



Corso Residenziale  
di Formazione  
per Giovani Medici

**AME-FADOI**

13-15 Febbraio 2014  
Hotel Europa Bologna



**Segreteria Scientifica**

**Mauro Silingardi**  
Direttore Dipartimento  
per la Formazione  
e Aggiornamento FADOI

**Michele Zini**  
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Formazione AME

# ***La Medicina Nucleare nella diagnosi e nella terapia dei NETs***

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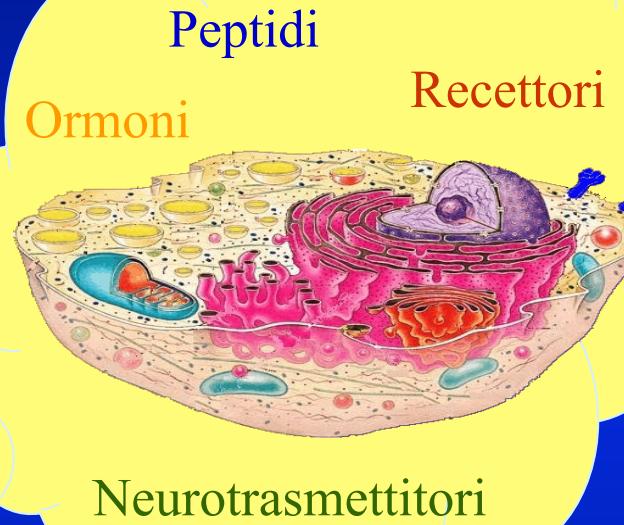
**SERVIZIO SANITARIO REGIONALE  
EMILIA-ROMAGNA  
Azienda Ospedaliera di Reggio Emilia**  
  
Arcispedale S. Maria Nuova

Istituto in tecnologie avanzate e modelli assistenziali in oncologia  
Istituto di Ricovero e Cura a Carattere Scientifico

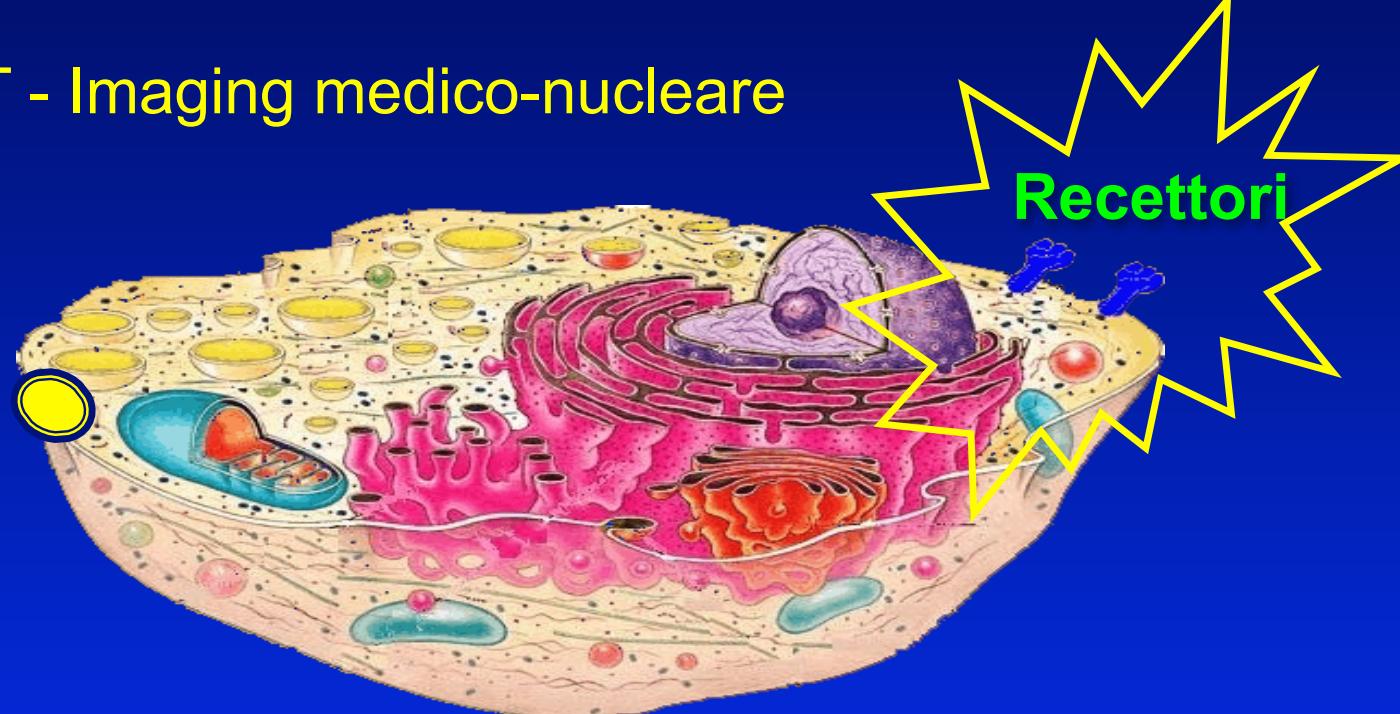


# *Imaging medico-nucleare=Imaging molecolare*

**Le immagini sono  
espressione delle  
caratteristiche  
biochimiche e  
metaboliche dei tessuti**



# NET - Imaging medico-nucleare



*Recettori per Peptidi Espressi  
Preferenzialmente dai Tumori GEP*

- Somatostatina (5 sotto-tipi)
- Bombesina (3 sotto-tipi)
- Colecistochinina (2 sotto-tipi)
- VIP (2 sotto-tipi)
- Glucagone (1 principale)

# Imaging medico-nucleare

## Presupposti fisiopatologici



## Metodiche

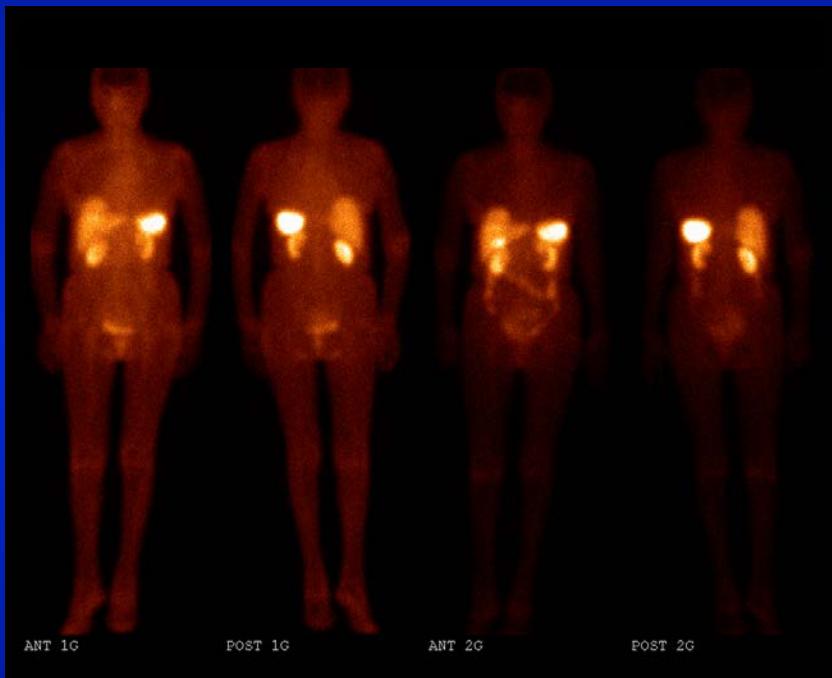
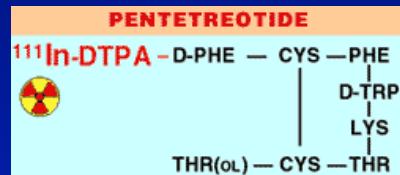
**Scintigrafia, SPECT, SPECT/CT con**  
•  $^{111}\text{In}$ -Octreoscan

**PET/CT con**  
•  $^{68}\text{Ga}$ -DOTATOC  
•  $^{68}\text{Ga}$ -DOTANOC  
•  $^{68}\text{Ga}$ -DOTATATE

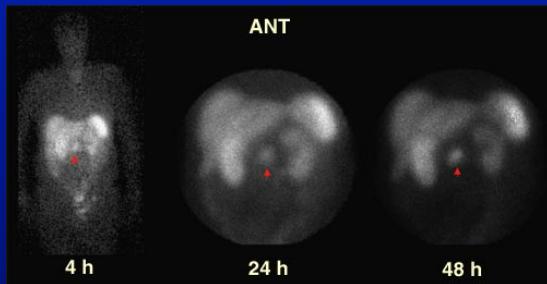
*Tumori Neuroendocrini  
e  
Diagnostica Medico-Nucleare*

- Localizzazione
- Stadiazione
- Selezione dei pazienti per terapia medico-nucleare

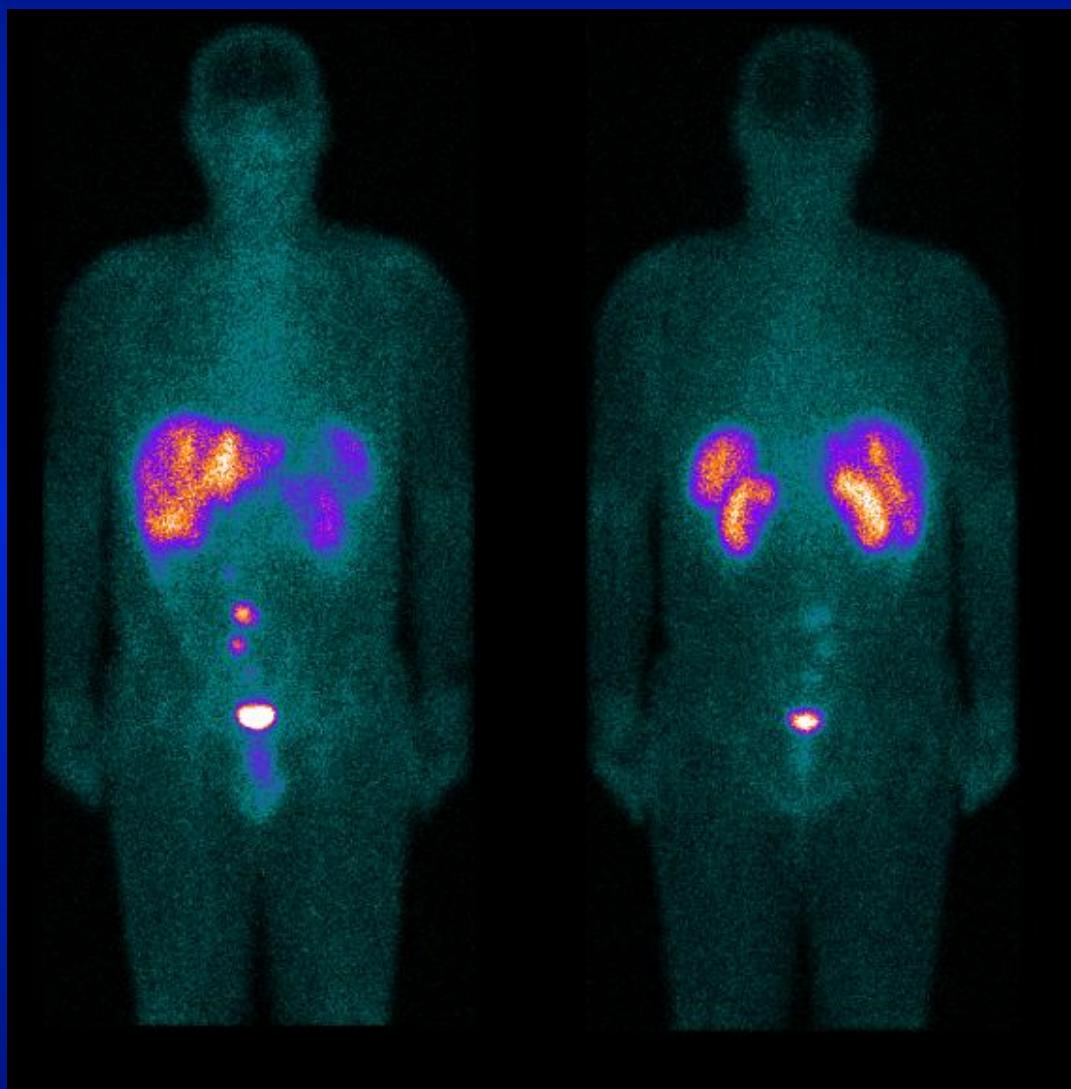
# Pentetreotide (Octreoscan)



- Acquisizioni: 4 ore, 24 ora (48 ora)
- Risoluzione spaziale > 1,5 cm
- Elevato uptake fegato, milza e reni
- Attività tardiva (aspecificità intestinale?)



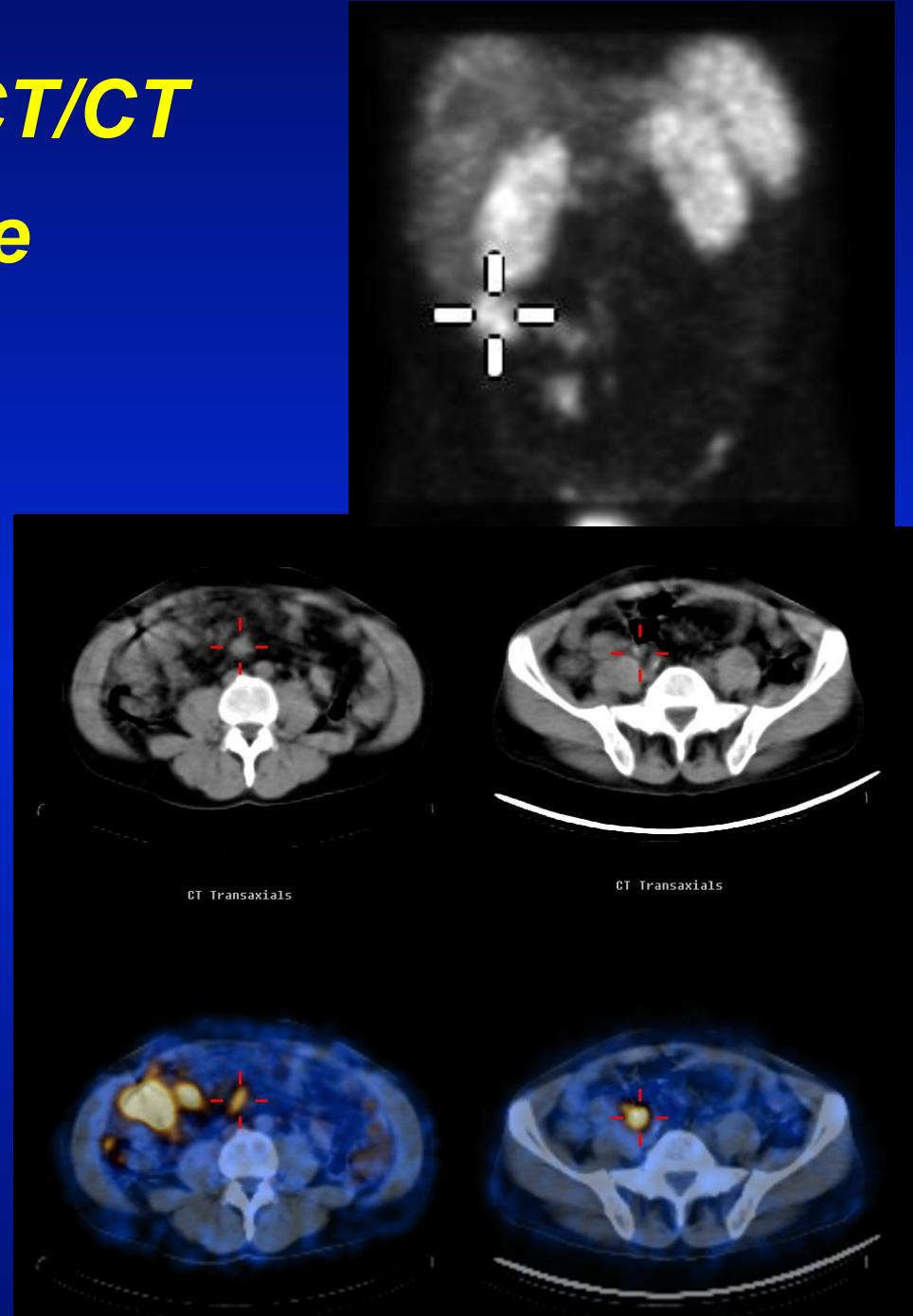
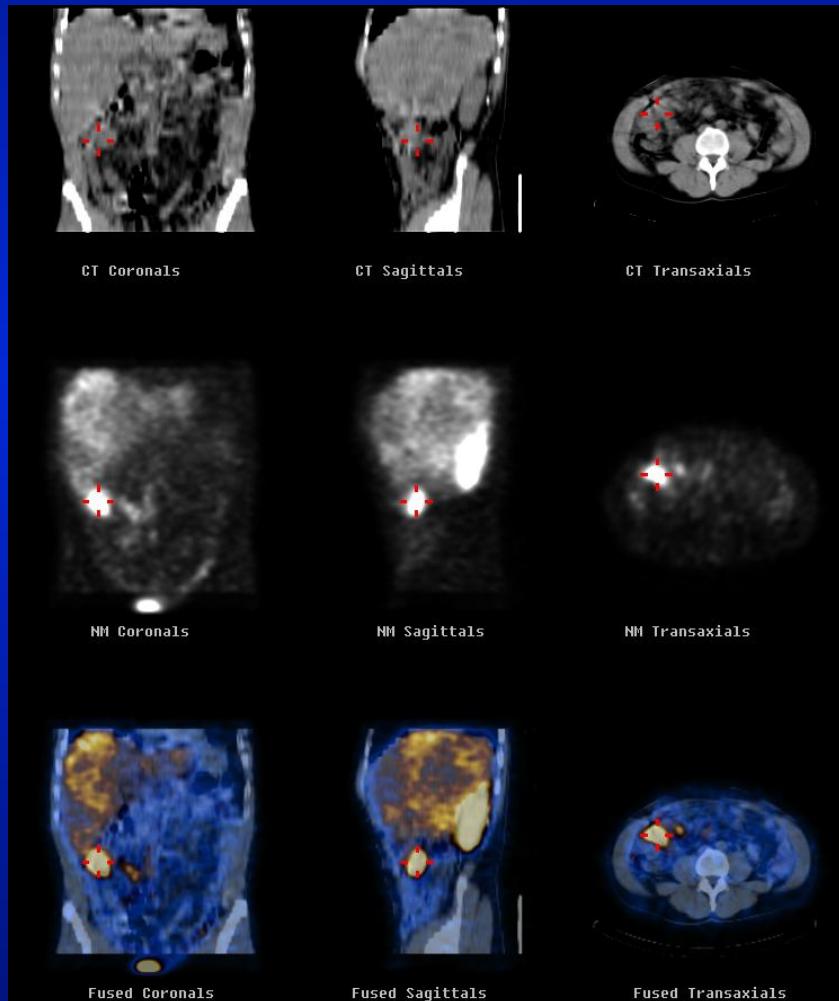
# *Scintigrafia con $^{111}\text{In}$ -Octreoscan*



*Carcinoide Ileale*

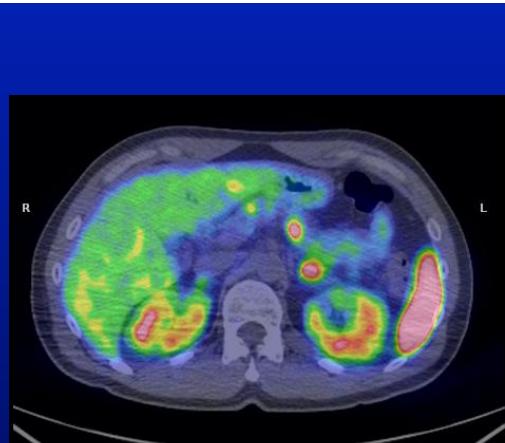
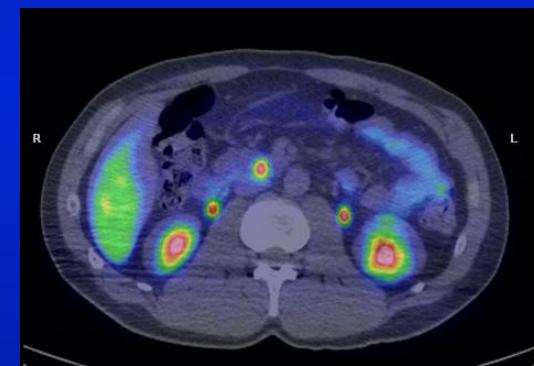
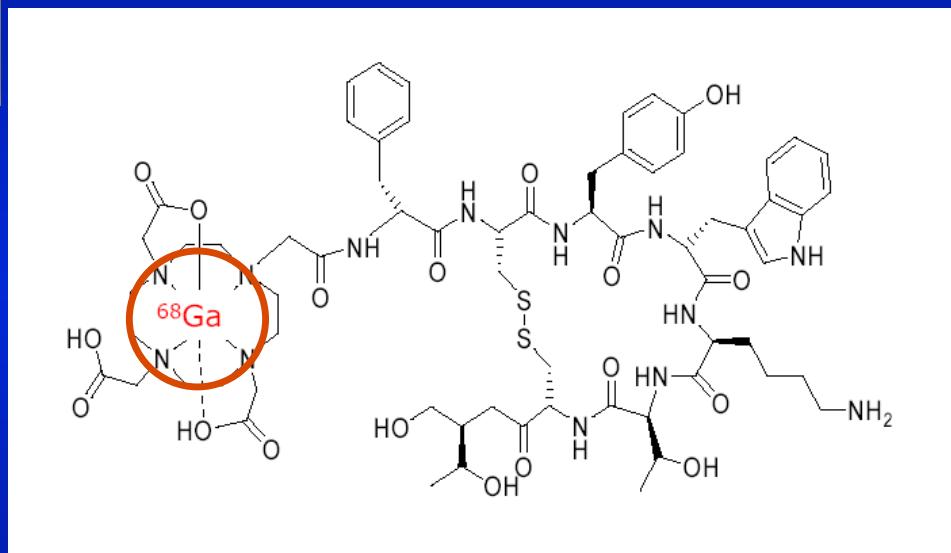
# *Octreoscan®: SPECT/CT*

## *Carcinoide Ileale*



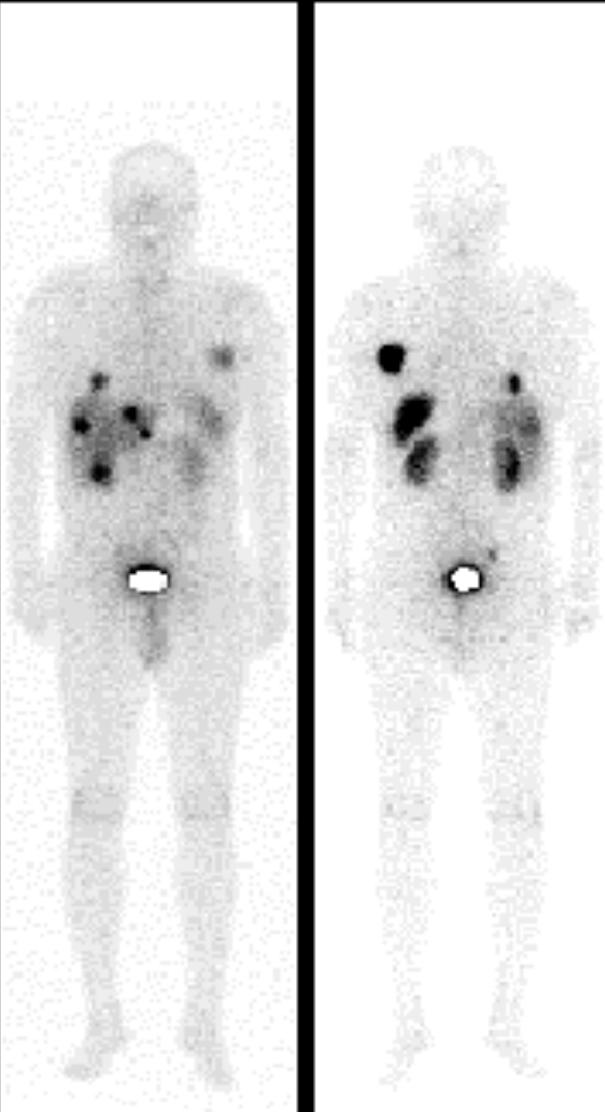
Prof. Giuliano Mariani - Pisa

# ***<sup>68</sup>Ga DOTATOC PET/CT***

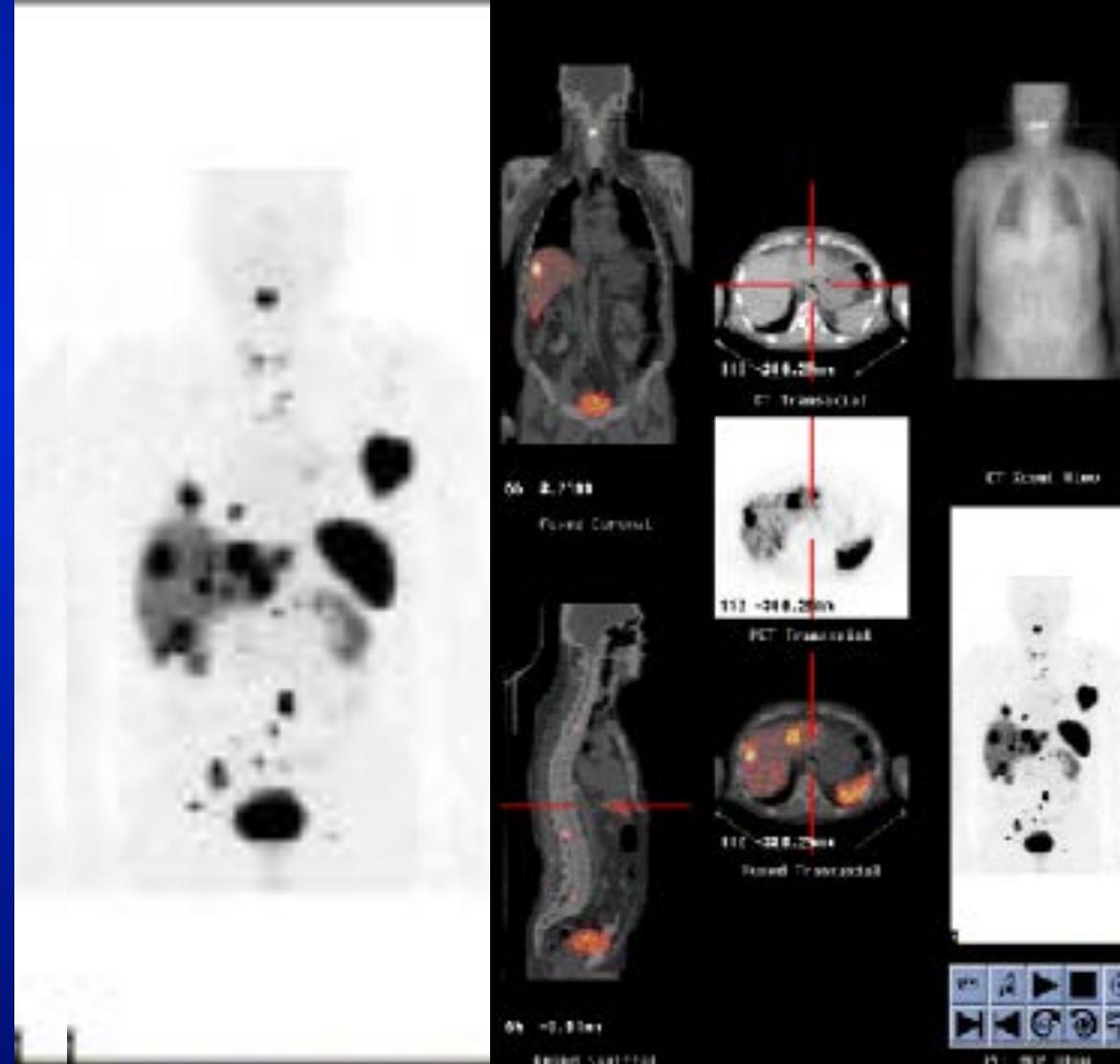


# Tumore neuroendocrino del tratto gastroenteropancreatico metastatico

**<sup>111</sup>In-Octreoscan**



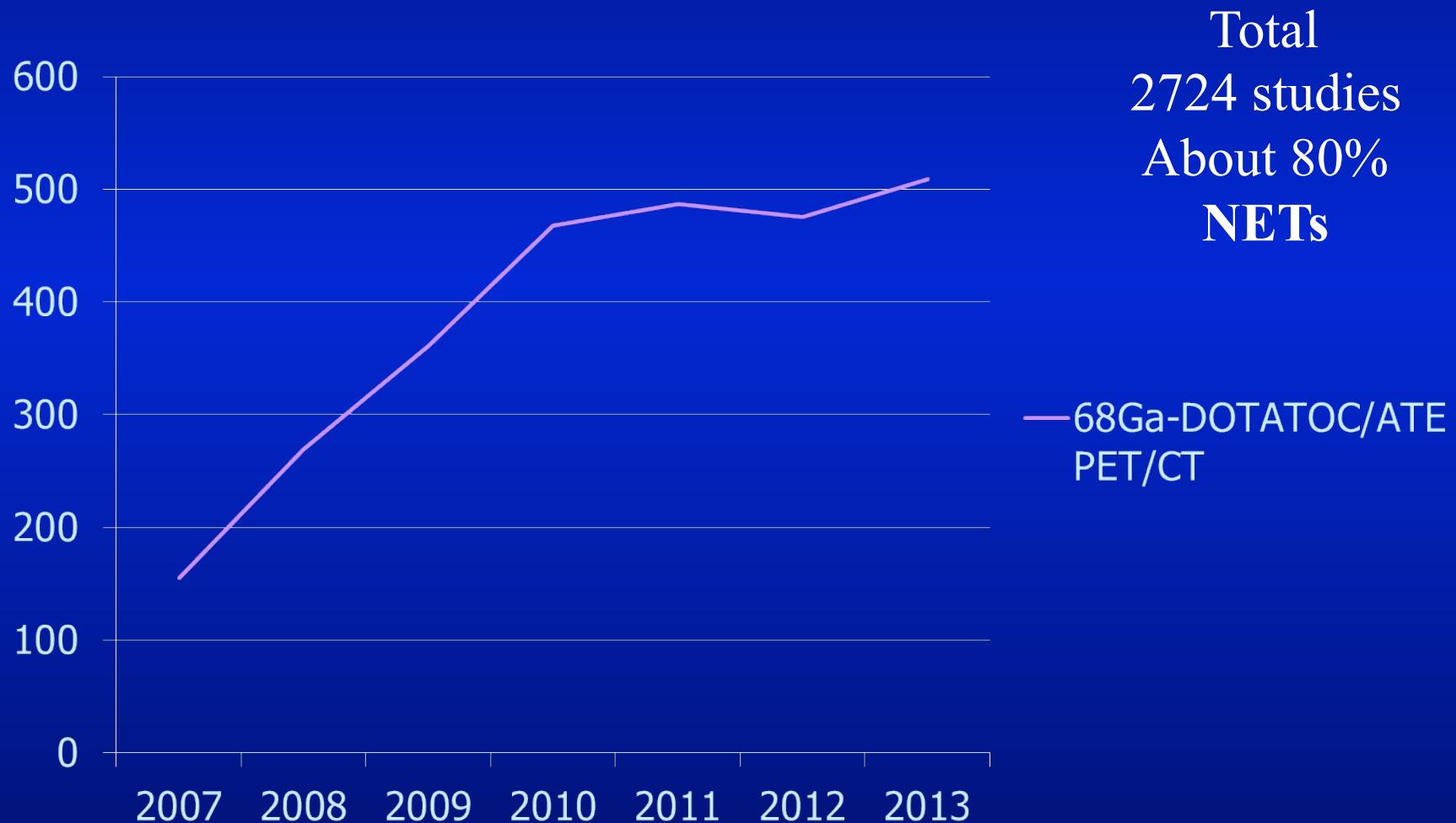
**<sup>68</sup>Ga-Dotatoc PET/CT**



# 68Ga-DOTATOC/ATE PET/CT

## Experience of Reggio Emilia

### January 2007 – December 2013



# **<sup>68</sup>Ga-DOTANOC PET/CT Clinical Impact in Patients with Neuroendocrine Tumors**

**J Nucl Med 2010; 51:669–673**

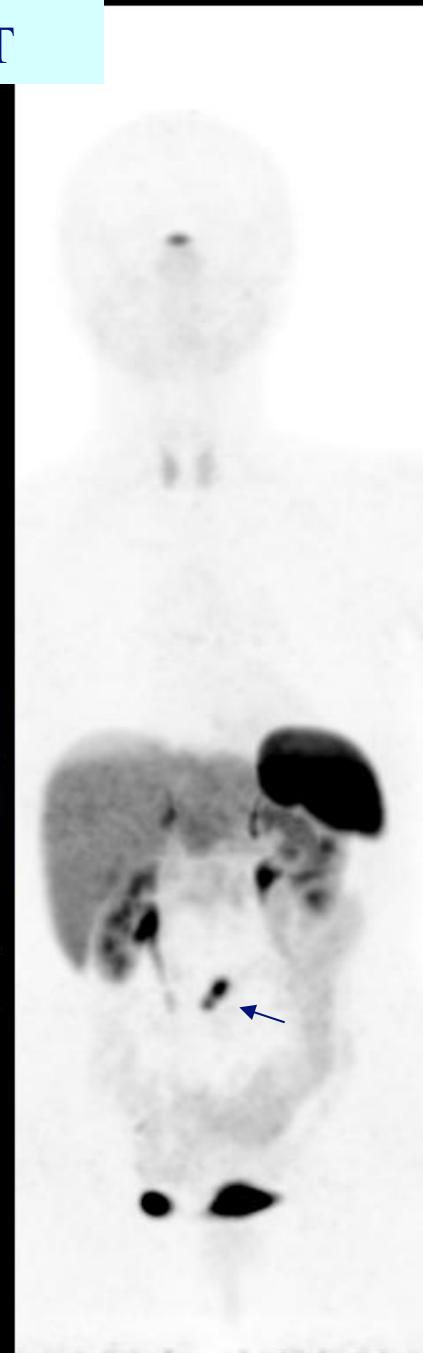
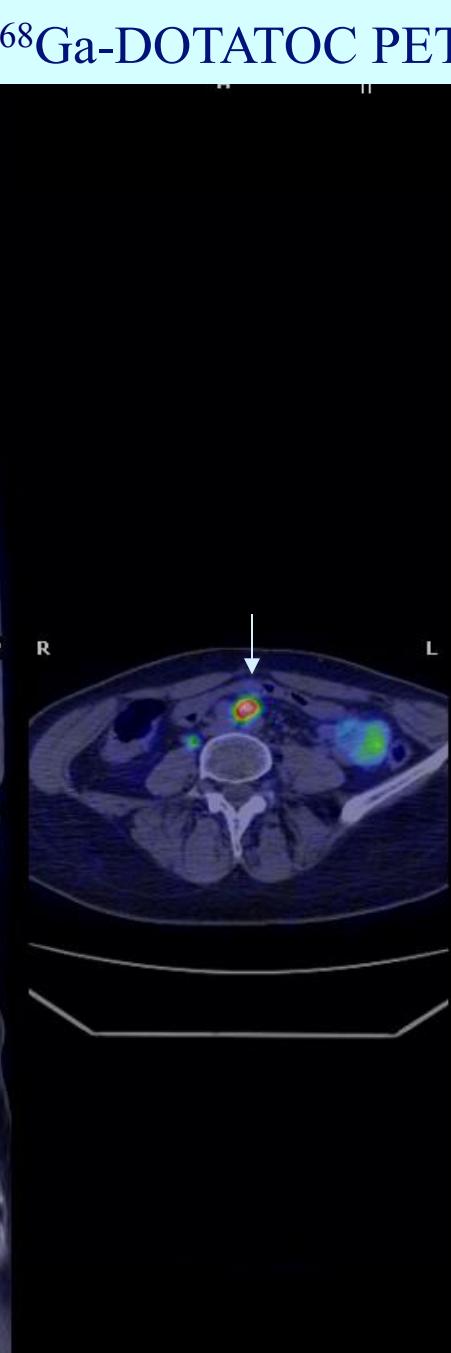
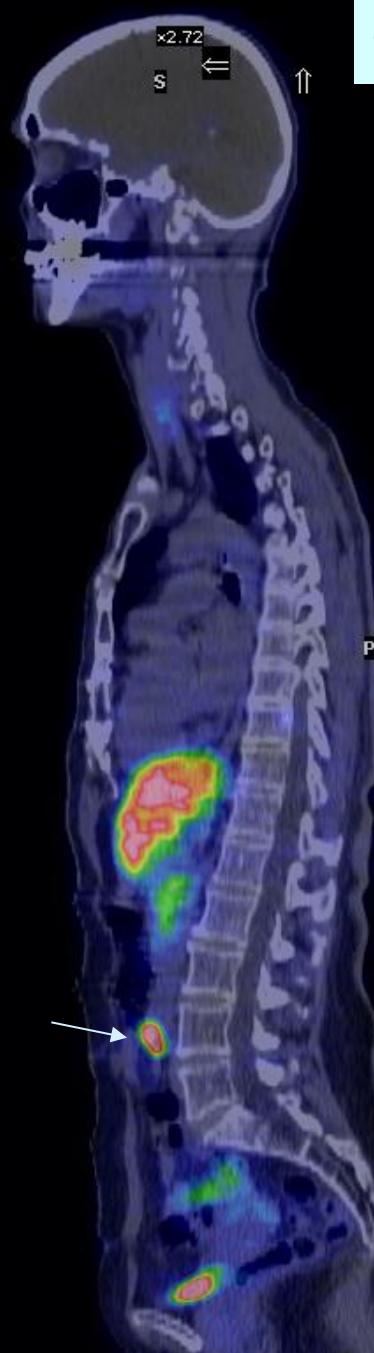
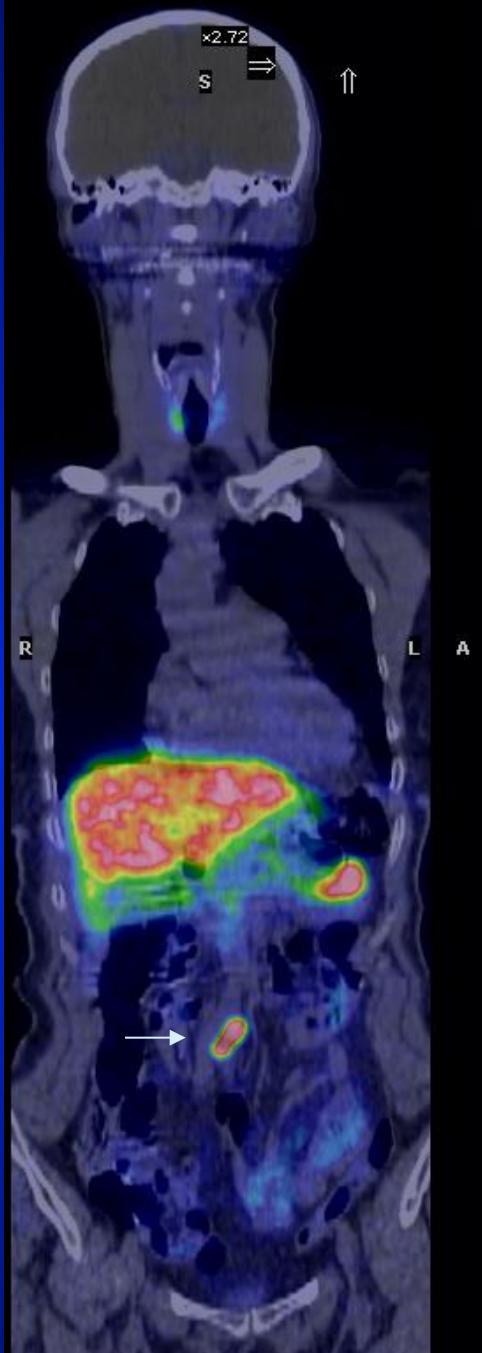
Valentina Ambrosini<sup>1</sup>, Davide Campana<sup>2</sup>, Lisa Bodei<sup>3</sup>, Cristina Nanni<sup>1</sup>, Paolo Castellucci<sup>1</sup>, Vincenzo Allegri<sup>1</sup>, Gian Carlo Montini<sup>1</sup>, Paola Tomassetti<sup>2</sup>, Giovanni Paganelli<sup>3</sup>, and Stefano Fanti<sup>1</sup>

<sup>1</sup>Department of Nuclear Medicine, Azienda Ospedaliero-Universitaria di Bologna, S. Orsola-Malpighi University Hospital, Bologna, Italy; <sup>2</sup>Department of Internal Medicine, Azienda Ospedaliero-Universitaria di Bologna, S. Orsola-Malpighi University Hospital, Bologna, Italy; and <sup>3</sup>Division of Nuclear Medicine, European Institute of Oncology, Milano, Italy

**TABLE 2.** Comparison of <sup>68</sup>Ga-DOTANOC PET/CT and CI Findings and Their Impact on Stage or Therapy Modifications

| Finding                   | n     | %     |
|---------------------------|-------|-------|
| PET and CI in concordance | 47/90 | 52.2  |
| PET impact on stage       | None  |       |
| PET impact on therapy     | 17/47 | 36.2  |
| PET and CI in discordance | 42/90 | 46.7  |
| PET impact on stage       | 12/42 | 28.6  |
| PET impact on therapy     | 32/42 | 76.2  |
| PET and CI equivocal      | 1     | 1.1   |
| PET impact                | 1     | 100.0 |

$^{68}\text{Ga}$ -DOTATOC PET



Carcinoid dell' ileo operato

Follow up: Metastasi linfonodali

# Bone Metastases in Patients with Neuroendocrine Tumor: $^{68}\text{Ga}$ -DOTA-Tyr<sup>3</sup>-Octreotide PET in Comparison to CT and Bone Scintigraphy

J Nucl Med 2009; 50:1214–1221

Daniel Putzer<sup>1</sup>, Michael Gabriel<sup>1</sup>, Benjamin Henninger<sup>2</sup>, Dorota Kendler<sup>1</sup>, Christian Uprimny<sup>1</sup>, Georg Dobrozemsky<sup>1</sup>, Clemens Decristoforo<sup>1</sup>, Reto Josef Bale<sup>2</sup>, Werner Jaschke<sup>2</sup>, and Irene Johanna Virgolini<sup>1</sup>

<sup>1</sup>Department of Nuclear Medicine, Innsbruck Medical University, Innsbruck, Austria; and <sup>2</sup>Department of Radiology, Innsbruck Medical University, Innsbruck, Austria

**TABLE 2.** Comparison of PET and CT in Detection of Bone Metastases from Neuroendocrine Tumor

| Parameter   | $^{68}\text{Ga}$ -DOTATOC PET (%) | CT (%)      |
|-------------|-----------------------------------|-------------|
| Sensitivity | 92 (37/38)                        | 58 (22/38)  |
| Specificity | 97 (12/13)                        | 100 (13/13) |
| Accuracy    | 96 (49/51)                        | 69 (35/51)  |

Numbers of patients are in parentheses.

# Bone Metastases in Patients with Neuroendocrine Tumor: $^{68}\text{Ga}$ -DOTA-Tyr<sup>3</sup>-Octreotide PET in Comparison to CT and Bone Scintigraphy

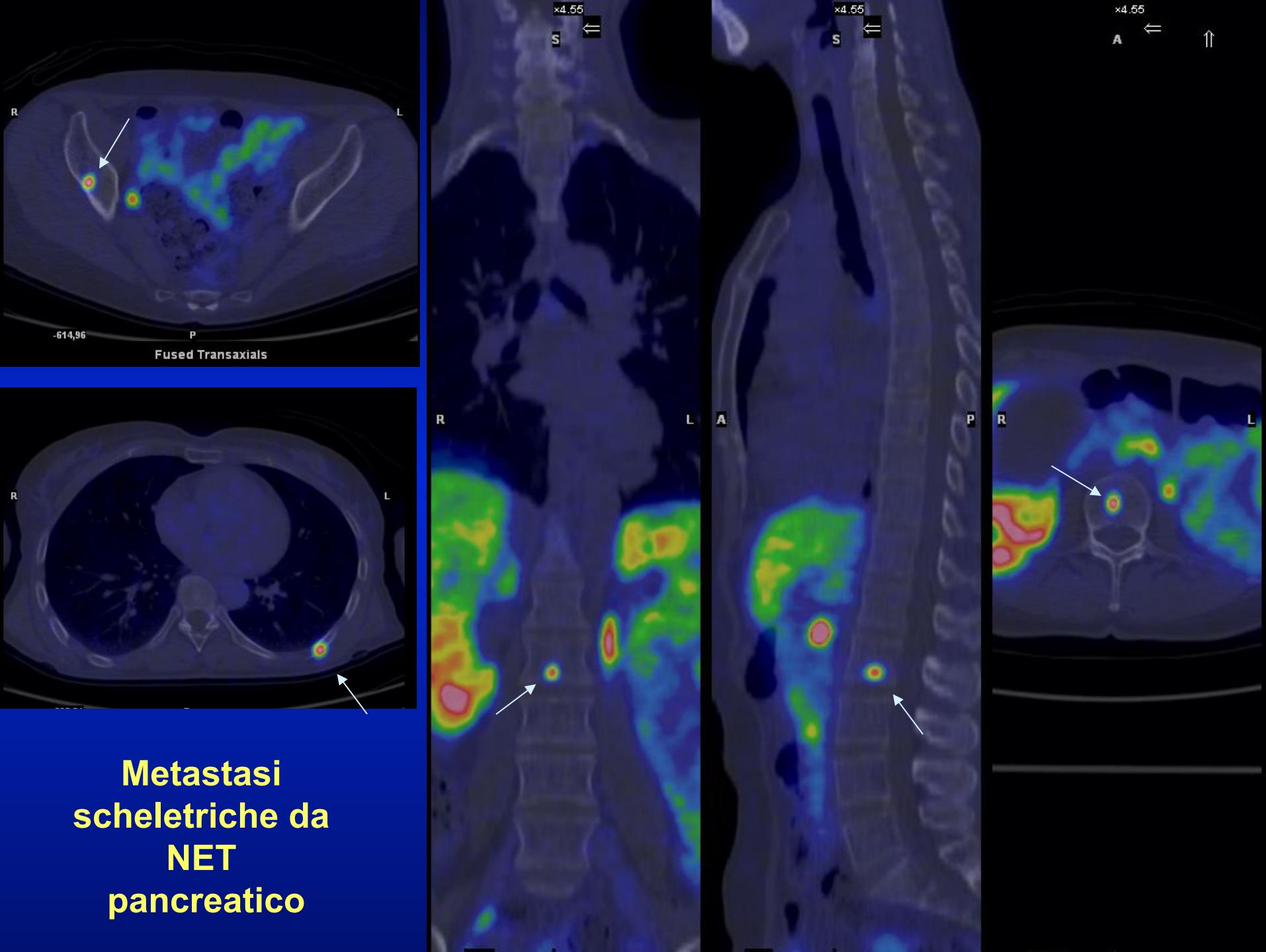
J Nucl Med 2009; 50:1214–1221

Daniel Putzer<sup>1</sup>, Michael Gabriel<sup>1</sup>, Benjamin Henninger<sup>2</sup>, Dorota Kendler<sup>1</sup>, Christian Uprimny<sup>1</sup>, Georg Dobrozemsky<sup>1</sup>, Clemens Decristoforo<sup>1</sup>, Reto Josef Bale<sup>2</sup>, Werner Jaschke<sup>2</sup>, and Irene Johanna Virgolini<sup>1</sup>

<sup>1</sup>Department of Nuclear Medicine, Innsbruck Medical University, Innsbruck, Austria; and <sup>2</sup>Department of Radiology, Innsbruck Medical University, Innsbruck, Austria

## CONCLUSION

Our study proved that  $^{68}\text{Ga}$ -DOTATOC PET is more useful than CT for the early detection of bone metastases in patients with neuroendocrine tumor. Negative  $^{68}\text{Ga}$ -DOTATOC PET findings in a patient with neuroendocrine tumor exclude the presence of somatostatin receptor-positive bone metastases.  $^{68}\text{Ga}$ -DOTATOC PET should replace conventional bone scintigraphy in patients with neuroendocrine tumor.

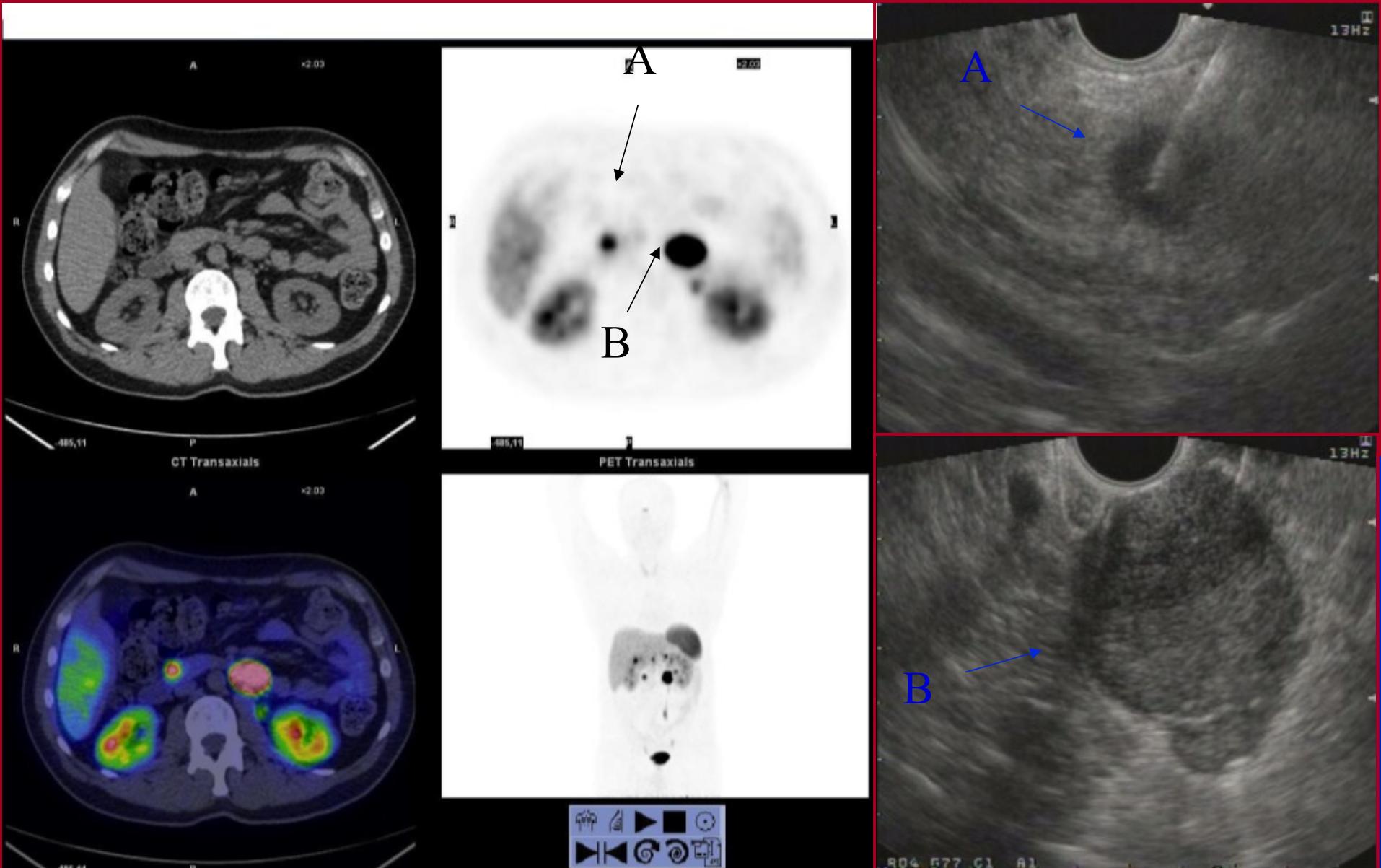


# Ga-68 DOTATOC PET, Endoscopic Ultrasonography, and Multidetector CT in the Diagnosis of Duodenopancreatic Neuroendocrine Tumors

*A Single-Centre Retrospective Study*

Annibale Versari, MD,\* Lorenzo Camellini, MD,† Gabriele Carlinfante, MD,‡ Andrea Frasoldati, MD,\* Franco Nicoli, MD,§ Elisa Grassi, ●●●,¶ Carmine Gallo, MD,‡ Francesco Giunta, MD,\* Alessandro Fraternali, MD,\* Diana Salvo, MD,\* Mattia Asti, ●●●,\* Francesco Azzolini, MD,† Veronica Iori, MD,† and Romano Sassatelli, MD†

*Clin Nucl Med 2010;*



Head pancreatic NET (A) with lymph node metastasis (B)

# Ga-68 DOTATOC PET, Endoscopic Ultrasonography, and Multidetector CT in the Diagnosis of Duodenopancreatic Neuroendocrine Tumors

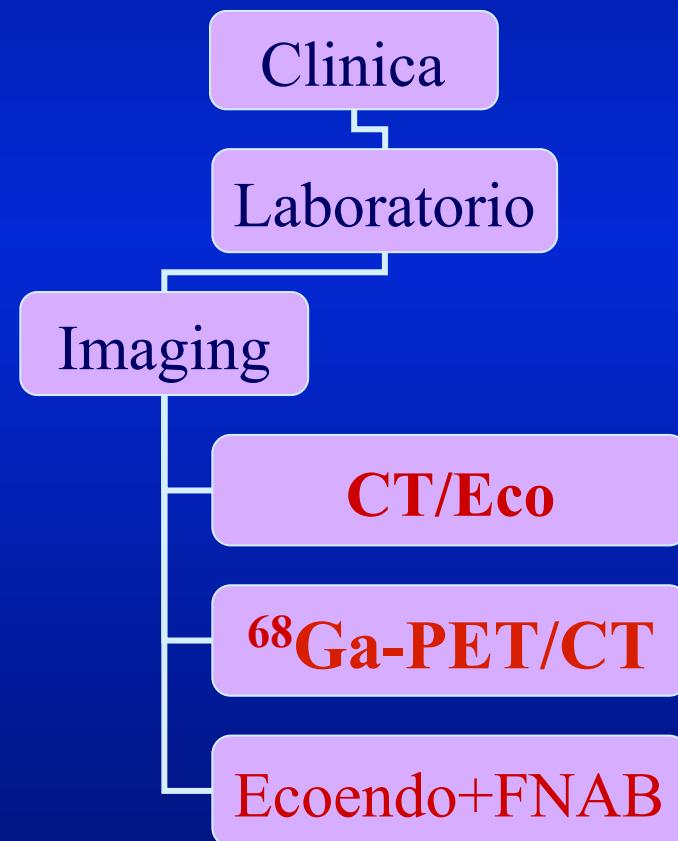
*A Single-Centre Retrospective Study*

Annibale Versari, MD,\* Lorenzo Camellini, MD,† Gabriele Carlinfante, MD,‡ Andrea Frasoldati, MD,\* Franco Nicoli, MD,§ Elisa Grassi, ●●●,¶ Carmine Gallo, MD,‡ Francesco Giunta, MD,\* Alessandro Fraternali, MD,\* Diana Salvo, MD,\* Mattia Asti, ●●●,\* Francesco Azzolini, MD,† Veronica Iori, MD,† and Romano Sassatelli, MD†

**Conclusions:** EUS, Ga-68 DOTATOC PET, and MDCT seem to have comparable accuracy in diagnosis of duodenopancreatic NET and their combination may allow an optimal preoperative diagnosis.

# Tumori neuroendocrini duodeno-pancreatici

## Proposta di percorso diagnostico



# **Accuracy and clinical impact of 68-Ga-labeled octreotide analogues PET in diagnosis and staging of duodeno-pancreatic neuroendocrine tumours. Proposal of a multicenter, prospective clinical trial**

Proponenti:

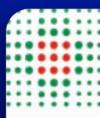
Bologna - 10 dicembre 2007  
Annibale Versari (Medicina Nucleare - PI)

Lorenzo Camellini (Endoscopia Digestiva)

Andrea Frasoldati (Endocrinologia)

Gabriele Carlinfante (Anatomia Patologica)

Pierpaolo Pattacini (Radiologia)



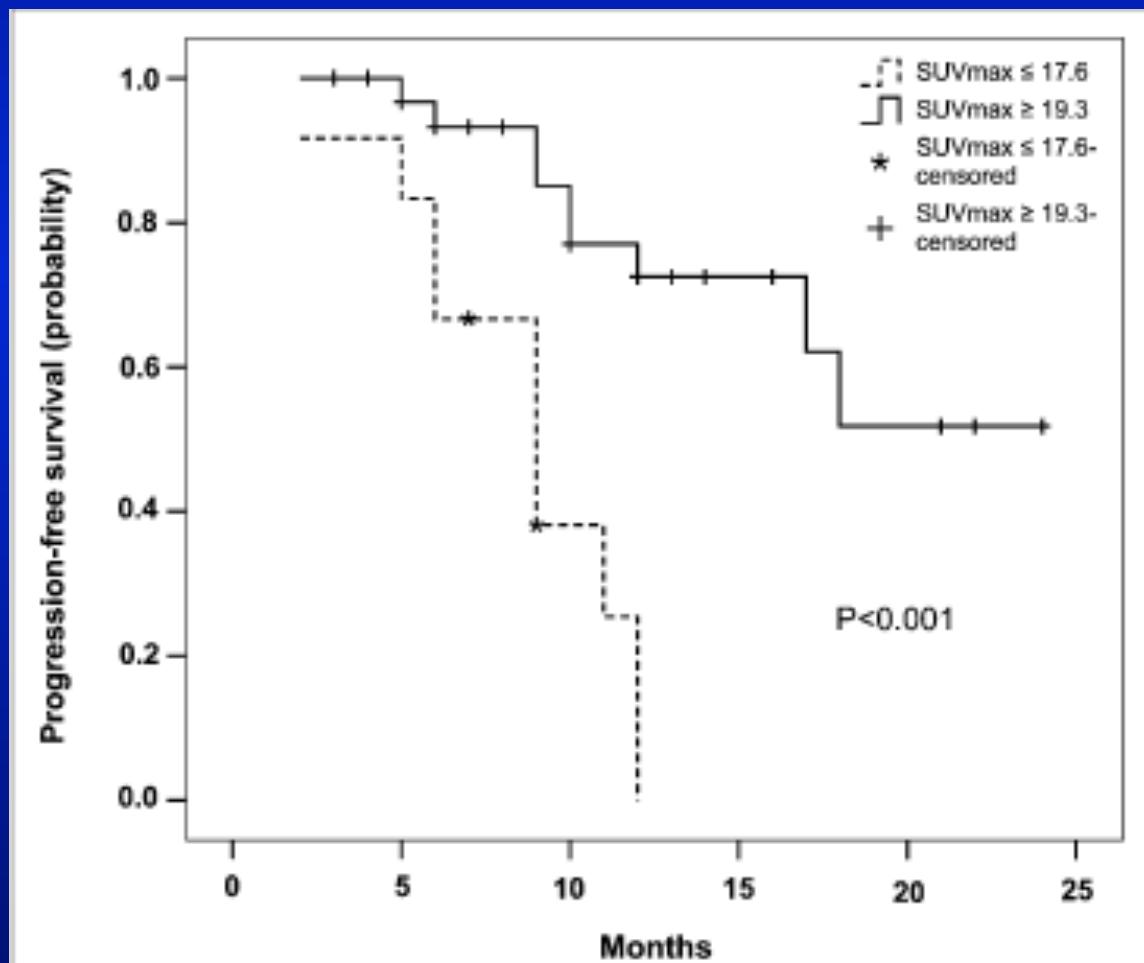
**SERVIZIO SANITARIO REGIONALE  
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Azienda Ospedaliera di Reggio Emilia  
Arcispedale S. Maria Nuova

Istituto in tecnologie avanzate e modelli assistenziali in oncologia  
Istituto di Ricovero e Cura a Carattere Scientifico

# Standardized Uptake Values of $^{68}\text{Ga}$ -DOTANOC PET: A Promising Prognostic Tool in Neuroendocrine Tumors

J Nucl Med 2010; 51:353–359

Davide Campana<sup>1</sup>, Valentina Ambrosini<sup>2</sup>, Raffaele Pezzilli<sup>1</sup>, Stefano Fanti<sup>2</sup>, Antonio Maria Morselli Labate<sup>1</sup>, Donatella Santini<sup>3</sup>, Claudio Ceccarelli<sup>3</sup>, Francesca Nori<sup>1</sup>, Roberto Franchi<sup>2</sup>, Roberto Corinaldesi<sup>1</sup>, and Paola Tomassetti<sup>1</sup>



# Functional Imaging of Neuroendocrine Tumors With Combined PET/CT Using $^{68}\text{Ga}$ -DOTATATE (Dota-DPhe<sup>1</sup>,Tyr<sup>3</sup>-octreotate) and $^{18}\text{F}$ -FDG

TABLE 2

Numbers of Patients Showing Predominant Uptake of  $^{68}\text{Ga}$ -DOTATATE or  $^{18}\text{F}$ -FDG According to Tumor Grade

|                             | Predominant uptake of $^{68}\text{Ga}$ -DOTATATE | Predominant uptake of $^{18}\text{F}$ -FDG | Total |
|-----------------------------|--------------------------------------------------|--------------------------------------------|-------|
| High/intermediate-grade NET | 3                                                | 11                                         | 14    |
| Low-grade NET               | 21                                               | 0                                          | 21    |
| Total                       | 24                                               | 11                                         | 35    |

Two-tailed  $P < .0001$ . Fisher exact T-test.

NET indicates neuroendocrine tumors;  $^{68}\text{Ga}$ -DOTATATE,  $^{68}\text{Ga}$ -DOTA-[SCAP]D[R]Phe<sup>1</sup>,Tyr<sup>3</sup>-octreotate;  $^{18}\text{F}$ -FDG,  $^{18}\text{F}$ -Fluorodeoxyglucose.

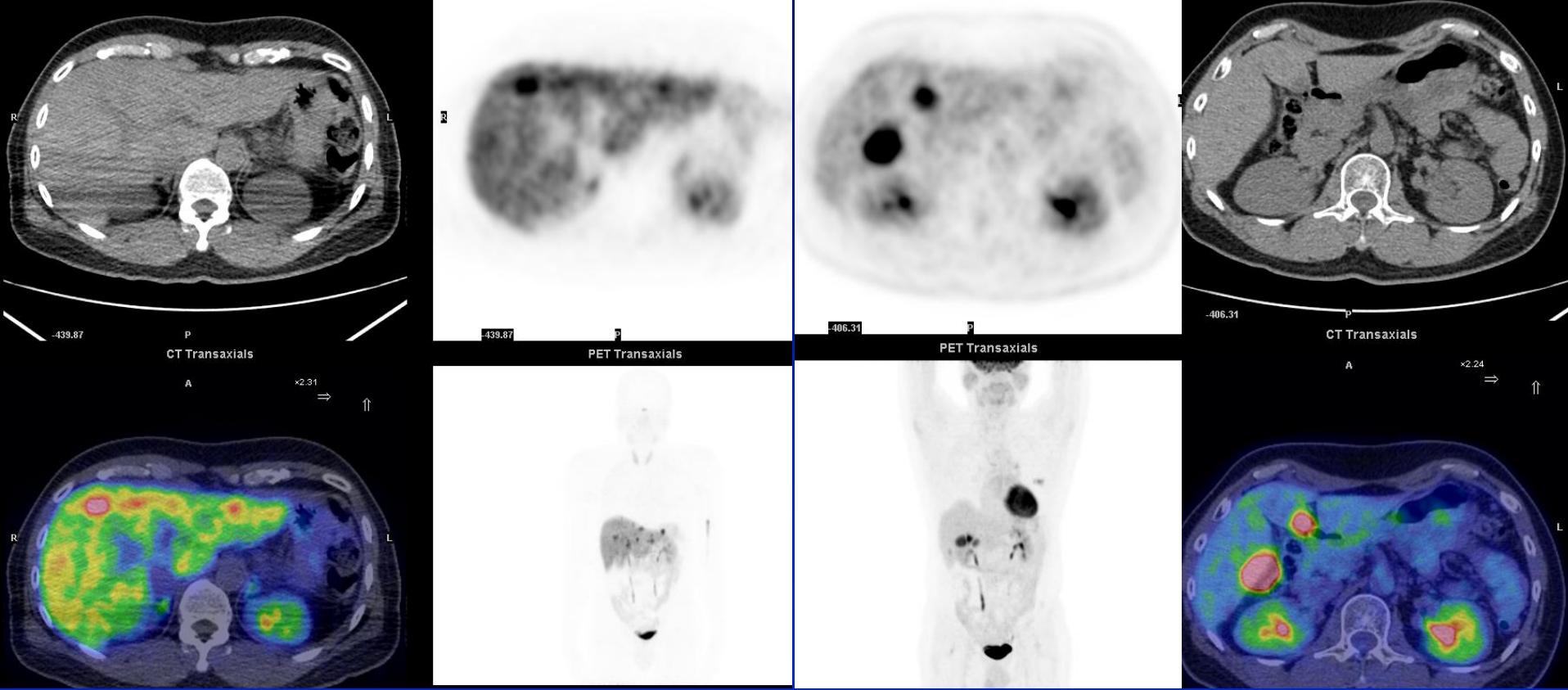
Irfan Kayani, FRCR<sup>1</sup>  
Jamshed B. Bomanji, MD, PhD, FRCR<sup>1</sup>  
Ashley Groves, MD<sup>1</sup>  
Gerard Conway, MD<sup>2</sup>  
Sveto Gacinovic, MD<sup>1</sup>  
Thida Win, MD<sup>3</sup>  
John Dickson, PhD<sup>1</sup>  
Martyn Caplin, FRCP<sup>4</sup>  
Peter Joseph Ell, FRCR, FRCP<sup>1</sup>

TABLE 3  
SUVmax of  $^{68}\text{Ga}$ -DOTATATE and  $^{18}\text{F}$ -FDG According to Tumor Grade

|                                     | $^{68}\text{Ga}$ -DOTATATE | $^{18}\text{F}$ -FDG | $P$   |
|-------------------------------------|----------------------------|----------------------|-------|
| All NET                             | 16.9 (1.6-50)              | 4.2 (1.4-16.4)       | .005  |
| Low-grade NET Ki67 index $\leq 2\%$ | 29 (3.3-45)                | 2.9 (1.5-12)         | <.001 |
| Intermediate NET Ki67 index 3%–20%  | 15.5 (1.8-50)              | 10.5 (2.0-13.9)      | NS    |
| High-grade NET Ki67 index $> 20\%$  | 4.4 (1.6-8.9)              | 11.7 (4.1-16.4)      | .03   |

SUVmax is the median SUVmax with range in parentheses.

SUVmax indicates maximum standardized uptake value; NET, neuroendocrine tumor;  $^{68}\text{Ga}$ -DOTATATE,  $^{68}\text{Ga}$ -DOTA-[SCAP]D[R]Phe<sup>1</sup>,Tyr<sup>3</sup>-octreotate;  $^{18}\text{F}$ -FDG,  $^{18}\text{F}$ -Fluorodeoxyglucose.



68Ga-DOTATOC

Gen 2011

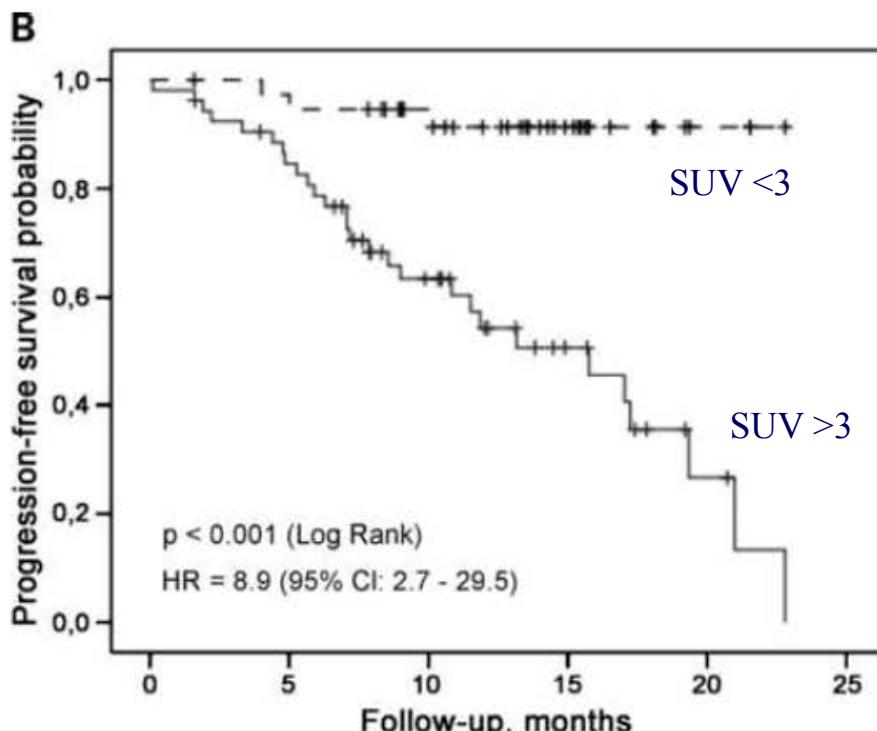
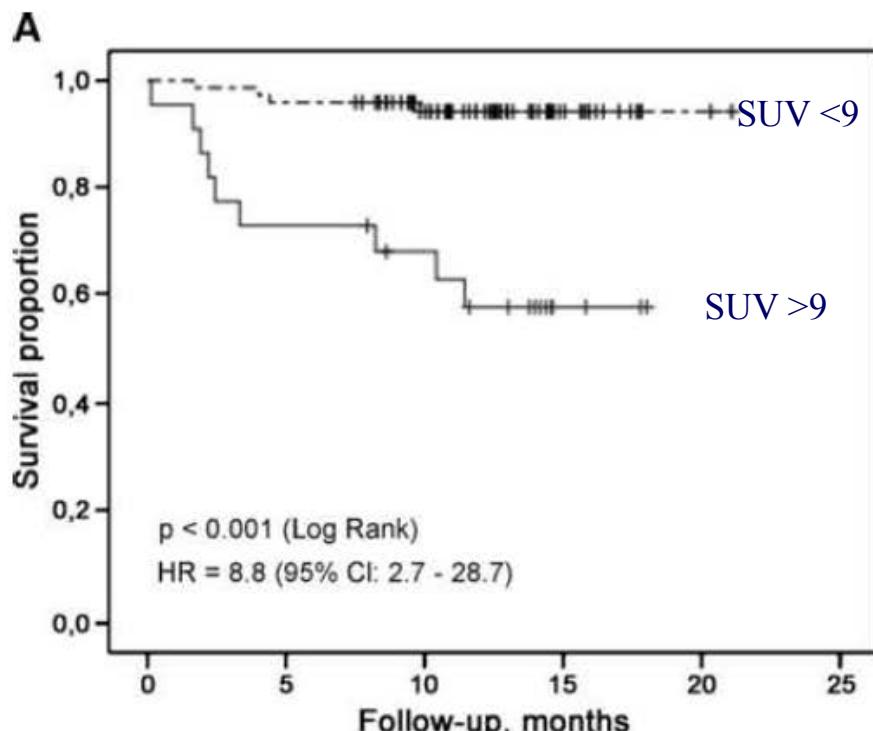
FDG-PET/CT

Feb 2011

**Imaging, Diagnosis, Prognosis**

# **<sup>18</sup>F-Fluorodeoxyglucose Positron Emission Tomography Predicts Survival of Patients with Neuroendocrine Tumors**

Tina Binderup<sup>1,2</sup>, Ulrich Knigge<sup>2,3</sup>, Annika Loft<sup>1</sup>, Birgitte Federspiel<sup>4</sup>, and Andreas Kjaer<sup>1,2</sup>



**Fig. 2.** A, survival distribution among patients with SUV<sub>max</sub> below (black, dashed line) or above (black, solid line) 9. B, PFS distribution among patients with SUV<sub>max</sub> below (black, dashed line) or above (black, solid line) 3.

# **$^{111}\text{In}$ -Octreoscan and $^{68}\text{Ga}$ -DOTA peptide PET/CT**

## **EANM guidelines**

- Primary tumor localization and staging
- Restaging (detection of residual, recurrent or progressive disease)
- SSTR status evaluation (patients with high positivity are more likely to respond to octreotide therapy)
- Response to therapy monitoring
- Selection of patients for peptide receptor radionuclide therapy (PRRT)

# **<sup>18</sup>F-Fluorodihydroxyphenylalanine PET/CT in Patients with Neuroendocrine Tumors of Unknown Origin: Relation to Tumor Origin and Differentiation**

**J Nucl Med 2014; 55:1–6**

Alessio Imperiale<sup>1,2</sup>, Edmond Rust<sup>1</sup>, Sophie Gabriel<sup>3</sup>, Julien Detour<sup>4</sup>, Bernard Goichot<sup>5</sup>, Bernard Duclos<sup>6</sup>, Jean-Emmanuel Kurtz<sup>7</sup>, Philippe Bachellier<sup>8</sup>, Izzie-Jacques Namer<sup>1,2</sup>, and David Taieb<sup>3</sup>

<sup>1</sup>Biophysics and Nuclear Medicine, Hautepierre University Hospital, Strasbourg, France; <sup>2</sup>ICube, University of Strasbourg/CNRS (UMR 7357) and FMTS, Faculty of Medicine, Strasbourg, France; <sup>3</sup>Nuclear Medicine, La Timone University Hospital, European Center for Research in Medical Imaging, Aix-Marseille University, Provence, France; <sup>4</sup>Radiopharmacy, Hautepierre University Hospital, Strasbourg, France; <sup>5</sup>Internal Medicine, Hautepierre University Hospital, Strasbourg, France; <sup>6</sup>Gastroenterology, Hautepierre University Hospital, Strasbourg, France; <sup>7</sup>Oncology, Hautepierre University Hospital, Strasbourg, France; and <sup>8</sup>Visceral Surgery and Transplantation, Hautepierre University Hospital, Strasbourg, France

Retrospective study of NET patients with negative conventional and somatostatin receptor scintigraphy (SRS) results

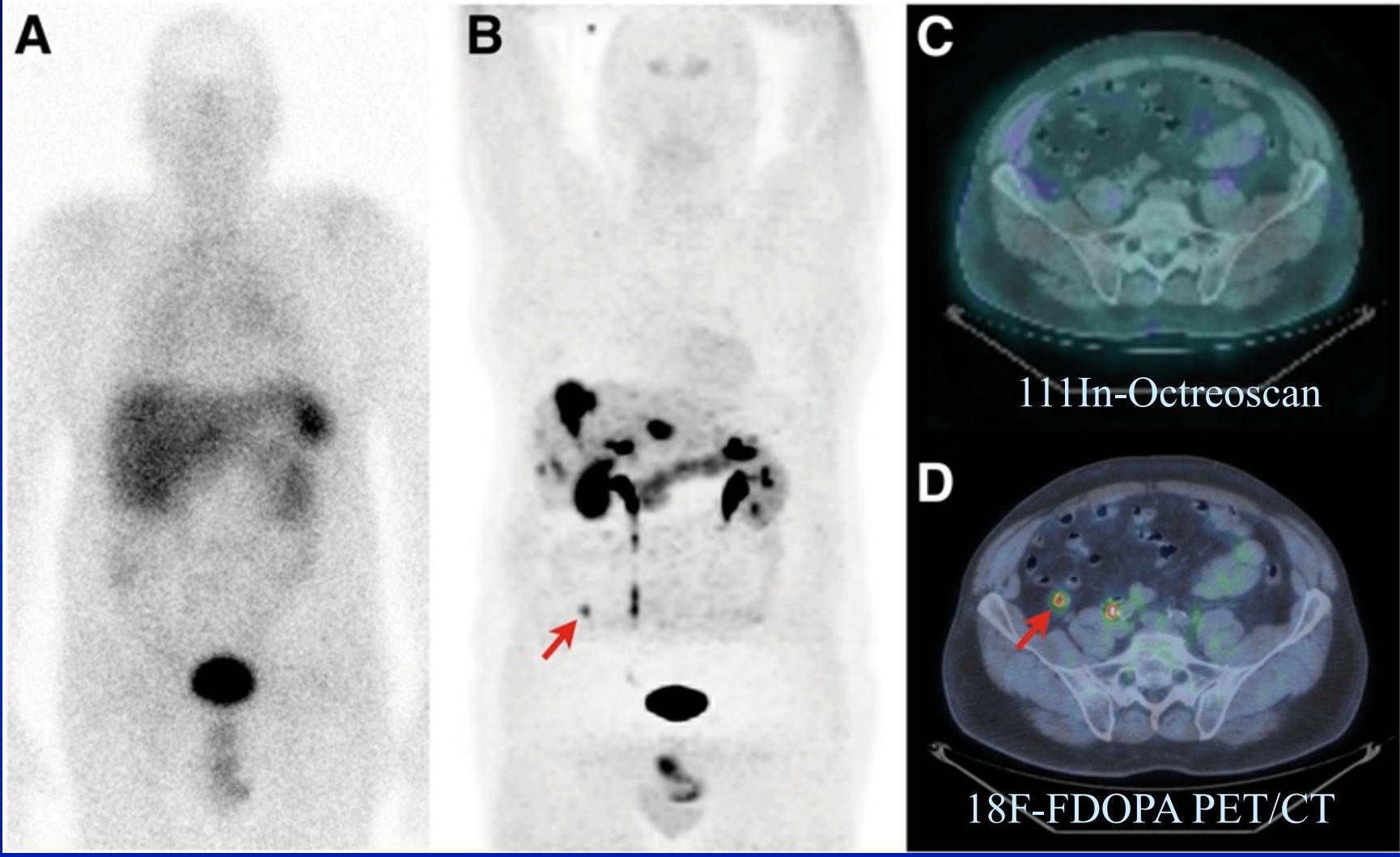
27 patients were evaluated with <sup>18</sup>F-FDOPA PET/CT

The primary occult NET was localized by <sup>18</sup>F-FDOPA PET/CT in 12 patients (overall

sensitivity, 44%; 52% in patients evaluated at initial diagnosis

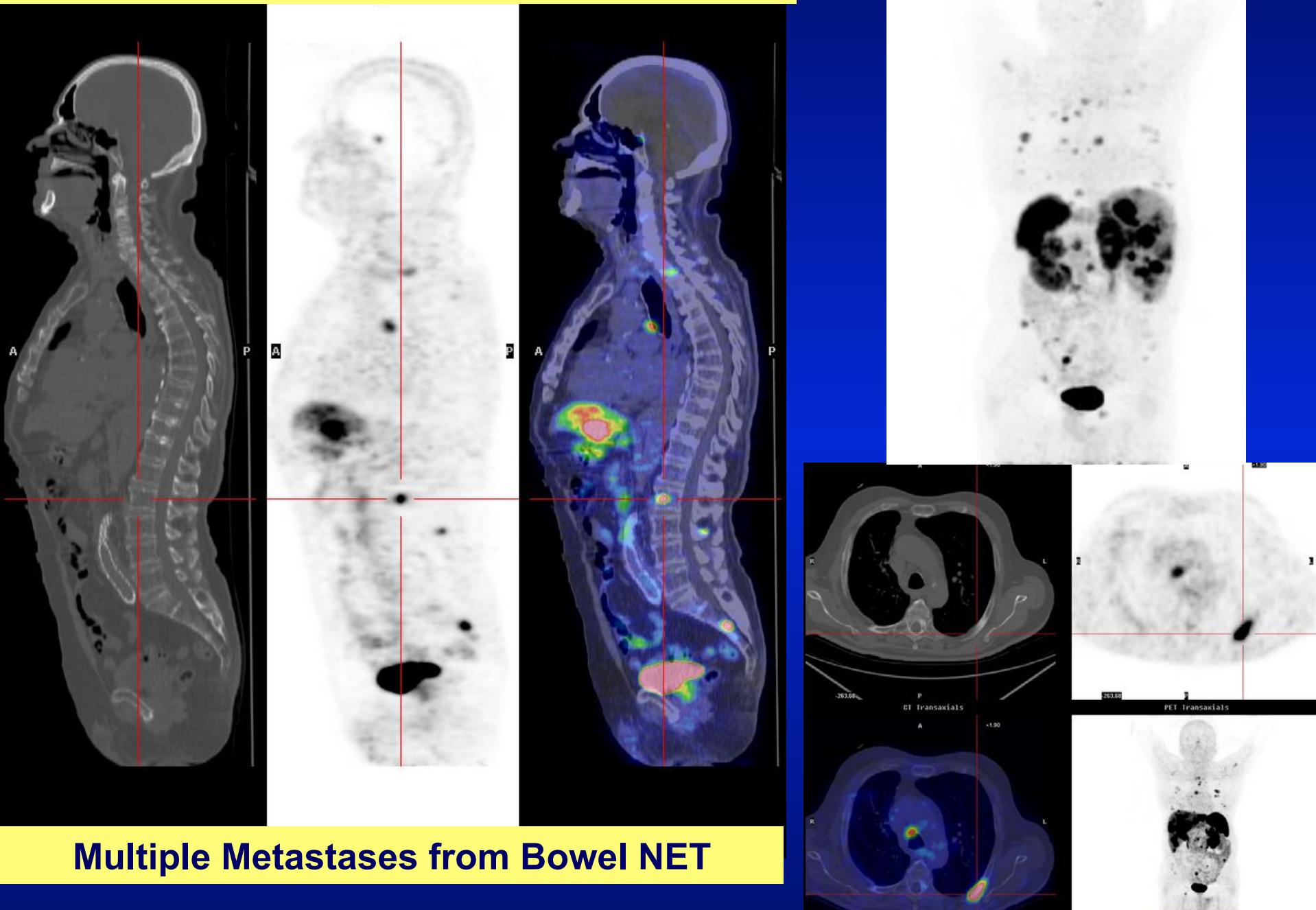
Conclusion:

<sup>18</sup>F-FDOPA PET appears to be a sensitive functional imaging tool for the detection of primary NETs occult on SRS, **especially tumors with a well-differentiated pattern and serotonin secretion**



A 56-y-old patient with metastatic NET of unknown origin. 18F-FDOPA PET/CT confirmed presence of liver metastases and identified primary tumor in ileum occult on both conventional imaging and SRS.

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



# Molto importante!!!!!!

## Discussione Interdisciplinare



# Dalla Diagnosi al Trattamento



Diagnosi  
 $^{68}\text{Ga}$

DOTA-TOC/TATE

Terapia  
 $^{90}\text{Y} / ^{177}\text{Lu}$

# *Physics properties (LET)*

|                   | $\beta$ -<br>(Mev) | $\gamma$<br>(Kev) | T1/2<br>(days) |
|-------------------|--------------------|-------------------|----------------|
| $^{177}\text{Lu}$ | <b>0.49</b>        | <b>110-210</b>    | <b>6.7</b>     |
| $^{90}\text{Y}$   | <b>2.27</b>        |                   | <b>2.7</b>     |

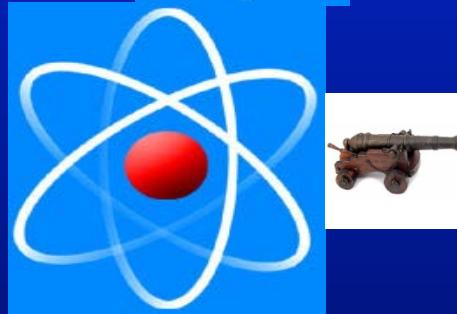
mean range in body tissue

$^{177}\text{Lu}$



**0.5-2mm**

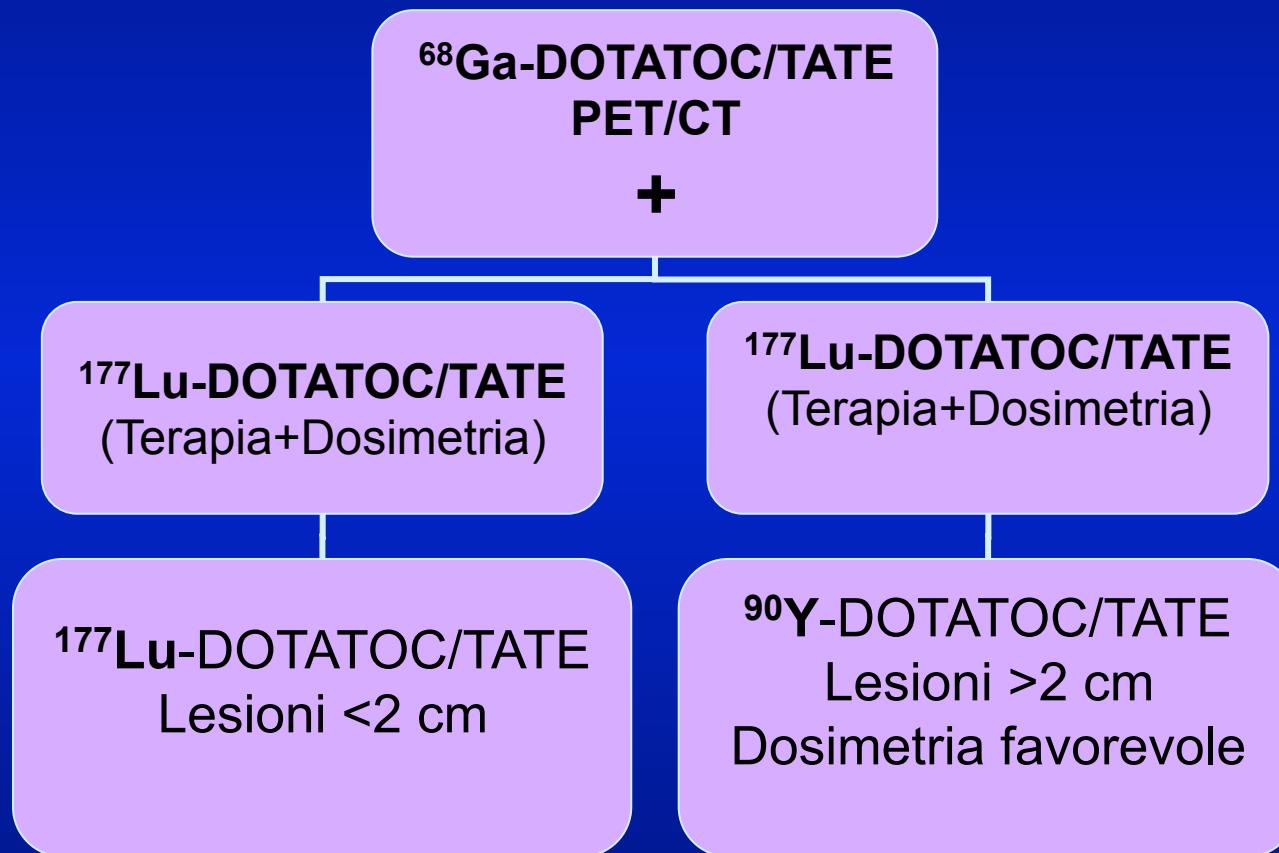
$^{90}\text{Y}$



**3-11 mm**

# Terapia Radiorecettoriale

## Algoritmo di Reggio Emilia

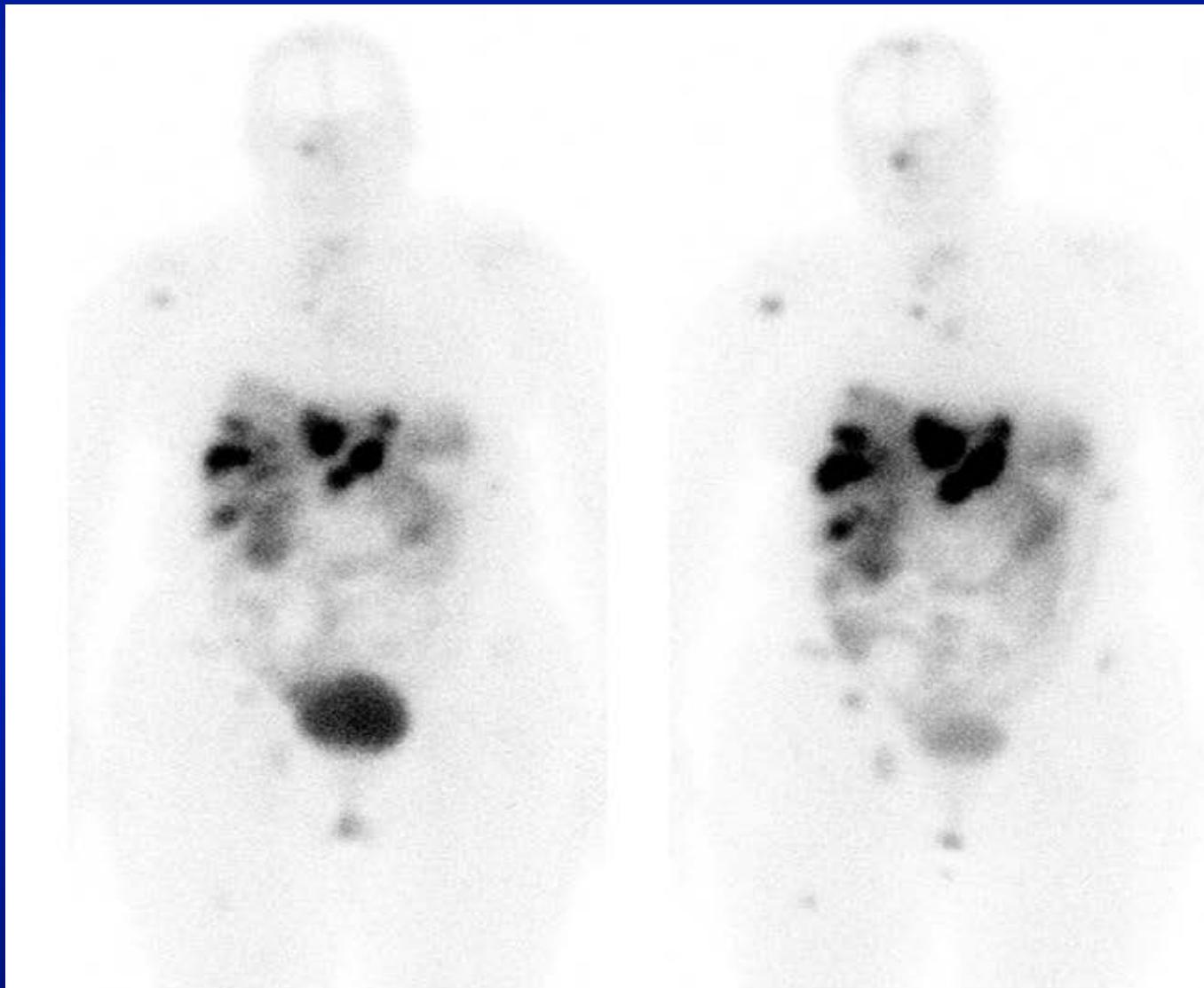


Creatinina <1.5; Hb >10; Leucociti >2.5; Piastrine >100; Bilirubina <2.5

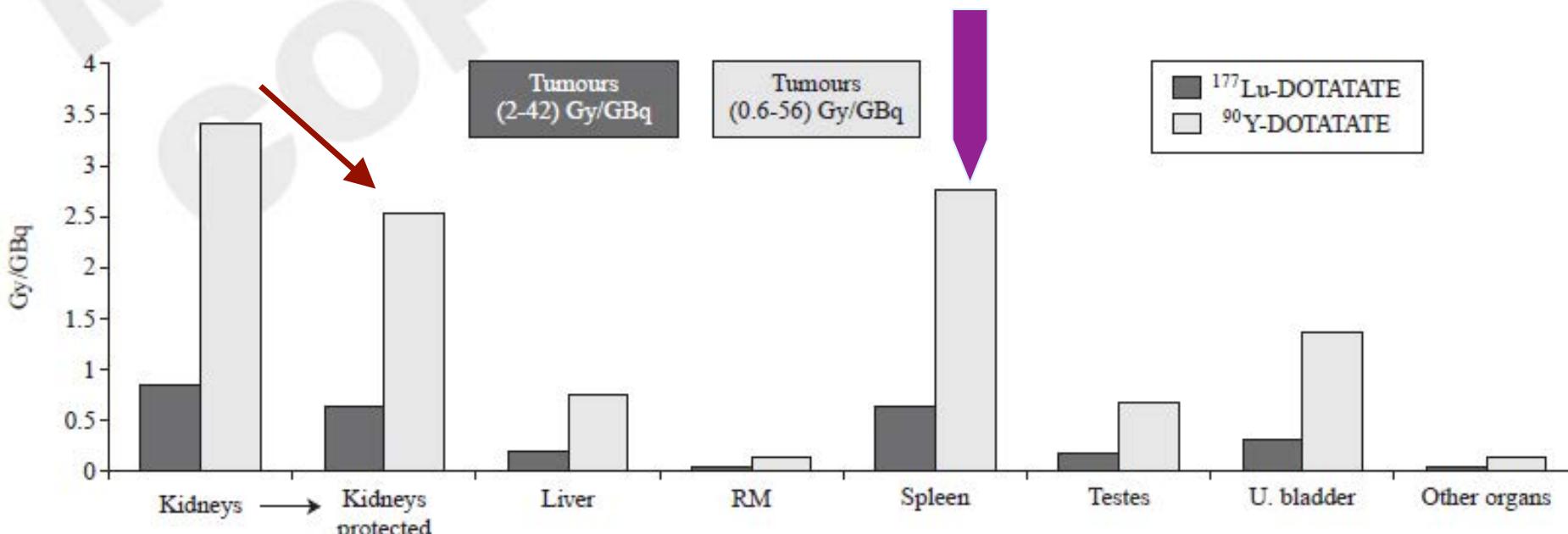
177Lu-DOTATOC

24 h

177Lu-DOTATATE



# Organs and tumour doses estimates for $^{90}\text{Y}$ / $^{177}\text{Lu}$ -DOTATATE



Estimates of tumour and OAR doses per unit activity in patient undergoing PRRT trial

# Terapia Radiorecettoriale Radiofarmaci

•<sup>90</sup>Y-DOTATATE

50-70 mCi (1850-2590 MBq)/ciclo

•<sup>177</sup>Lu-DOTATATE

100-150 mCi (3700-5550 MBq)/ciclo

# Terapia Radiorecettoriale

## Procedura di Reggio Emilia

Esami ematologici



**Follow up**

0

2

4

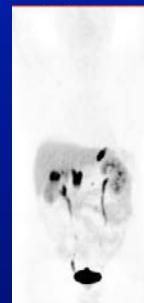
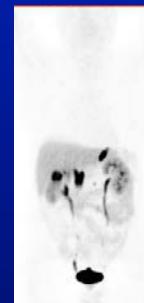
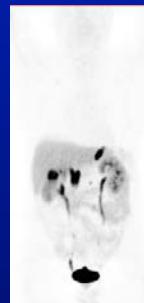
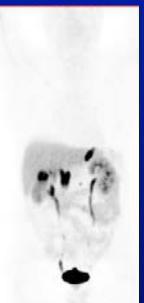
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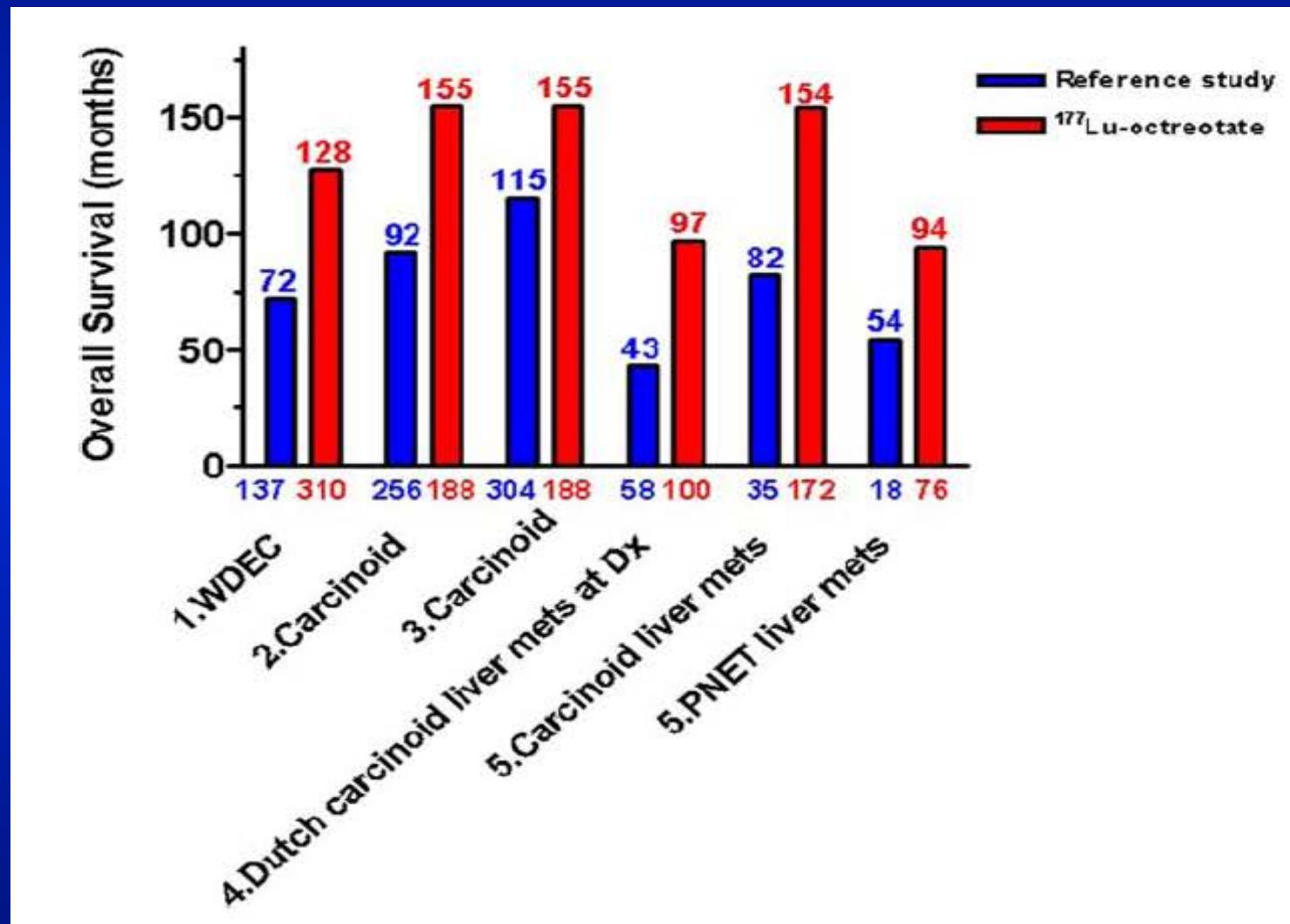


# Peptide Receptor Radionuclide Therapy (PRRT)

| Author     | Year | Radiopharmaceutical | Nº Pts. | Primary NET | Response (%) |    |    |    |    |
|------------|------|---------------------|---------|-------------|--------------|----|----|----|----|
|            |      |                     |         |             | CR           | PR | MR | SD | PD |
| Waldherr   | 2001 | 90Y-DOTATOC         | 41      | GEP+lung    | 2            | 22 | 12 | 49 | 15 |
| Waldherr   | 2002 | 90Y-DOTATOC         | 39      | GEP+lung    | 5            | 18 | -  | 65 | 11 |
| Valkema    | 2006 | 90Y-DOTATOC         | 58      | GEP         | 0            | 9  | 12 | 61 | 19 |
| Kwekkeboom | 2008 | 177Lu-DOTATATE      | 310     | GEP         | 2            | 28 | 16 | 35 | 20 |
| Bodei      | 2011 | 177Lu-DOTATATE      | 51      | GEP+lung    | 2            | 27 | 26 | 27 | 18 |
| Filice     | 2012 | 90Y/177Lu-DOTATOC   | 59      | GEP+lung    | 2            | 40 | -  | 40 | 18 |
| Vinjamuri  | 2013 | 90Y-DOTATOC         | 57      | GEP+lung    | -            | 25 | -  | 47 | 28 |

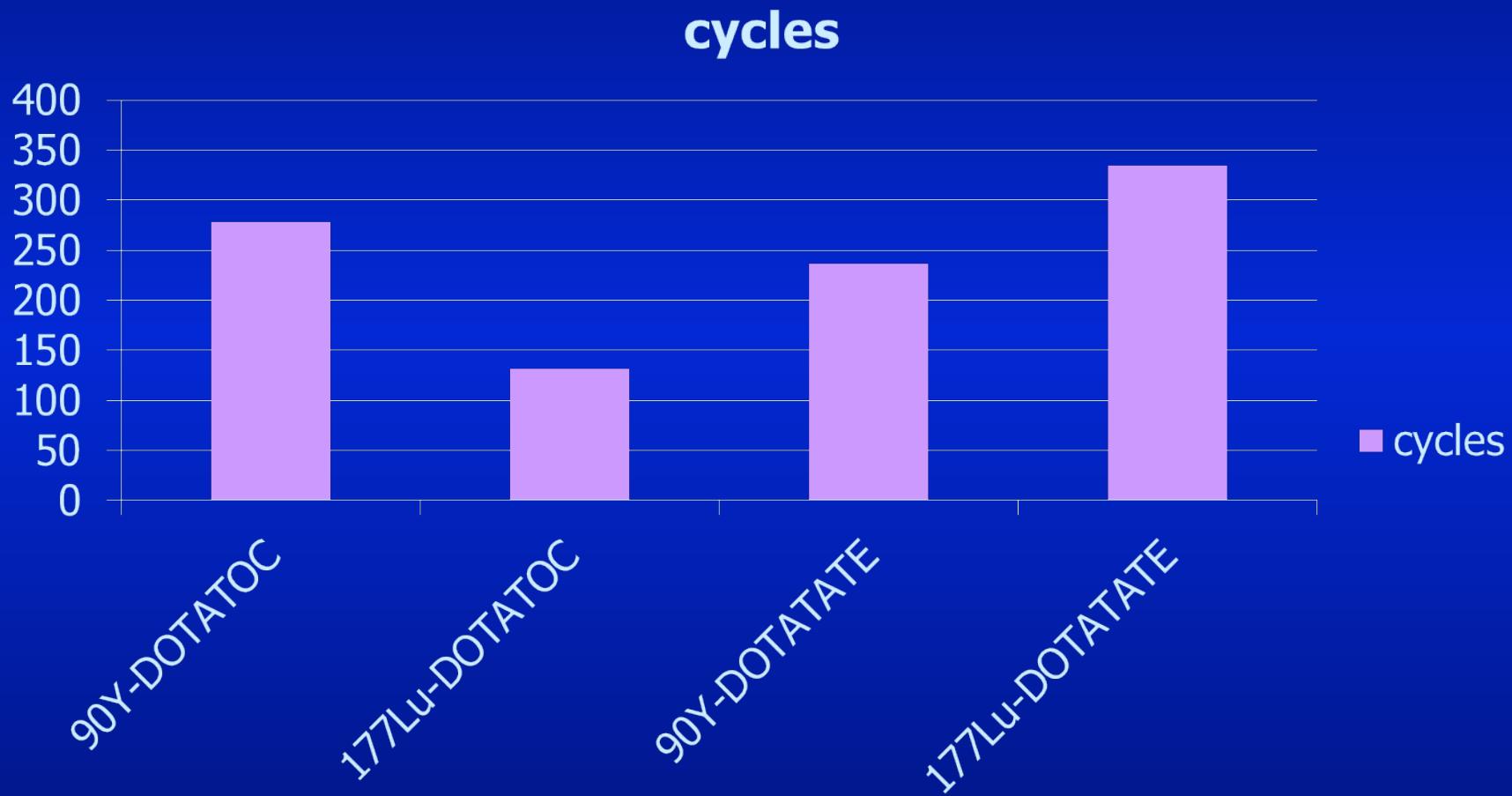
# Overall Survival

## Confronto Terapia Radiorecettoriale/Gruppo di controllo



# 90Y/177Lu-DOTATOC/ATE Experience of Reggio Emilia

January 2007 – August 2013

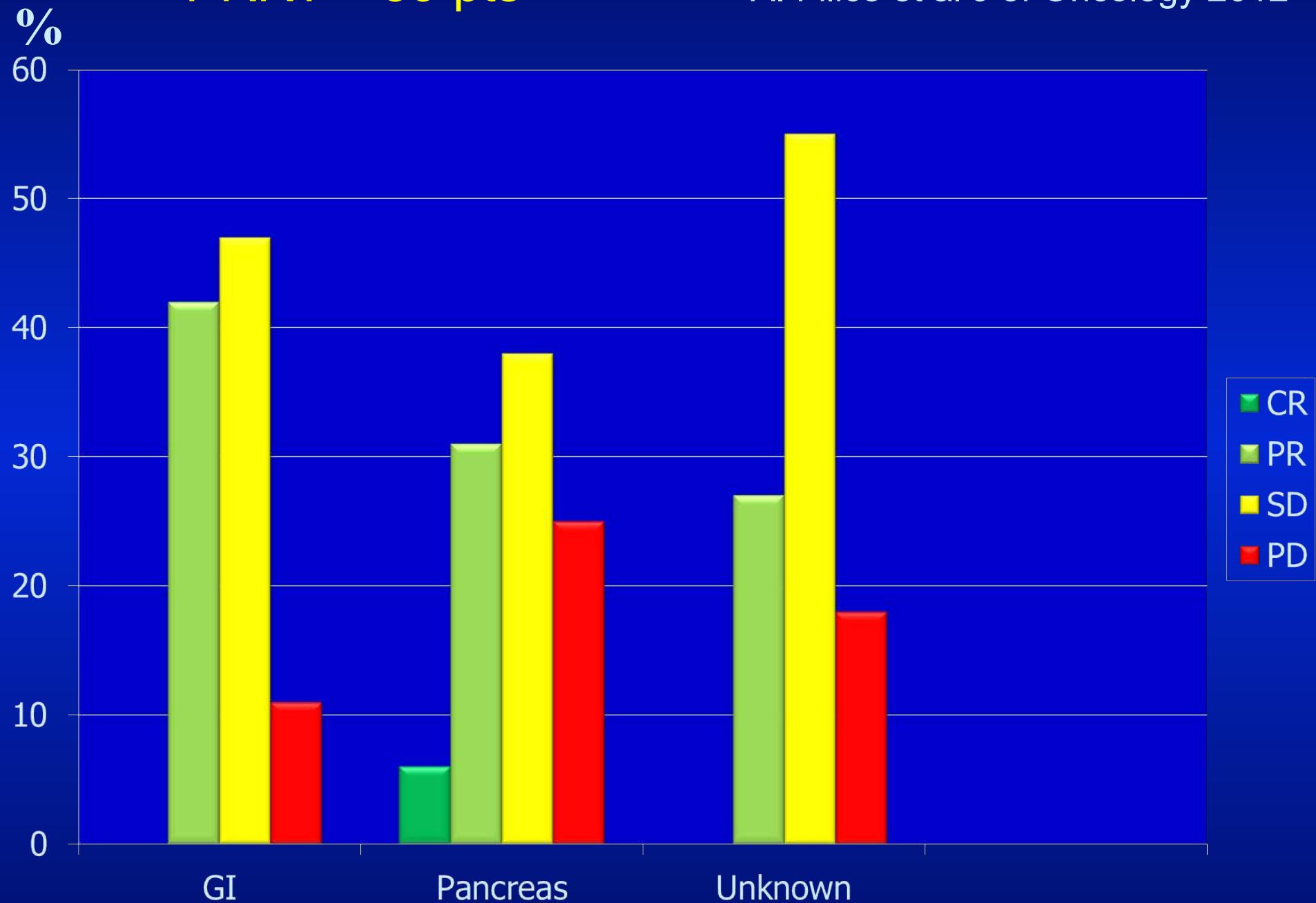


261 patients

982 cycles of treatment

PRRT 59 pts

A. Filice et al J of Oncology 2012



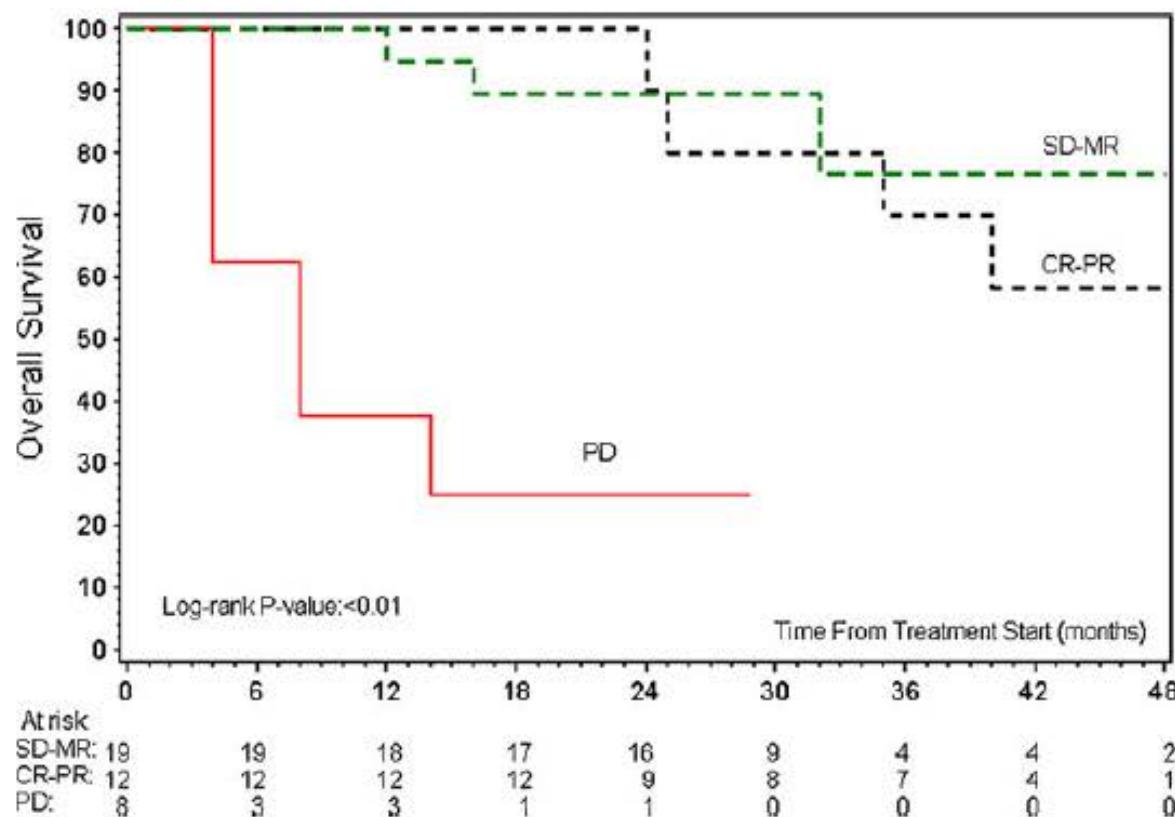
# Peptide receptor radionuclide therapy with $^{177}\text{Lu}$ -DOTATATE: the IEO phase I-II study

Lisa Bodei · Marta Cremonesi · Chiara M. Grana · Nicola Fazio · Simona Iodice · Silvia M. Baio · Mirco Bartolomei · Dario Lombardo · Mahila E. Ferrari · Maddalena Sansovini · Marco Chinol · Giovanni Paganelli

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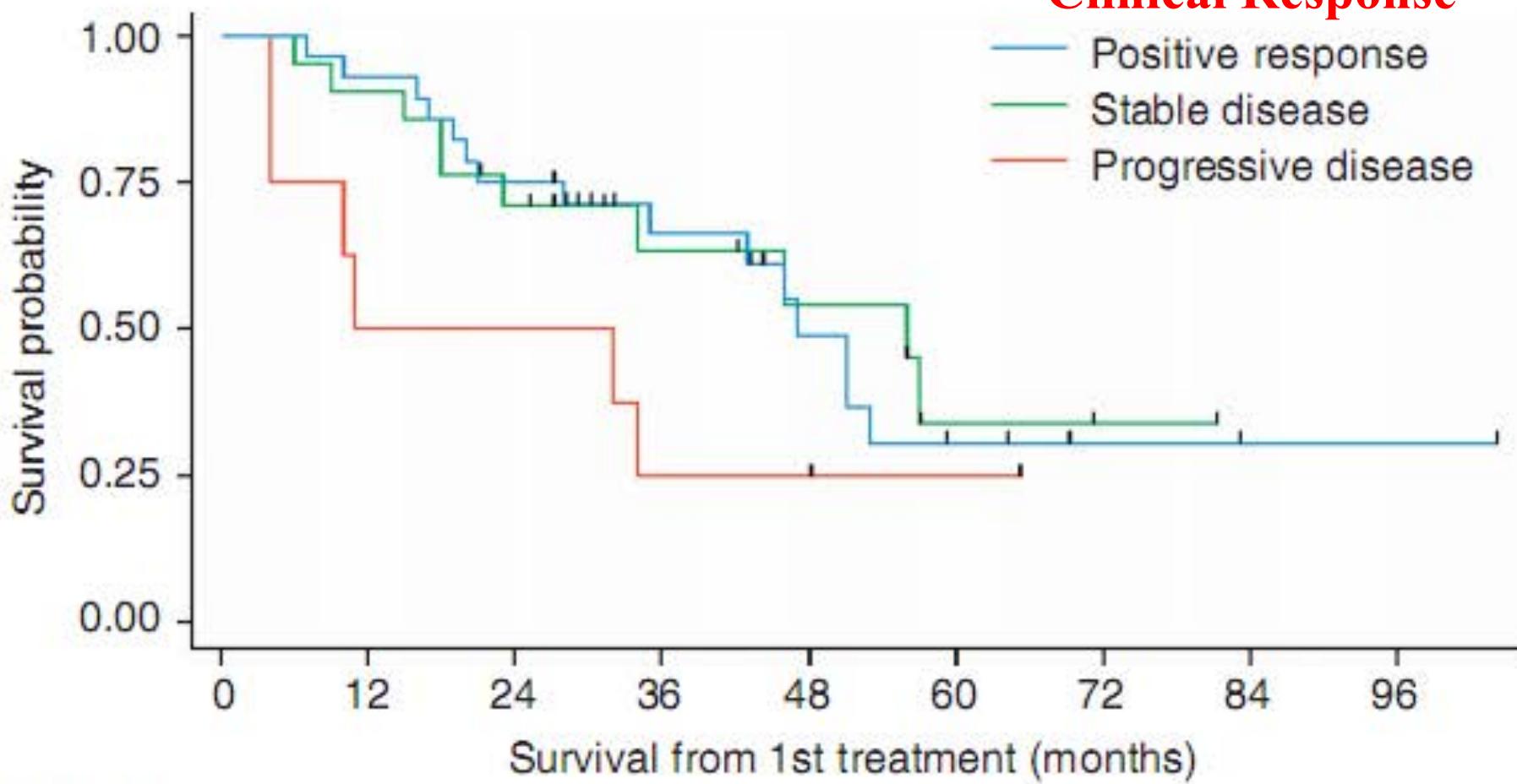
Eur J Nucl Med Mol Imaging (2011) 38:2125–2135

**Fig. 5** Overall survival in progressing patients at baseline. From a prognostic point of view, stabilizations and objective responses showed the same survival probability



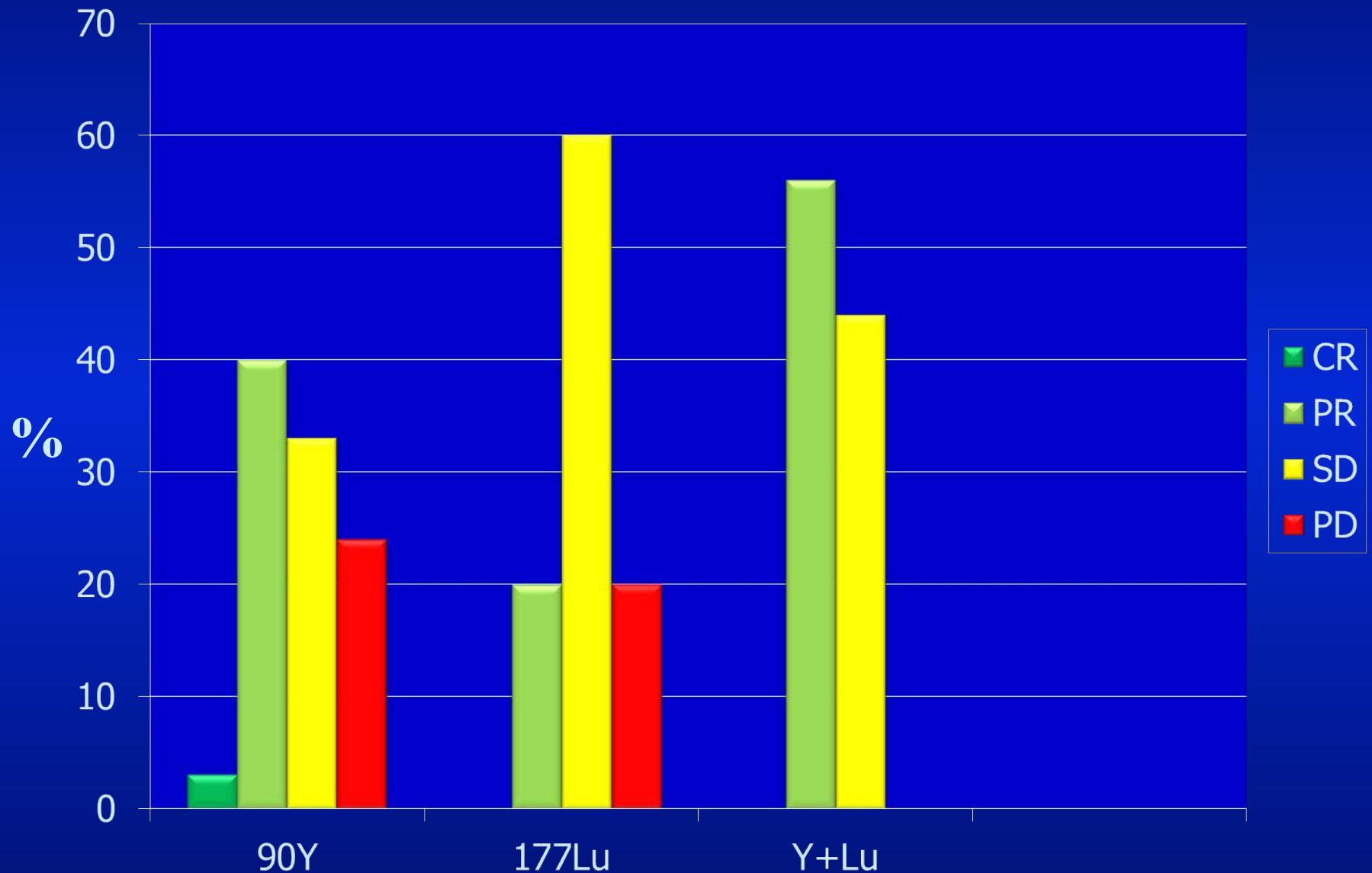
S Vinjamuri<sup>1,8</sup>, T M Gilbert<sup>2,8</sup>, M Banks<sup>3</sup>, G McKane<sup>1</sup>, P Maltby<sup>1</sup>, G Poston<sup>3</sup>, H Weissman<sup>4</sup>, D H Palmer<sup>5</sup>,  
J Vora<sup>6</sup>, D M Pritchard<sup>7</sup> and D J Cuthbertson<sup>\*2</sup>

### Clinical Response



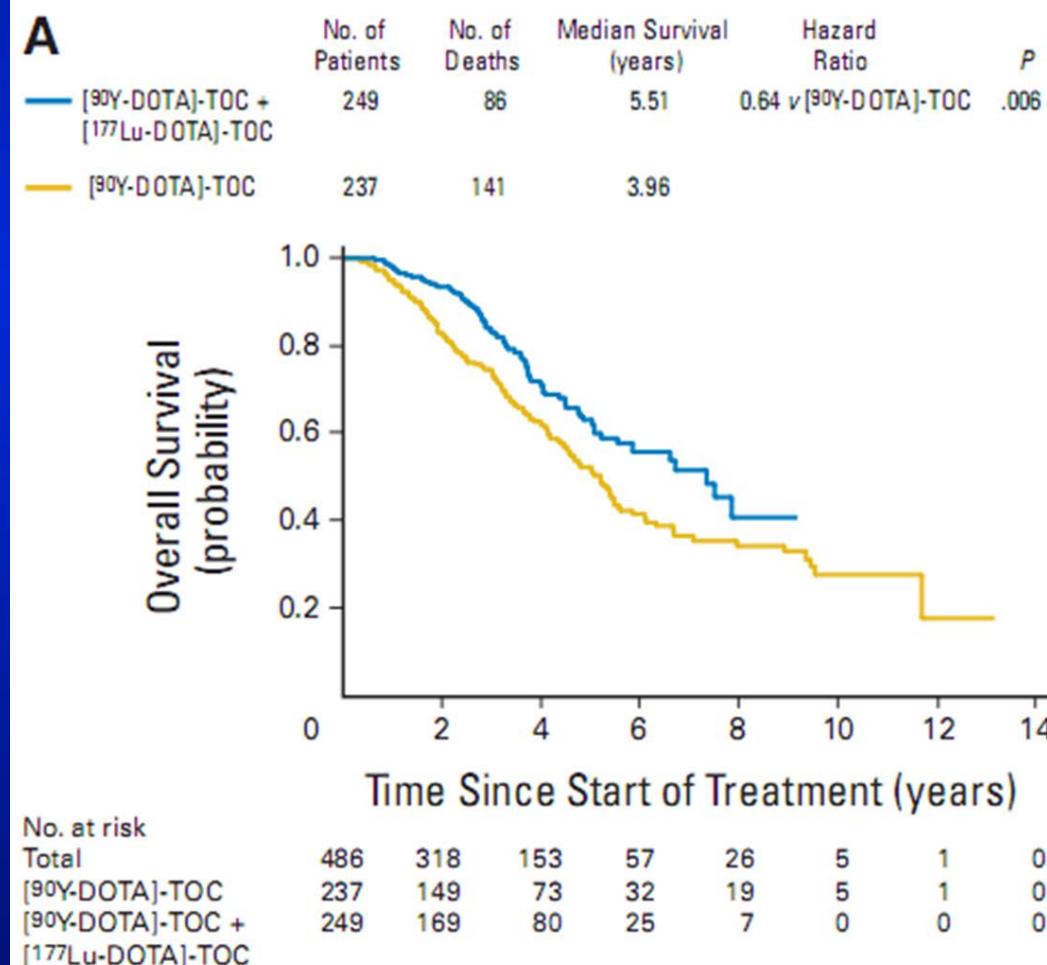
PRRT 59 pts

A. Filice et al J of Oncology 2012



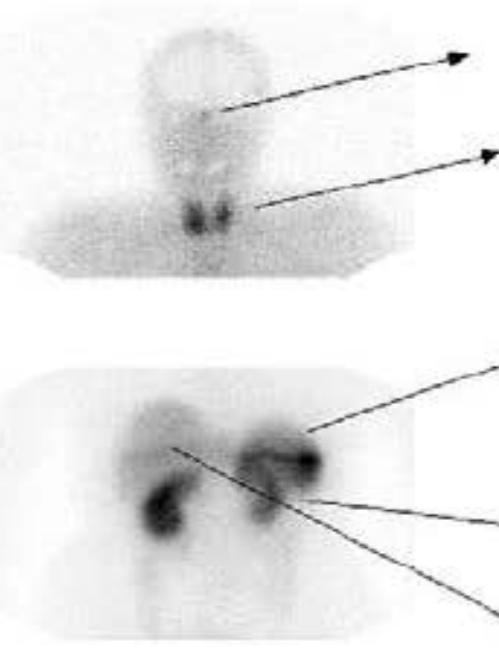
## Cohort Study of Somatostatin-Based Radiopeptide Therapy With [<sup>90</sup>Y-DOTA]-TOC Versus [<sup>90</sup>Y-DOTA]-TOC Plus [<sup>177</sup>Lu-DOTA]-TOC in Neuroendocrine Cancers

Linda Villard, Anna Romer, Nicolas Marinck, Philippe Brunner, Michael T. Koller, Christian Schindler, Quinn K.T. Ng, Helmut R. Macke, Jan Müller-Brand, Christoph Rochlitz, Matthias Briel, and Martin A. Walter



# Terapia Radiorecettoriale

## Effetti collaterali

- 
- No important effect on pituitary function
  - No important effect on thyroid function
  - Common: mild bone marrow suppression
  - Common: Lymphocytopenia
  - Rare: MDS, Leukemia
  - Rare: Kidney impairment
  - Rare: Liver toxicity

Fattori di rischio per insuff.renale

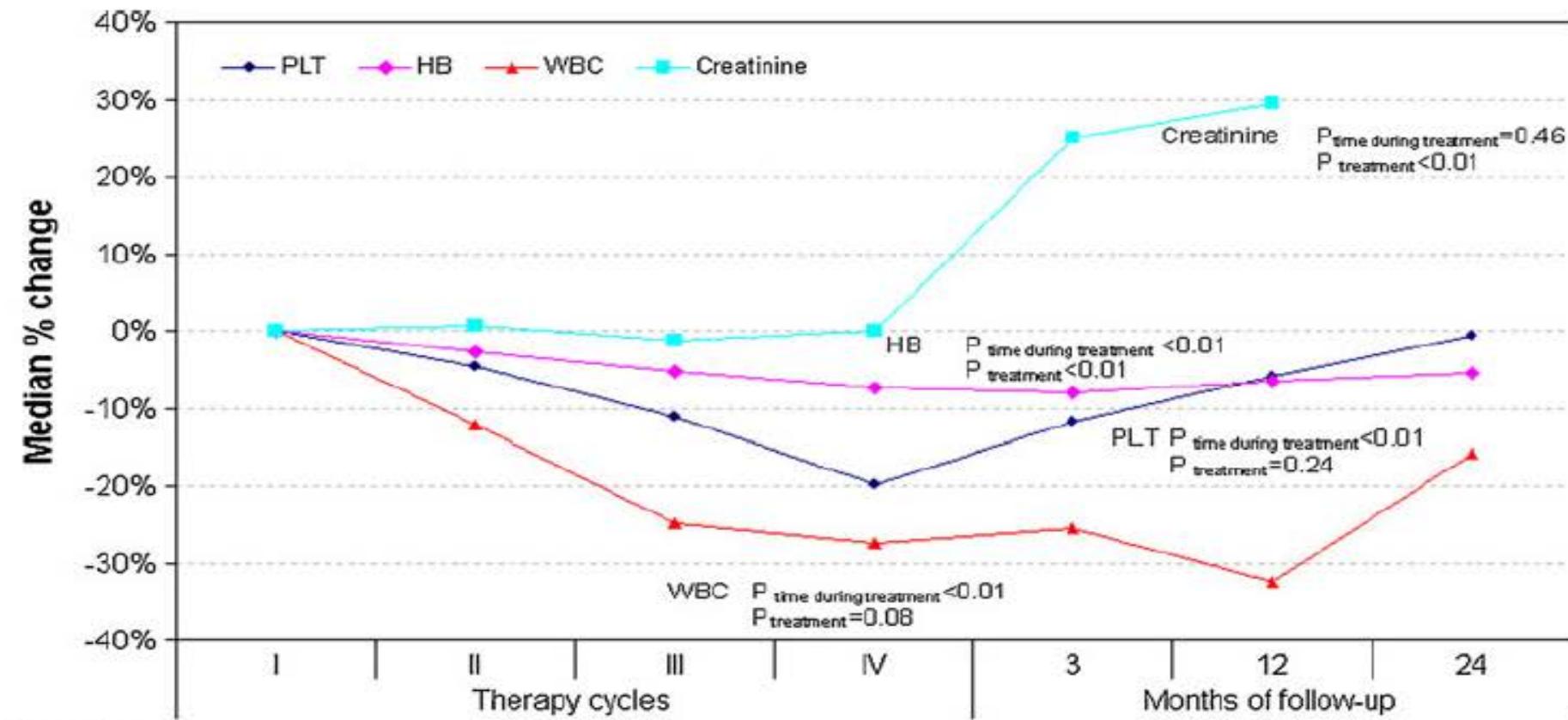
Diabete  
Ipertensione arteriosa

# Peptide receptor radionuclide therapy with $^{177}\text{Lu}$ -DOTATATE: the IEO phase I-II study

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Maddalena Sansovini · Marco Chinol · Giovanni Paganelli

## Haematological and renal toxicity

Eur J Nucl Med Mol Imaging (2011) 38:2125–2135

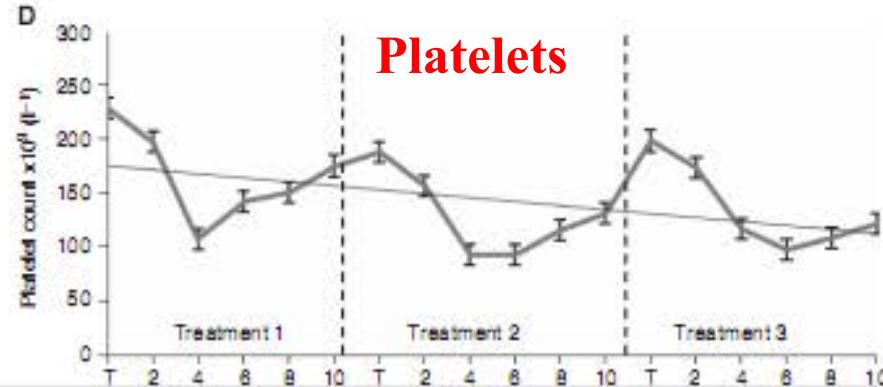
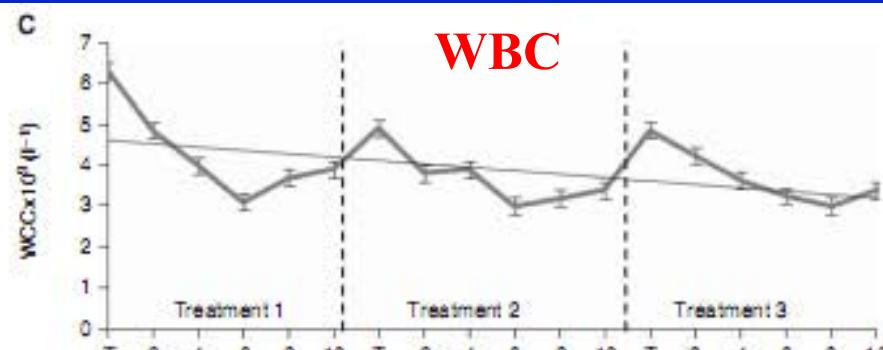
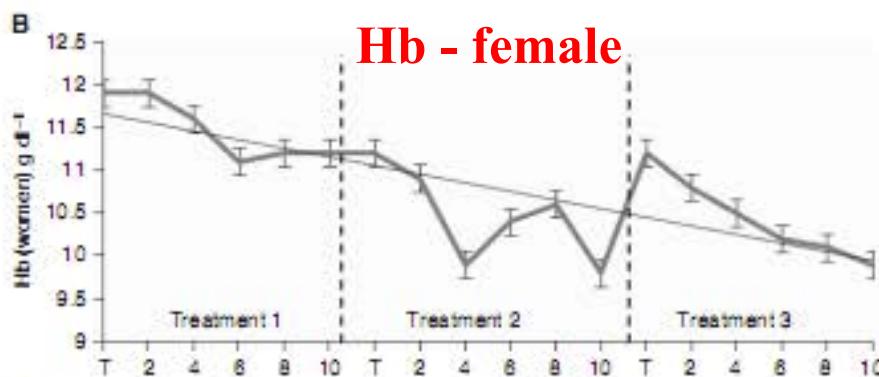
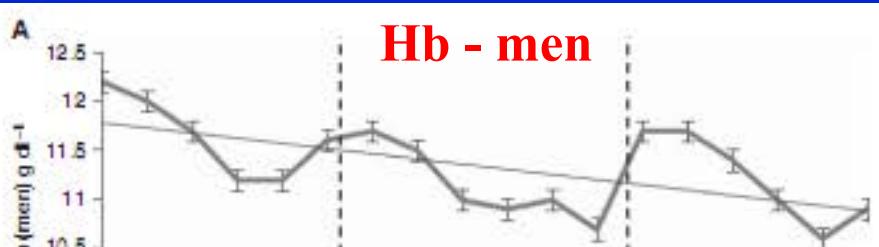


No. patients

|     | I  | II | III | IV | 3  | 12 | 24 |
|-----|----|----|-----|----|----|----|----|
| CR  | 51 | 50 | 49  | 45 | 41 | 25 | 7  |
| HB  | 51 | 51 | 51  | 46 | 29 | 9  | 9  |
| PLT | 51 | 51 | 51  | 46 | 46 | 8  | 8  |
| WBC | 51 | 51 | 49  | 46 | 46 | 29 | 9  |

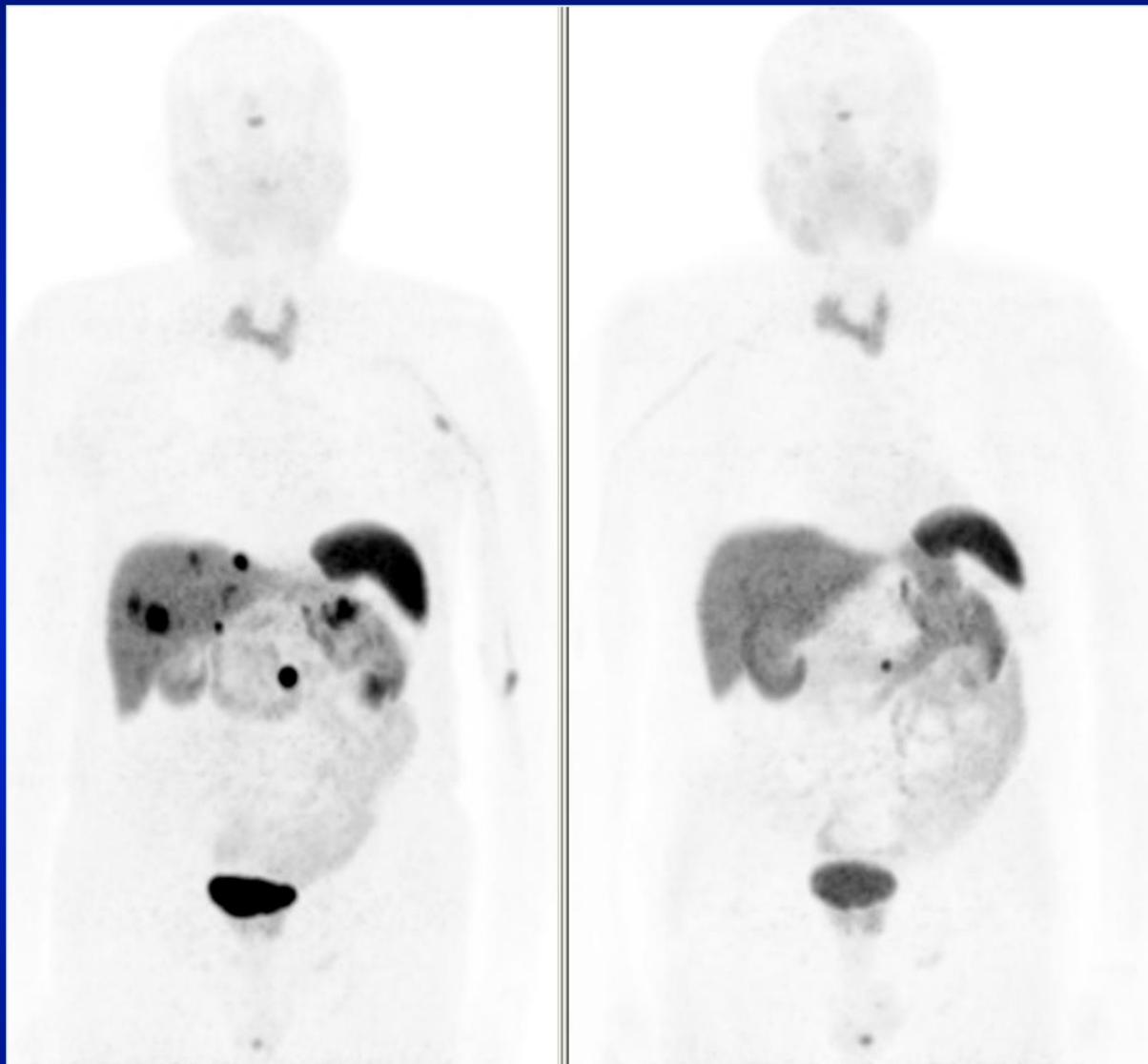
S Vinjamuri<sup>1,8</sup>, T M Gilbert<sup>2,8</sup>, M Banks<sup>3</sup>, G McKane<sup>1</sup>, P Maltby<sup>1</sup>, G Poston<sup>3</sup>, H Weissman<sup>4</sup>, D H Palmer<sup>5</sup>,  
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## PRRT - Hematological toxicity



<sup>68</sup>Ga-DOTATATE PET/CT

Pre-terapia

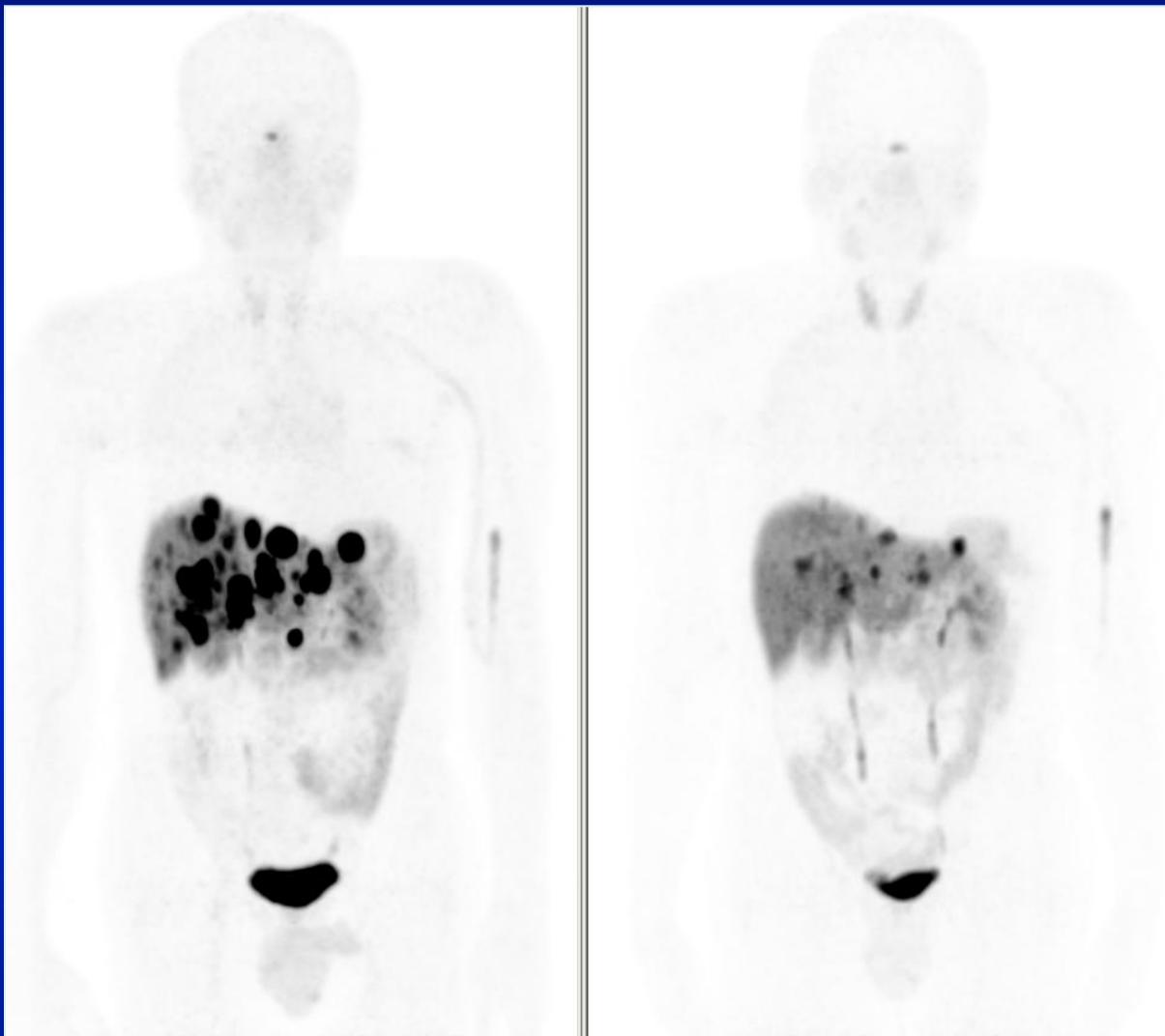


Post-terapia

M, 73 aa: Carcinoma neuroendocrino pancreatico con metastasi epatiche.  
2 cicli di 90Y e 4 cicli di 177Lu. Risposta parziale alla terapia.

<sup>68</sup>Ga-DOTATATE PET/CT

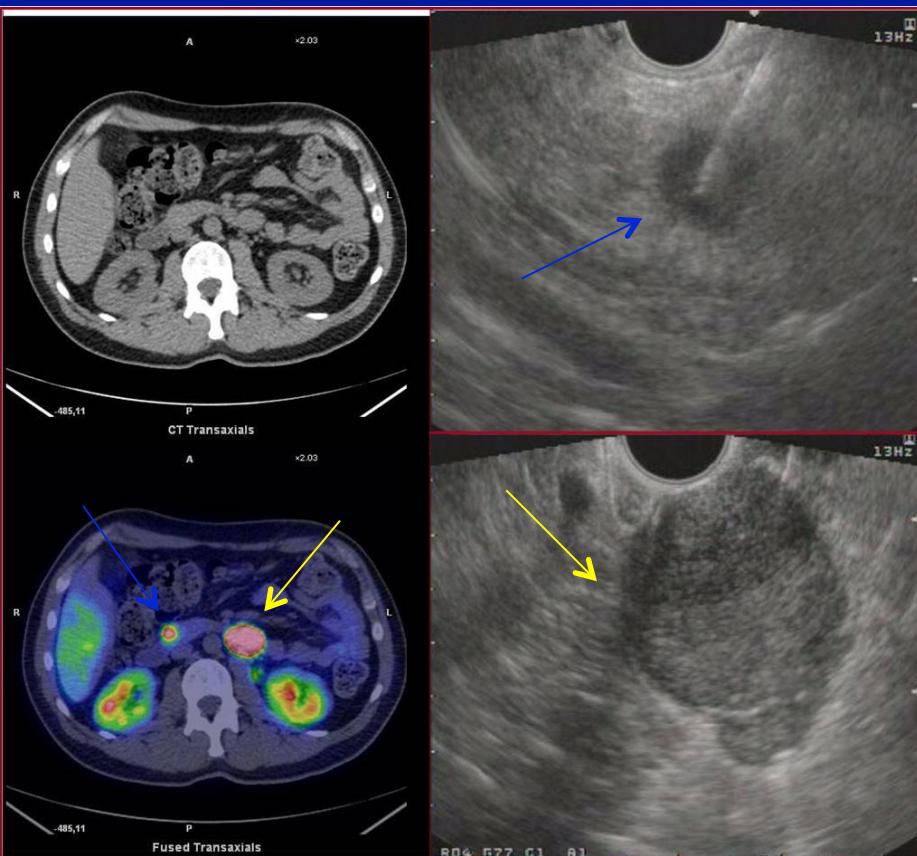
Pre-terapia



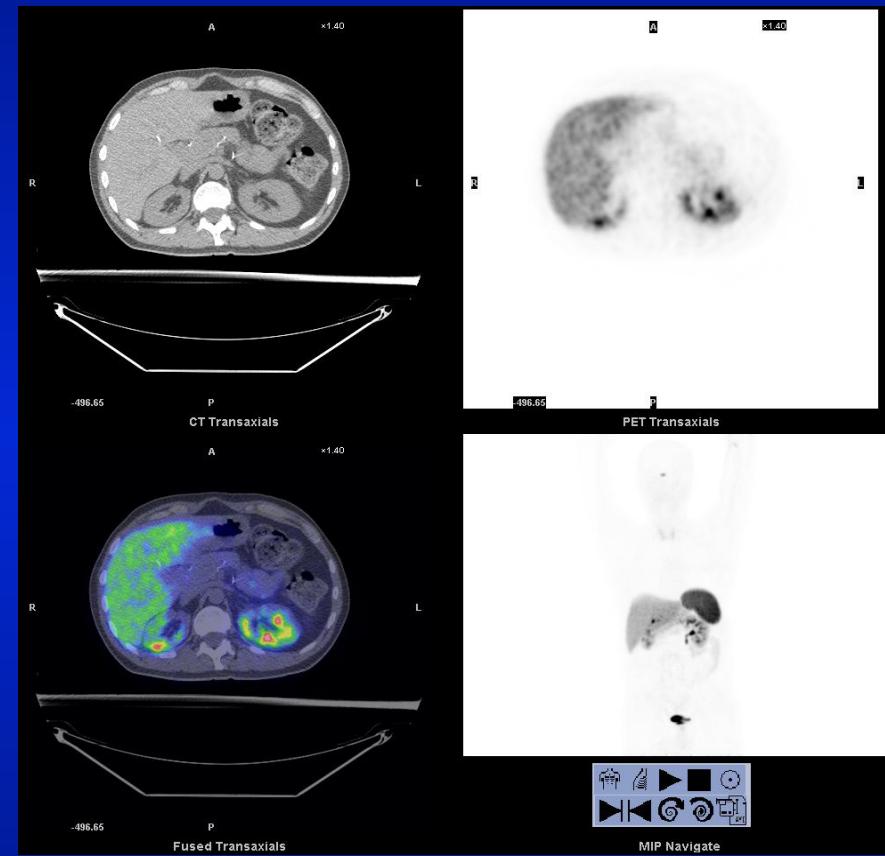
Post-terapia

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

# Pre-terapia

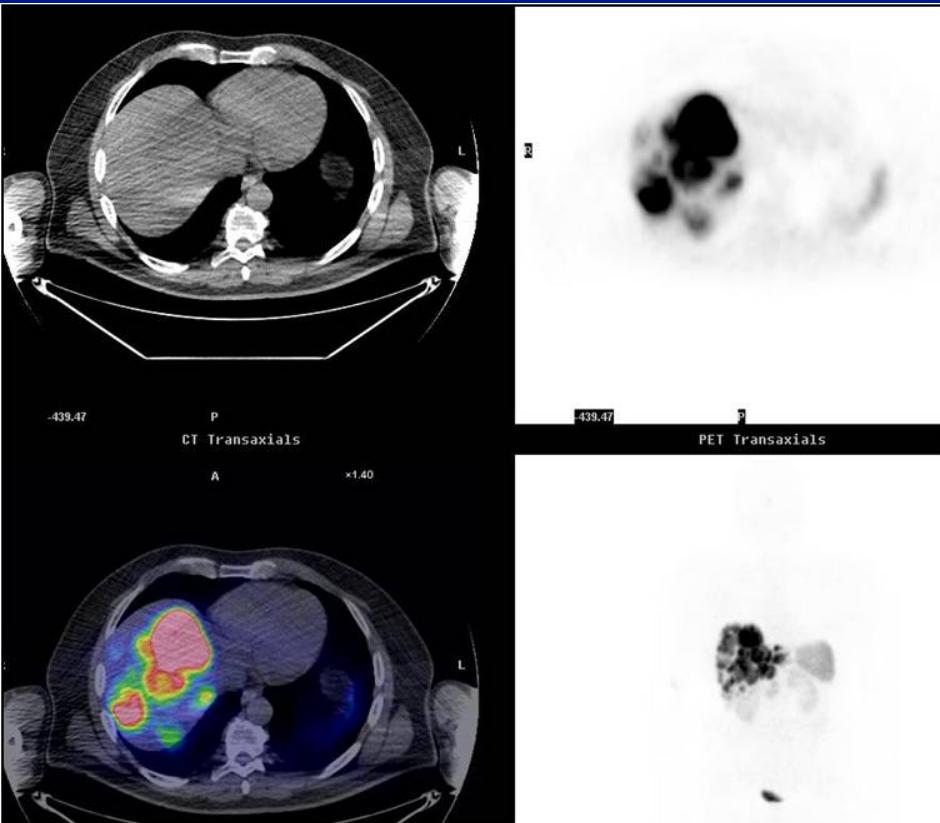


# Post-terapia

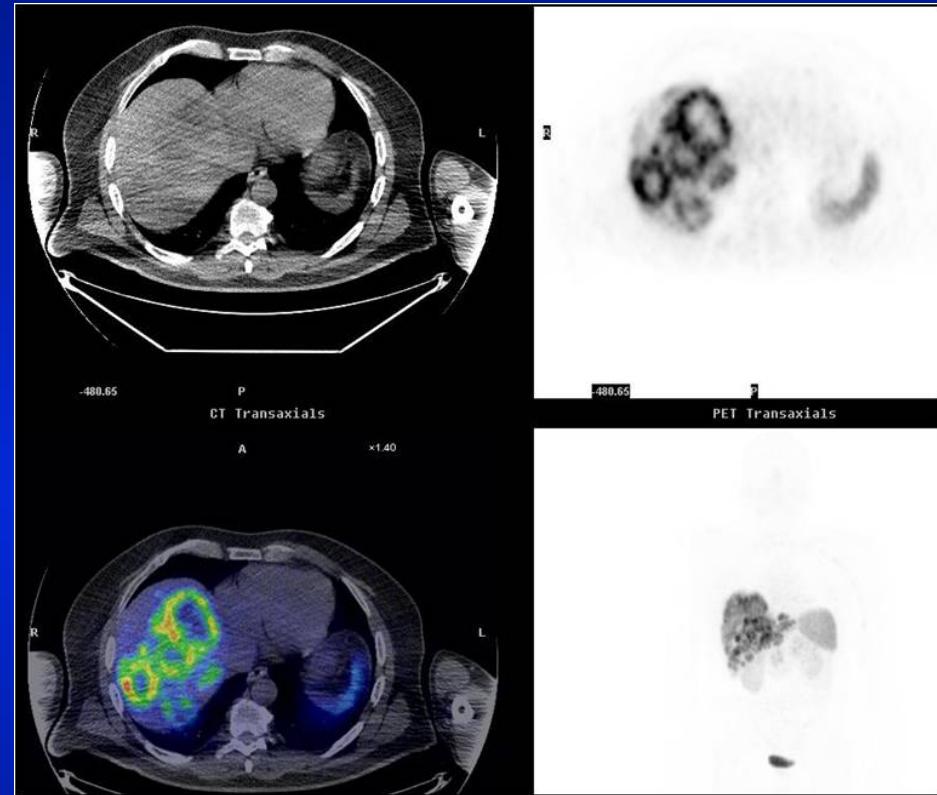


Pz. V.R.: NET della testa del pancreas con metastasi linfonodale .  
Risposta completa alla terapia con 90Y.

## $^{68}\text{Ga}$ -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  $^{90}\text{Y}+^{177}\text{Lu}$ .

# Terapia Radiorecettoriale

## Costi

**DRG (Emilia Romagna)  
(per ciclo)**

- € 3260 (paz. fuori regione)
- € 8500 (paz. intra-regione)

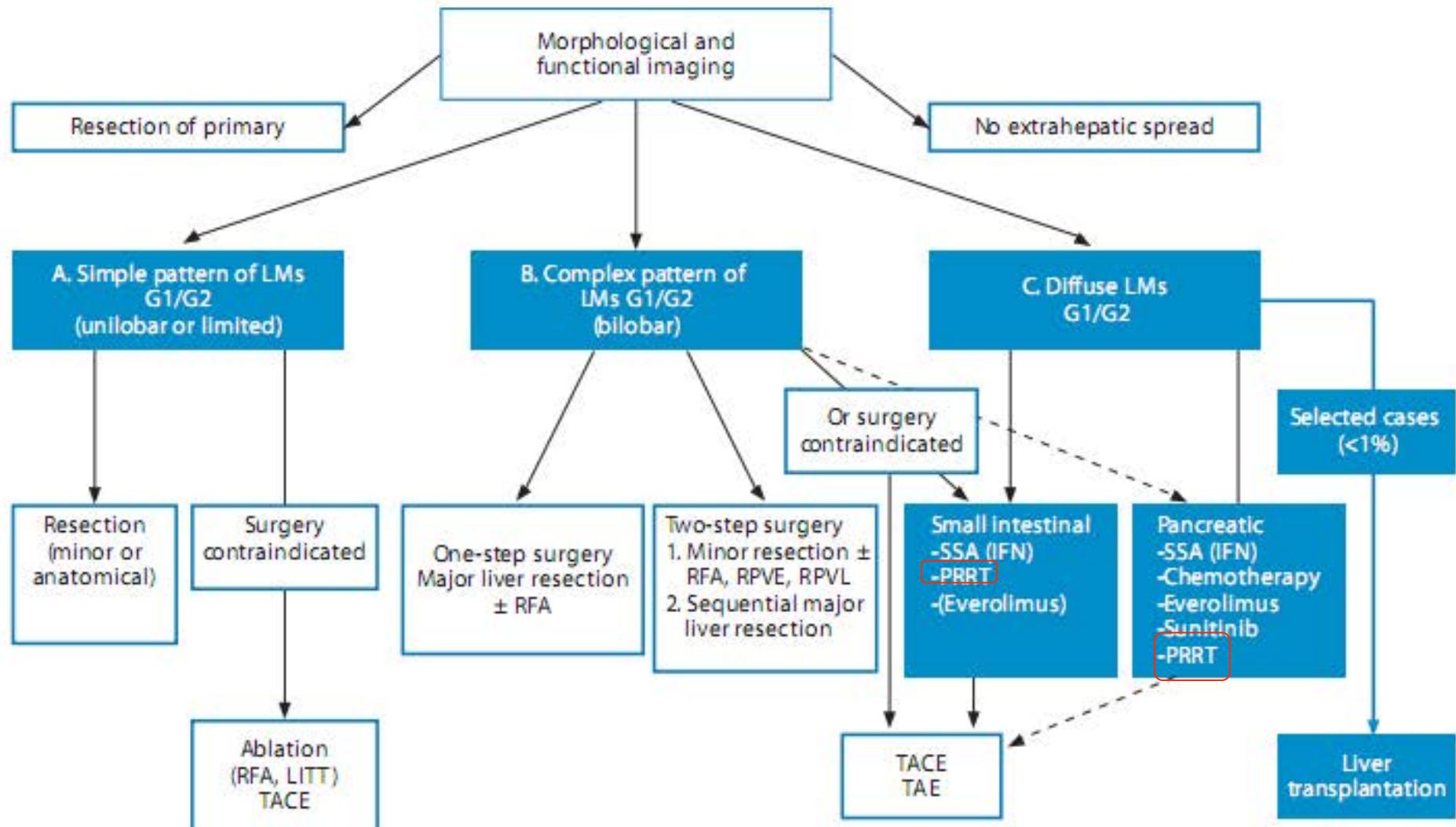
**Costo sociale**

- **Ricovero**  
3 giorni/ciclo
- **Spostamenti** dovuti  
al ridotto numero di centri

# 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>

2012



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

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**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.

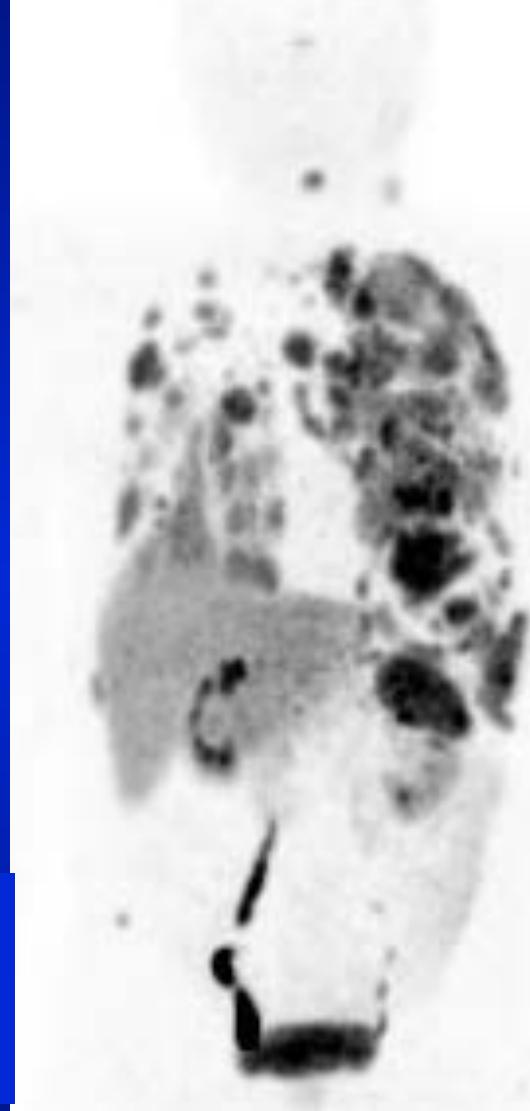
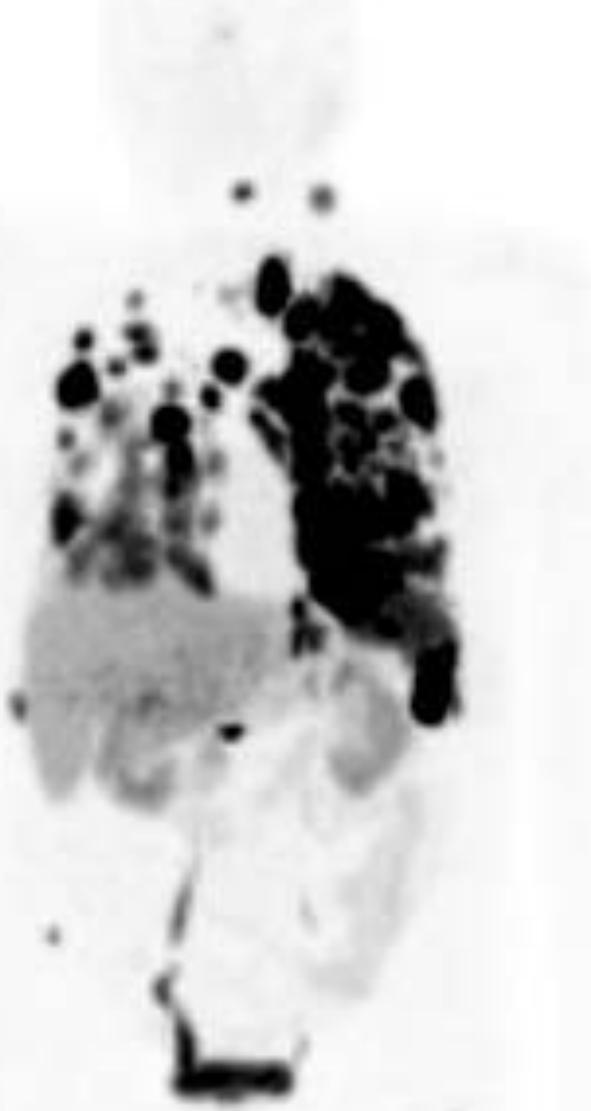
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Ramon Salazar<sup>h</sup> all other Barcelona Consensus Conference participants<sup>1</sup>

## **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.

# Carcinoma differenziato della tiroide plurimetastatico non iodio-captante



Pre-terapia



Dopo 4 cicli



**$^{90}\text{Y}$ -DOTATOC**

(dose cumulativa 268 mCi)

B.M. M, 75 aa

Set 2007

Mar 2009

Grazie per  
l'attenzione

