

**ENETS Consensus Guidelines for the Management of Patients with Liver and Other Distant Metastases from Neuroendocrine Neoplasms of Foregut, Midgut, Hindgut, and Unknown Primary**

Marianne Pavel<sup>a</sup> Eric Baudin<sup>b</sup> Anne Couvelard<sup>c</sup> Eric Krenning<sup>d</sup>  
 Kjell Öberg<sup>e</sup> Thomas Steinmüller<sup>f</sup> Martin Anlauf<sup>g</sup> Bertram Wiedenmann<sup>a</sup>  
 Ramon Salazar<sup>h</sup> all other Barcelona Consensus Conference participants<sup>1</sup>

**Table 1.** Therapeutic options and conditions for preferential use as first-line therapy

Drug	Func-tionality	Grading	Primary site	SSTR status	Special considerations
Octreotide	+	G1	midgut	+	low tumor burden
Lanreotide	+	G1		+	placebo-controlled data on antiproliferative activity pending
STZ+5-FU	+/-	G1-G2	pancreas		progressive in short-term <sup>1</sup> or high tumor burden or symptomatic
TEM/CAP	+/-	G2	pancreas		progressive in short-term <sup>1</sup> or high tumor burden or symptomatic; contraindication for STZ-based regimen
Everolimus	+/-	G1-G2	pancreas		insulinoma; contraindication for CTX
Sunitinib	+/-	G1-G2	pancreas		contraindication for CTX
PRRT	+/-	G1-G2	any	+	extended disease; extrahepatic disease, e.g. bone metastases (if tumor burden not too high); high uptake of tumor lesions on Octreoscan and limited disease amenable to surgery after down-staging
Cisplatin + etoposide	+/-	G3	any	+/-	all poorly differentiated NEC

CTX = Chemotherapy; STZ = streptozotocin; SSTR = somatostatin receptor.

<sup>1</sup> 3-6 months.

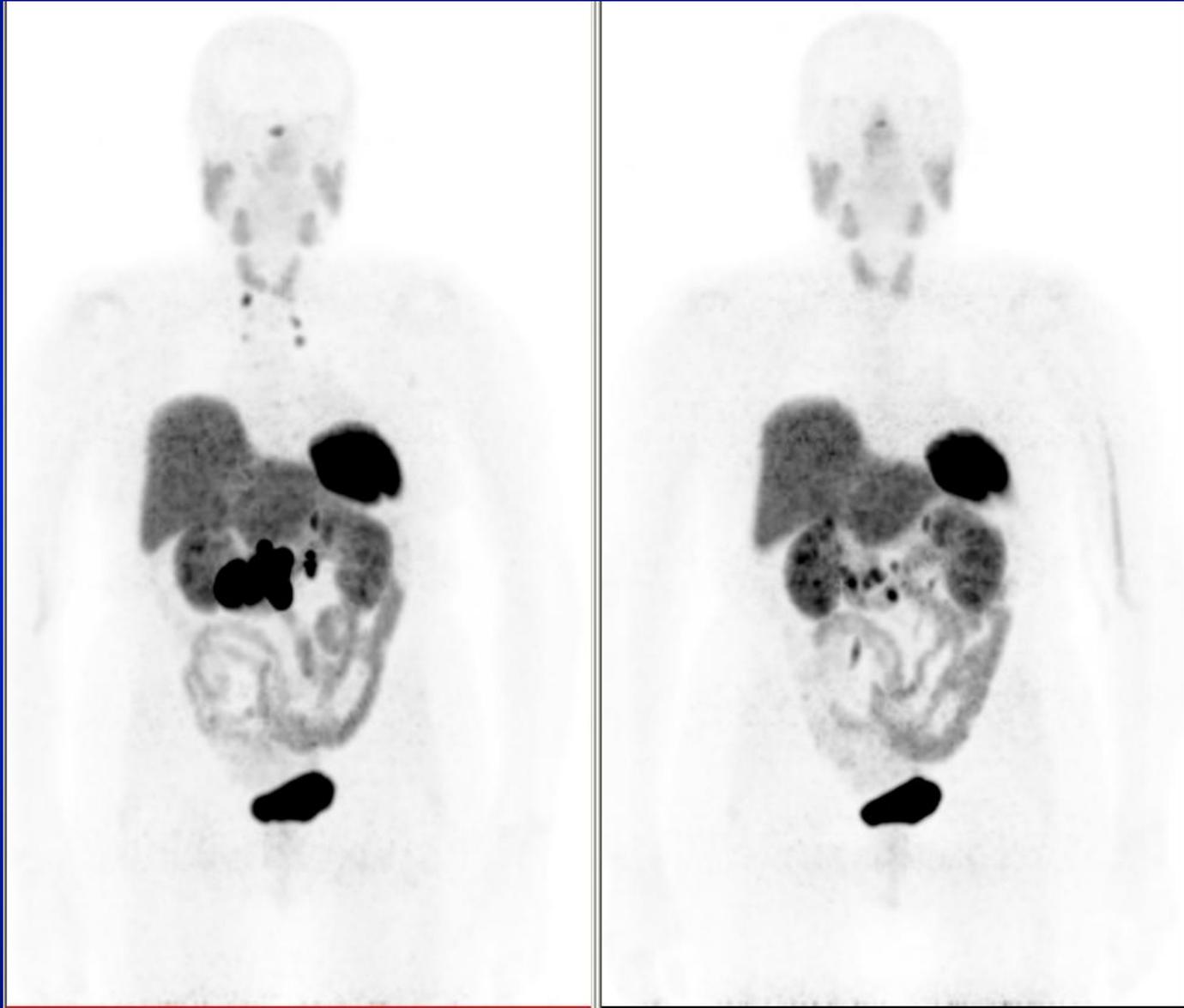
# ENETS Consensus Guidelines for the Management of Patients with Liver and Other Distant Metastases from Neuroendocrine Neoplasms of Foregut, Midgut, Hindgut, and Unknown Primary

Marianne Pavel<sup>a</sup> Eric Baudin<sup>b</sup> Anne Couvelard<sup>c</sup> Eric Krenning<sup>d</sup>  
Kjell Öberg<sup>e</sup> Thomas Steinmüller<sup>f</sup> Martin Anlauf<sup>g</sup> Bertram Wiedenmann<sup>a</sup>  
Ramon Salazar<sup>h</sup> all other Barcelona Consensus Conference participants<sup>1</sup>

## Conclusions

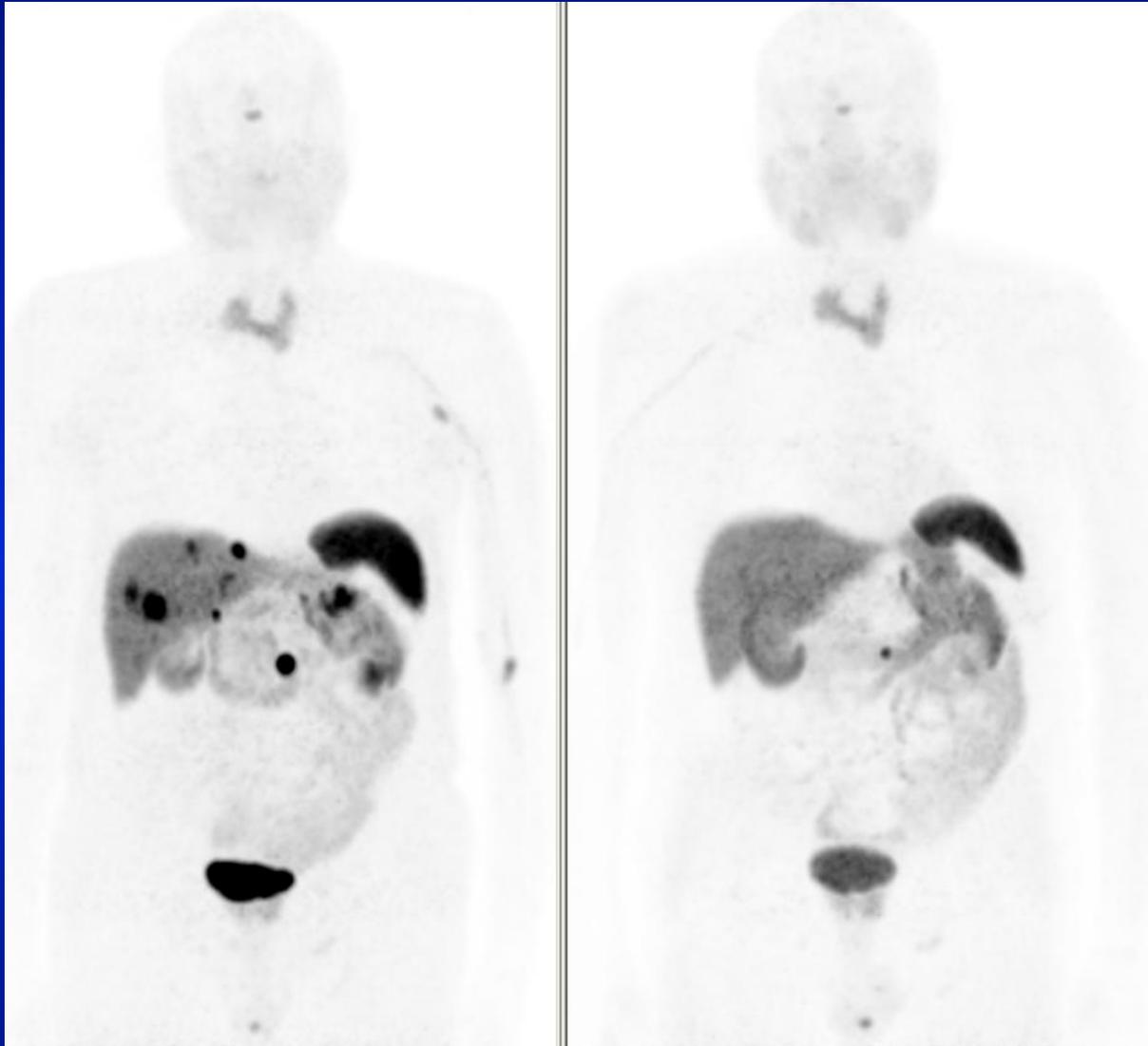
PRRT may be used to treat metastases of NET G1/G2, with <sup>90</sup>Y- and/or <sup>177</sup>Lu-DOTATOC or -DOTATATE showing particular promise, but prospective randomized clinical trial results are warranted.

$^{68}\text{Ga}$ -DOTATATE PET/CT



Valutazione precoce dopo 2 trattamenti

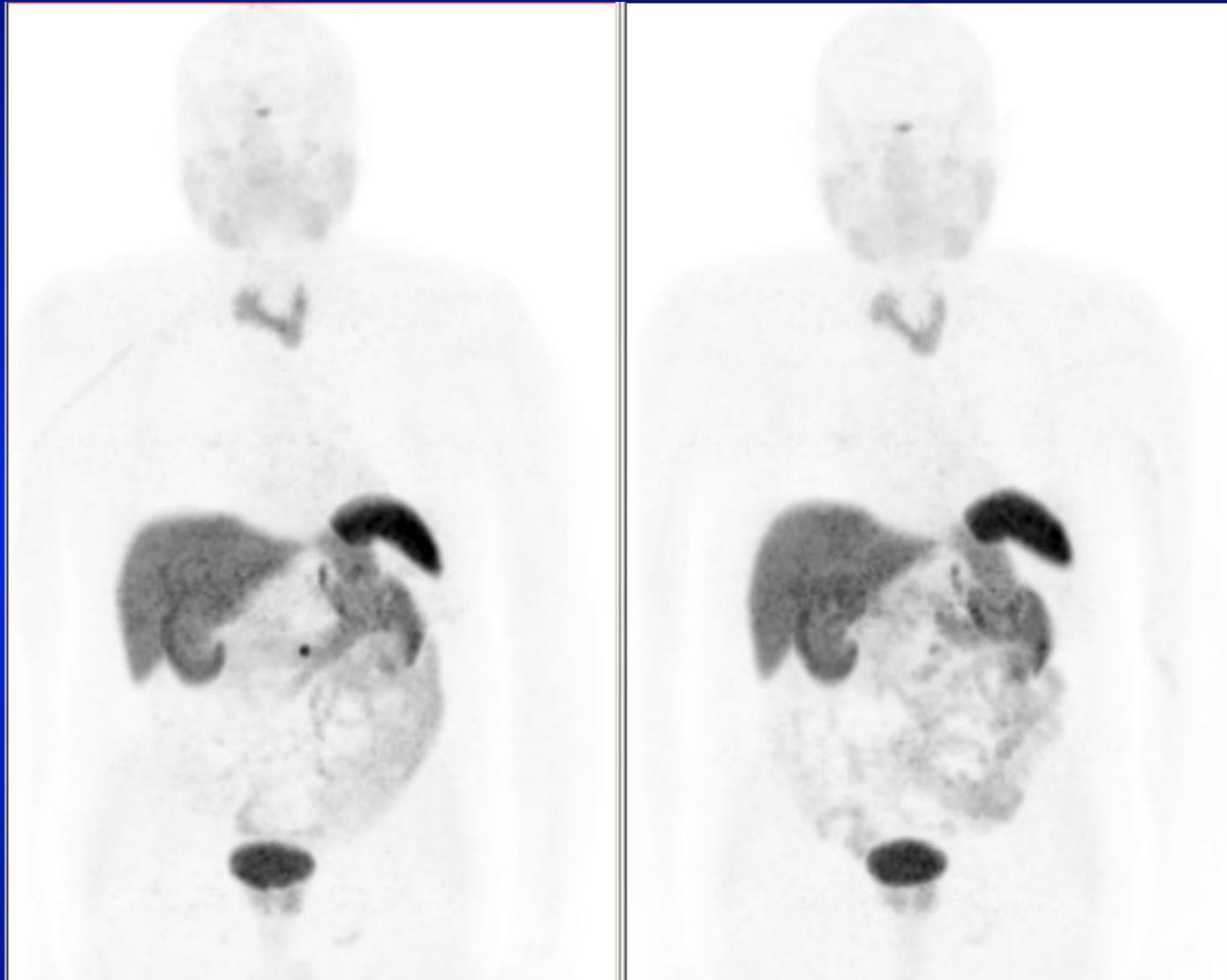
$^{68}\text{Ga}$ -DOTATATE PET/CT



carcinoma neuroendocrino pancreatico  
con metastasi epatiche

M  
73 aa  
2 cicli di  $^{90}\text{Y}$  e 4 cicli di  $^{177}\text{Lu}$

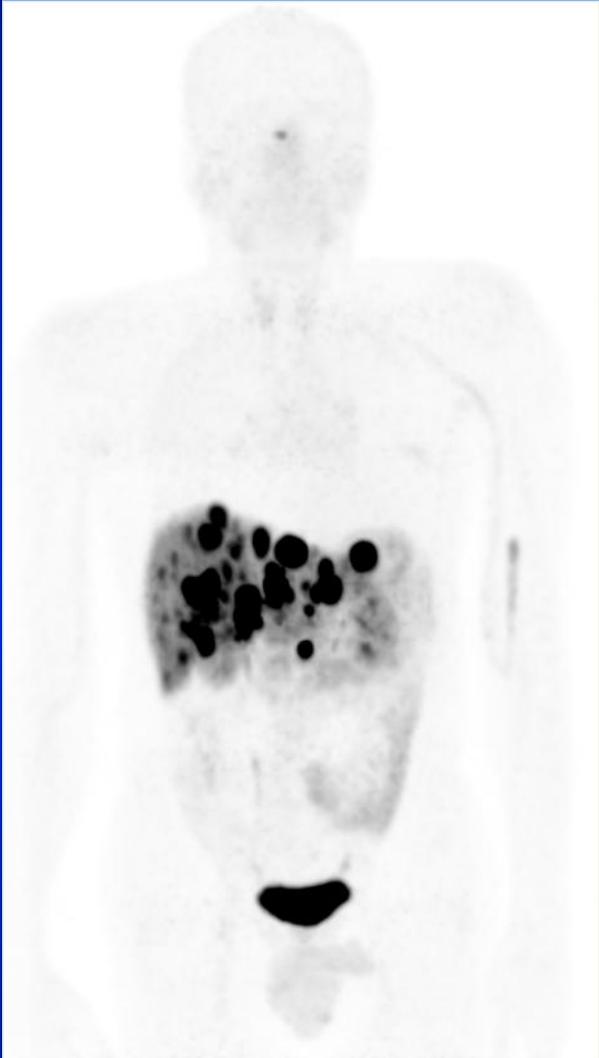
$^{68}\text{Ga}$ -DOTATATE PET/CT



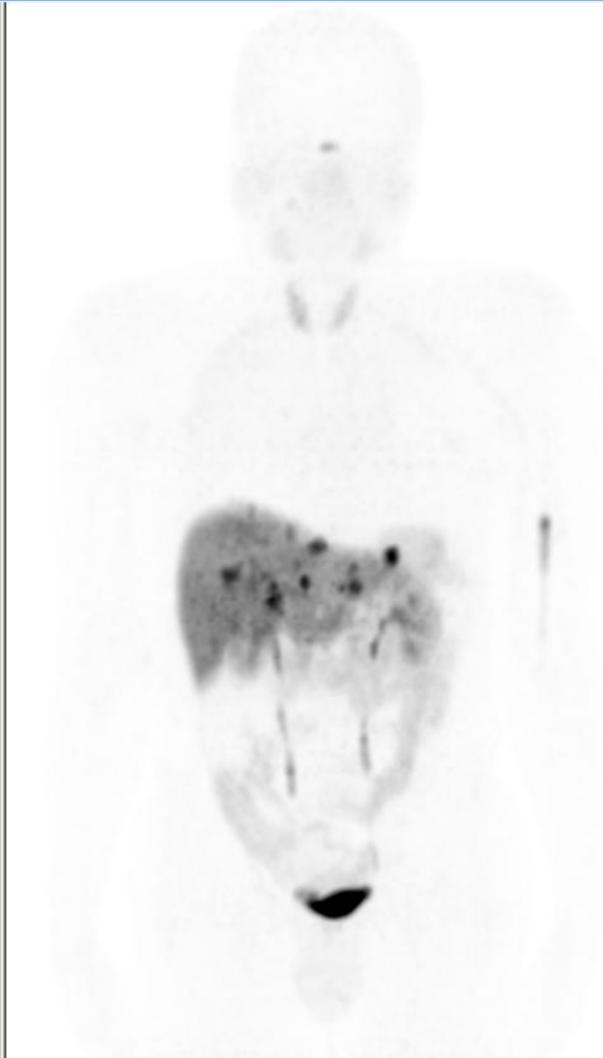
carcinoma neuroendocrino pancreatico  
con metastasi epatiche

M  
73 aa  
2 cicli di  $^{90}\text{Y}$  ed 4 ciclo di  $^{177}\text{Lu}$

**Pre-terapia**

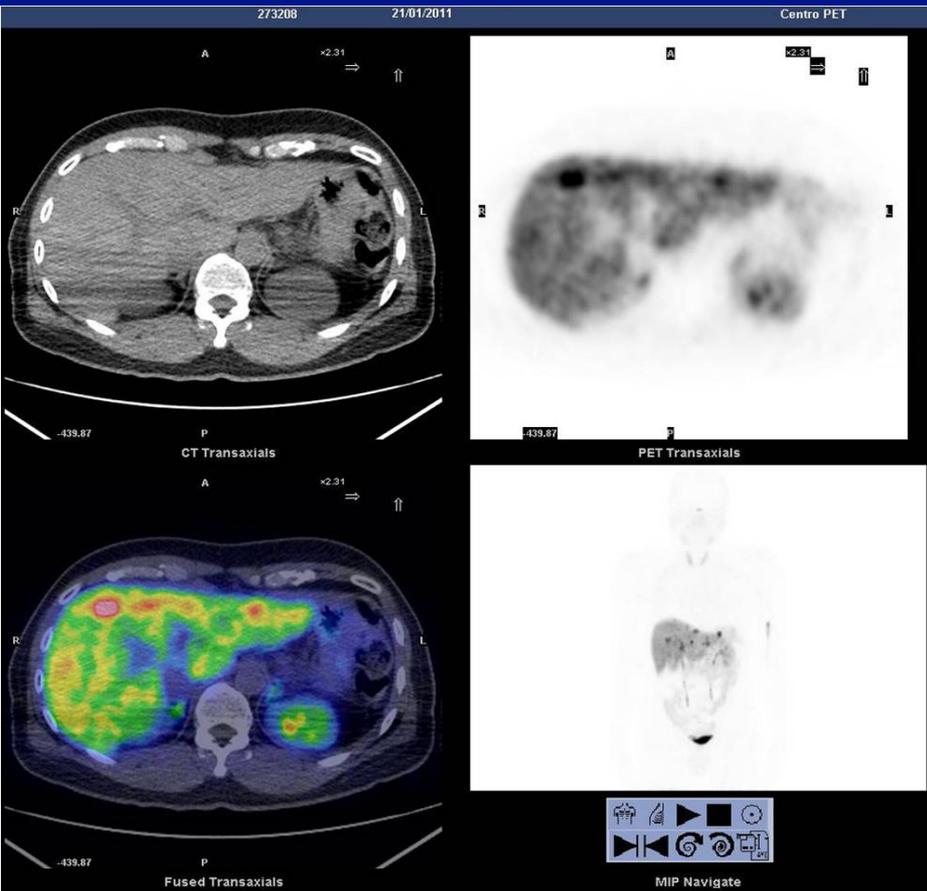


**Post-terapia**

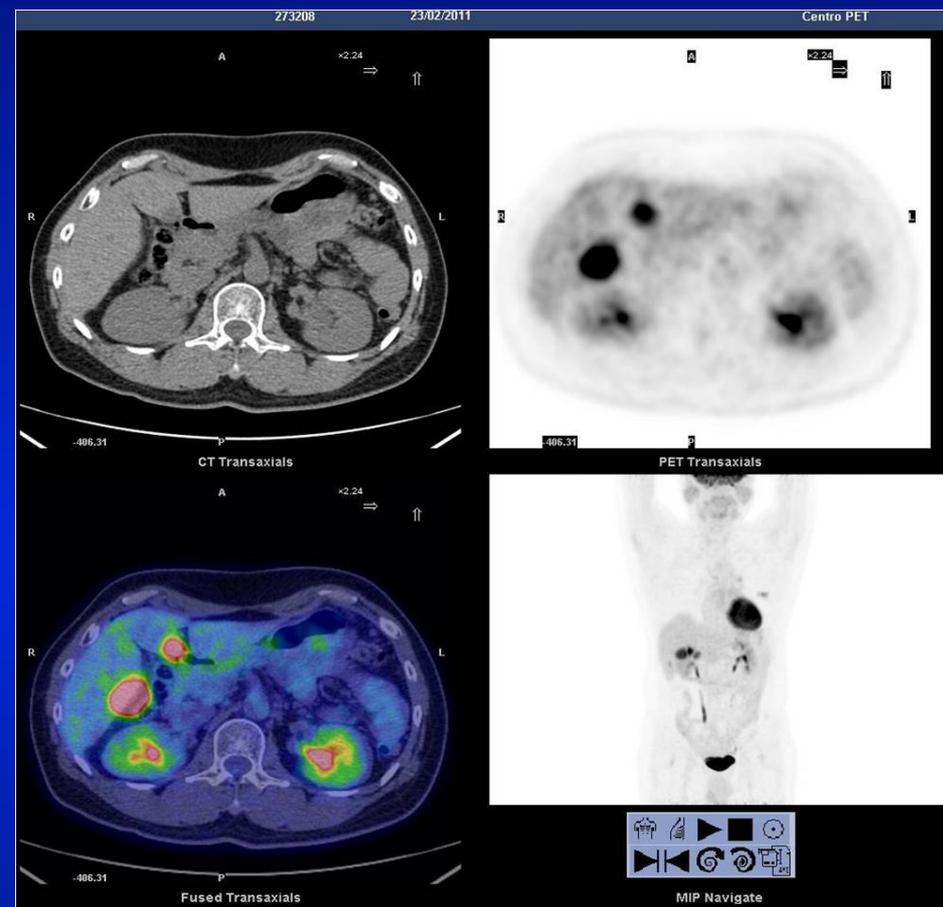


M, 56 aa: carcinoma neuroendocrino pancreatico con metastasi epatiche.  
4 cicli di  $^{90}\text{Y}$  e 1 di  $^{177}\text{Lu}$ . Risposta parziale alla terapia.

## $^{68}\text{Ga}$ -DOTATOC PET/CT



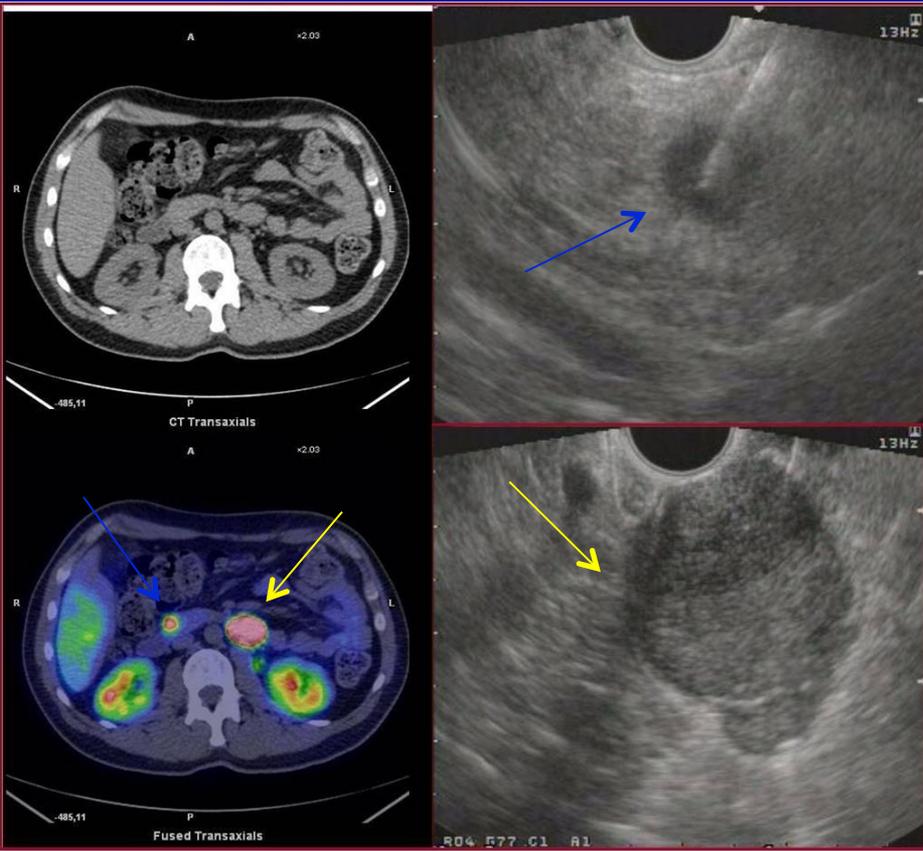
## $^{18}\text{F}$ -FDG PET/CT



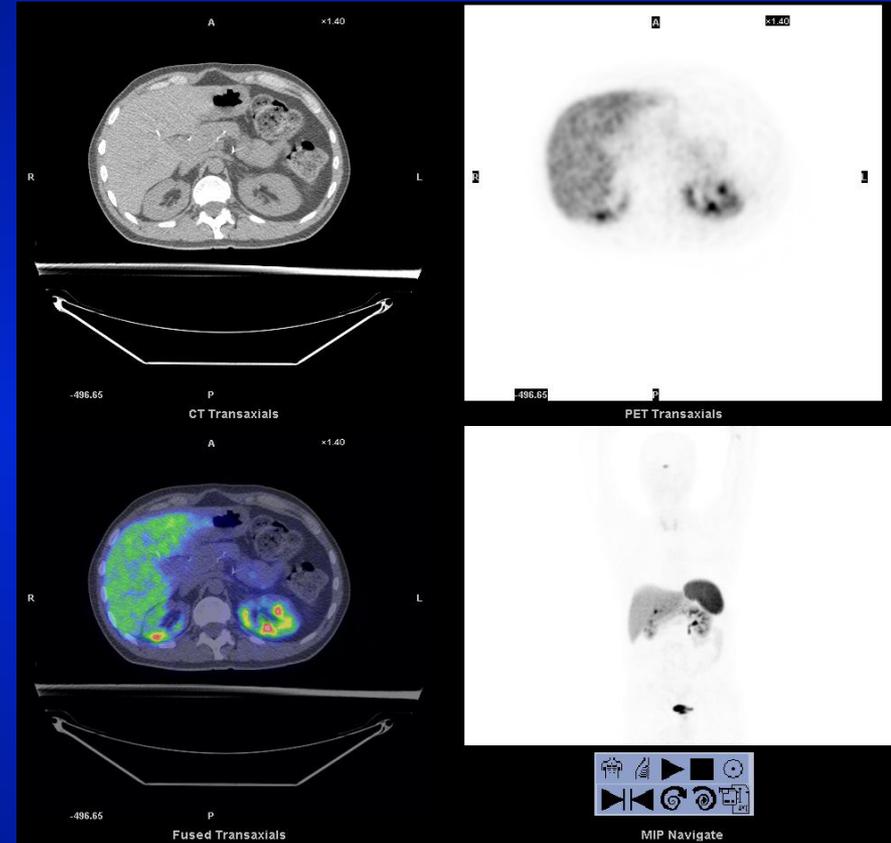
## Post-terapia

Stesso paziente. Buona risposta alla terapia (4 cicli di  $^{90}\text{Y}$ + 1 ciclo di  $^{177}\text{Lu}$ ) sulle lesioni captanti il  $^{68}\text{Ga}$ -DOTATOC. Presenza di nuove lesioni captanti il  $^{18}\text{F}$ -FDG

# Pre-terapia

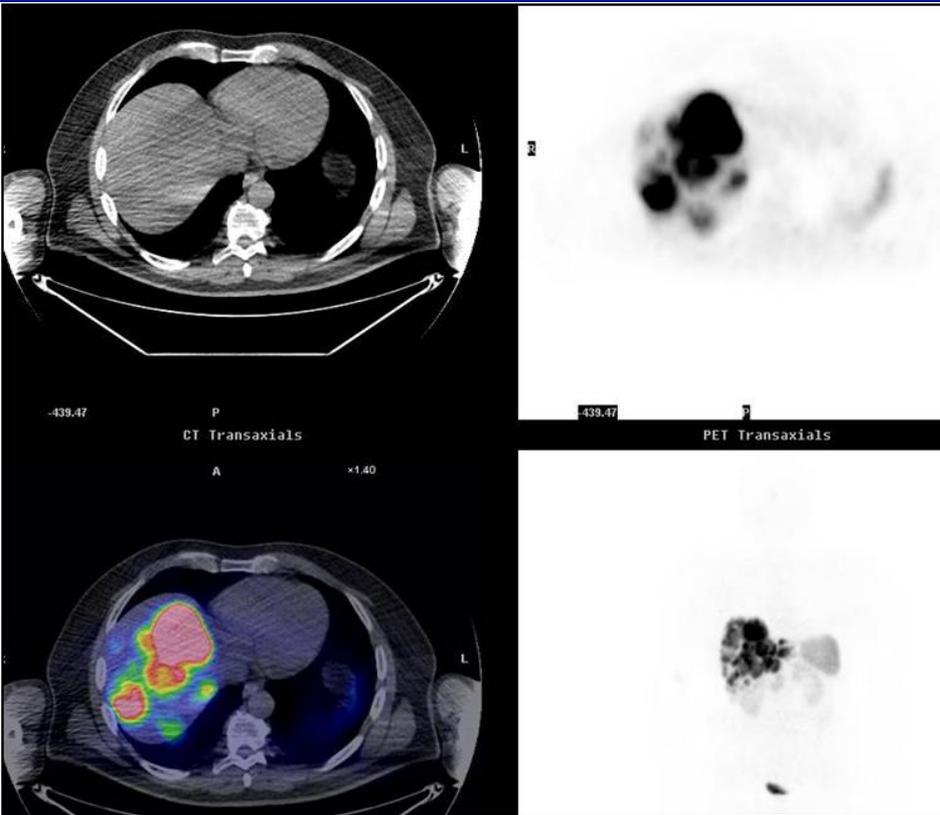


# Post-terapia

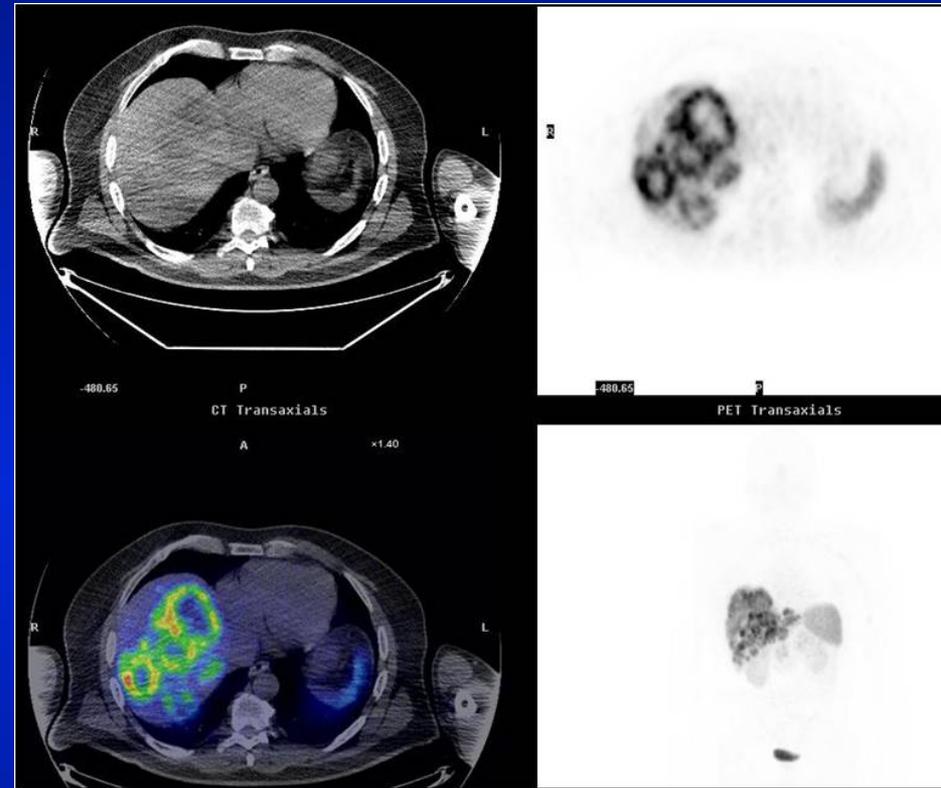


Pz. V.R.: NET della testa del pancreas (freccia blu) con metastasi linfonodale (freccia gialla). Risposta completa alla terapia con 90Y.

## $^{68}\text{Ga}$ -DOTATOC PET/CT



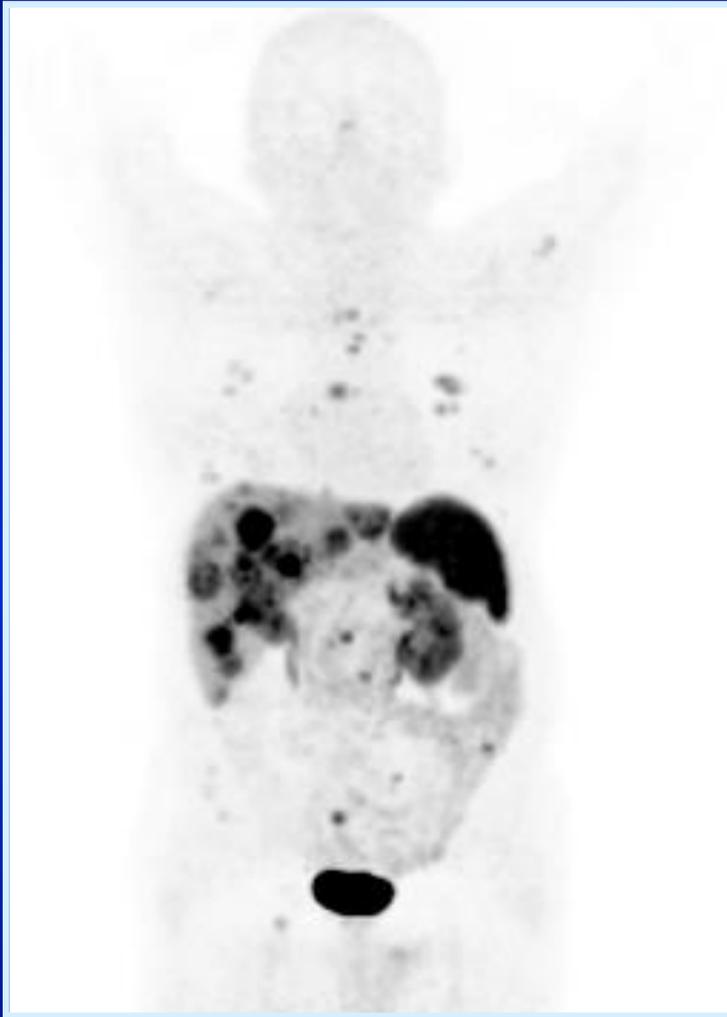
**Pre-terapia**



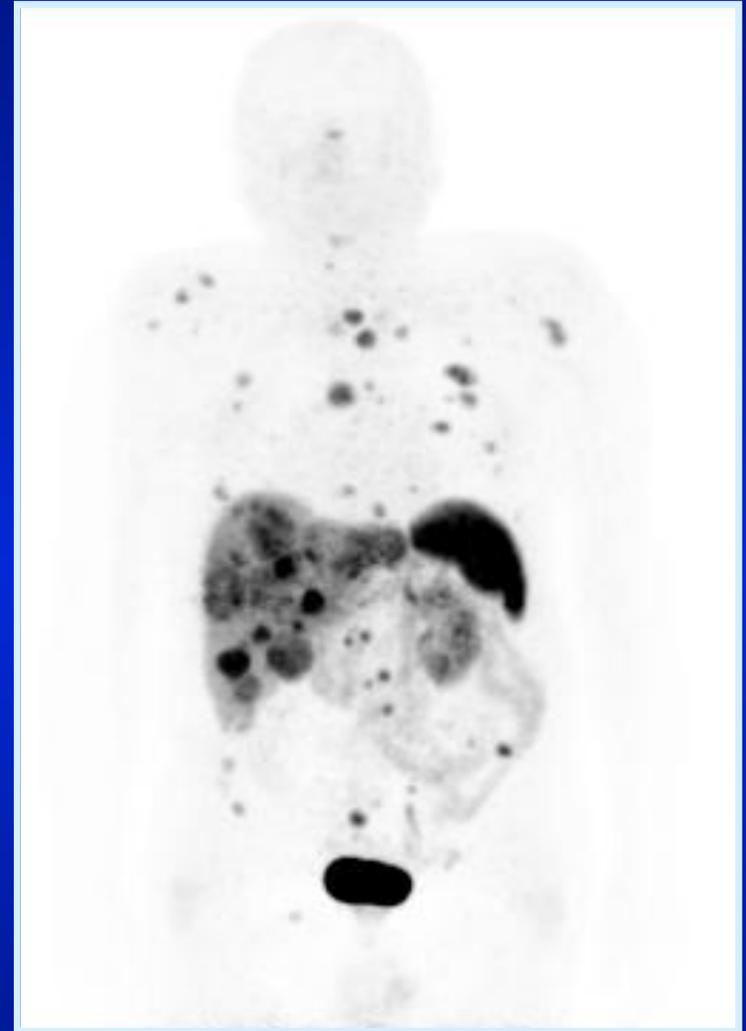
**Post-terapia**

R.A., M, 59aa: metastasi epatiche da ca neuroendocrino da primitivo a sede ignota. Risposta parziale alla terapia combinata  $^{90}\text{Y}$ + $^{177}\text{Lu}$ .

$^{68}\text{Ga}$ -DOTATATE PET/CT

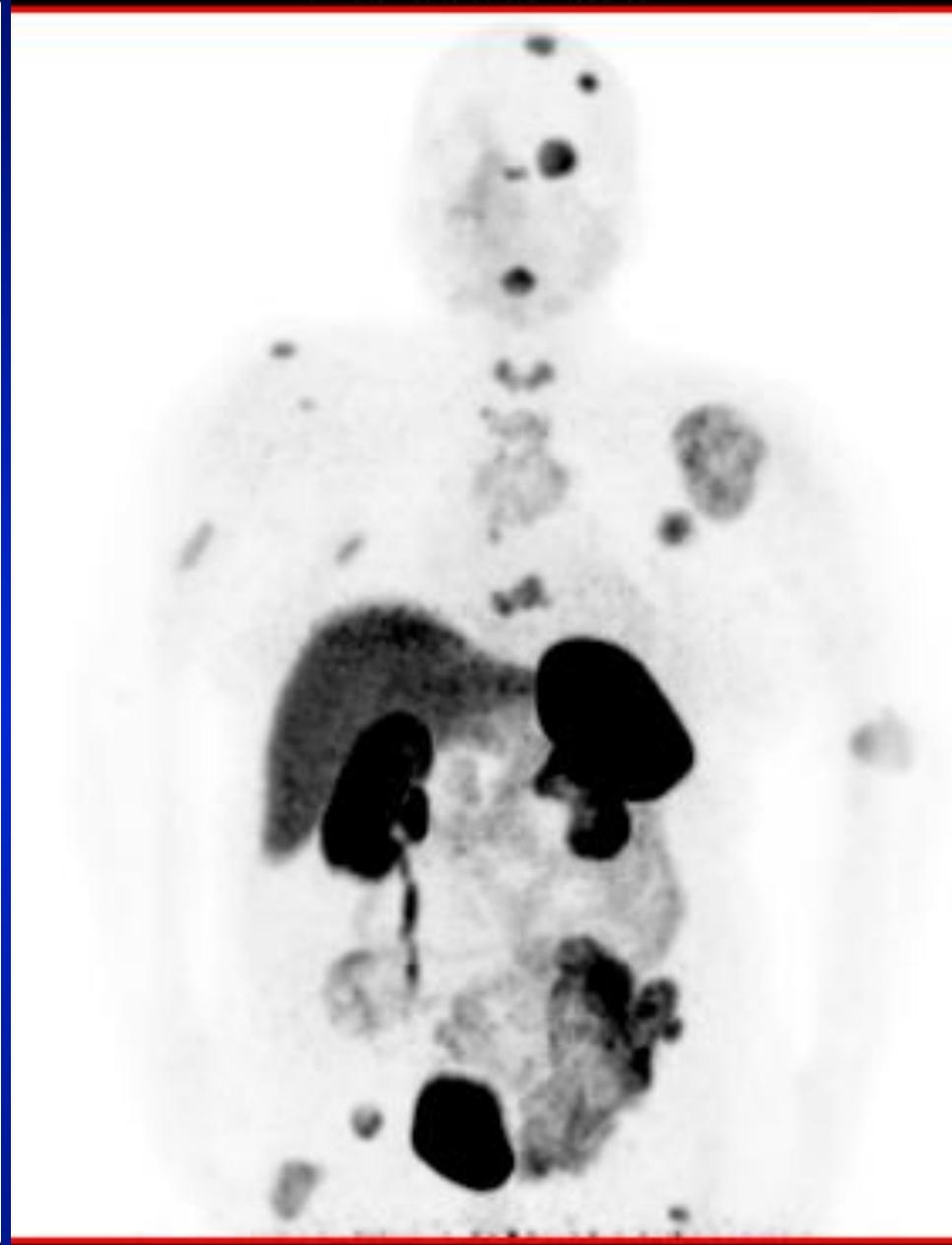
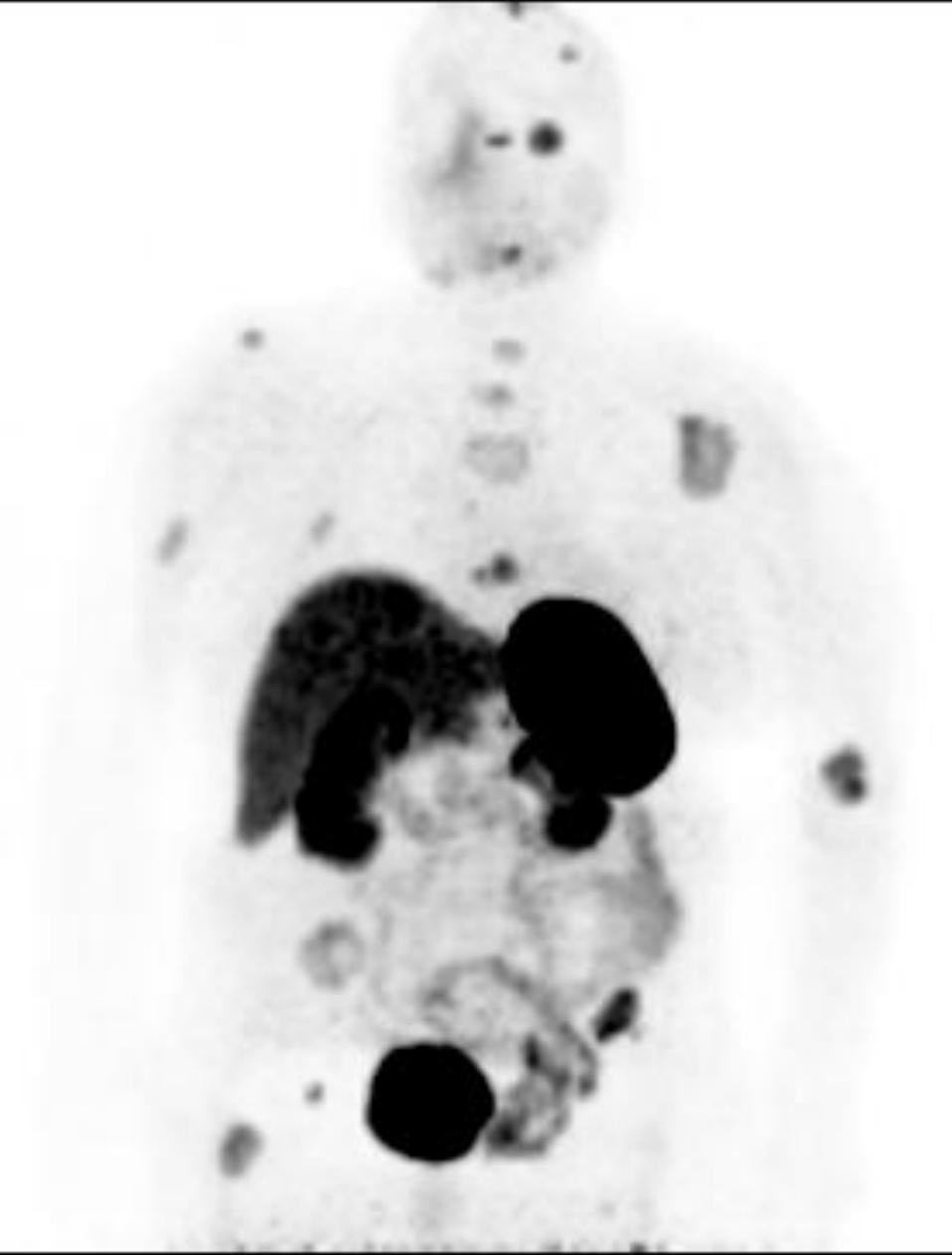


**Pre-  
terapia**



**Post-terapia**

R.I., M, 76 anni : Ca neuroendocrino del polmone con metastasi epatiche, ossee e linfonodali. Malattia in progressione dopo trattamento con  $^{90}\text{Y}$ .



Pre-therapy

**P.M. female, 61 year old**

Post-therapy

**Severe dyspnea**  
**O<sub>2</sub>-therapy: 6-7 hours/day**

**No dyspnea**  
**No O<sub>2</sub>-therapy**

**Before therapy**

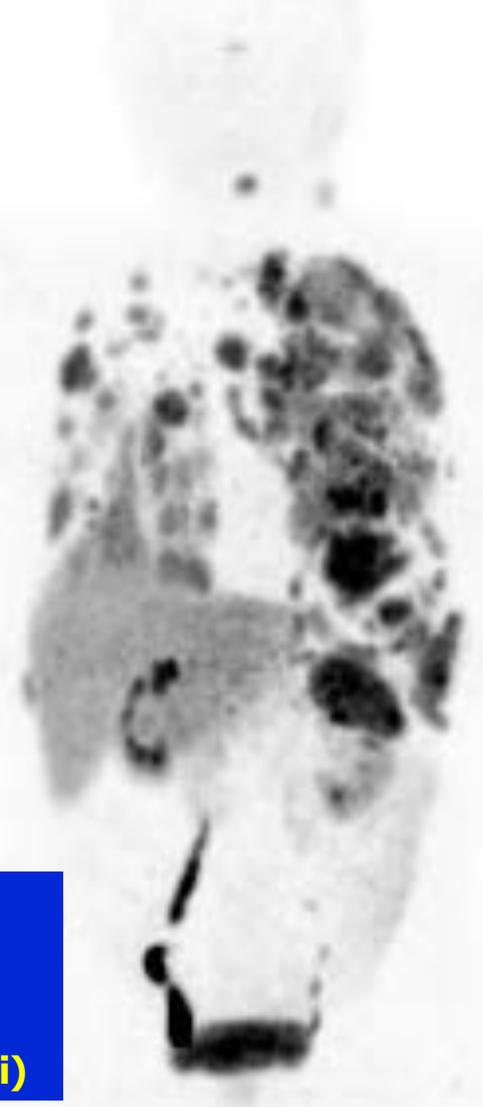


**After 4 cycles**  
**<sup>90</sup>Y-DOTATOC**  
**(cumulative dose 268 mCi)**

**Sept 2007**

**Mar 2009**

**B.M. male, 75 year old**



## Differentiated Thyroid Cancer: A New Perspective with Radiolabeled Somatostatin Analogues for Imaging and Treatment of Patients

Annibale Versari,<sup>1</sup> Martina Sollini,<sup>1</sup> Andrea Frasoldati,<sup>2</sup> Alessandro Fraternali,<sup>1</sup> Angelina Filice,<sup>1</sup> Armando Froio,<sup>1</sup> Mattia Asti,<sup>1</sup> Federica Fioroni,<sup>3</sup> Nadia Cremonini,<sup>4</sup> Daniel Putzer,<sup>5</sup> and Paola Anna Erba<sup>6</sup>

TABLE 3. SITE OF METASTATIC DISEASE DETECTED BY <sup>68</sup>Ga-DOTATOC PET/CT DETAILED FOR EACH TREATED PATIENT; <sup>90</sup>Y-DOTATOC ADMINISTRATION DATA AND TREATMENT RESPONSE IN PATIENTS TREATED WITH PRRT

Pt	Site of disease according to <sup>68</sup> Ga-DOTATOC	Administrations of <sup>90</sup> Y-DOTATOC (n)	Days between PRRT administration	Total cumulative activity <sup>90</sup> Y-DOTATOC (GBq)	Best response (RECIST)	Duration (months)
#1	Lung, bone	2	91	4.329	PD	N/A
#2	Thyroid bed, LNs, lung	4	56; 45; 63	14.911	PR	8
#3	Thyroid bed, LNs, lung	4	91; 84; 70	11.729	SD	7
#4	Thyroid bed, LNs, lung, bone	6	126; 92; 90; 91; 112	12.987	SD	11.5
#5	LNs, lung, bone	3	70; 56	11.050	PR	7.5
#6	Bone	6	126; 92; 90; 91; 140	12.765	PD	N/A
#7	Thyroid bed, LNs, bone	4	63; 63; 56	14.870	SD	3.5
#8	Bone	5	61; 70; 49; 39	14.393	N/A	N/A
#9	LNs, lung, bone	5	63; 63; 77; 56	17.950	SD	8
#10	Bone	3	63; 63	11.170	PD	N/A
#11	Liver, bone	4	56; 42; 70	14.689	PD	N/A

DOTATOC, DOTA<sup>0</sup>-Tyr<sup>3</sup>-octreotide; PET, positron emission tomography; CT, computed tomography; PRRT, peptide receptor radionuclide therapy; RECIST, Response Evaluation Criteria in Solid Tumors.

# Take Home Messages

- La possibilità di usare lo **stesso peptide** per la **diagnostica** e, nei pazienti PET/CT positivi, per la **terapia** rappresenta il punto di forza del trattamento radiorecettoriale.
- Circa il 48% dei Pazienti che esegue la PET/CT con  $^{68}\text{Ga}$ -DOTATOC/TATE risulta positivo all'indagine e questo cambia il management clinico fornendo nuove prospettive terapeutiche.

# Take Home Messages

- La risposta clinica è stata più precoce e spesso superiore rispetto alla risposta morfologico-funzionale.
- Nella nostra casistica il 42,5% ha una risposta al trattamento (PR+CR) ed il 40,5% presenta una SD.

# Take Home Messages

## Punti critici:

- Valutazione della risposta
- Tutti i risultati pubblicati derivano da studi di fase I-II, non omogenei per quanto attiene ai criteri di inclusione ed agli schemi di trattamento, pertanto un confronto tra loro risulta oggi praticamente impossibile.
- Mancanza di protocolli condivisi

Picture by *Armando Froio* 03/03/2013; Vellir, Iceland

