PATOLOGIE RARE IN ONCOLOGIA
"TUMORI RARI":
FONDAMENTI SCIENTIFICI ED ASPETTI LEGISLATIVI

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I Tumori Neuroendocrini

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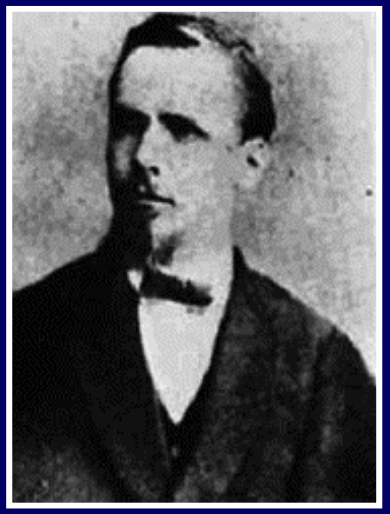
di Oncologia

NENs NELLA STORIA UMANA



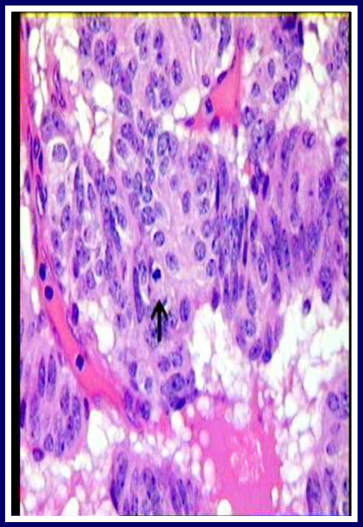
1552 a.c
Papiro Ebers



1867 d.c.
Insulae di Langerhans



1890 d.c.
Ransom
Sindrome da Carcinoide



1907 d.c.
Oberndorfer
Karzinoid

RARE CANCERS EUROPE

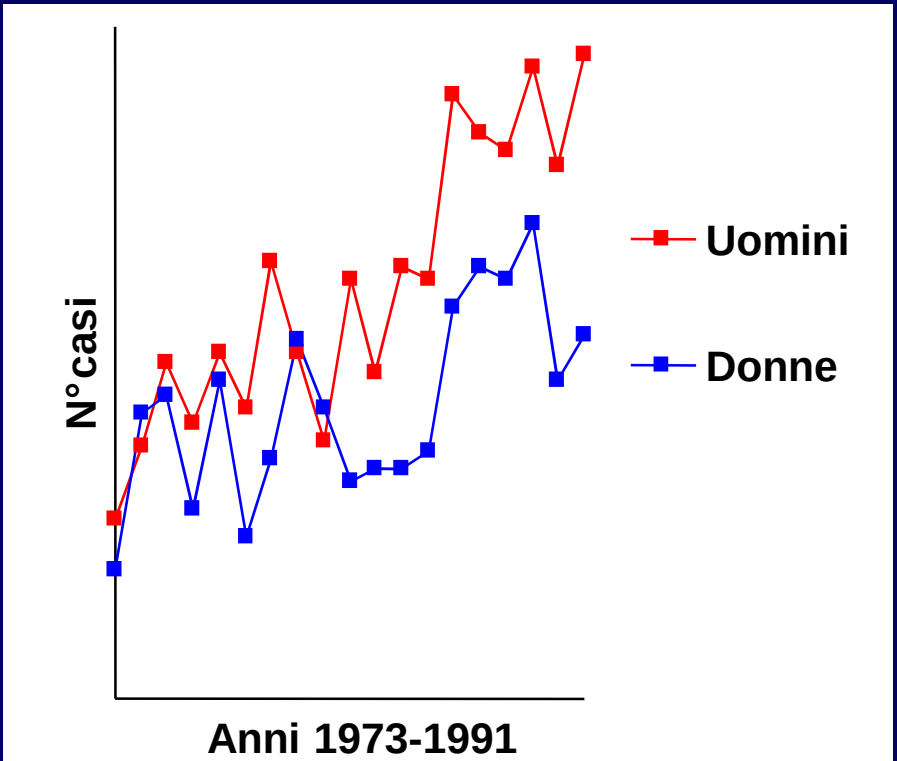
Incidence: (<6/100,000/year).

- ❖Rare SKIN cancers and NON-CUTANEOUS MELANOMA
- ❖Rare THORACIC cancers (mesothelioma, thymoma, rare lung cancers, rare breast cancers)
- ❖Rare UROGENITAL cancers (kidney cancers, bladder cancers, urinary tract cancers)
- ❖Rare FEMALE GENITAL cancers (cervical and ovarian cancers)
- ❖Rare MALE GENITAL cancers (prostate and testicular cancers)

- ❖NEUROENDOCRINE cancers

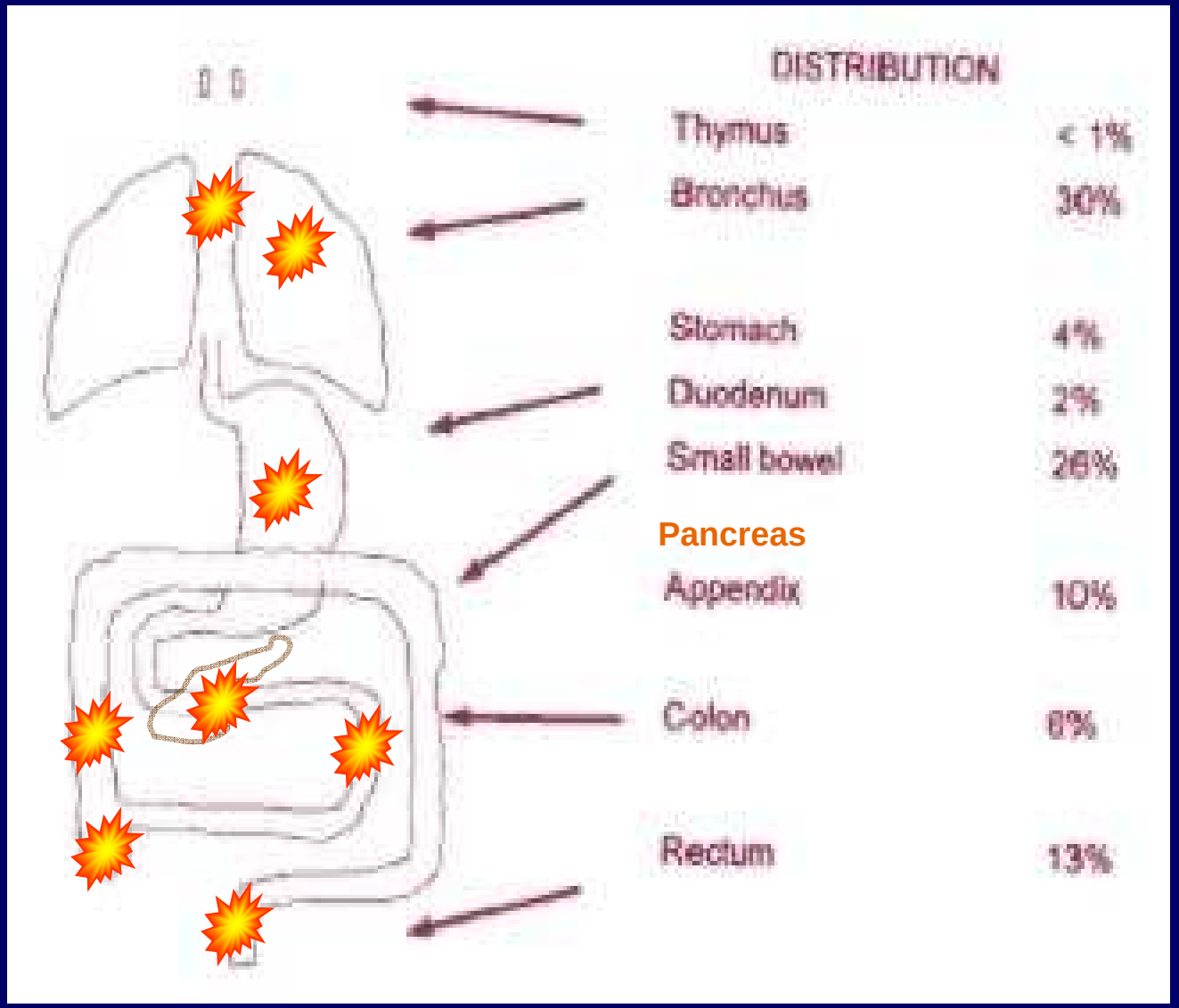
- ❖ENDOCRINE ORGAN cancers (adrenal cancer, thyroid and parathyroid cancer)
- ❖Rare CNS cancers (brain cancer)
- ❖SARCOMAS
- ❖Rare DIGESTIVE cancers (oesophageal cancers, stomach and small intestine cancer, colorectal and anal cancers, liver cancers, gallbladder cancers and cancers of the Intrahepatic/Extrahepatic Bile Tract (IBT/EBT), pancreatic cancers)
- ❖Rare cancers of HEAD & NECK
- ❖Rare HAEMATOLOGIC cancers (lymphomas, leukaemias, myelodysplastic and myeloproliferative disorders/neoplasms)
- ❖PAEDIATRIC solid cancers

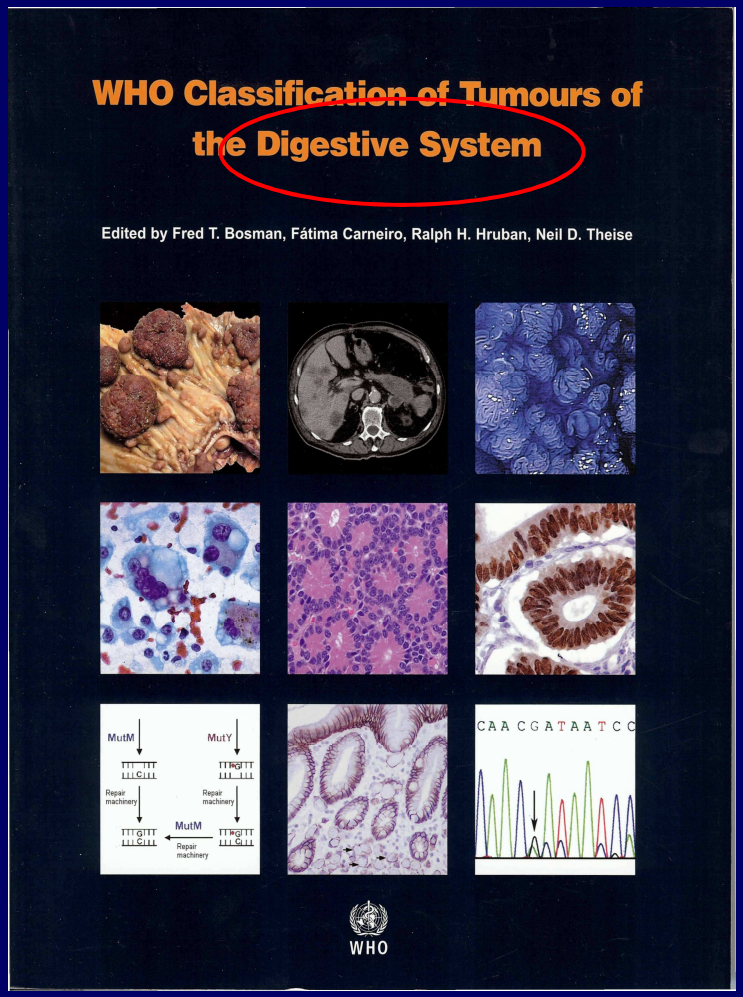
Incidenza diagnostica dei tumori neuroendocrini



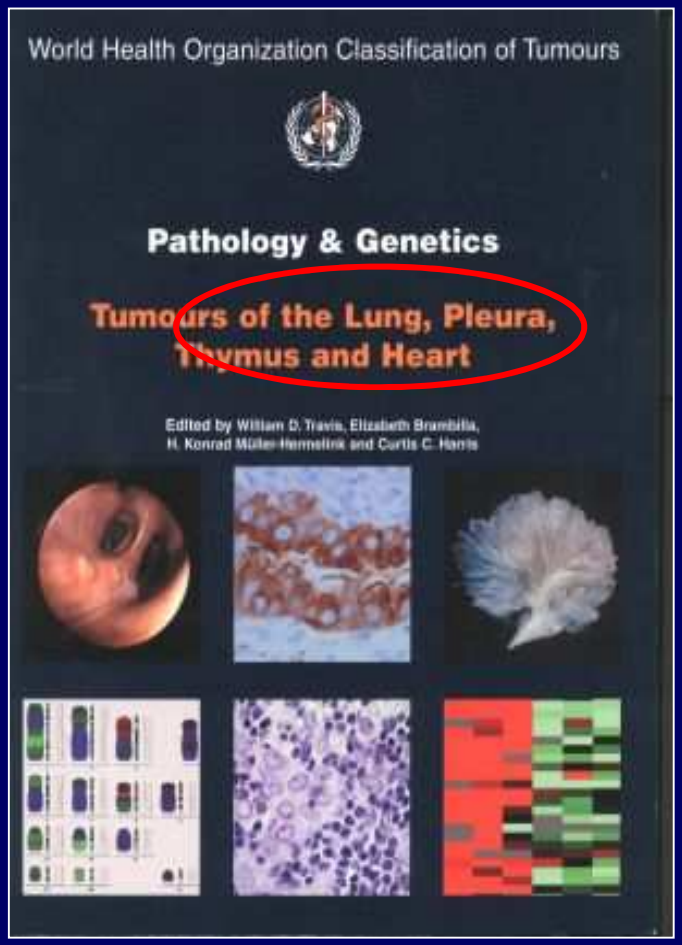
Severson RK, Cancer Epidem Biomarkers Prevent, 5: 81-84, 1996.

SEDI delle NENs



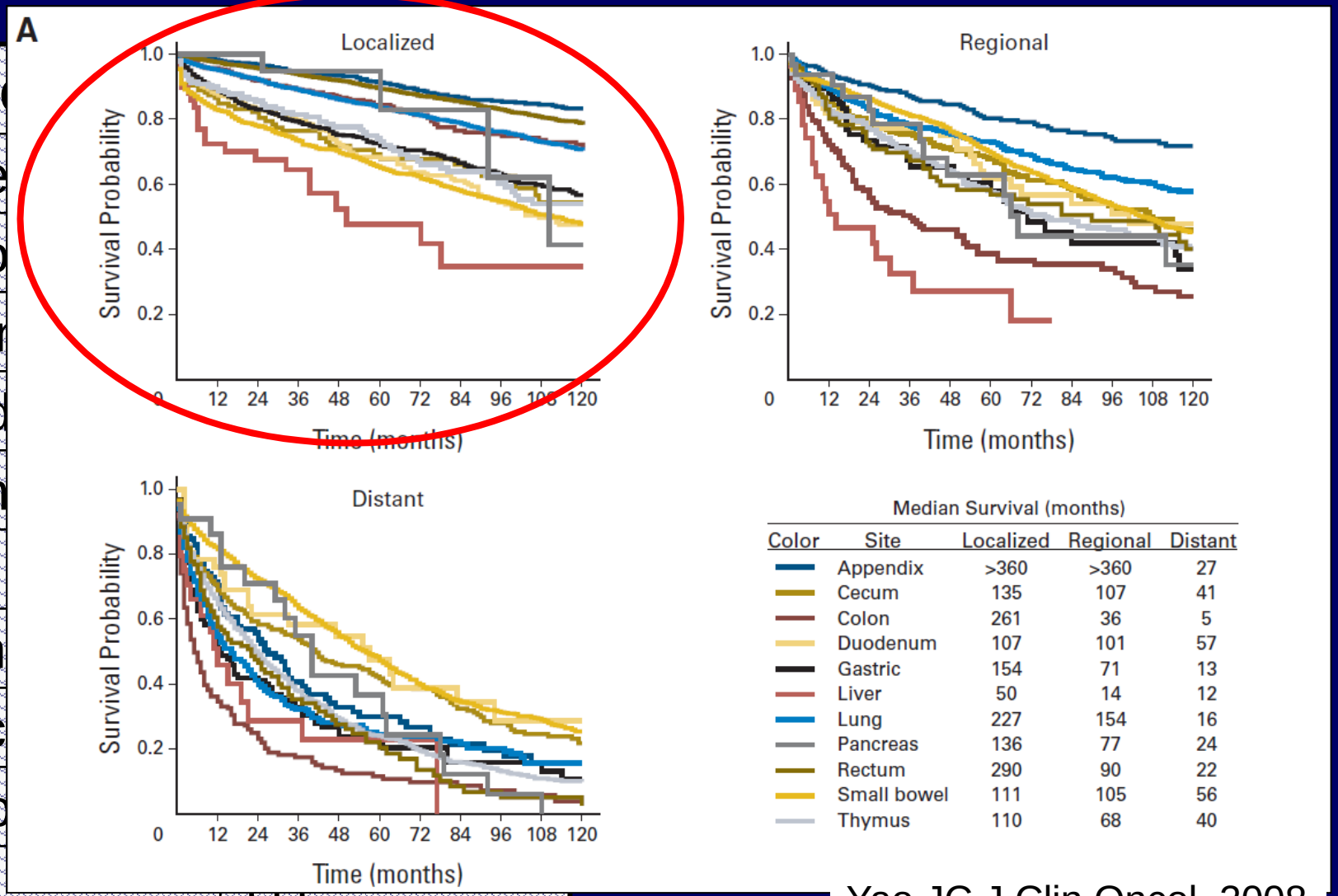


	Conta mitotica (HPF)	Ki-67 (%)
NET G1	< 2 x10HPF	≤ 2
NET G2	2-20 x10HPF	3-20
NEC G3	> 20 x10HPF	> 20
Ca misto adenoneuroendocrino	n.a	n.a
Lesioni iperplastiche e paraneoplastiche	n.a	n.a



- Carcinoide Tipico
- Carcinoide Atipico
- SCLC
- LCNEC
- DIPNECH
- Tumorlets

La sede del tumore primitivo



Median Survival (months)

Color	Site	Localized	Regional	Distant
	Appendix	>360	>360	27
	Cecum	135	107	41
	Colon	261	36	5
	Duodenum	107	101	57
	Gastric	154	71	13
	Liver	50	14	12
	Lung	227	154	16
	Pancreas	136	77	24
	Rectum	290	90	22
	Small bowel	111	105	56
	Thymus	110	68	40

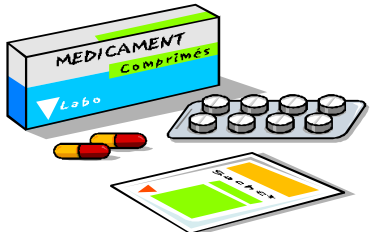
Yao JC J Clin Oncol, 2008

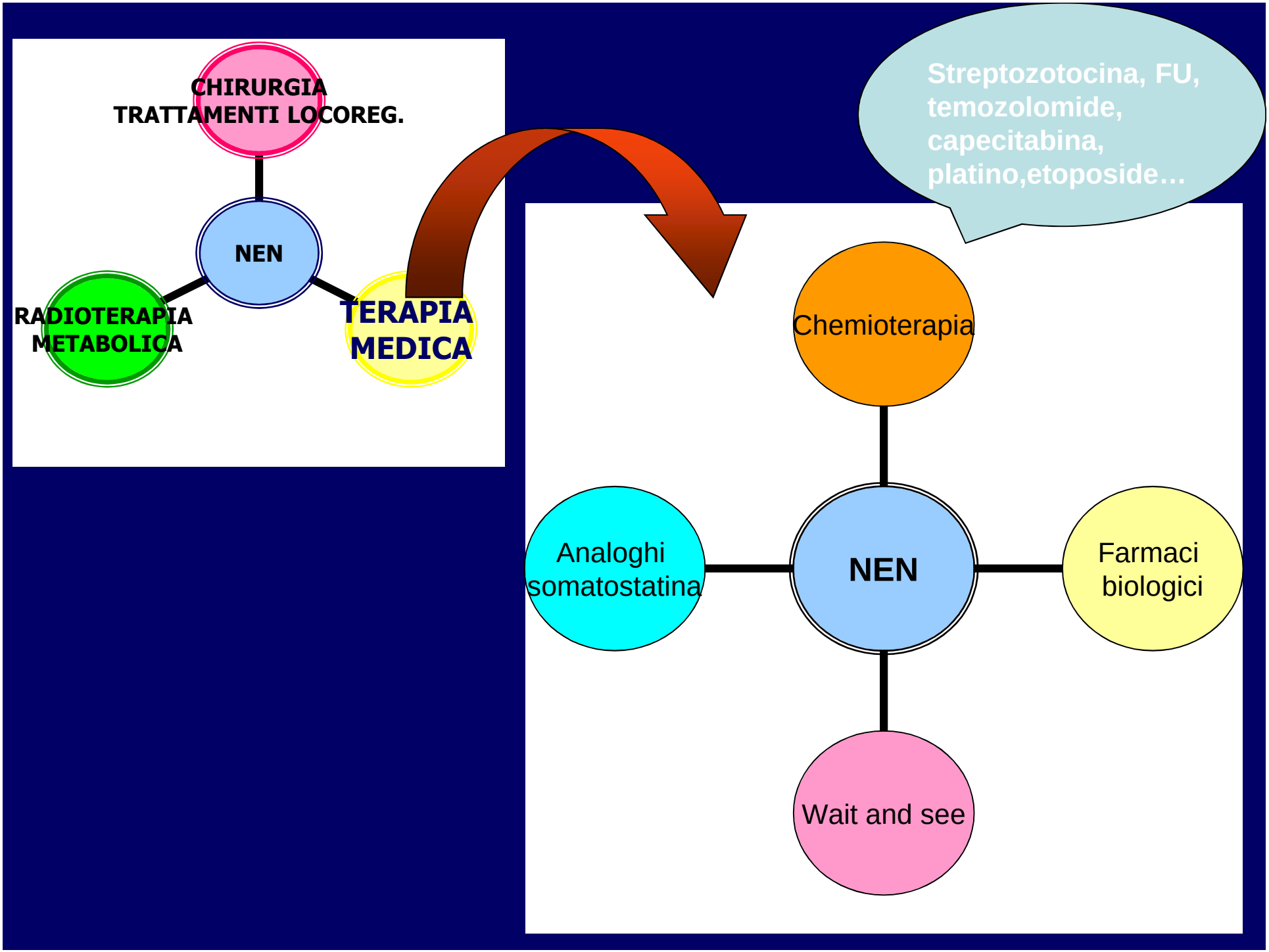
Estensione di malattia

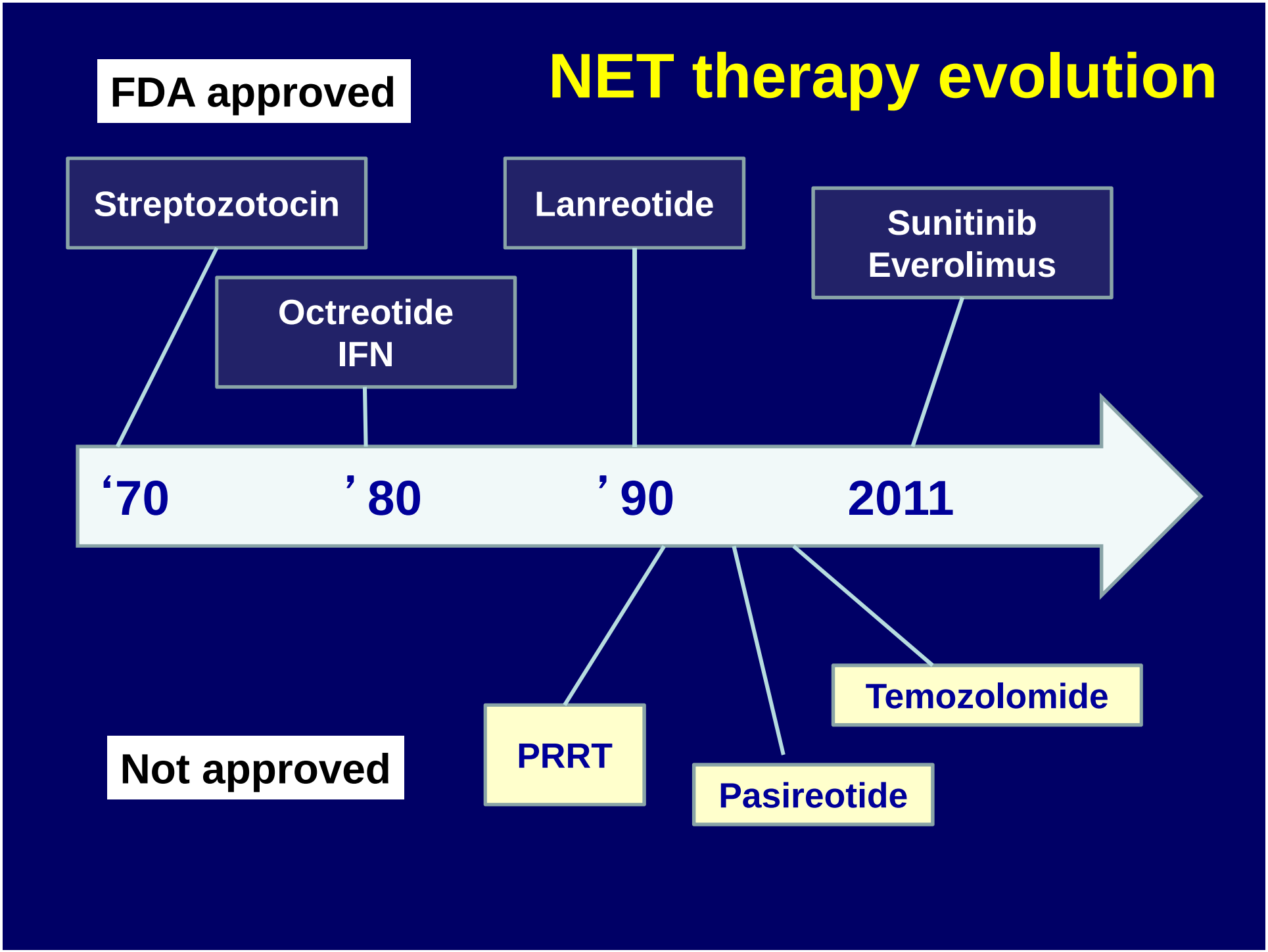
- Malattia operabile



- Malattia avanzata




CHIRURGIA
TRATTAMENTI LOCOREG.
NEN
RADIOTERAPIA
METABOLICA
TERAPIA
MEDICA
Streptozotocina, FU,
temozolomide,
capecitabina,
platino,etoposide…
Chemioterapia
Analoghi
somatostatina
NEN
Farmaci
biologici
Wait and see


NET therapy evolution
FDA approved
Streptozotocin
Octreotide
IFN
Lanreotide
Sunitinib
Everolimus
‘70
’80
’90
2011
Not approved
PRRT
Pasireotide
Temozolomide

NET: guidelines

NET societes

Oncological societes

Country guidelines

UK

NORDIC

CANADIAN

ITALIAN (upcoming)

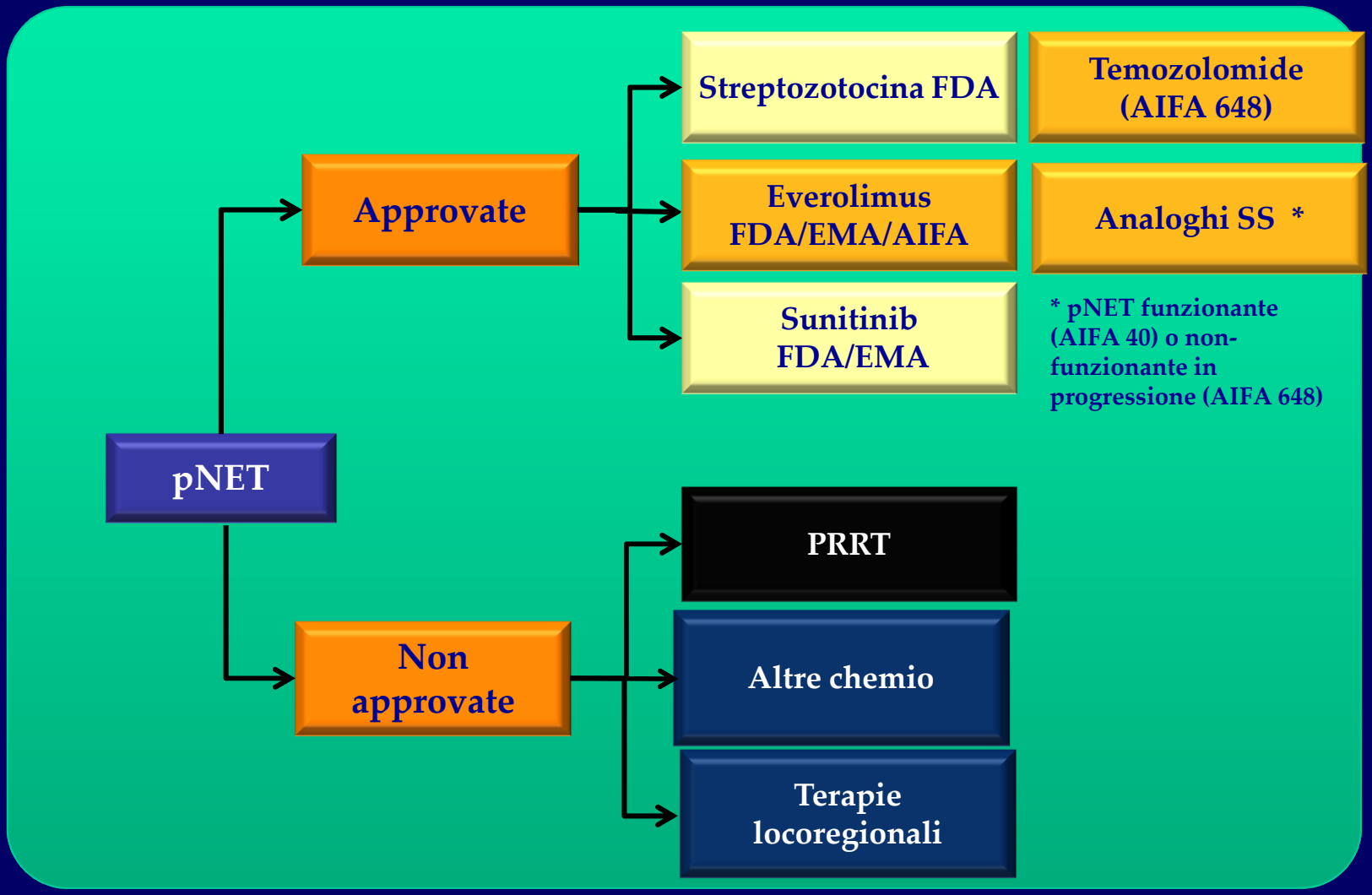
Local guidelines

ROL

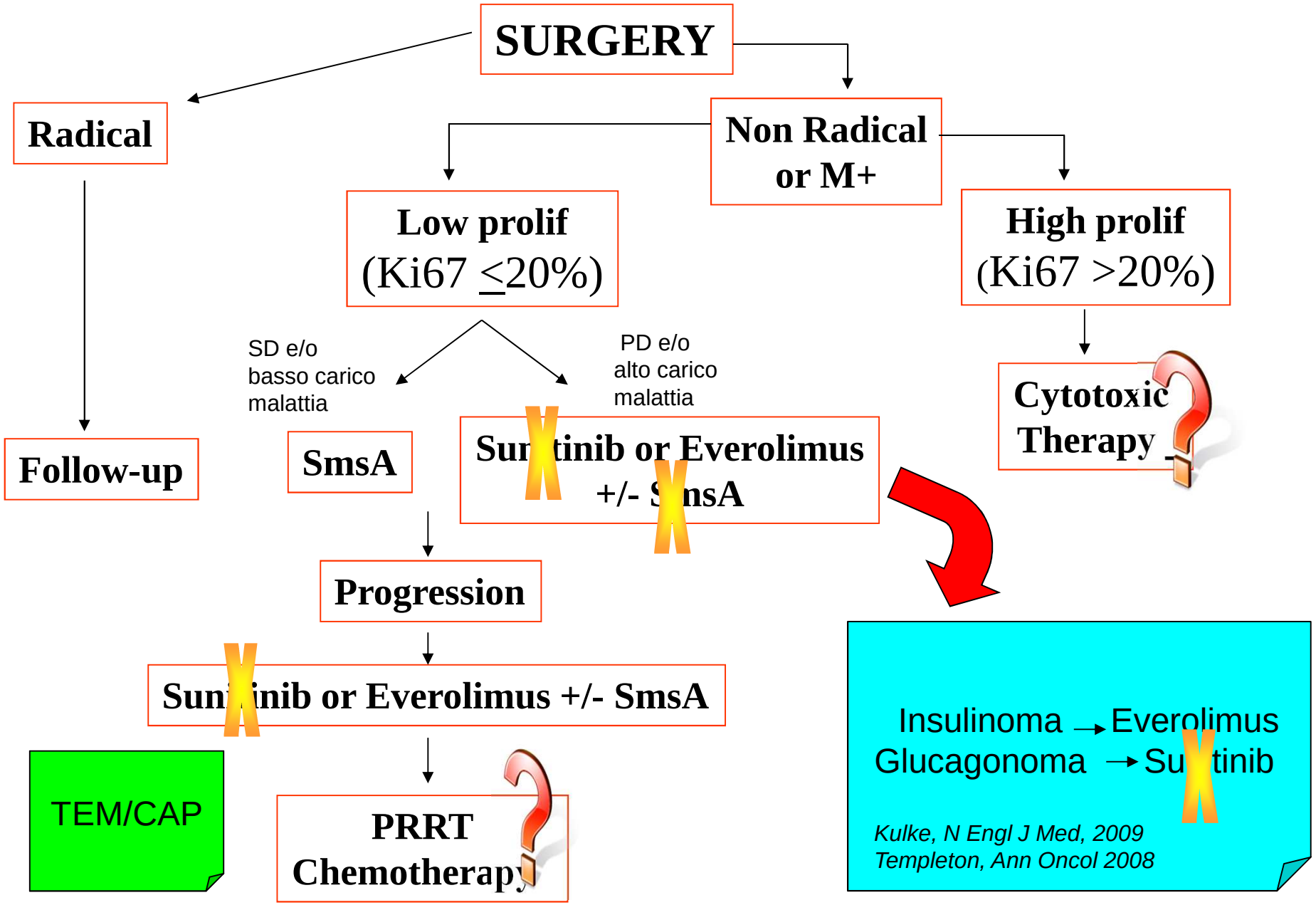
Literature Data

Drugs	N pts	Ki67	SSTR+	PR	TTP	Type	Author
STZ/ADM/FU	84	?	?	34 %	9 m	Retrosp.	Kouvaraki 2004
TMZ	12	?	?	14 %	7 m	Retrosp	Ekeblad 2007
XELOX	11	?	?	27 %	20 m	**Phase II**	Bajetta 2007
STZ/DDP/FU	49 (tot)	25	39	38 %	9 m	Retrosp.	Turner 2010
TMZ/Xeloda	30	?	?	70 %	18 m	Retrosp.	Strosberg 2010
PRRT (Lu)	91	?	91	43 %	40 m(tot)	Retrosp.	Kweek. JCO 2008
PRRT (Lu)	52	?	52	29 %	29 m	Phase II	Sansovini 2013
Sunitinib	86	36	?	7 %	11.4 m	**Phase III**	Reymond,
Placebo	85	36		0 %	5.5 m		NEJM 2011
Everolimus	207	?	?	5 %	11 m	**Phase III**	Yao , NEJM 2011
Placebo	203				4.6 m		

pNET avanzati:
Terapie approvate e non approvate



Algoritmo terapeutico NETs pancreatici



Decisione terapeutica

Evidenza

Raccomandazioni / linee-guida

Norme regolatorie

Logistica / Expertise

Studi clinici


Grazie
Mahalo
Koszonom
Obrigado
THANK
YOU
arigato
Спасибо
Takk
Рахмет
Prasom
Gracias
Danke
Dziekuje
Merci
Multumesc