Gestione delle terapie biologiche nei pazienti con NET

Caso clinico 2

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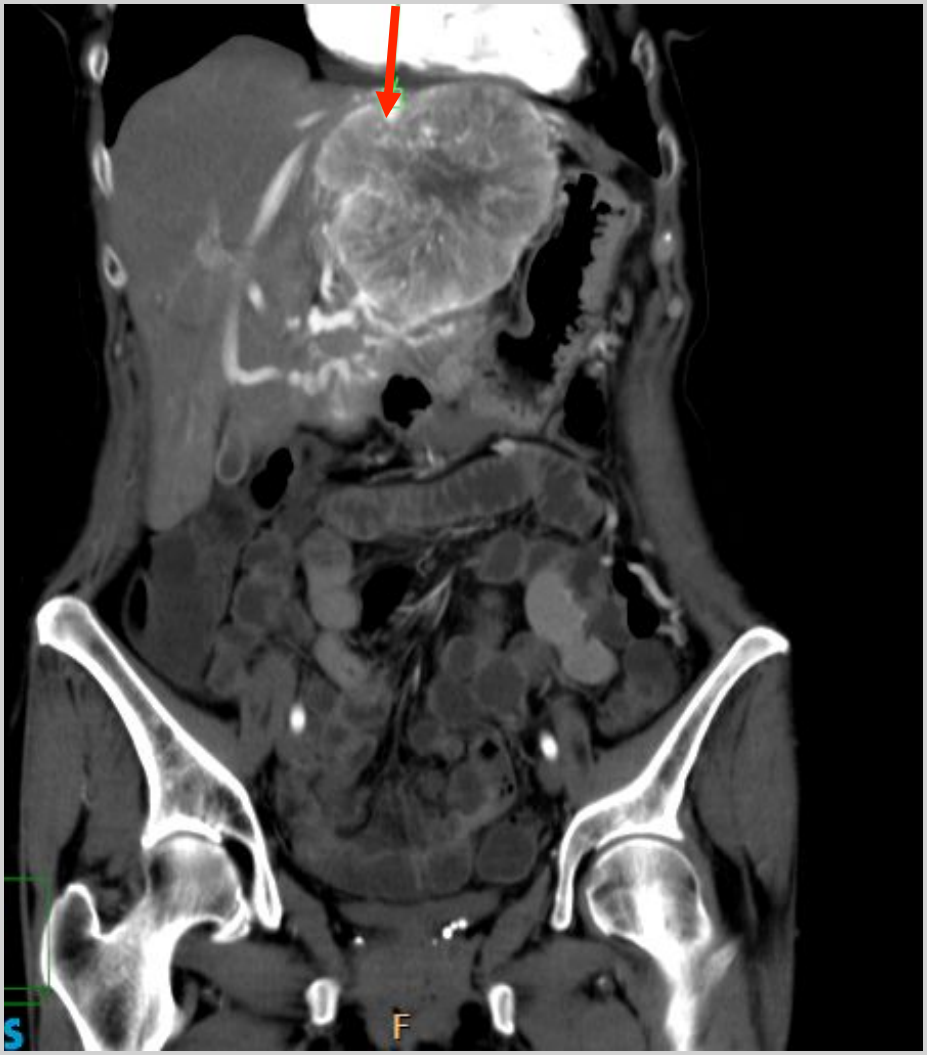
Caso clinico

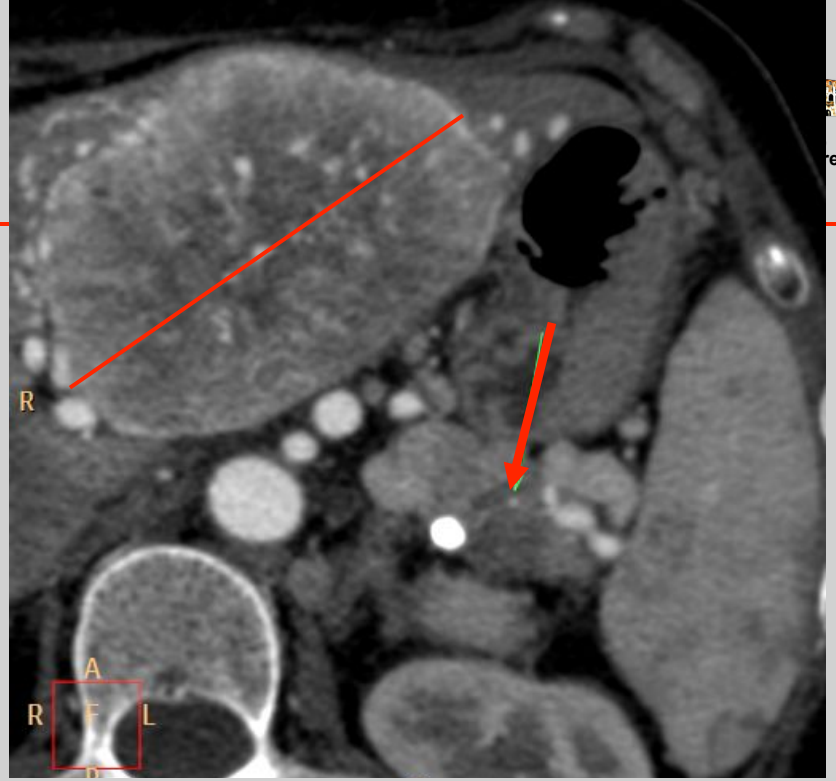
- F, 62 anni
- Familiarita' per neoplasia pancreatica e gastrica
- Anamnesi patologica remota negativa
- Da 6 mesi dolore addominale ingravescente in regione epigastrica e ipocondrio ds associato a calo ponderale di 18 kg.

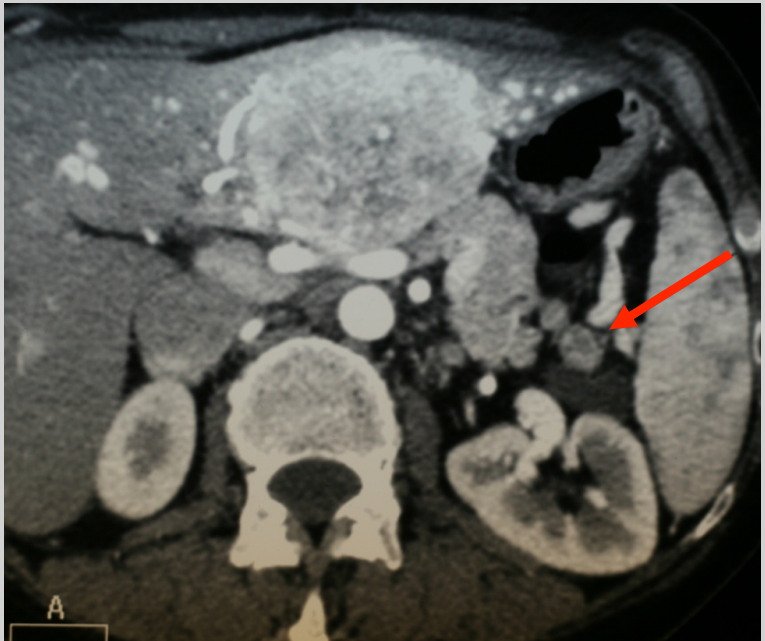
Sett/Ott 2009:

- **EGDS:** gastrite erosiva
- **Colonscopia**: diverticolosi del colon
- **Ecografia addome**: lesione al lobo epatico sn di 9,7 cm

TC nov 2009







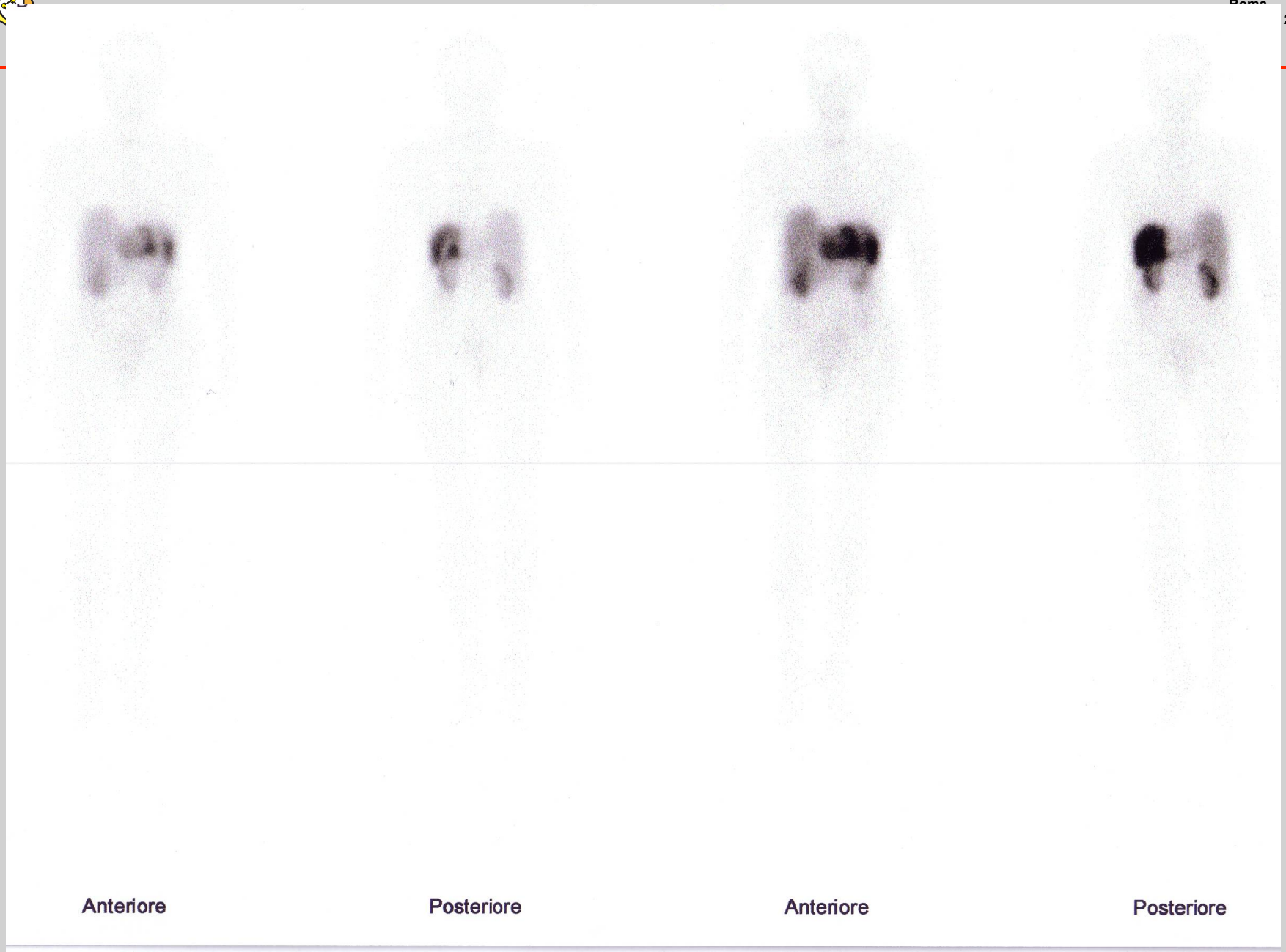
Biospia epatica ecoguidata :

metastasi epatica di carcinoma endocrino ben differenziato

Cromogranina +, sinaptofisina +, serotonina -

Ki67: 3-5%.

Octreoscan



Laboratorio

- **Cromogranina A** 1200 ng/ml (n.v. 19-98)
- NSE, gastrina, glucagone, calcitonina normali
- **5-HIAA** 180 mg/24 h (2-7)
- **Calcemia** 14,3 mg/dl, **PTH** 13 pg/ml (v.n. 10-65)

Pre-operatorio: idratazione e ac. Zoledronico 4 mg e.v.

→ calcemia 10,5 mg/dl

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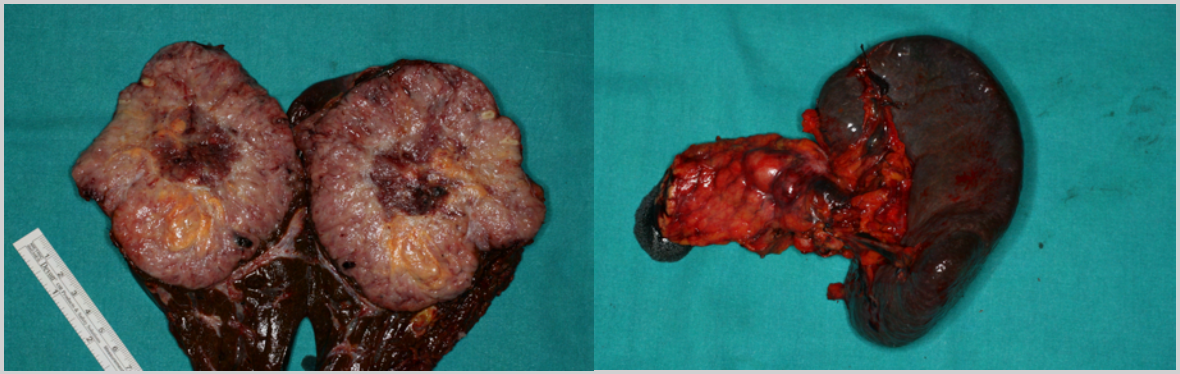
Feb 2010:

Ecografia intraoperatoria: no metastasi al lobo epatico ds

Intervento: splenopancreasectomia sn, lobectomia epatica sn, colecistectomia e ampia linfoadenectomia regionale



Esame istologico:

NET G2 della coda del pancreas (3 cm) con invasione perineurale, vascolare, del tessuto peripancreatico e della v. splenica

Ki67: 2-3%;

Metastasi in 7/15 linfonodi peripancreatici

Metastasi epatica di 12 cm, **Ki67: 5%.**

Classificazione dei GEP-NET

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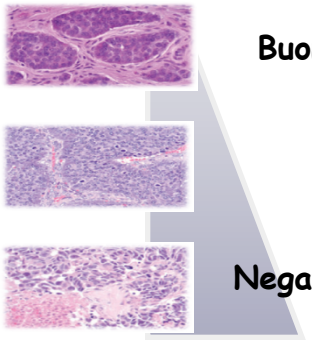
WHO 1980	WHO 2000	WHO 2010
Carcinoide	Tumore endocrino ben differenziato (WDET)[a]	NET G1 (carcinoide)[b]
	Carcinoma endocrino ben differenziato (WDEC)[a]	NET G2[b]
Modificato da (1)	Tumore endocrino poco differenziato/ carcinoma a piccole cellule (PDEC)	NEC (tipo a larghe cellule o a piccole cellule)[b,c]

Prognosi dei pazienti



Modificato da (2,3)

Criteri di *grading* istopatologico (1,4,5)

G1	<2 mitosi x 10 HPF e/o <2% Ki-67
G2	2-20 mitosi x 10 HPF e/o 3-20% Ki-67
G3	>20 mitosi x 10 HPF e/o >20% Ki-67

Elaborazione da (1,4,5)

1. Bosman FT, et al. WHO Classification of Tumours of the Digestive System, Fourth Edition, p. 13-14, 2010; 2. Strosberg JR, et al. Gastrointest Cancer Res 2008; 2(3): 113-25. 3.Pape UF et al. Cancer 2008;113:256–65; 4. Rindi G, et al. Virchows Arch 2006; 449: 395-401; 5. Rindi G, et al. Virchows Arch 2007; 451: 757-62.

TNM

Table 3. TNM Classification and Staging Proposed by the European Neuroendocrine Tumor Society[a]

T—Primary Tumor	
Tx	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor limited to the pancreas and size <2 cm
T2	Tumor limited to the pancreas and size 2–4 cm
T3	Tumor limited to the pancreas and size >4 cm or invading duodenum or bile duct
T4	Tumor invading adjacent organs (stomach, spleen, colon, adrenal gland, or the wall of large vessels)
N—Regional Lymph Nodes	
Nx	Regional lymph node cannot be assessed
N0	No regional lymph node metastases
N1	Regional lymph node metastases
M—Distant Metastases	
Mx	Distant metastases cannot be assessed
M0	No distant metastases
M1	Distant metastases

TNM Stage Groupings

Stage I	T1	N0	M0
Stage IIA	T2	N0	M0
Stage IIB	T3	N0	M0
Stage IIIA	T4	N0	M0
Stage IIIB	Any T	N1	M0
Stage IV	Any T	Any N	M1

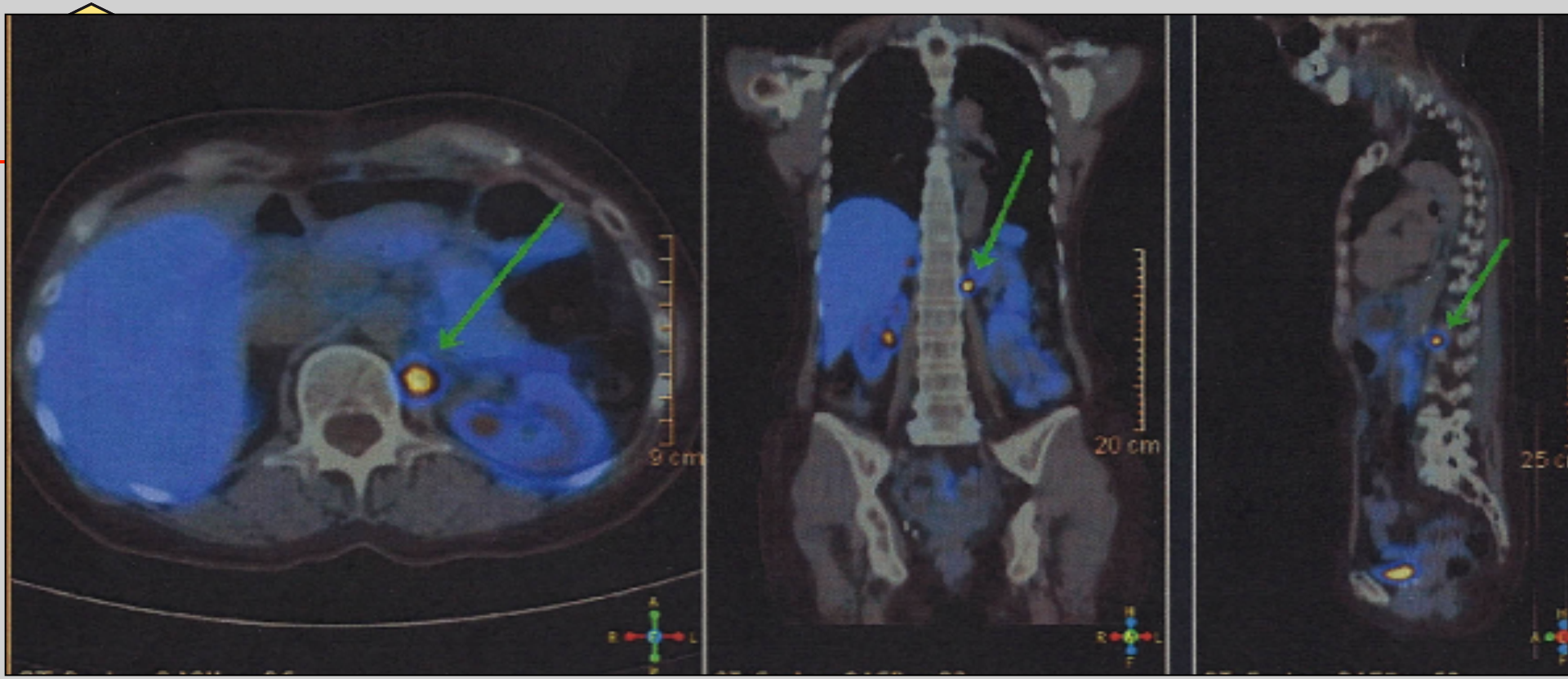
[a] Data from Rindi et al.[96]

Rindi et al. 2006

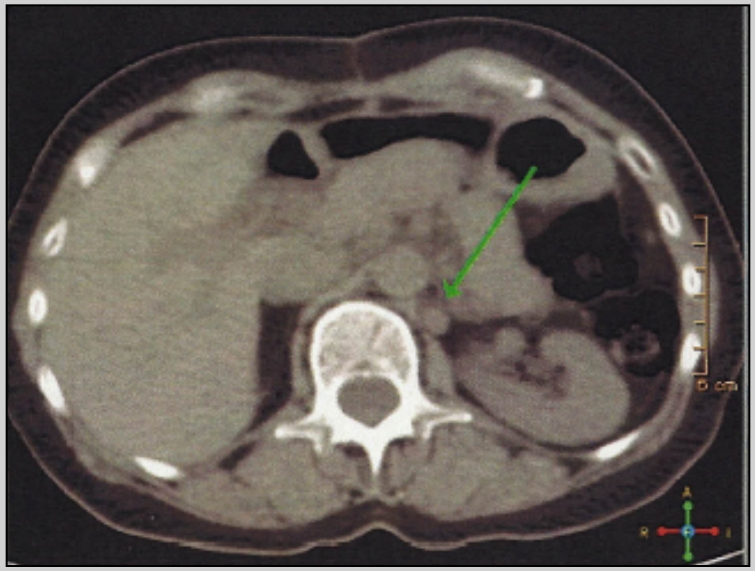
FOLLOW-UP a 6 mesi
(giugno 2010)

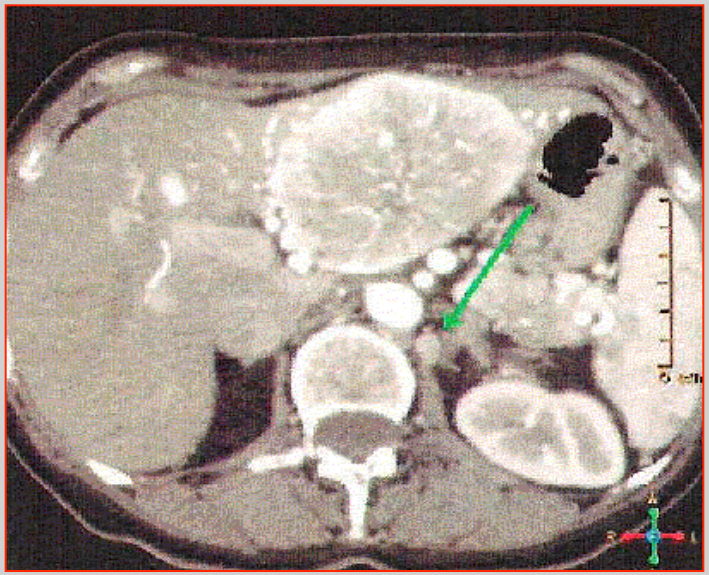
- Karnofsky 100%
- Cromogranina A 129 ng/ml
- 5-HIAA 5,8 mg/24 h, Ca 8,8 mg/dl, PTH 52 pg/ml

- ^{68}Ga-DOTANOC- PET-CT: elevato uptake corrispondente a linfoadenopatia di 12 mm in regione addominale para-aortica sn



^{68}GA-DOTANOC PET-CT





Trattamento

- Octreotide s.c. 0,1 mg 1 fl x 2/die s.c. x 7 gg
- Octreotide LAR 20 mg 1 fl/28 gg i.m.

- Controllo RMN addome dopo 6 mesi: metastasi linfonodale paraortica sn stazionaria

- Prosegue octreotide LAR ⟹ 30 mg/28 gg

Follow up successivo

SD: giugno 2010 ➡ febbraio 2012:

Giugno 2012:

Karnofsky 100%, ECOG0

CrgA 281 ng/ml, **5-HIAA 10,8 mg/24 h,**

Ca, PTH normali

RMN ADDOME:

comparsa di multiple lesioni epatiche ipervascolarizzate, le maggiori al V segmento (20-14 mm) e al IV (10 mm), immodificata la linfoadenopatia paraortica sn

RMN (19-6-12)

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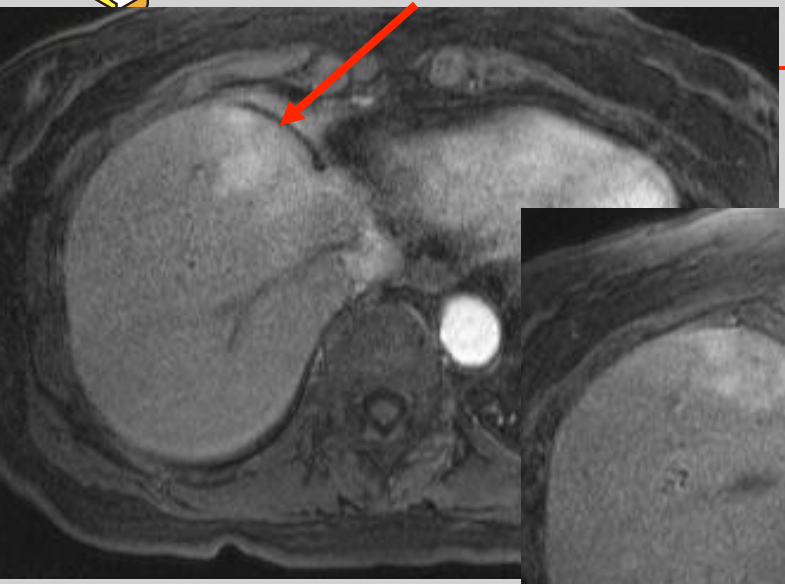

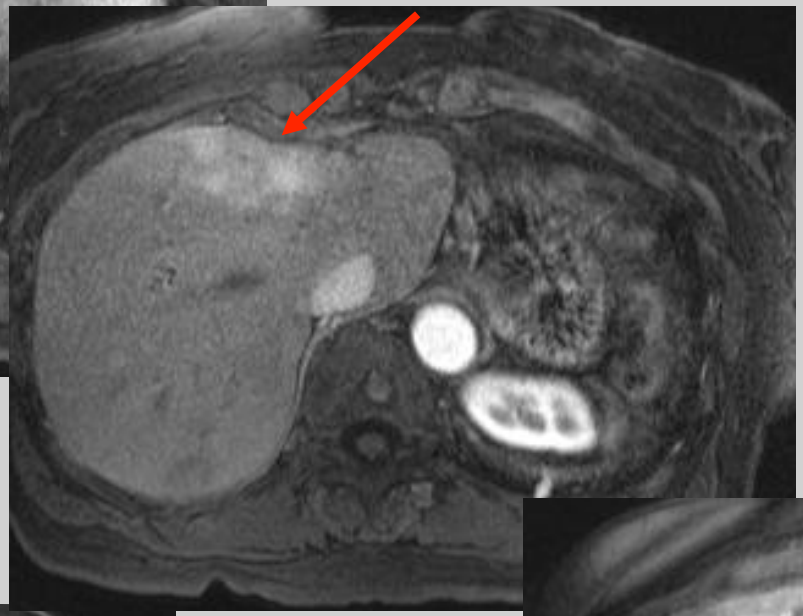

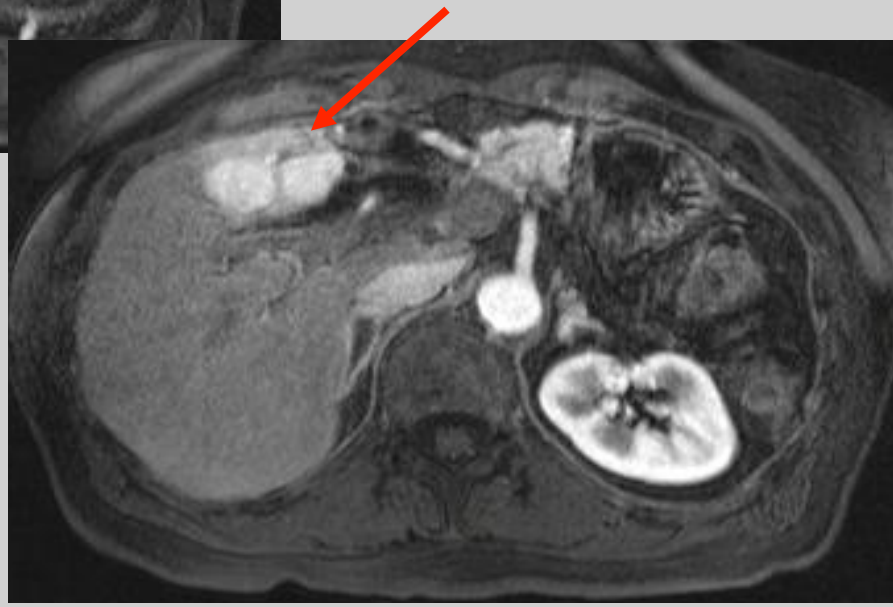

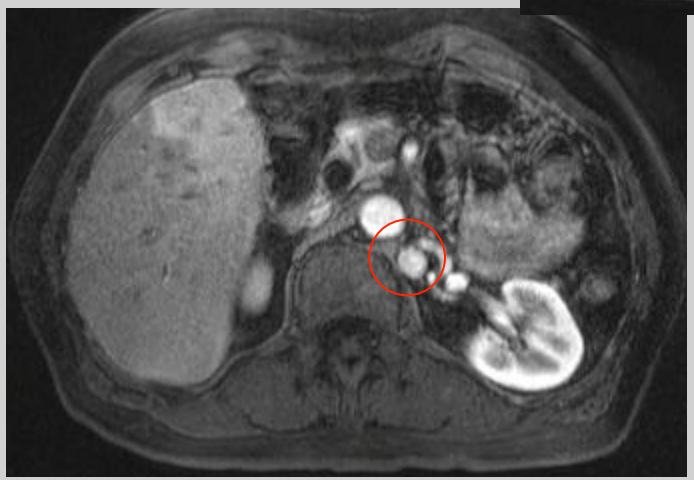

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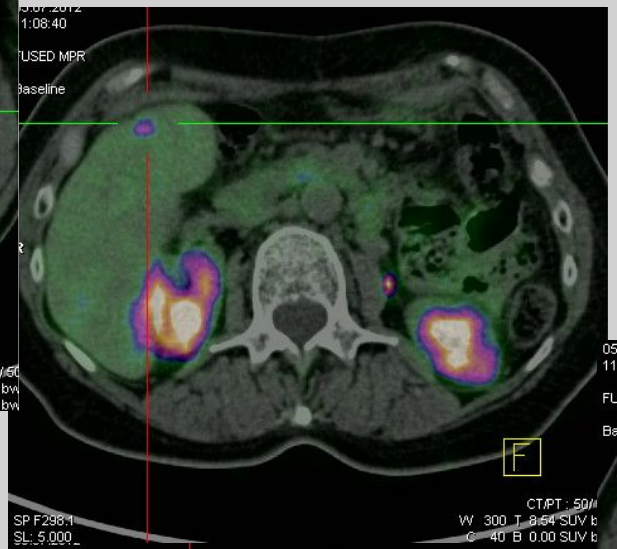
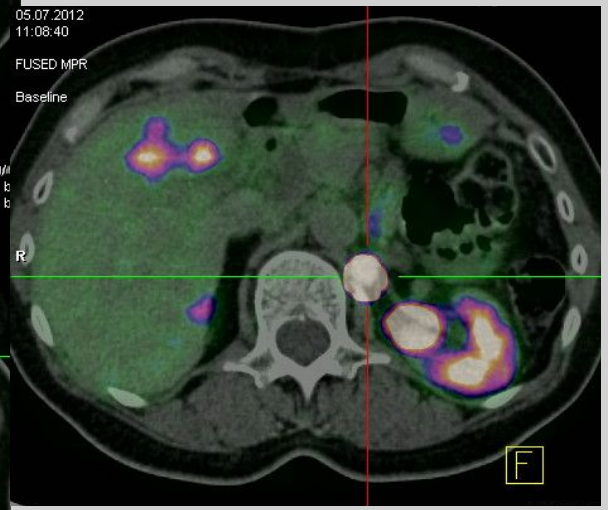
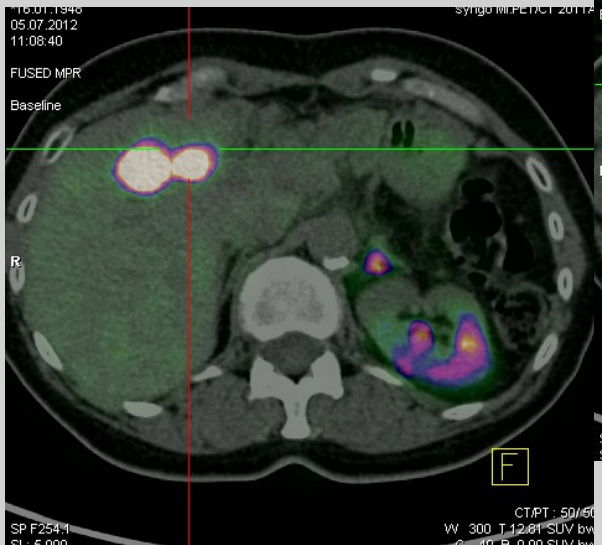
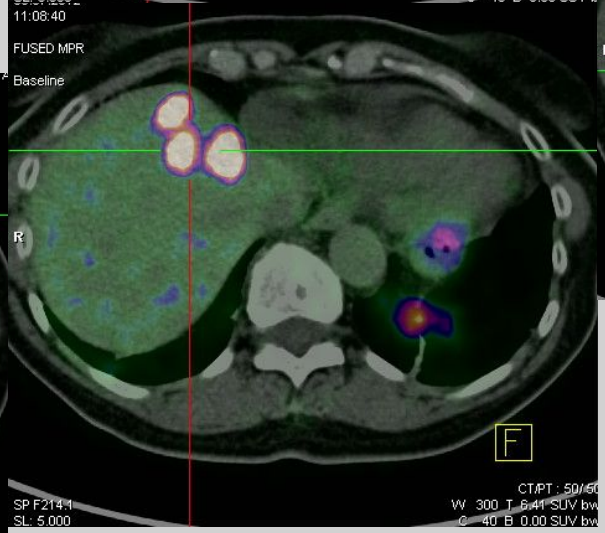
^{68}GA-DOTANOC PET-CT (5/7/12)









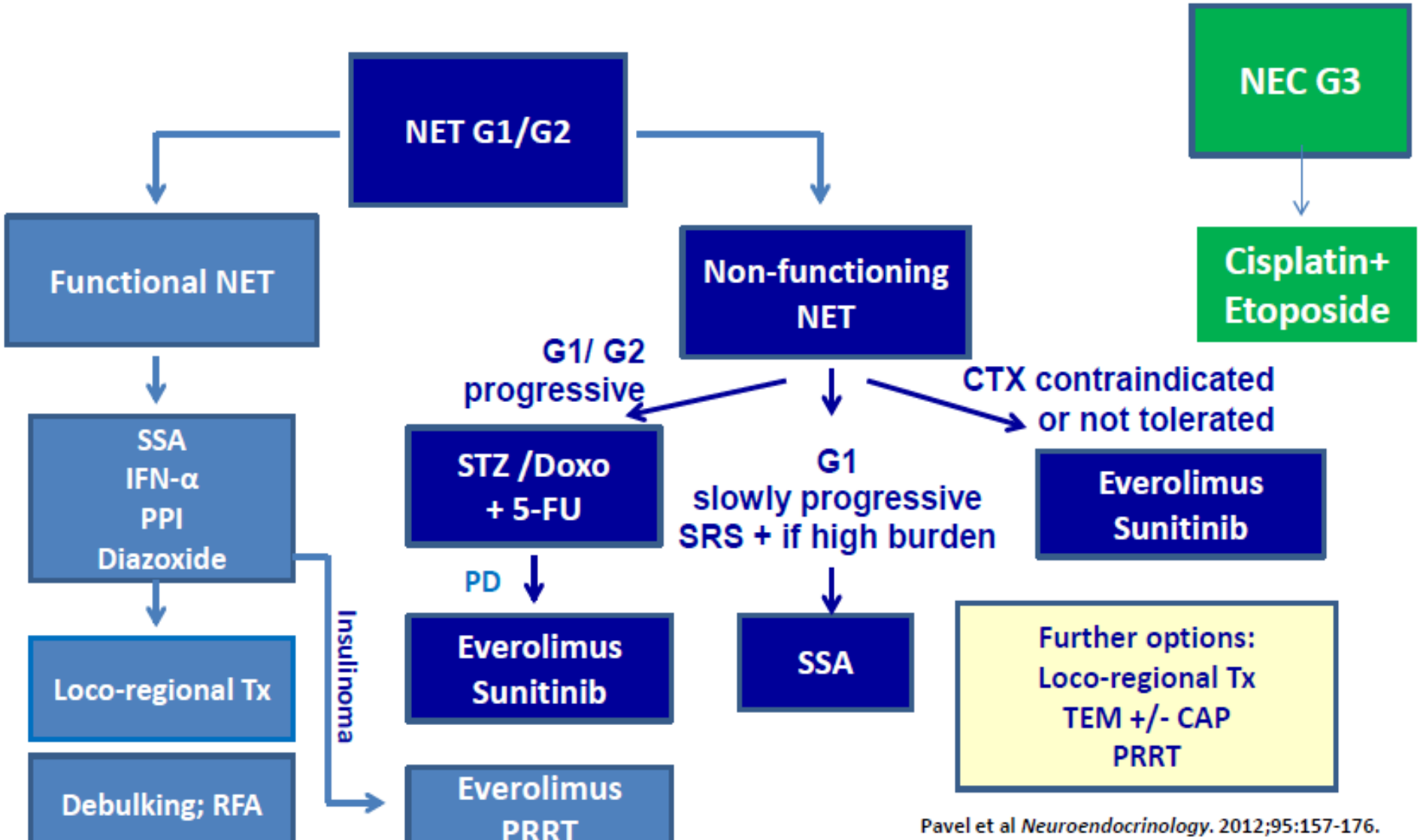
NET pancreas G2 in progressione epatica cosa fare?

- Aumento dosaggio (intervalli) di octreotide?
- Terapia radiometabolica con ^{90}Y-dotatoc o ^{177}Lu-dotatate?
- HAE/TACE/SIRT?
- Everolimus/sunitinib?
- Chemioterapia?

Fattori che influenzano la scelta terapeutica

- Istologia: grading
- Sindrome ormonale associata
- Positivita' ai recettori della somatostatina
- Carico tumorale/malattia extraepatica
- Sede del primitivo (pancreas vs intestino)

Pharmcacological Therapy in Metastatic Nonresectable Pancreatic NET
ENETS Consensus Guidelines 2011



Pavel et al *Neuroendocrinology*. 2012;95:157-176.


10 Novembre 2012
Giornata mondiale
dei tumori neuroendocrini
NET CANCER DAY