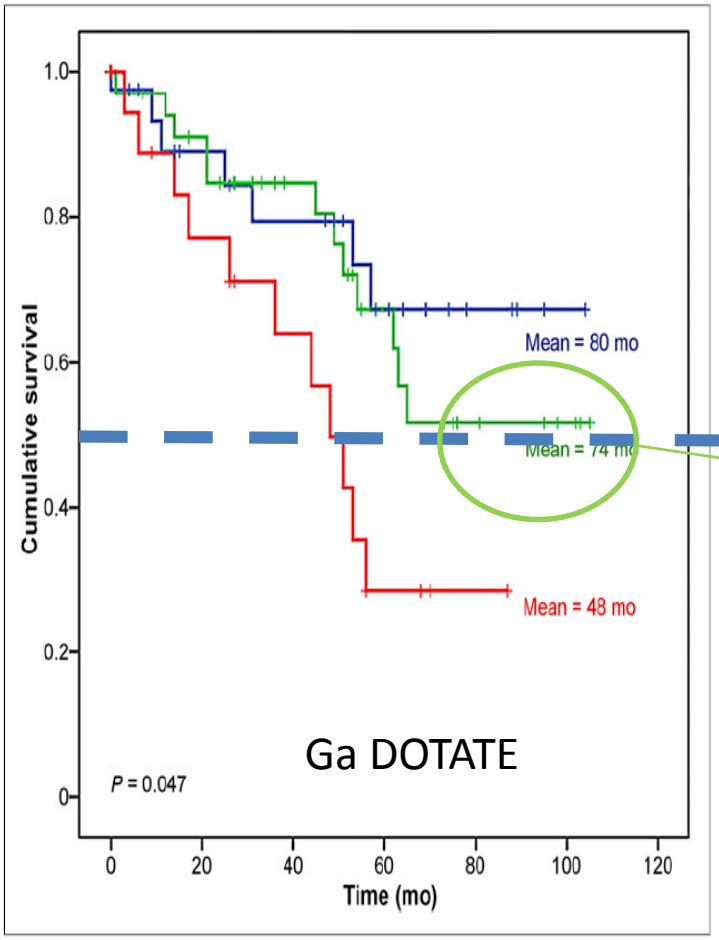


FIGURE 3. Survival curves for patients with bone metastasis (red) vs. soft-tissue metastasis (green) or no metastasis (blue) detected using ^{18}F-FDG.

No Mets

Visceral mets

Bone Mets



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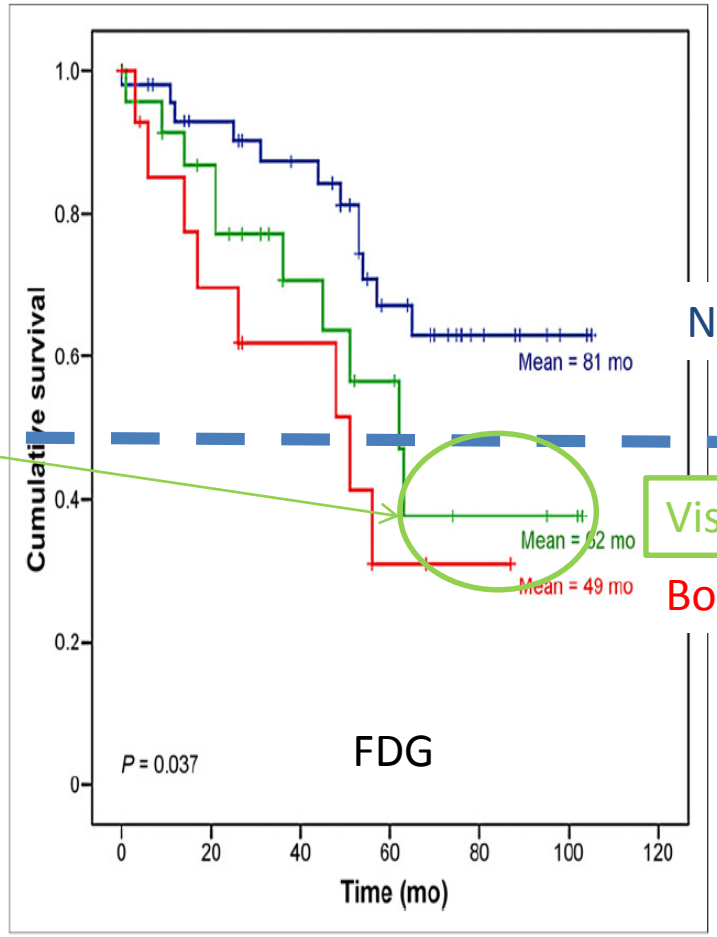


FIGURE 3. Survival curves for patients with bone metastasis (red) vs. soft-tissue metastasis (green) or no metastasis (blue) detected using ^{18}F-FDG.

No Mets

Visceral mets

Bone Mets

Comparison of the Impact of ^{68}Ga-DOTATATE and ^{18}F-FDG PET/CT on Clinical Management in Patients with Neuroendocrine Tumors

JNM 2017

Emmanouil Panagiotidis[1], Alshaima Alshammari[1], Sofia Michopoulou[1], Evangelia Skoura[1], Keval Naik[2], Emmanouil Maragkoudakis[2], Mullan Mohmaduvesh[2], Mohammed Al-Harbi[1], Maria Belda[1], Martyn E. Caplin[2], Christos Toumpanakis[2], and Jamshed Bomanji[1]

[1]Institute of Nuclear Medicine, University College London Hospital, London, United Kingdom; and [2]Neuroendocrine Tumour Unit, ENETS Centre of Excellence, Royal Free Hospital, London, United Kingdom

104 patients 68Ga-DOTATATE + 18F-FDG PET/CT
- 55 H et 49 F ; age médian 58 ans ; (20–90 a).
- 28pts (26.9%) peu différenciée
- 76pts (73.1%) bien différenciée
- SUVs vs grade (G1, G2, or G3), CgA, Ki67

Clinical and Epidemiologic Characteristics of the Patients

Characteristic	*n*	Characteristic	*n*
Sex (*n*)		Primary site (*n*)	
Female	49 (47.1%)	CUP	33 (31.7%)
Male	55 (52.9%)	Midgut	31 (29.8%)
Age (y)		Lung	16 (15.4%)
Median	58	Pancreas	11 (10.6%)
Interquartile range	20–90	Stomach	5 (4.8%)
PET/CT indication		Ovary	4 (3.8%)
Recurrence	57 (54.8%)	Esophagus	3 (2.9%)
Follow-up	13 (12.5%)	Grade (*n*)	
Equivocal CI	13 (12.5%)	G1	36 (34.6%)
Staging	11 (10.6%)	G2	40 (38.5%)
Before PRRT	10 (9.6%)	G3	28 (26.9%)
Recurrence	57 (54.8%)	Chromogranin A (*n*)	
Ki-67 (%)		Strongly positive	88 (84.6%)
Median	6.5	Negative	13 (12.5%)
Interquartile range	1–80	Weakly positive	3 (2.9%)

CUP = cancer of unknown primary; CI = conventional imaging.

NB 68Ga-DOTATATE après SEVRAGE des analogues SMS

TABLE 2
Treatment Before ^{18}F-FDG and ^{68}Ga-DOTATATE PET/CT

Treatment	*n*
Surgery	21 (20.2%)
Active surveillance	20 (19.2%)
Long-acting SSA	13 (12.5%)
None	12 (11.5%)
CMT	11 (10.6%)
Surgery, CMT	10 (9.6%)
Further diagnostic procedure	5 (4.8%)
Surgery, interferon	4 (3.8%)
Surgery, ^{90}Y, SSA	4 (3.8%)
PRRT	1 (1.0%)
Surgery, CMT, SSA, TACE, LDT	1 (1.0%)
Surgery, radiofrequency ablation	1 (1.0%)
LDT	1 (1.0%)

SSA = somatostatin analogs; CMT = chemotherapy; ^{90}Y = ^{90}Y-DOTATATE therapy; TACE = transcatheter arterial chemoembolization; LDT = liver-directed therapy.

TABLE 3
Management Based on ^{18}F-FDG and ^{68}Ga-DOTATATE PET/CT Findings

	Findings on which management was based			
Management	^{68}Ga-DOTATATE	^{18}F-FDG	Both	Total
Active surveillance	5	4	22	31 (29.8%)
Chemotherapy	8	10	2	20 (19.2%)
Chemotherapy, TACE	0	0	1	1 (1%)
Everolimus	1	0	0	1 (1%)
Interferon	0	0	2	2 (1.9%)
PRRT	14	0	1	15 (14.4%)
Radiofrequency ablation	0	1	0	1 (1%)
Somatostatin analogs	11	2	2	15 (14.4%)
Surgery	9	5	2	16 (15.4%)
Liver-directed therapy	2	0	0	2 (1.9%)
Total	50	22	32	104

TACE = transcatheter arterial chemoembolization.

Cas des G1 et des G2 TEP FDG modifie prise en charge dans 2,7% et 12,5% des pts
Cas des peu dif TEP FDG modifie prise en charge dans 39,2%

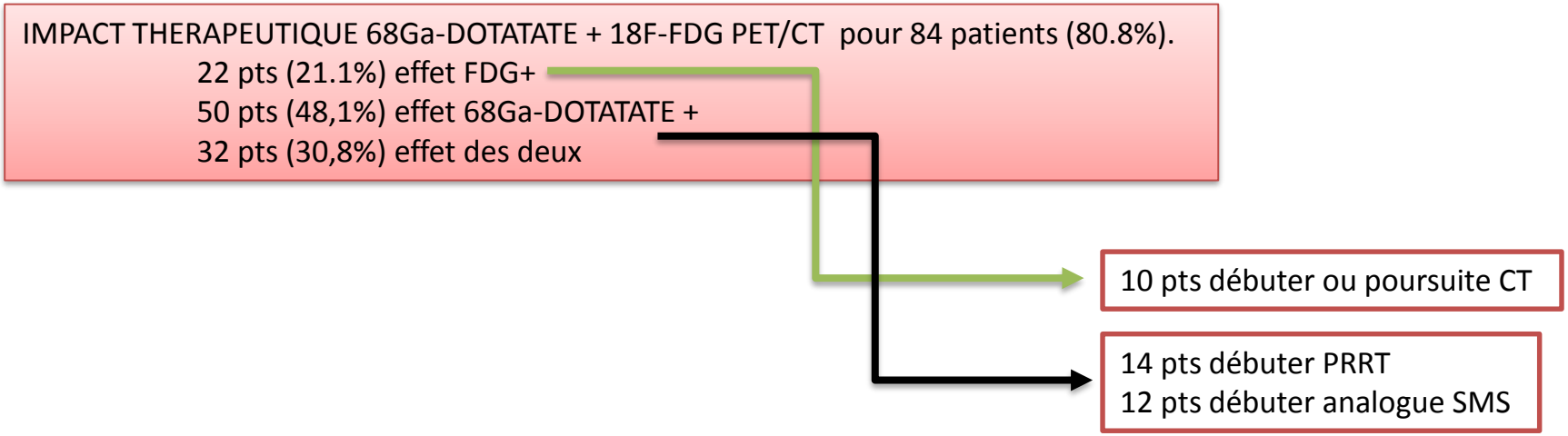

IMPACT THERAPEUTIQUE 68Ga-DOTATATE + 18F-FDG PET/CT pour 84 patients (80.8%).
22 pts (21.1%) effet FDG+
50 pts (48,1%) effet 68Ga-DOTATATE +
32 pts (30,8%) effet des deux
10 pts débuter ou poursuite CT
14 pts débuter PRRT
12 pts débuter analogue SMS

TABLE 4
Correlation of Grade with ^{18}F-FDG and ^{68}Ga-DOTATATE PET/CT Findings

Grade	Findings on which management was based			Total
	^{68}Ga-DOTATATE	^{18}F-FDG	Both	
G1	25	1	10	36 (34.6%)
G2	16	10	14	40 (38.4%)
G3	9	11	8	28 (27%)
Total	50	22	32	104

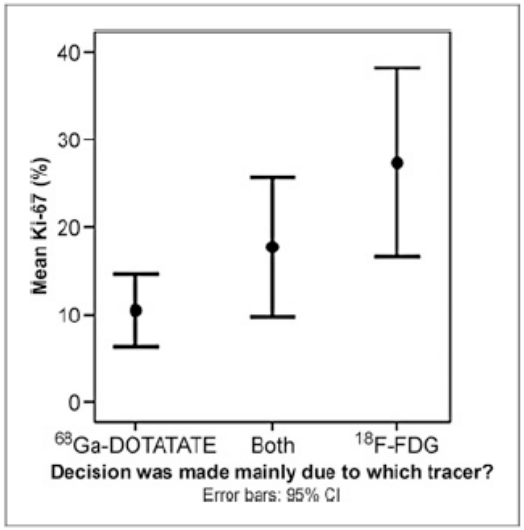


FIGURE 1. Correlation between mean Ki-67 of NETs and PET/CT tracer results on which clinical management decision was based.

- Pour les G1 pas de routine use of both 68Ga-DOTATATE + 18F-FDG PET/CT
- Pour les G3 68Ga-DOTATATE + 18F-FDG PET/CT intéret du 18F-FDG PET/CT pour les valeurs élevées de Ki- 67

G3 NET : FDG more likely to be + 93% vs 40% for G1 Binderup et al

Combined ^{68}Ga-DOTATATE and ^{18}F-FDG PET/CT is useful in the individual therapeutic approach of GEPNETs in clinically challenging intermediate-grade GEPNETs Simsek et al

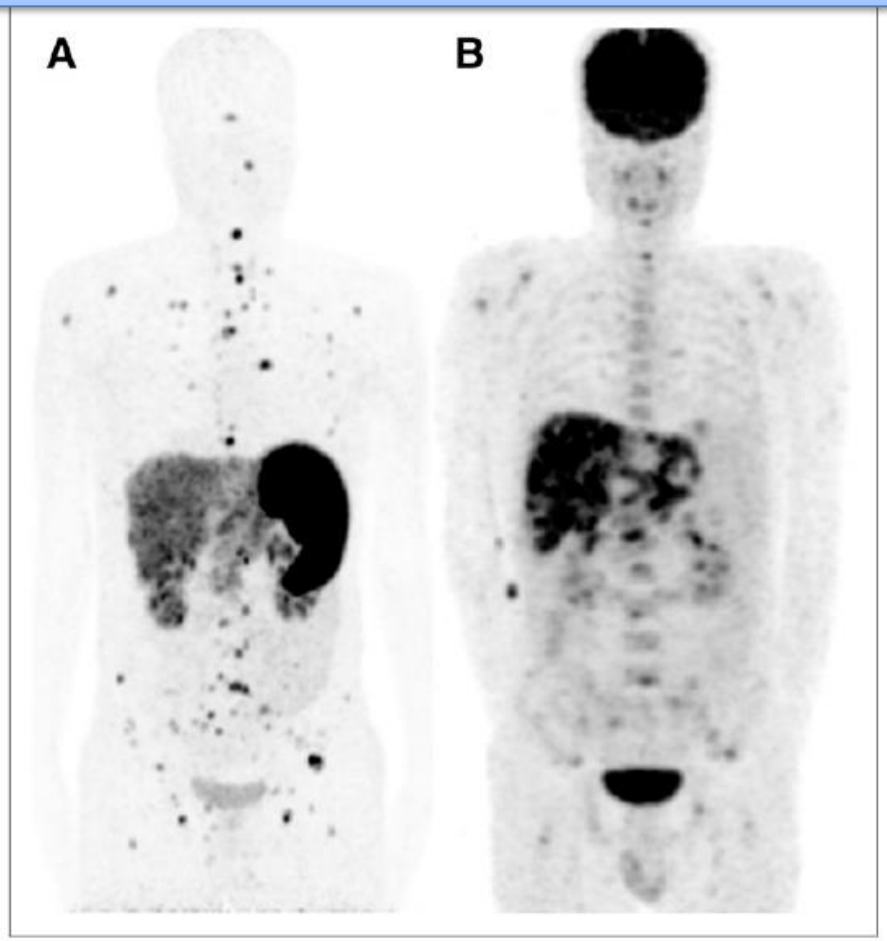
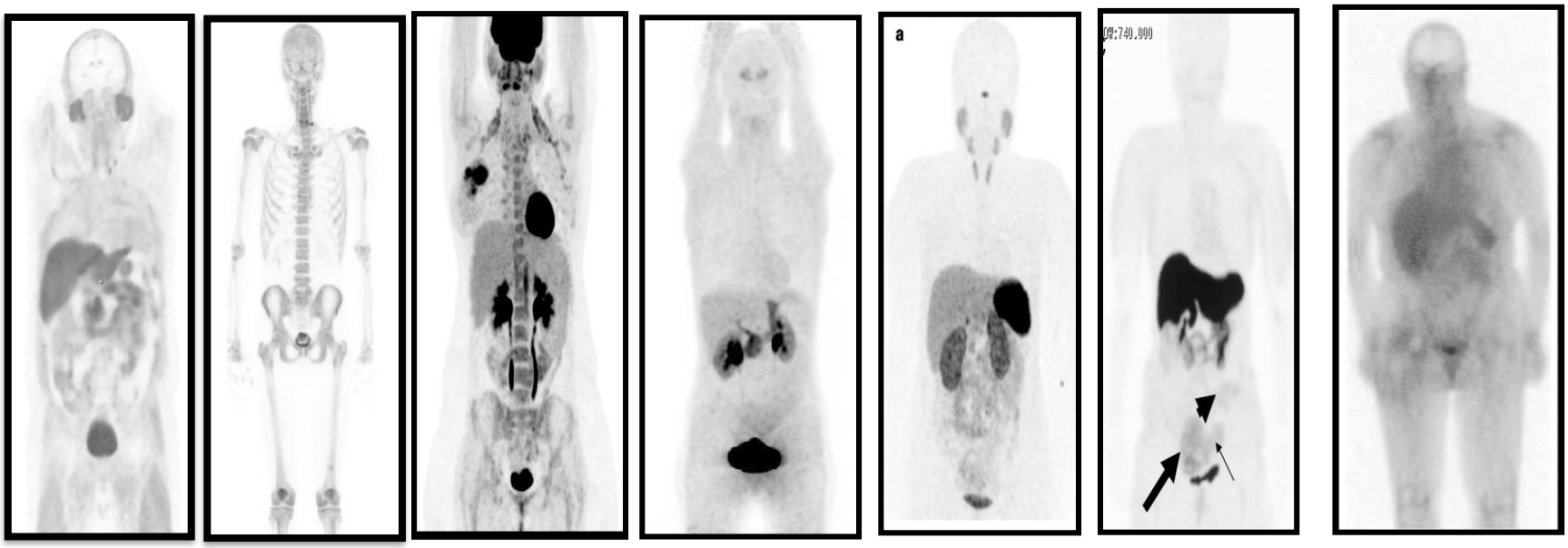


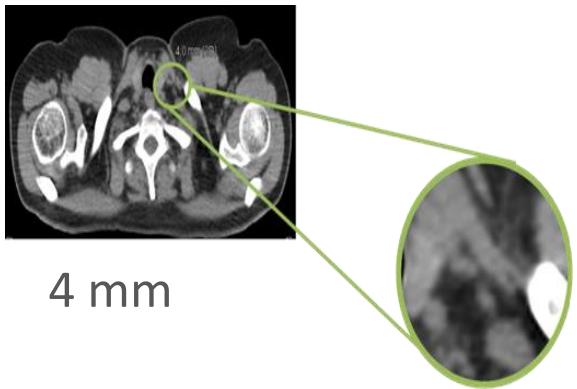
FIGURE 4. Maximum-intensity-projection images of high-grade (Ki67, 25%) pancreatic NET patient demonstrate multiple ^{18}F-FDG(+) bone and liver metastasis (A); however, unexpectedly higher ^{68}Ga-DOTATATE uptake (B) in metastatic lesions was mainstay of switching to PRRT.

we have a Problem

This does not seem right! .

MOLECULAR IMAGING AT A GLANCE !





^{111}InDTPA Octreotide

^{18} F CHOLINE

^{18} F-DOPA

?

^{18} F-Na

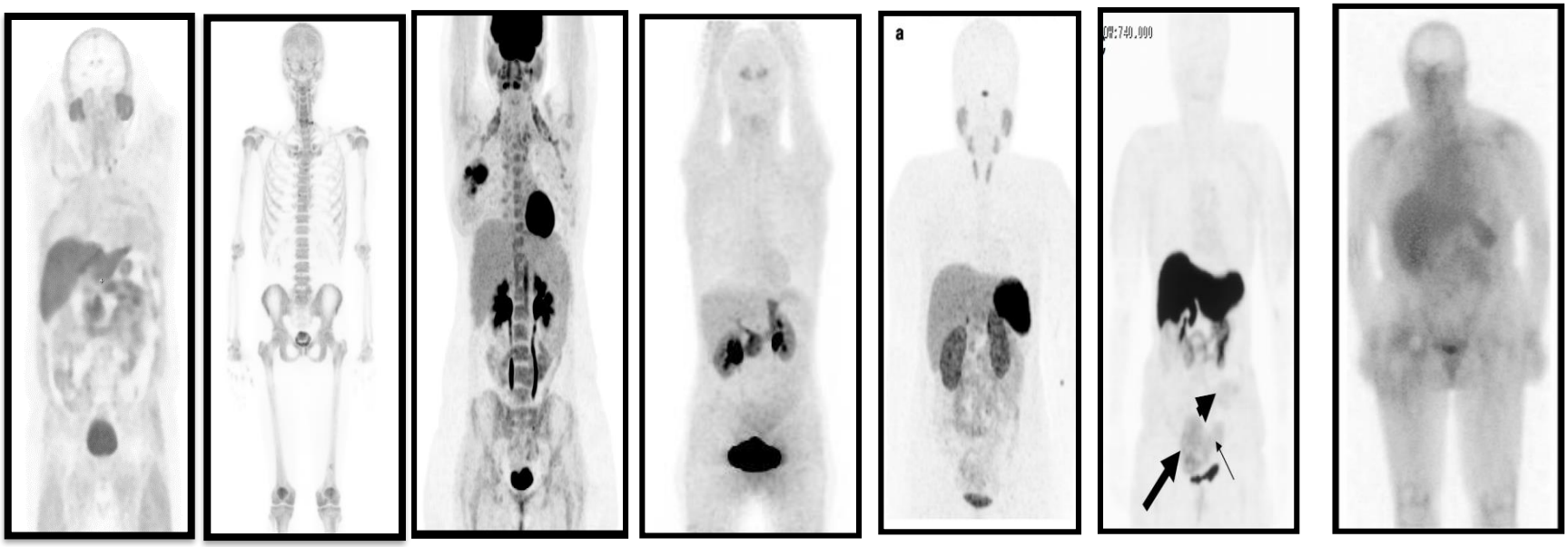
^{68} Ga-DOTATE

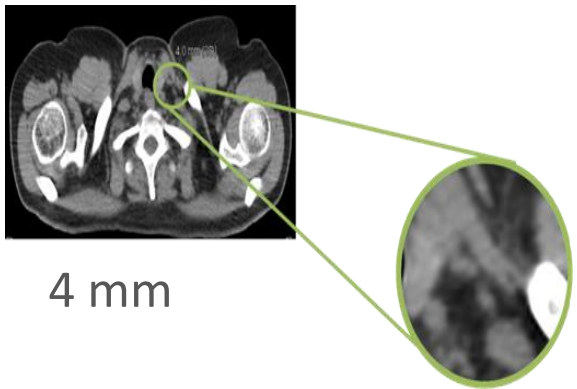
^{18} FDG

^{18} FES

MOLECULAR IMAGING AT A GLANCE !

^{18}F CHOLINE | ^{18}F-Na | ^{18}FDG | ^{18}F-DOPA | ^{68}Ga-DOTANOC | ^{18}FES | ^{111}InDTPA Octreotide





^{111}InDTPA Octreotide

^{18}F CHOLINE

^{18}F-DOPA

?

^{18}F-Na

^{68}Ga-DOTATE

^{18}FDG

^{18}FES

PRRT Experience

Center (reference)	Ligand	*n*	Tumor response					
			CR	PR	MR	SD	PD	CR+PR (%)
Rotterdam (6)	[^{111}In-DTPA^{0}]octreotide	26	0	0	5 (19%)	11 (42%)	10 (38%)	0
New Orleans (7)	[^{111}In-DTPA^{0}]octreotide	26	0	2 (8%)	NA	21 (81%)	3 (12%)	8
Milan (13)	[^{90}Y-DOTA^{0},Tyr^{3}]octreotide	21	0	6 (29%)	NA	11 (52%)	4 (19%)	29
Basel (14, 15, 41)	[^{90}Y-DOTA^{0},Tyr^{3}]octreotide	74	3 (4%)	15 (20%)	NA	48 (65%)	8 (11%)	24
Basel (15, 41)	[^{90}Y-DOTA^{0},Tyr^{3}]octreotide	33	2 (6%)	9 (27%)	NA	19 (57%)	3 (9%)	33
Multicenter (1)	[^{90}Y-DOTA^{0},Tyr^{3}]octreotide	58	0	5 (9%)	7 (12%)	33 (61%)	10 (19%)	9
Multicenter (2)	[^{90}Y-DOTA^{0},Tyr^{3}]octreotide	90	0	4 (4%)	NA	63 (70%)	11 (12%)	4
Copenhagen (3)	[^{90}Y-DOTA^{0},Tyr^{3}]octreotide	53	2 (4%)	10 (19%)	NA	34 (64%)	7 (13%)	23
Warsaw (4)	[^{90}Y-DOTA^{0},Tyr^{3}]octreotate	58	0	13 (23%)	NA	44 (73%)	3 (5%)	23
Rotterdam (5)	[^{177}Lu-DOTA^{0},Tyr^{3}]octreotate	310	5 (2%)	86 (28%)	51 (16%)	107 (35%)	61 (20%)	29
Gothenburg (42)	[^{177}Lu-DOTA^{0},Tyr^{3}]octreotate	26	0	6 (38%)	NA	8 (50%)	2 (13%)	38
Lund (43)	[^{177}Lu-DOTA^{0},Tyr^{3}]octreotate	12	0	2 (17%)	3 (25%)	5 (40%)	2 (17%)	17
Milan (10)	[^{177}Lu-DOTA^{0},Tyr^{3}]octreotate	42	1 (2%)	12 (29%)	9 (21%)	11 (26%)	9 (21%)	31

van der Zwan et al Eur J Endocrinol 2015 Jan; 172(1):R1-8

NETTER -1

Aim

Evaluate the efficacy and safety of ^{177}Lu-Dotatate plus Octreotide30 mg compared to Octreotide LAR 60mg (off-label use)[1] in patients with inoperable, somatostatin receptor positive (111in SRS) , midgut NET, progressive under Octreotide LAR 30mg (label use)

Design

International, multicenter, randomized, comparator-controlled, parallel-group

Treatment and Assessments

Tumour burden assessment (RECIST criteria) **every 12 weeks**

Dose 1 | Dose 2 | Dose 3 | Dose 4

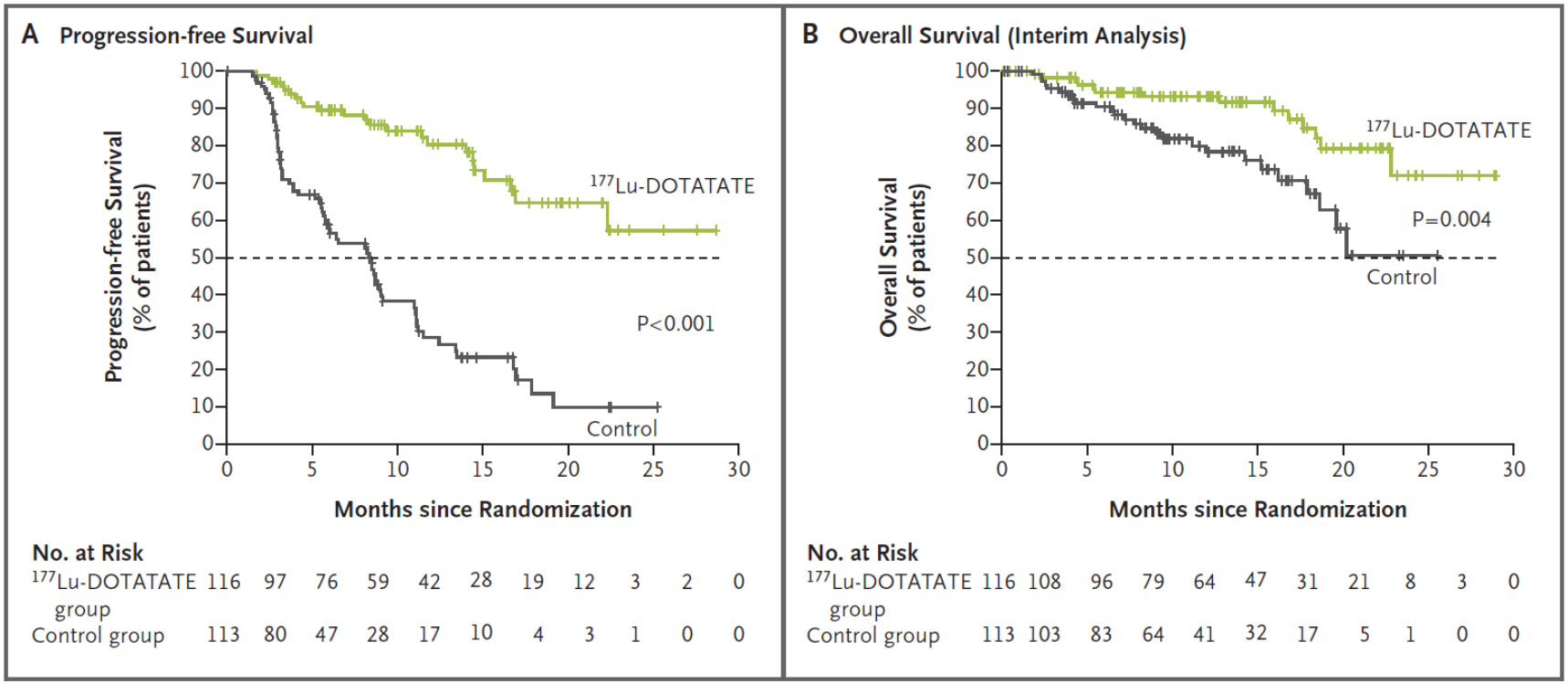
Baseline and Randomization

n = 115 — 4 administrations of 7.4 GBq of ^{177}Lu-Dotatate every 8 weeks + Octreotide 30 mg

n = 115 — Octreotide LAR 60mg every 4 weeks

5 Years follow up

1. FDA and EMA recommendation



Patients who completed treatment phase (N=103†)	no. (%)
Number of administrations	
4	79 (77)
3	6 (6)
2	12 (12)
1	5 (5)
0	1 (1)
All treated patients (N=111)	
No DMT	103 (93)
DMT	8 (7)

* DMT denotes dose-modifying toxicity.

† Excluding patients still under treatment (n=8) or no treatment (n = 5).

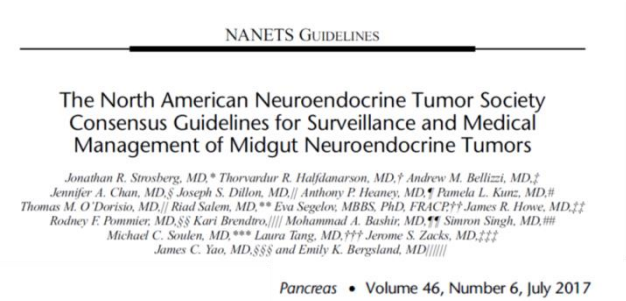
^{177}Lu-Dotatate
Median PFS: Not reached

EMA 2017

Lutathera is indicated for the treatment of **unresectable or metastatic**, **progressive,** well differentiated (G1 and G2), somatostatin receptor positive gastroenteropancreatic neuroendocrine tumours (GEP NETs) in adults.

FDA approval 2018

For the treatment of somatostatin receptor positive GEPNETs including foregut, midgut, and hindgut neuroendocrine tumors in adults.



NANETS GUIDELINES

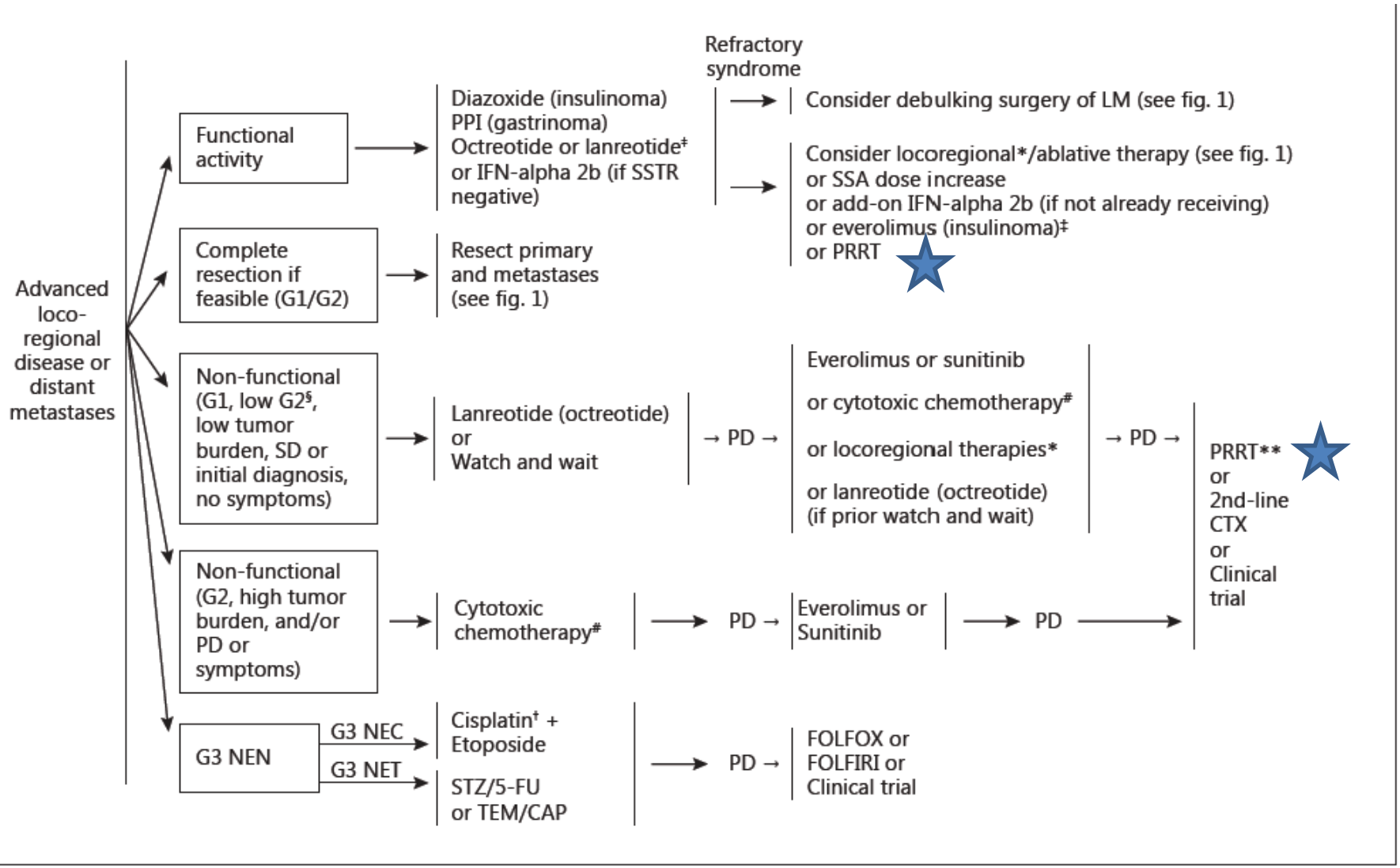
The North American Neuroendocrine Tumor Society Consensus Guidelines for Surveillance and Medical Management of Midgut Neuroendocrine Tumors

Jonathan R. Strosberg, MD, Thorvardur R. Halfdanarson, MD,† Andrew M. Bellizzi, MD,‡ Jennifer A. Chan, MD,§ Joseph S. Dillon, MD,|| Anthony P. Heaney, MD,¶ Pamela L. Kunz, MD,# Thomas M. O'Dorisio, MD,|| Riad Salem, MD,** Eva Segelov, MBBS, PhD, FRACP,†† James R. Howe, MD,‡‡ Rodney F. Pommier, MD,§§ Kari Brendtro,|||| Mohammad A. Bashir, MD,¶¶ Simron Singh, MD,## Michael C. Soulen, MD,*** Laura Tang, MD,††† Jerome S. Zacks, MD,‡‡‡ James C. Yao, MD,§§§ and Emily K. Bergsland, MD||||||*

Pancreas • Volume 46, Number 6, July 2017

- second-line (after SMSa) treatment in patients with somatostatin receptor–positive midgut NETs**, a significant majority of the expert panel selected 177Lu-DOTATATE**

The ENETS 2016 treatment algorithm for pancreatic NETs



** If STR imaging +

Place de la RIV dans le TNCD

TNE duodeno---pancréatique

1ère Ligne

- Analogues de la somatostatine*
- Chimiothérapie de référence notamment dans le but d'une réduction tumorale permettant une chirurgie secondaire
- Sinon thérapie ciblée

2ème Ligne

- Chimiothérapie de référence
- Thérapie ciblée
- Chimioembolisation

Options

- Autres chimiothérapies
- Analogues de la somatostatine*
- Embolisation
- Radiothérapie Interne vectorisée
- Transplantation Hépatique après exérèse du primitif

TNE Non pancréatique

pour TNE iléale, après résection de la tumeur primitive

Référence

- Analogues de la somatostatine*
- Chimioembolisation/embolisation
- Everolimus
- Radiothérapie interne vectorisée

Options

- Interféron (pégylé ?)
- Chimiothérapie
- Transplantation Hépatique après exérèse du primitif

* Envahissement Hépatique <25--50% et progression lente, Ki67 <2% (TNE grêle) ou 5% (TNE pancréas)

Source: www.tncd.gov

Uptake G4, G3

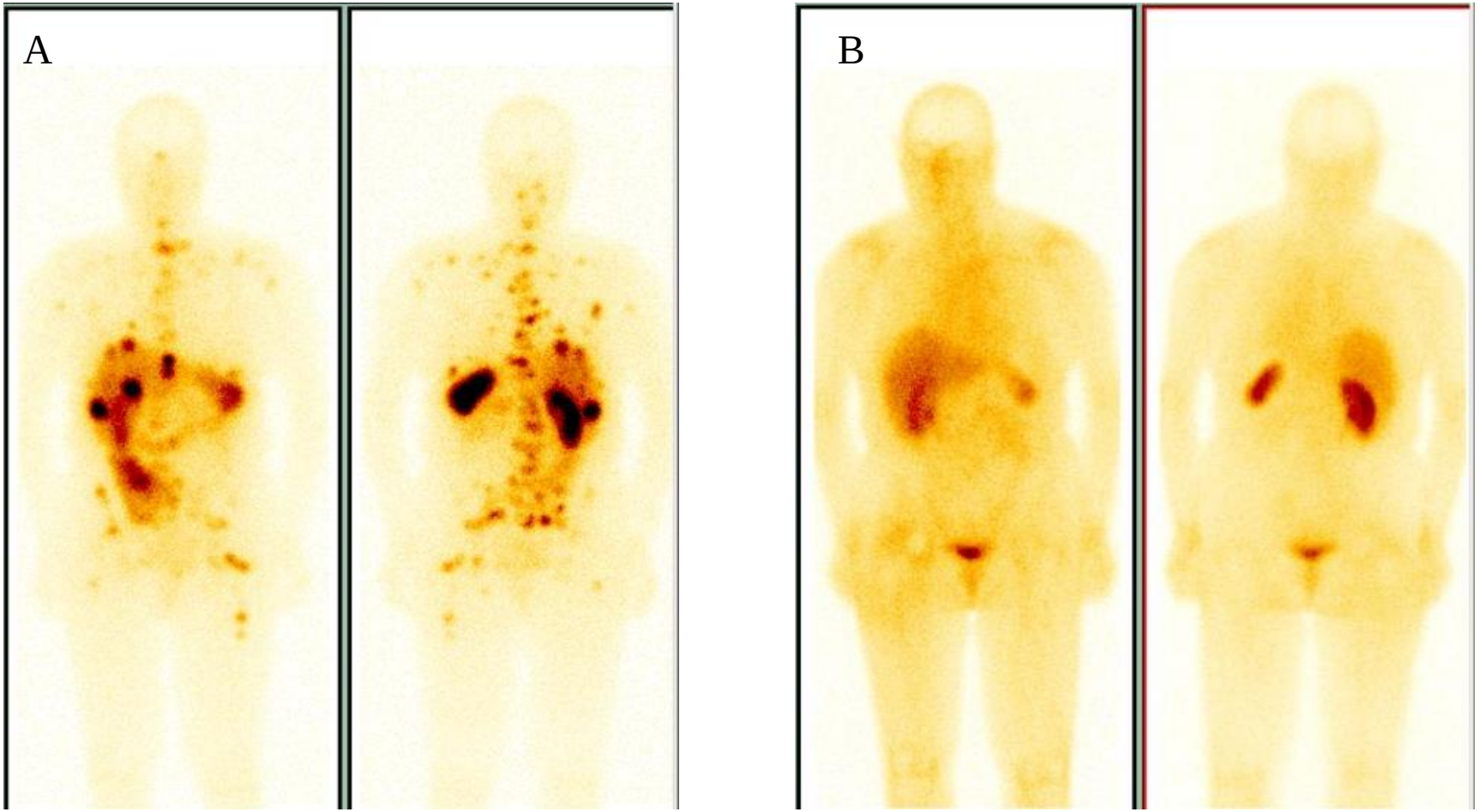


Fig. 2 PRRT partial response on ^{111}In-DTPA-octreotide @ 24h
A anterior and posterior view of a planar whole body image before treatment
B anterior and posterior view of a planar whole body image 1 year after treatment
This figures illustrates a partial remission in a 70 year old patient with advanced bone and liver metastases of a renal neuro endocrine tumor treated with 4 injections of 177Lu-DOTATATE (total cumulated activity of 30,05 GBq) and remaining without progression of disease for 5 years:

177 Lu PRRT

2002: pNETS T1N0 (0/6)

2003 : liver metastasectomy

2004-2006 ADRIAMYCINE-ZANOSAR (9 cycles stopped for heart failure)

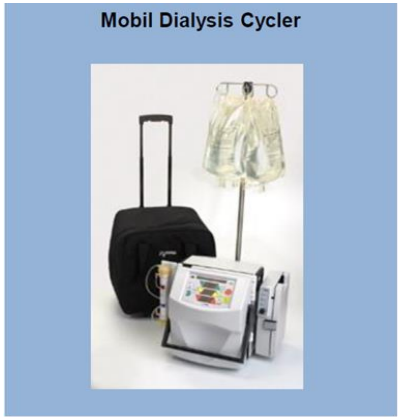
2006 -2012 SMS analogue

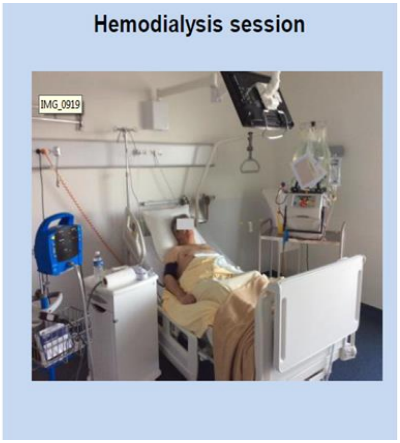
2012: ^{90}Y DOTATOC et 2 cycles ^{177}Lu-DOTATOC 20GBq

2015: TACE

2016 End stage renal Disease (hemodialyse: 3w)

2017 at the age of 73 y.o 4 cycles of **^{177}Lu-DOTATATE 17GBq**

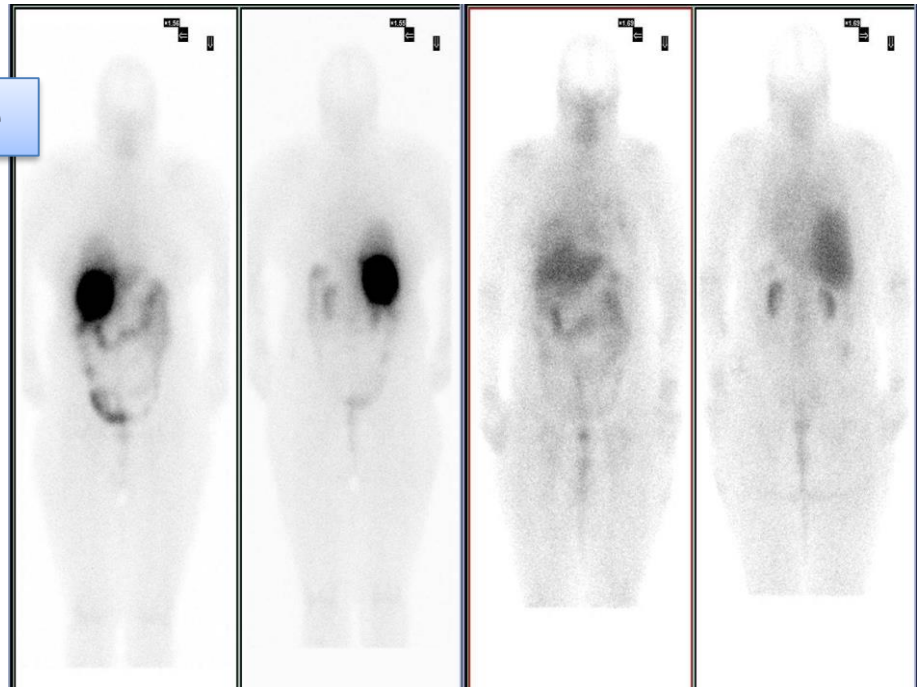




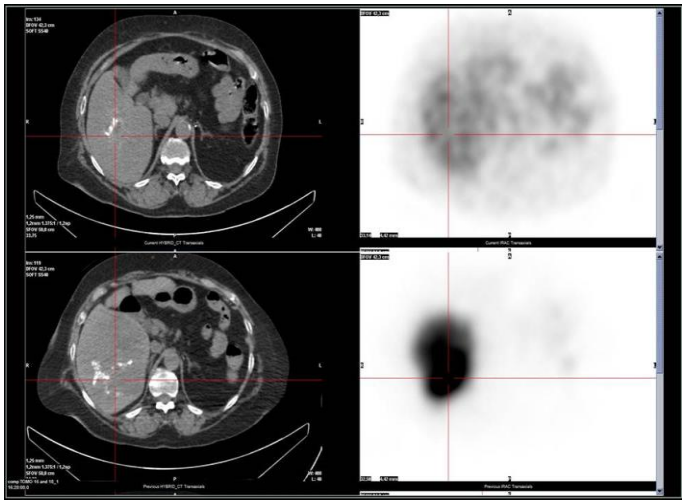
- CTCAE grade 2 anemia, thrombopenia et leucopenie et
- CTCAE grade 3 lymphopenia

Courtesy Dr L Dierickx

111- In DTPA Octreotide



SRSi wb before PRRT 1 année after PRRT



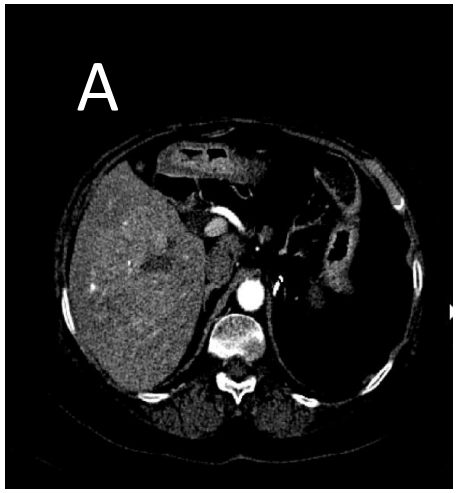
TDM SPECT fusion MIP

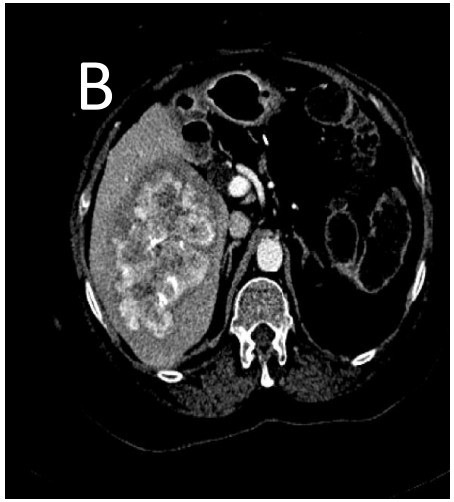
Post ^{177}Lu DOTATATE SPECT CT

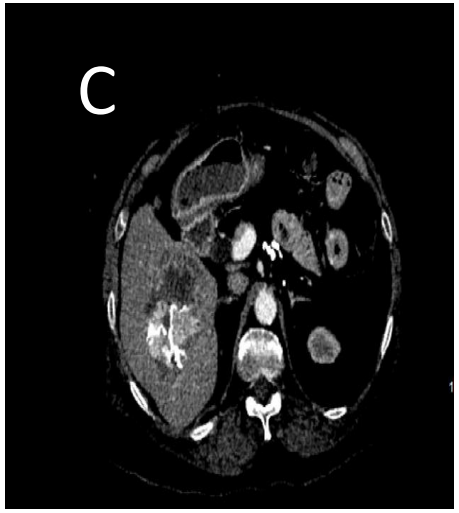
@ cycle 2

@ cycle 4

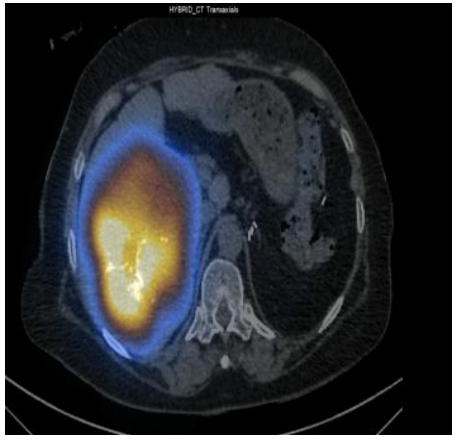
@ 3 mo

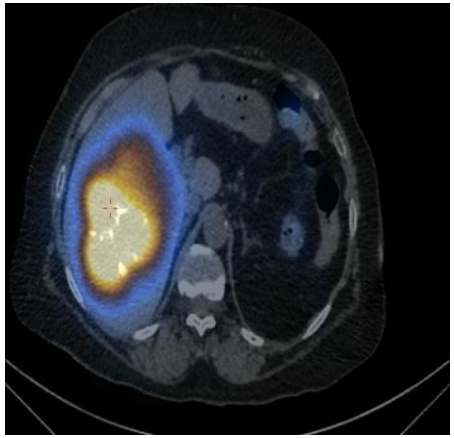


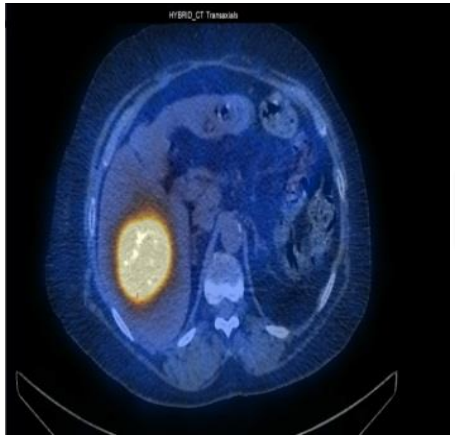




PR







PR ?

2019 Alive and CR on SRS imaging

SST2 expression score : ^{111}InDTPA-octreotide

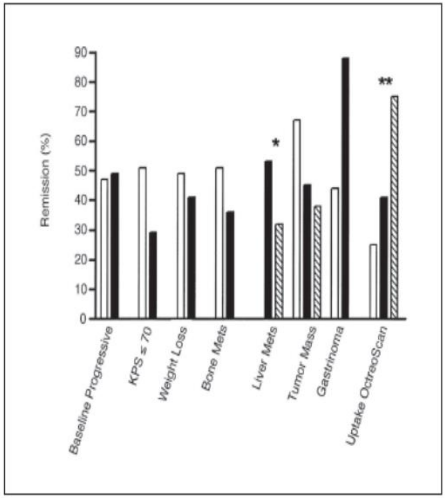
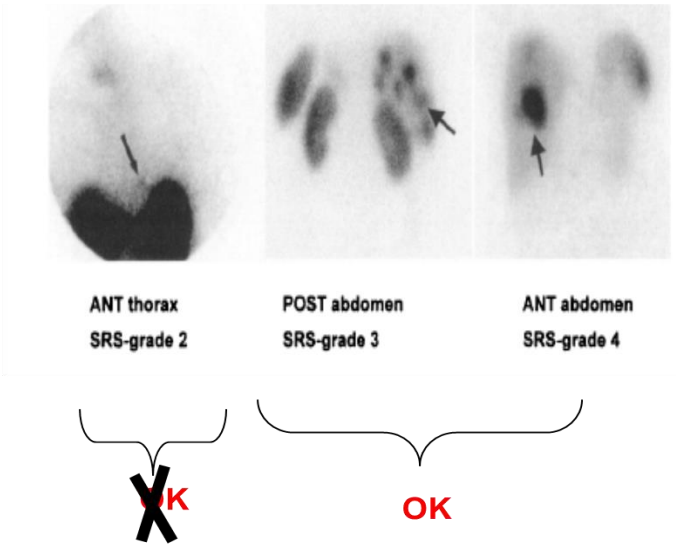


Fig 5. Analysis of factors that may predict tumor remission (minor response, partial remission, or complete remission). (*) $P < .05$; (**) $P < .01$, logistic regression. KPS, Karnofsky performance score.



^{111}In-pentetreotide scintigraphy vs. ^{68}Ga-DOTATATE PET: Impact on Krenning Scores Hope et al JNM 2019

- post-hoc comparison, 150pts

- **SSTR-PET substantially increases the Krenning Score (up grading?)**
- **^{68}Ga-DOTATATE PET may lead to recruit for PRRT pts with smaller lesion (<2cm) (overtreatment?)**

^{111}In-Pentetreotide Scintigraphy Versus ^{68}Ga-DOTATATE PET: Impact on Krenning Scores and Effect of Tumor Burden

Thomas A. Hope*[1–3], Jeremie Calais*[4], Li Zhang[3,5], William Dieckmann[6], and Corina Millo[6]

JNM 2019

Risque de SUR traitement

TABLE 1
Krenning Scores Broken Down by Reader and Imaging Modality Across All Patients Imaged

	Reader 1			Reader 2			Reader 3		
Krenning score	Planar	SPECT	PET	Planar	SPECT	PET	Planar	SPECT	PET
0–1 (*n*)	117 (78%)	93 (62%)	42 (28%)	106 (71%)	83 (55%)	43 (29%)	119 (79%)	102 (68%)	45 (30%)
2 (*n*)	5	16	0	13	17	3	4	5	3
3 (*n*)	17	23	25	18	31	17	14	24	14
4 (*n*)	11	18	83	13	19	87	13	19	88
2–4 (*n*)	33 (22%)	57 (38%)	108 (72%)	44 (29%)	67 (45%)	107 (71%)	31 (21%)	48 (32%)	105 (70%)

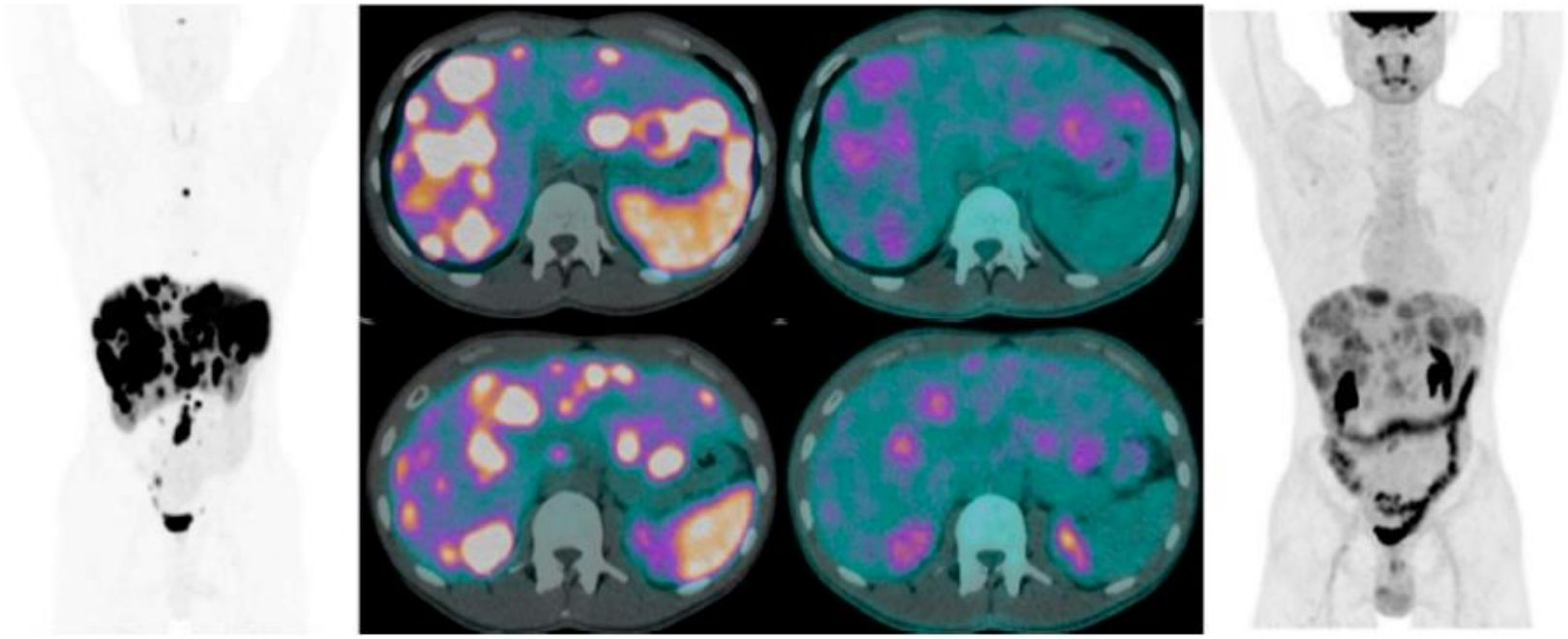
PERTINENT FINDINGS: A retrospective analysis was conducted on 150 patients imaged in NIH with ^{68}Ga-DOTATATE PET/CT and ^{111}In-pentetreotide PET/CT within 1 wk. The Krenning score was significantly higher with SSTR PET than with planar or SPECT ^{111}In-pentetreotide. This discrepancy was most pronounced for lesions <2 cm; lesion size did not affect SSTR PET score.

IMPLICATIONS FOR PATIENT CARE: Most patients with lesions <2 cm would not have qualified for PRRT based on ^{111}In-pentetreotide but appear as candidates based on SSTR PET. This implies the possibility that patients with numerous small lesions could benefit from PRRT. Integration of size, volume, and extent of tumor burden with the Krenning score might prove of benefit when selecting patients for PRRT based on SSTR PET.

Dual PET CT et l'hétérogénéité tumorale

Ga-68 DOTA

F-18 FDG



Patient, 24 ans, TNE iléale G2, M+: foie+ggl+os.
Hétérogénéité tumorale Ga-68 DOTA vs FDG

Carideo L et al, J Clin Med, 2019

Phenotype instability

Lindstrom LS, Karlsson E, Wilking UM, et al. Clinically used breast cancer markers such as estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 are unstable throughout tumor progression. *J Clin Oncol* 2012; **30**: 2601–08.

Breast Cancer Markers Are Unstable Throughout Tumor Progression

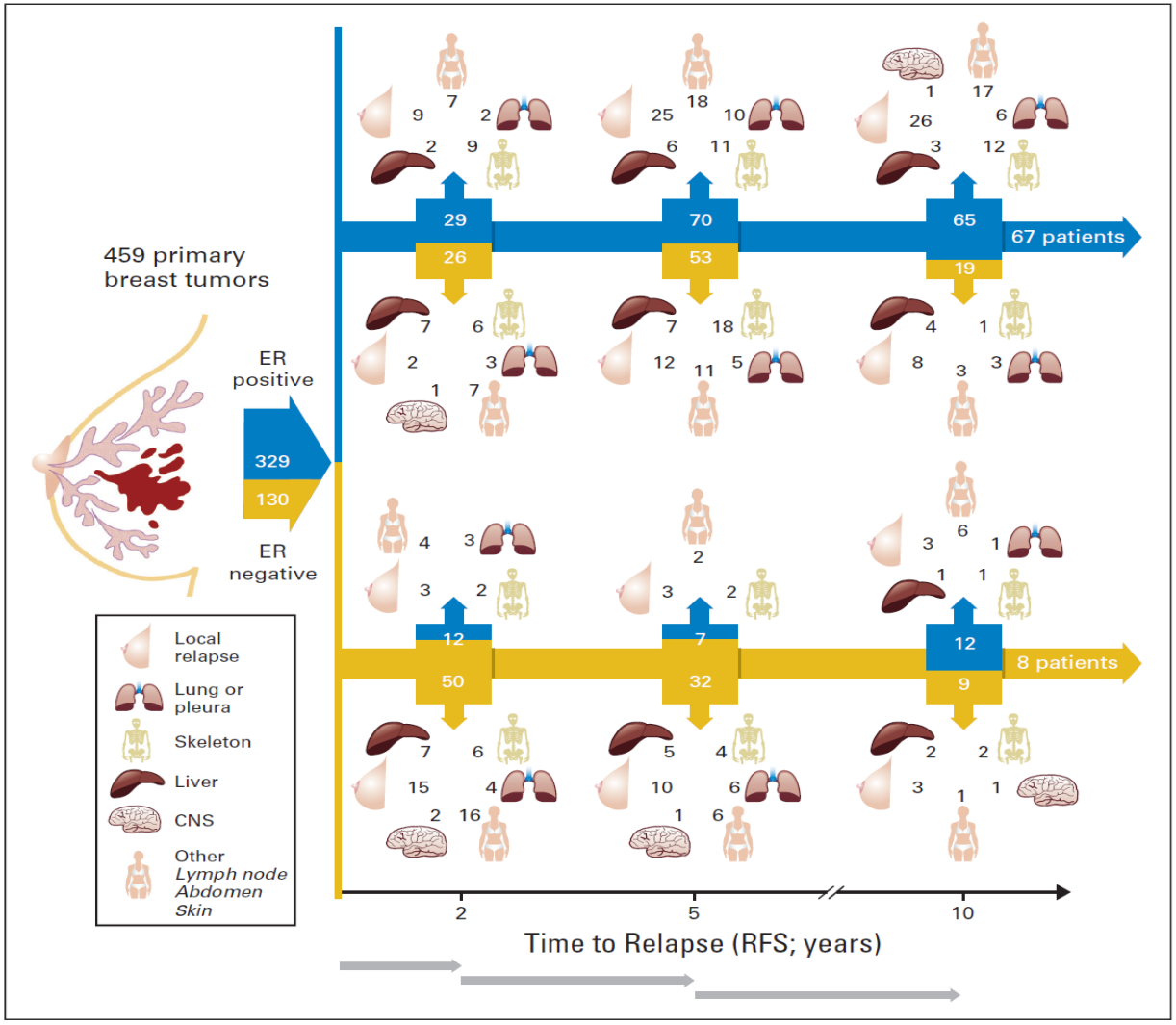


Fig 2. Patients by intraindividual estrogen receptor (ER) status (in primary tumor and first diagnosed site of relapse) were stratified according to relapse-free survival (RFS) at ≤ 2, 5, and 10 years. The sites of relapse were grouped into local relapse (ipsilateral breast), skeleton, lung and pleura combined, liver, CNS, or other (mainly defined as lymph node, abdomen, or skin).

Improving trageting efficiency

Loosing SST expression

Buscail L, et al. Loss of sst2 somatostatin receptor gene expression in human pancreatic and colorectal cancer. Cancer Res. 1996;56:1823–1827

Eur J Nucl Med Mol Imaging
DOI 10.1007/s00259-016-3486-2

ORIGINAL ARTICLE

The prognostic and predictive value of $sstr_2$-immunohistochemistry and $sstr_2$-targeted imaging in neuroendocrine tumors

Philippe Brunner[1,2] · Ann-Catherine Jörg[2] · Katharina Glatz[1] · Lukas Bubendorf[1] · Piotr Radojewski[3] · Maria Umlauft[3] · Nicolas Marincek[2,3] · Petar-Marko Spanjol[3] · Thomas Krause[3] · Rebecca A. Dumont[3] · Helmut R. Maecke[4] · Jan Müller-Brand[2] · Matthias Briel[5,6] · Anja Schmitt[7] · Aurel Perren[7] · Martin A. Walter[3]

PERSPECTIVES

Neuro-endocrinology
Neuroendocrinology (DOI:10.1159/000475526)
(Accepted, unedited article not yet assigned to an issue)
Advanced Release: April 13, 2017
© 2017 S. Karger AG, Basel
www.karger.com/nen
Received: December 12, 2016
Accepted after revision: April 6, 2017

ENETS Consensus Guidelines for the Standards of Care in Neuroendocrine Neoplasia: Peptide Receptor Radionuclide Therapy with Radiolabeled Somatostatin Analogues

Chemo + PRRT (PRCRT) feasible with minimal incremental toxicity.

In patients who retain SSTR expression but are FDG-avid, encouraging response rates and survival rates have been reported with PRCRT

Eur J Nucl Med Mol Imaging (2016) 43:2453–2455
DOI 10.1007/s00259-016-3497-z

LETTER TO THE EDITOR

The case for combined chemotherapy-peptide receptor radionuclide therapy (chemo-PRRT) strategy in metastatic neuroendocrine tumor: predicting and looking at the possible case scenarios

Sandip Basu[1] · Vikas Ostwal[2]

	Bone m.	Liver m.
GLU	-	+
SST2	+	-

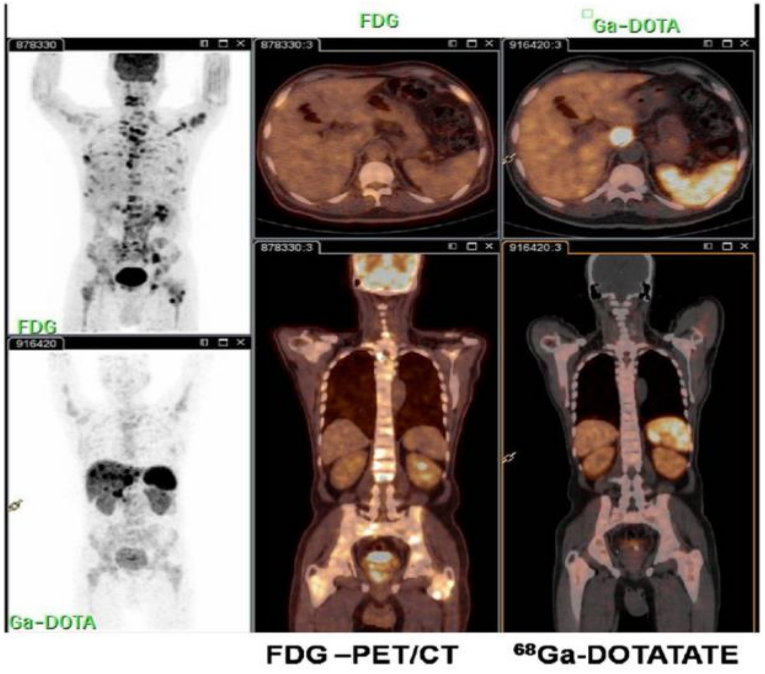
Tumor heterogeneity

Fig. 1 Dual tracer PET (^{68}Ga-DOTATATE/^{18}FDG) imaging findings in a 65-year-old male with a diagnosed case of grade I duodenal NET with liver and skeletal metastases (duodenal polyp biopsy was suggestive of well-differentiated NET with Mib1 LI <2 %) is illustrated. The ^{68}Ga-DOTATATE PET-CT demonstrated high uptake in the hepatic metastases (Krenning score 4), and there was faint uptake noted in the bone marrow (Krenning score 1). On FDG-PET/CT, the liver lesions did not demonstrate an appreciable focal uptake, while the bone marrow lesions were distinctly positive with irregularly increased uptake throughout the axial and proximal appendicular skeletal marrow

FDG –PET/CT

^{68}Ga-DOTATATE

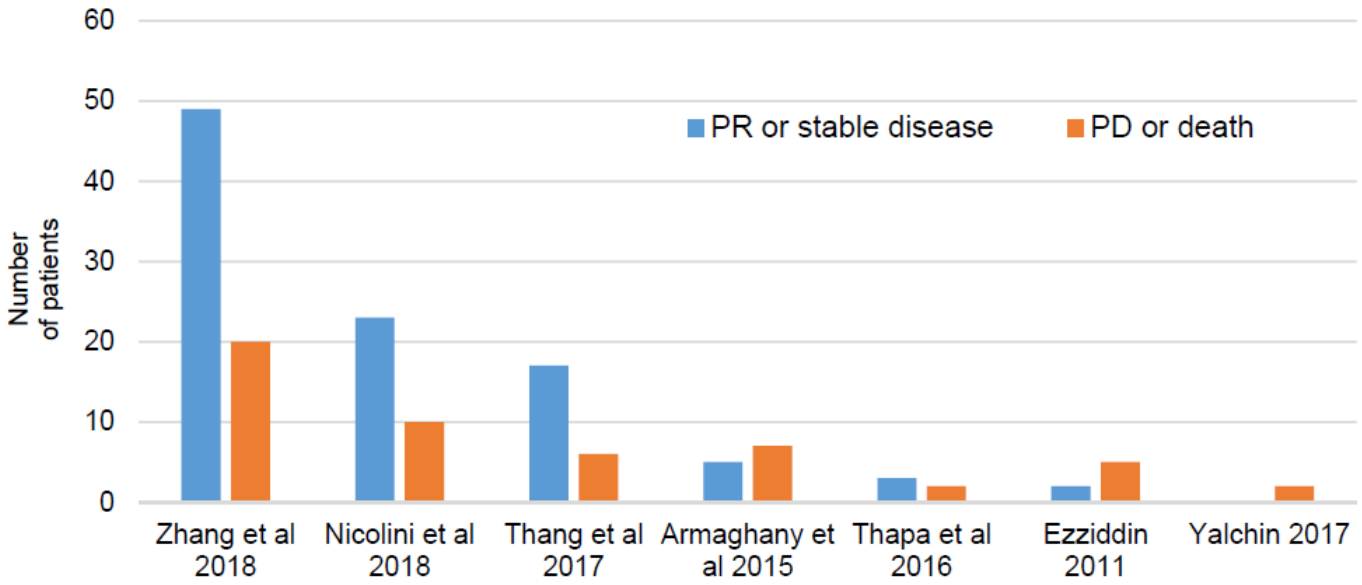
Mib 1 < 2%



PRRT for G3 ?

Waseem et al JNM 2019 ,
Med line review G3 PRRT (protocols are heterogenous 90Y or 177Lu)
151 pts (7 studies)
66% SD or PR

Figure 2. Comparison of responses reported in seven studies of patients with G3 NENs treated with PRRT



Abbrev: PRRT, peptide receptor radionuclide therapy; PR, partial response; PD, progressive disease

→ Warant further studies

Favourable outcomes of ^{177}Lu-DOTATATE PRRT in patients with FDG-avid NET

- *Induction* therapy:

3 to 5 cycles 6 – 10 GBq ^{177}Lu-DOTATATE / 6 – 8 we.

- *Maintenance* therapy:

as needed 12 – 18 months after induction therapy.

- *Radiosensitizing* regimen

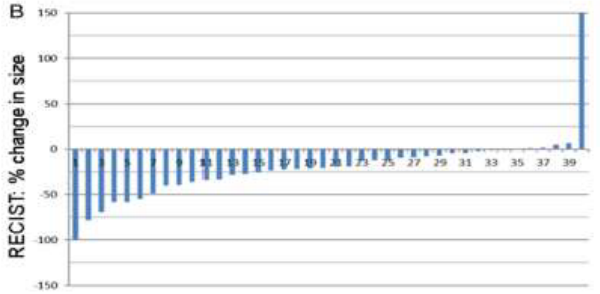
  5-FU (200 mg/m2/day) as a continuous infusion from the second cycle of PRRT starting 4 days prior to radionuclide administration and continuing for up to 3 weeks.

Grade 1 4 pts
Grade 2 28 pts
Grade 3 4 pts

Table 2 Imaging responses at 3 months after completion of PRCRT

	RECIST 1.1 (n=40)	FDG PET (n=31)	SSTR imaging (s=51)
Complete response	1	5	1
Partial response	11	17	32
Stable disease	27	5	1
Progressive disease	1	4	17[a]

[a] A proportion of these patients had a mixed response with response in dominant preexisting lesions but progression of existing small-volume disease defining progression



Kashyap R et al Eur J Nucl Med Mol Imaging 2015

Salvage PPRT

+ 2 cycles

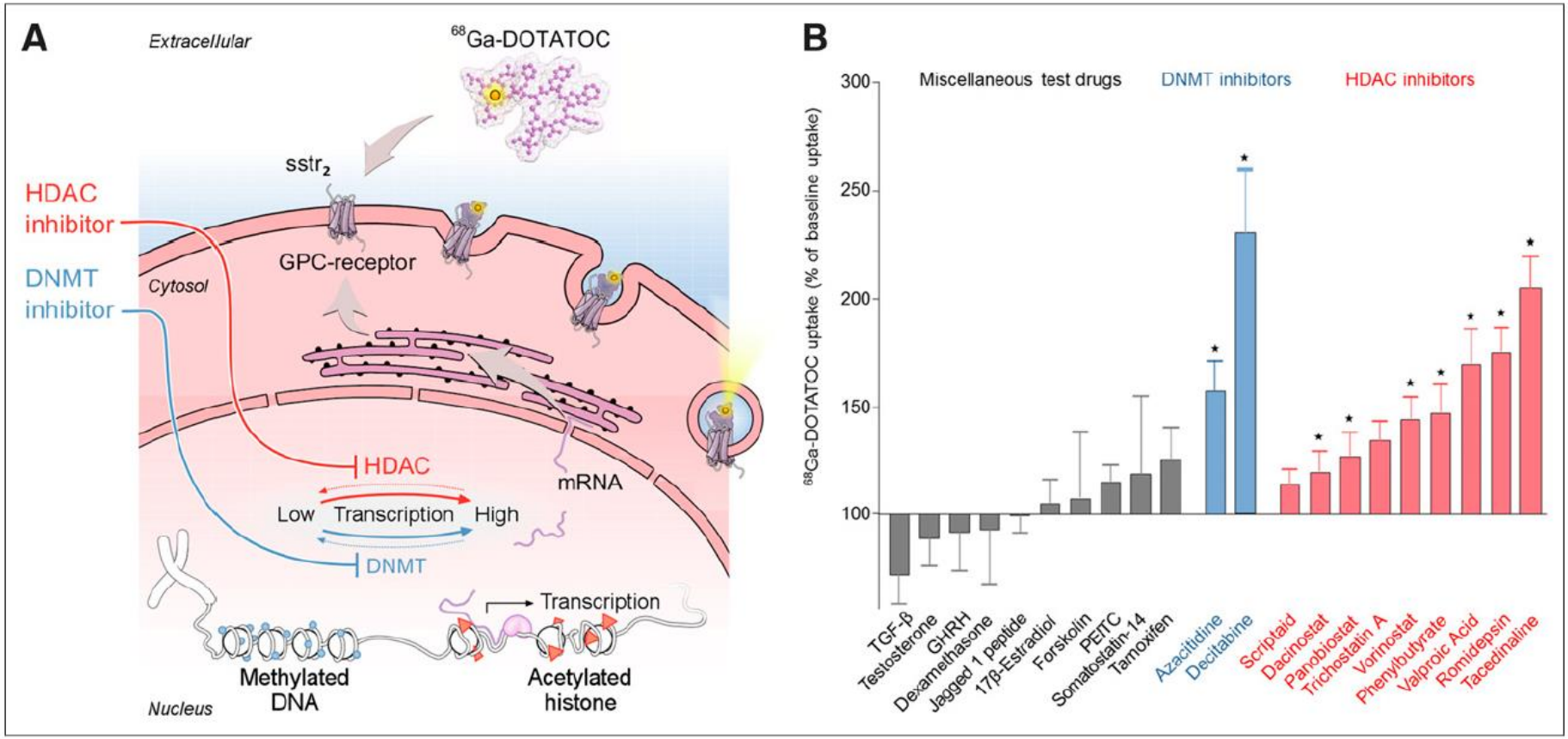
- Feasible
- No added toxicity
- Reponse duration seems shorter

van Essen M, Krenning EP, Kam BL, de Herder WW, Feelders RA, Kwekkeboom DJ. Salvage therapy with 177Lu-octreotate in patients with bronchial and gastroenteropancreatic neuroendocrine tumors. J Nucl Med. 2010;51:383–90. 51.

Sabet A, Haslerud T, Pape UF, Sabet A, Ahmadzadehfar H, Grünwald F, et al. Outcome and toxicity of salvage therapy with 177Lu-octreotate in patients with metastatic gastroenteropancreatic neuroendocrine tumours. Eur J Nucl Med Mol Imaging. 2014;41: 205–10.

Upregulation of Key Molecules for Targeted Imaging and Therapy

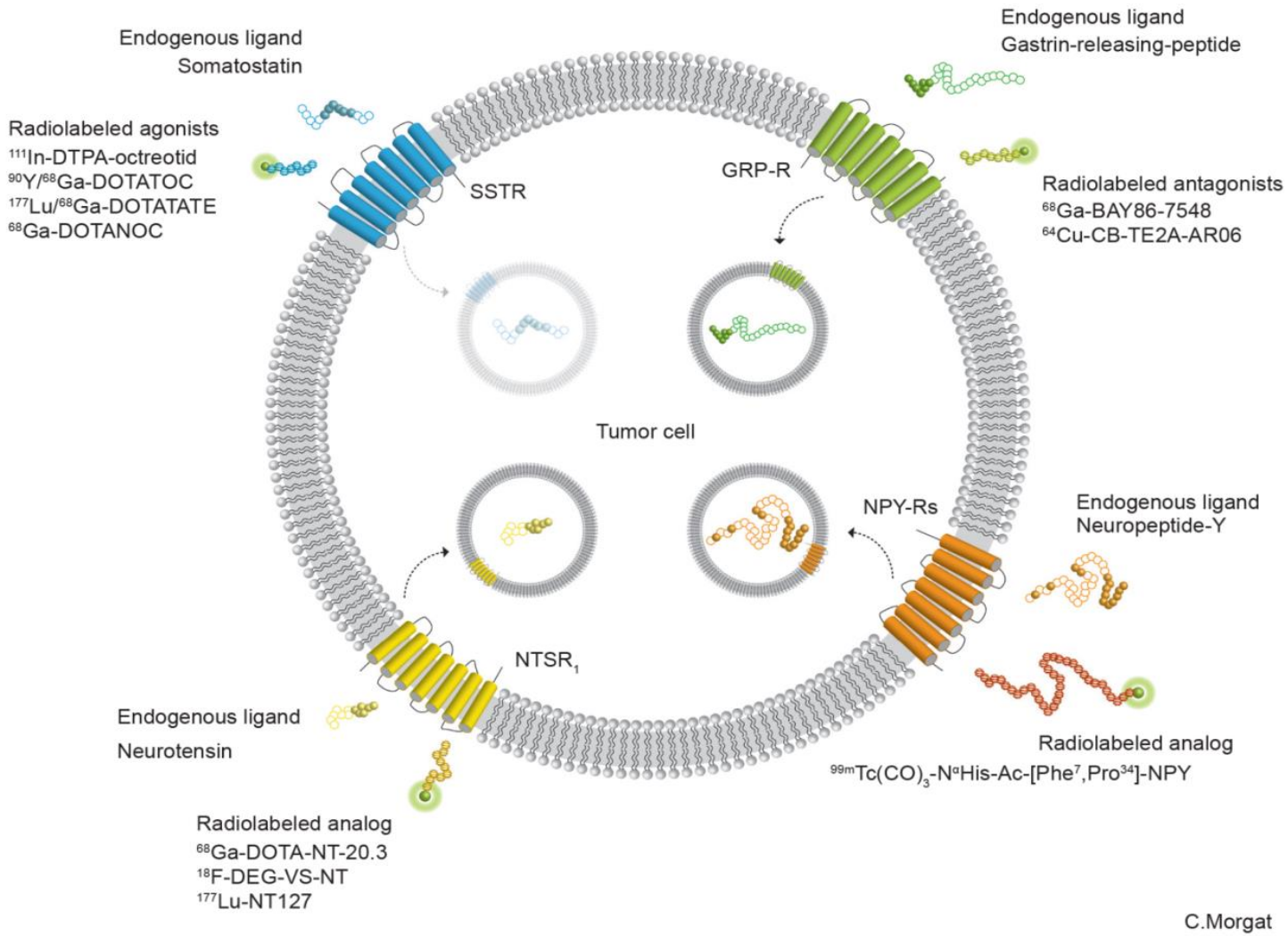
Vincent F. Taelman*[1,2], Piotr Radojewski*[1,2], Nicolas Marincek[1,2], Anat Ben-Shlomo[3], Andrea Grotzky[1,2], Cristina I. Olariu[1,2], Aurel Perren[4], Christoph Stettler[5], Thomas Krause[1,2], Lorenz P. Meier[1,2], Renzo Cescato[1,2], and Martin A. Walter[1,2,6]



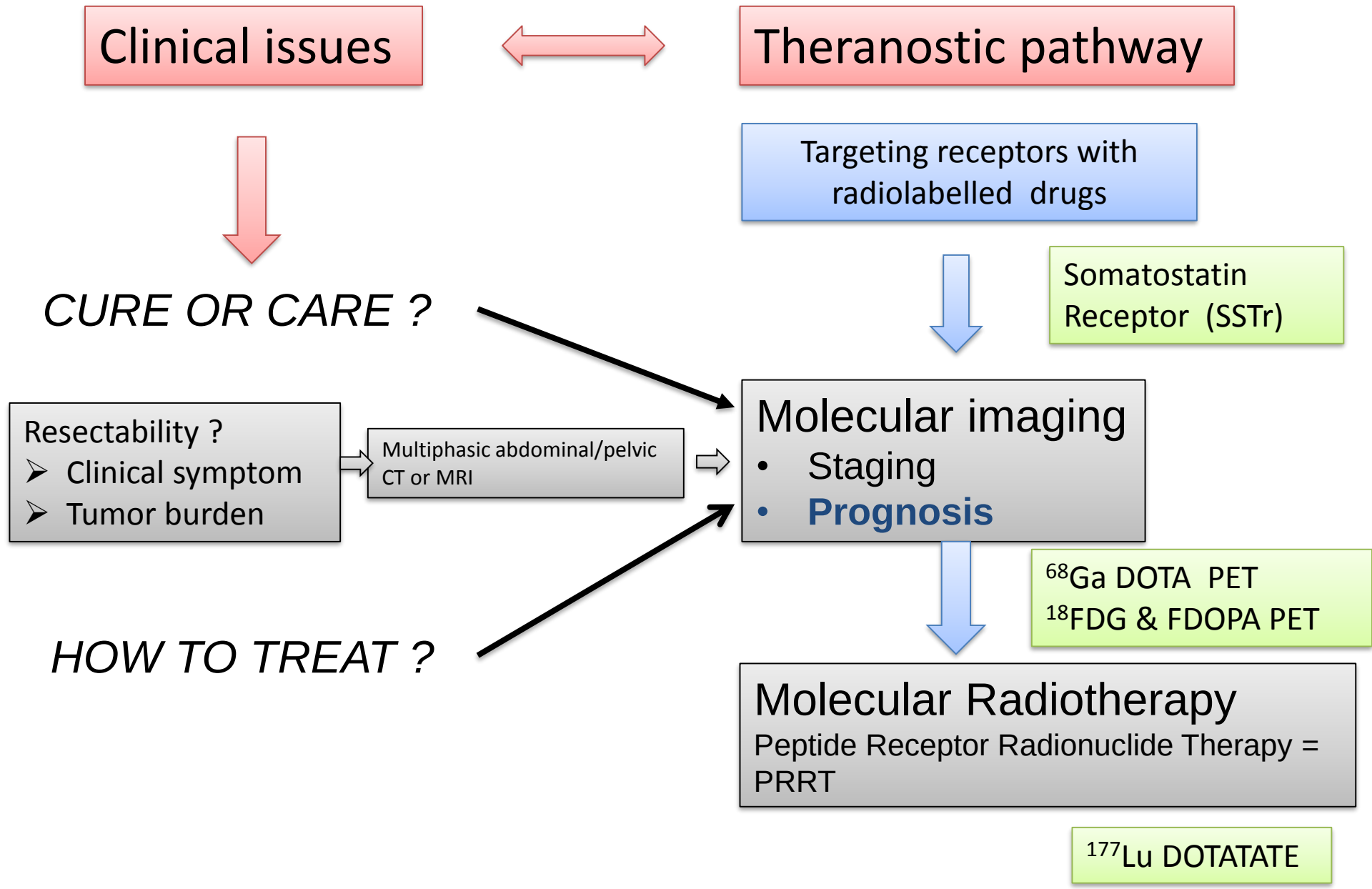
SST Antagonist

Ongoing trial OPS 201 (IPSEN)

NETs



Targeting neuropeptide receptors for cancer imaging and therapy: perspectives with bombesin, neurotensin, and neuropeptide-Y receptors
Morgat C, Mishra AK, Varshney R, Allard M, Fernandez P, Hindié E.J Nucl Med. 2014


Clinical issues
Theranostic pathway
Targeting receptors with radiolabelled drugs
Somatostatin Receptor (SSTr)
CURE OR CARE ?
Resectability ?
Clinical symptom
Tumor burden
Multiphasic abdominal/pelvic CT or MRI
Molecular imaging
Staging
Prognosis
68Ga DOTA PET
18FDG & FDOPA PET
HOW TO TREAT ?
Molecular Radiotherapy
Peptide Receptor Radionuclide Therapy = PRRT
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Merci