

What have we learnt in the management of NETs in the last decade?

Enrique Grande
Head of Medical Oncology
Director of Clinical Research

 @drenriquegrande



MD Anderson
~~Cancer Center~~
Madrid • España

Disclosures



Honoraria for speaker engagements, advisory roles or funding of continuous medical education:

Adacap, AMGEN, Angelini, Astellas, Astra Zeneca, Bayer, Blueprint, Bristol Myers Squibb, Caris Life Sciences, Celgene, Clovis-Oncology, Eisai, Eusa Pharma, Genetracer, Guardant Health, HRA-Pharma, IPSEN, ITM-Radiopharma, Janssen, Lexicon, Lilly, Merck KGaA, MSD, Nanostring Technologies, Natera, Novartis, ONCODNA (Biosequence), Palex, Pharmamar, Pierre Fabre, Pfizer, Roche, Sanofi-Genzyme, Servier, Taiho, Tecnofarma, Thermo Fisher Scientific

Research Grants:

Astellas, Astra Zeneca, IPSEN, Lexicon, MTEM/Threshold, Nanostring Technologies, Pfizer, Roche

Leadership roles in medical societies:

ENETS, GETNE and GETHI

Private Healthcare provider:

MD Anderson Cancer Center Madrid (workplace)

Commercial Medical Education provider:

Universidad Europea de Madrid (UEM), Universidad CEU Cardenal Herrera, Universidad Rey Juan Carlos, Oncinfo

Stocks or ownership interest:

None

Milestones in the history of NETs at a glance

~~Cancer.~~



Milestones in the history of NETs at a glance

~~cancer.~~



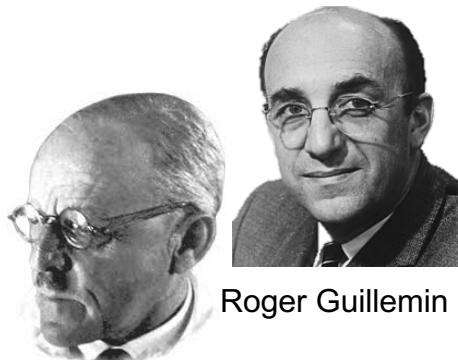
Siegfried Oberndorfer



**Discovery of
Karzinoids**

Milestones in the history of NETs at a glance

~~cancer.~~



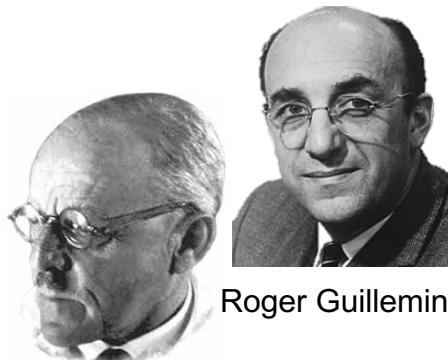
Roger Guillemin

Siegfried Oberndorfer



Milestones in the history of NETs at a glance

-cancer.



Roger Guillemin



Charles Moertel



Milestones in the history of NETs at a glance

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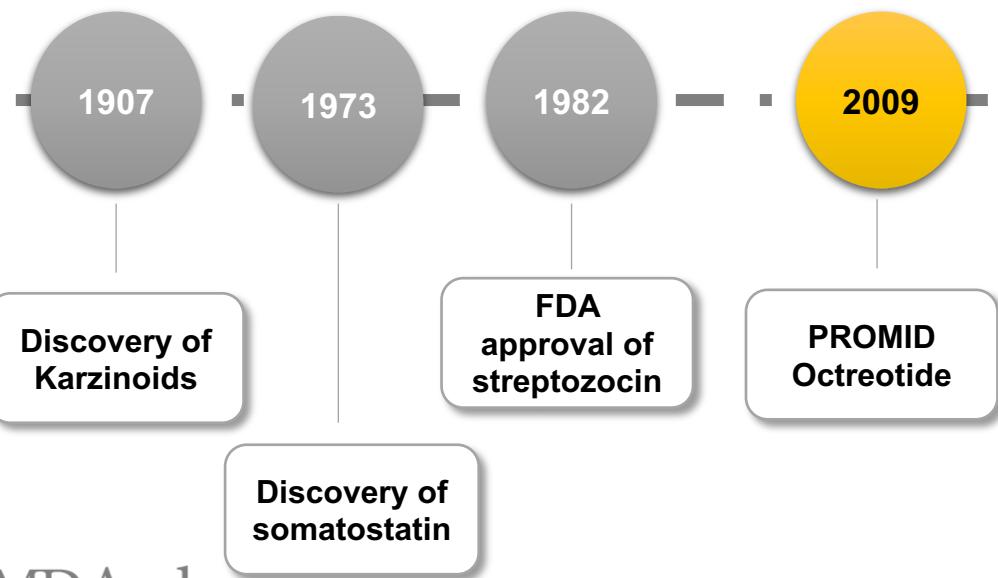
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Charles Moertel



Anja Rinke



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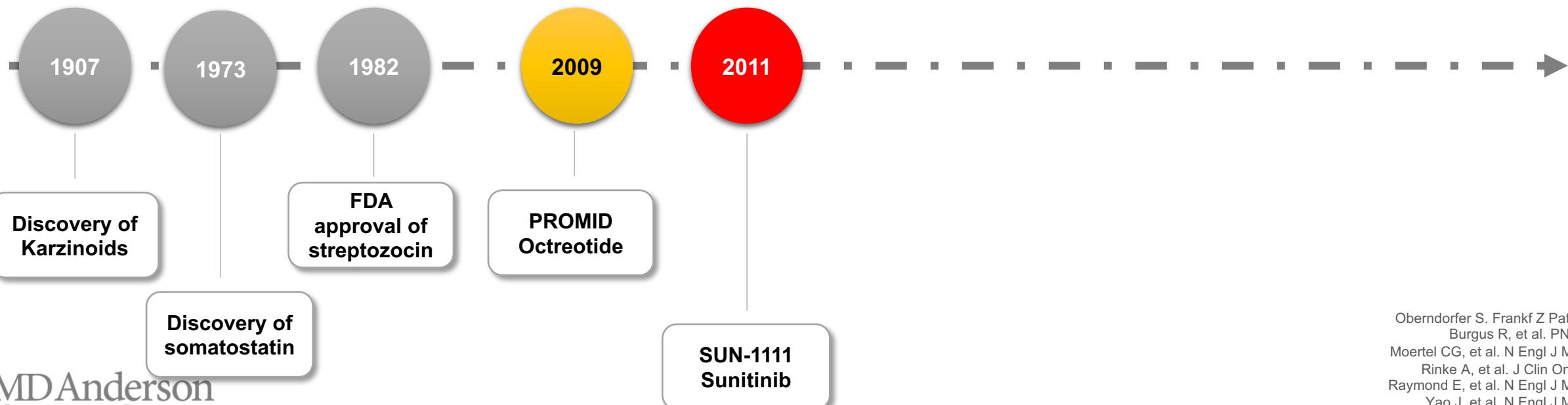


Anja Rinke



Eric Raymond

Siegfried Oberndorfer



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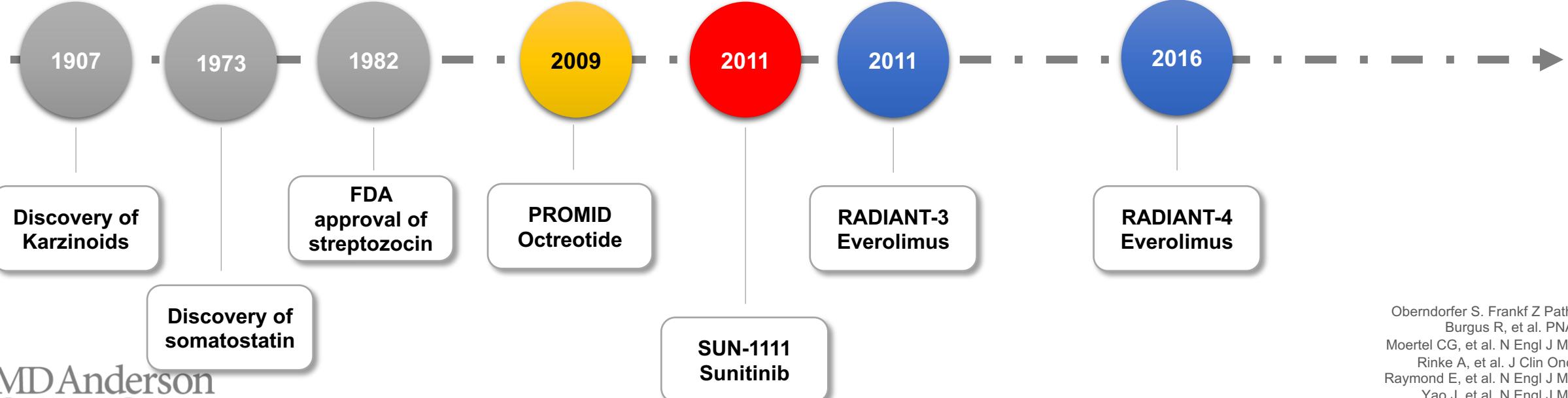
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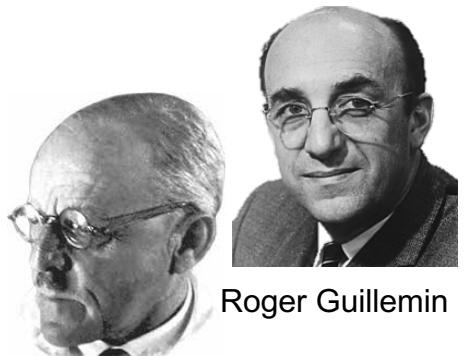


James Yao



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Martin Caplin

Siegfried Oberndorfer



Discovery of Karzinoids



Discovery of somatostatin



FDA approval of streptozocin



PROMID Octreotide



2011

RADIANT-3 Everolimus



2011

SUN-1111 Sunitinib



2015

CLARINET Lanreotide

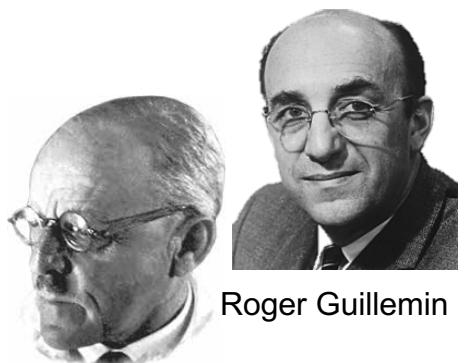


2016

RADIANT-4 Everolimus

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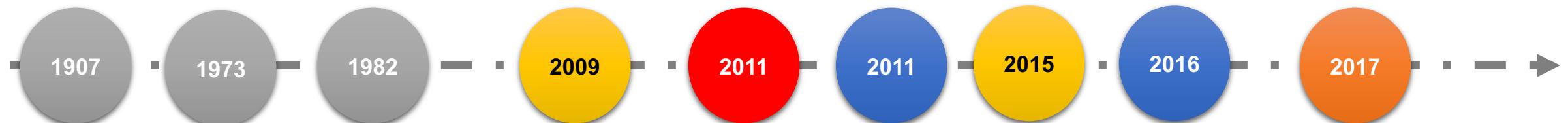
Martin Caplin



Jonathan Strosberg



Matt Kulke



Discovery of Karzinoids

FDA approval of streptozocin

PROMID Octreotide

RADIANT-3 Everolimus

RADIANT-4 Everolimus

NETTER-1 Lu¹⁷⁷-DOTATATE

TELESTAR Telotristat

Discovery of somatostatin

SUN-1111 Sunitinib

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Neuroendocrine Tumors ESMO Guidelines 2020

~~cancer.~~



ANNALS OF
ONCOLOGY
driving innovation in oncology

SPECIAL ARTICLE

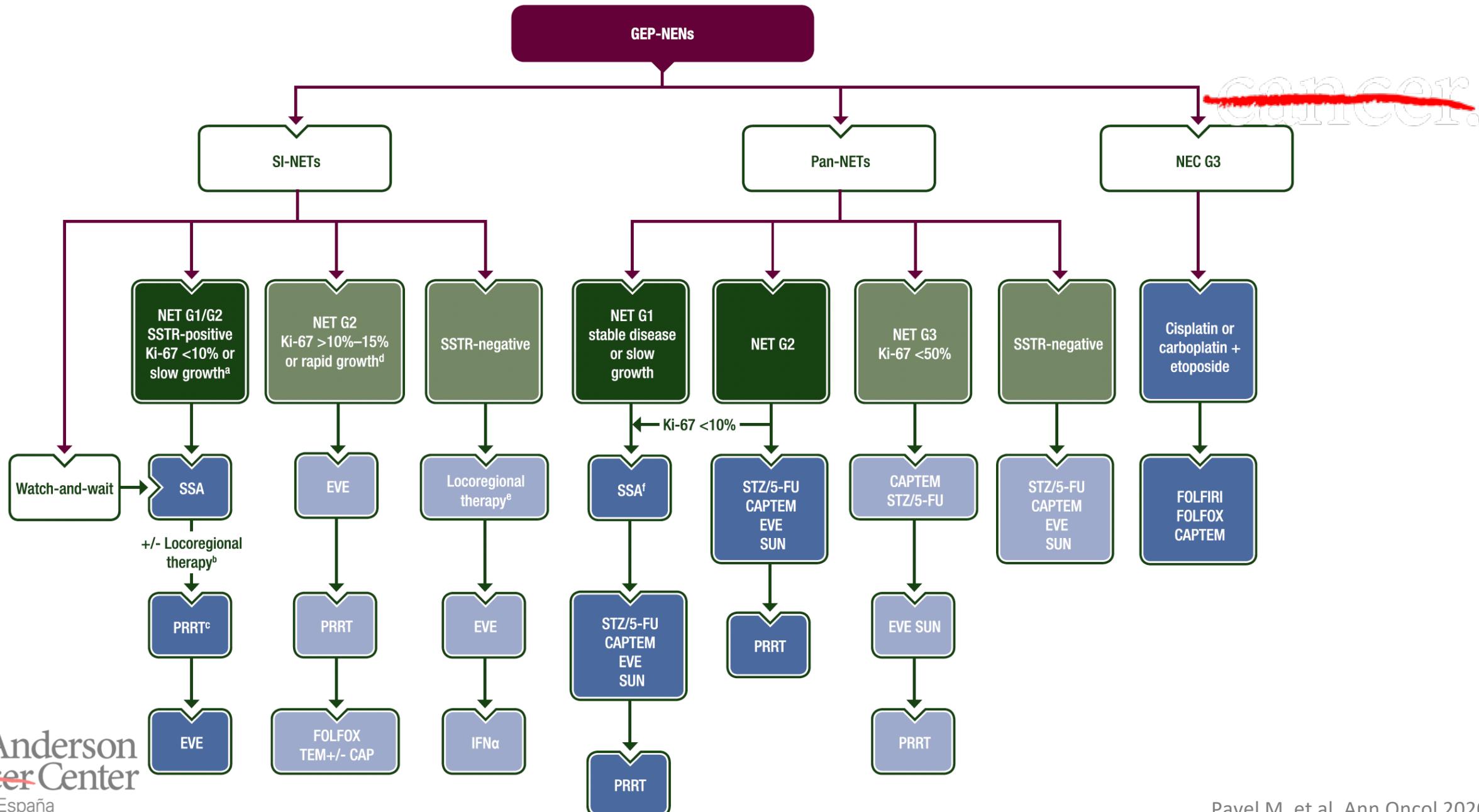
Gastroenteropancreatic neuroendocrine neoplasms: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up[†]

M. Pavel¹, K. Öberg², M. Falconi³, E. P. Krenning⁴, A. Sundin⁵, A. Perren⁶ & A. Berruti⁷, on behalf of the ESMO Guidelines Committee*

¹Department of Medicine 1, University Hospital Erlangen, Erlangen, Germany; ²Department of Endocrine Oncology, Uppsala University, Uppsala, Sweden; ³Department of Surgery, IRCCS San Raffaele Scientific Institute, Milan, Italy; ⁴Cyclotron Rotterdam BV, Erasmus Medical Centre, Rotterdam, The Netherlands; ⁵Department of Surgical Sciences, Uppsala University, Uppsala, Sweden; ⁶Institute of Pathology, University of Bern, Bern, Switzerland; ⁷Department of Medical and Surgical Specialties, Radiological Sciences and Public Health, Medical Oncology Unit, University of Brescia, ASST Spedali Civili, Brescia, Italy

Available online 6 April 2020





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~~cancer.~~



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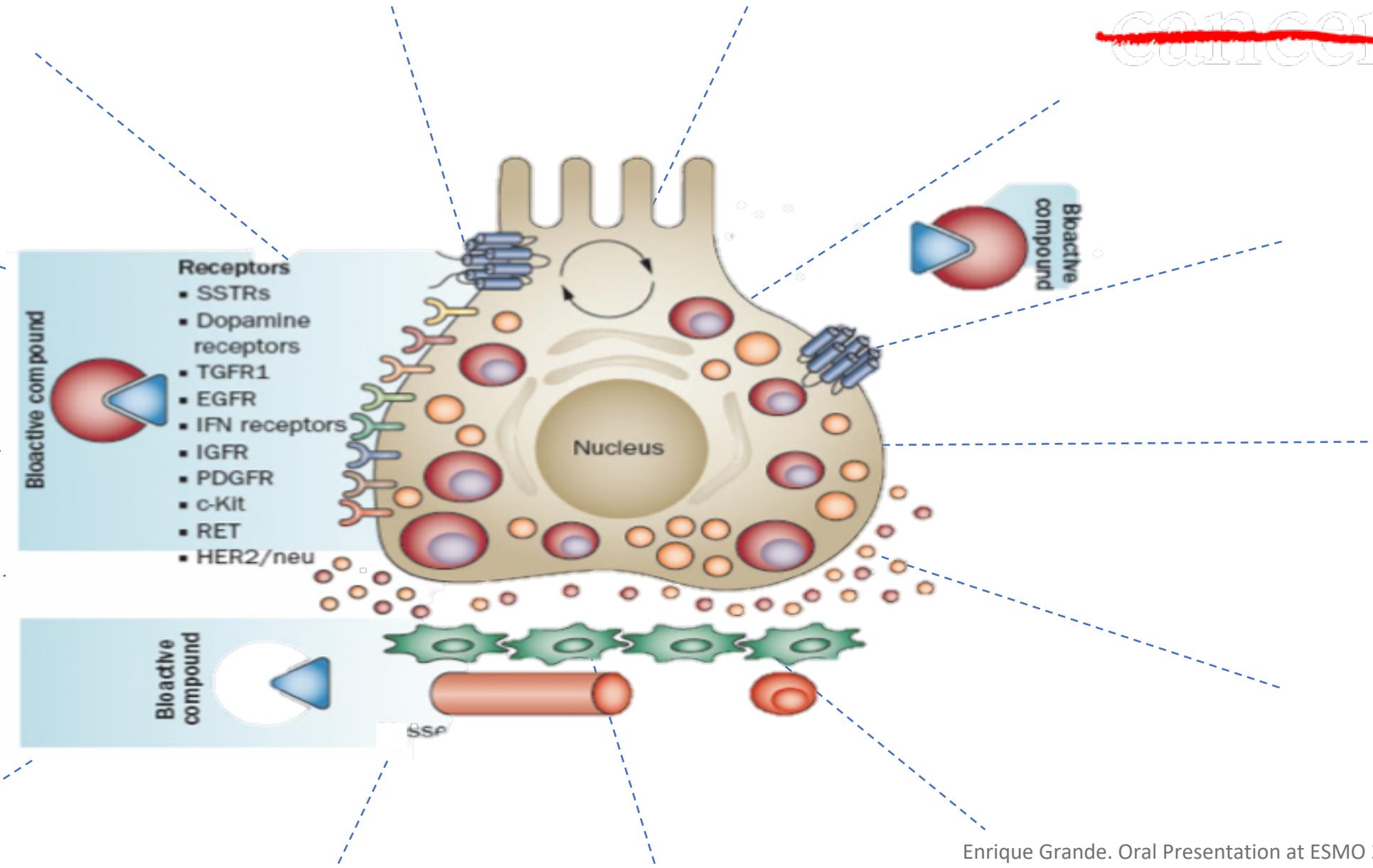
~~cancer.~~



- ✓ We realized we were in front of an extremely heterogenous disease

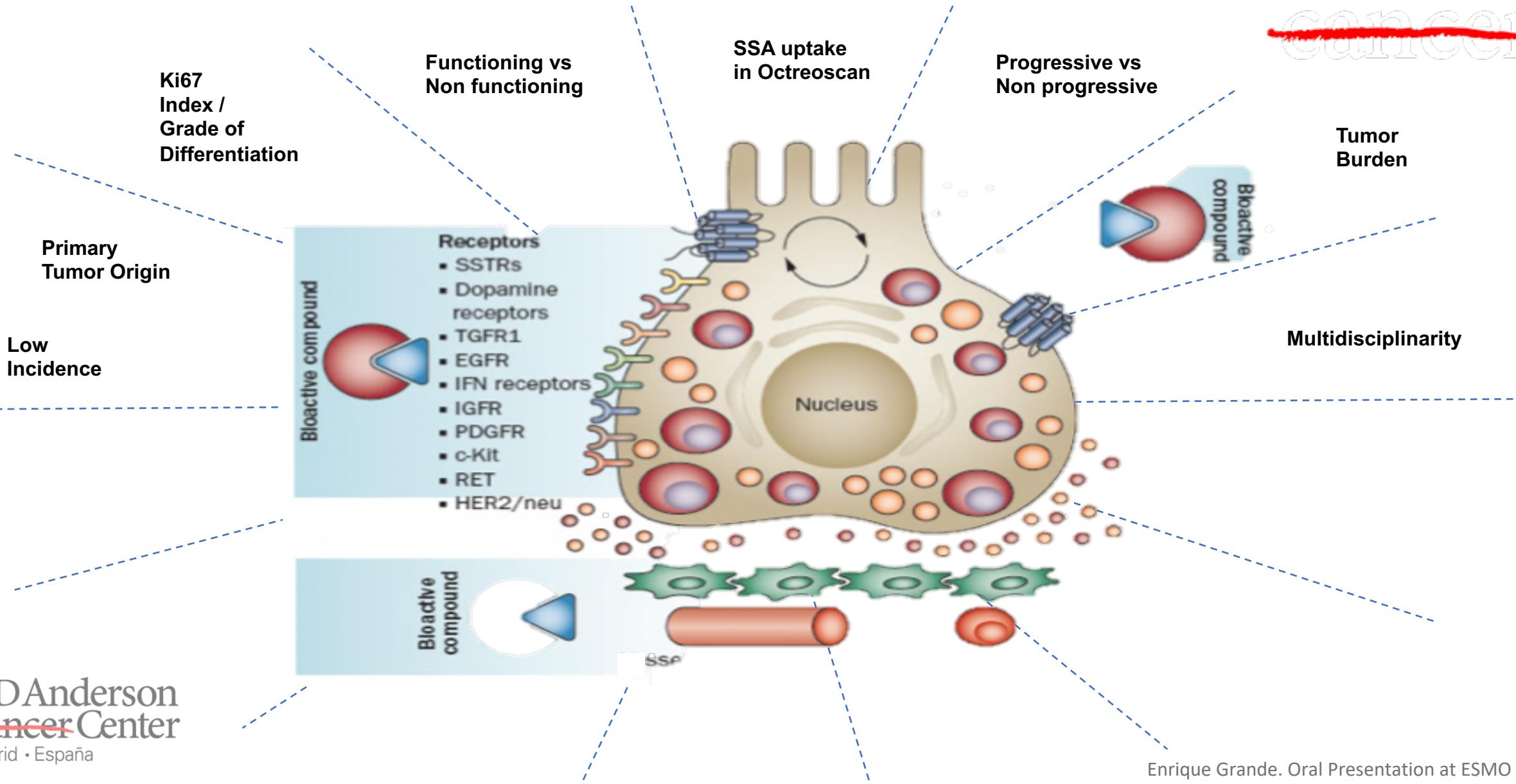
NETs are heterogeneous

~~cancer.~~



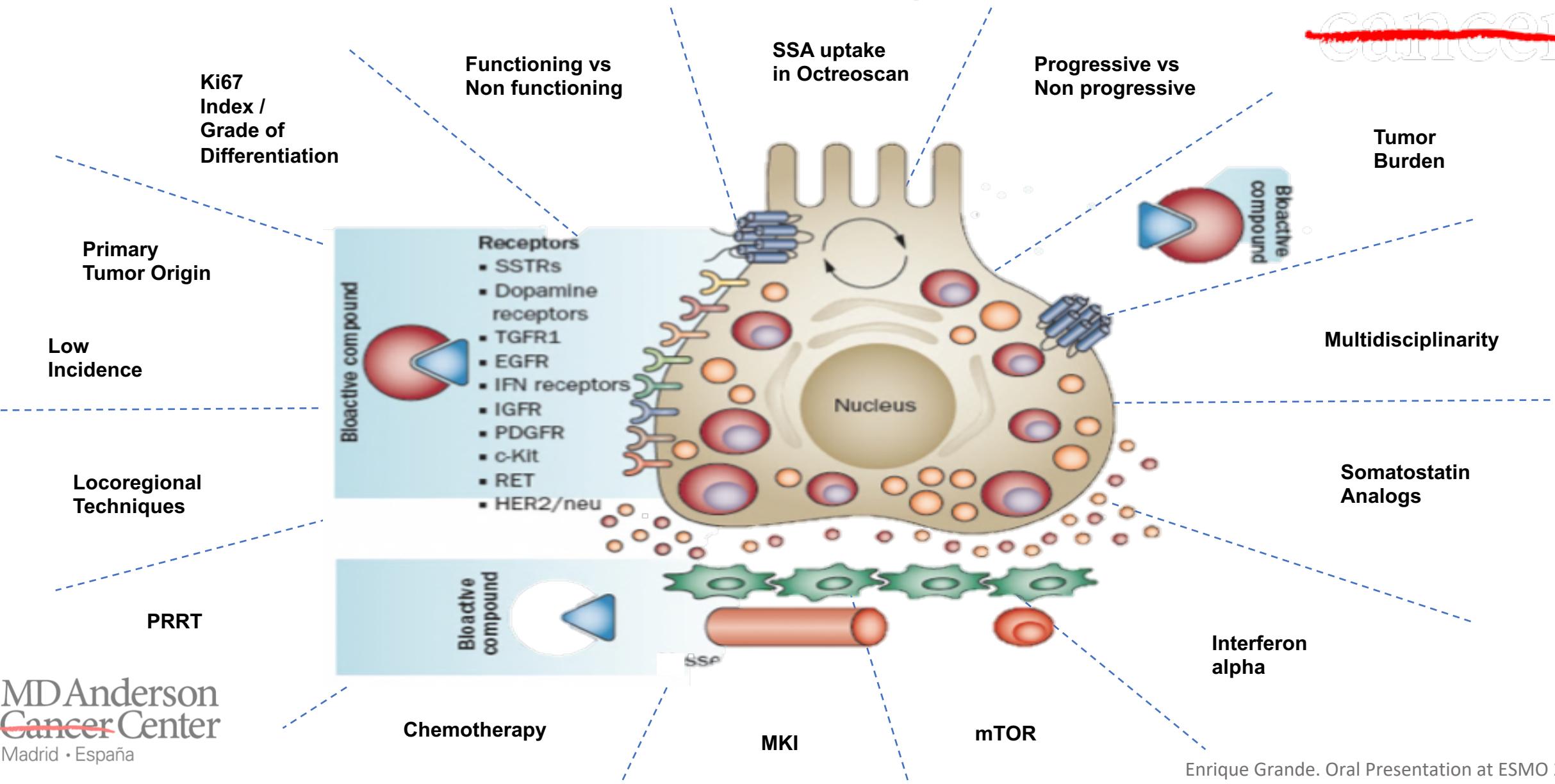
NETs are heterogeneous

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NETs are heterogeneous

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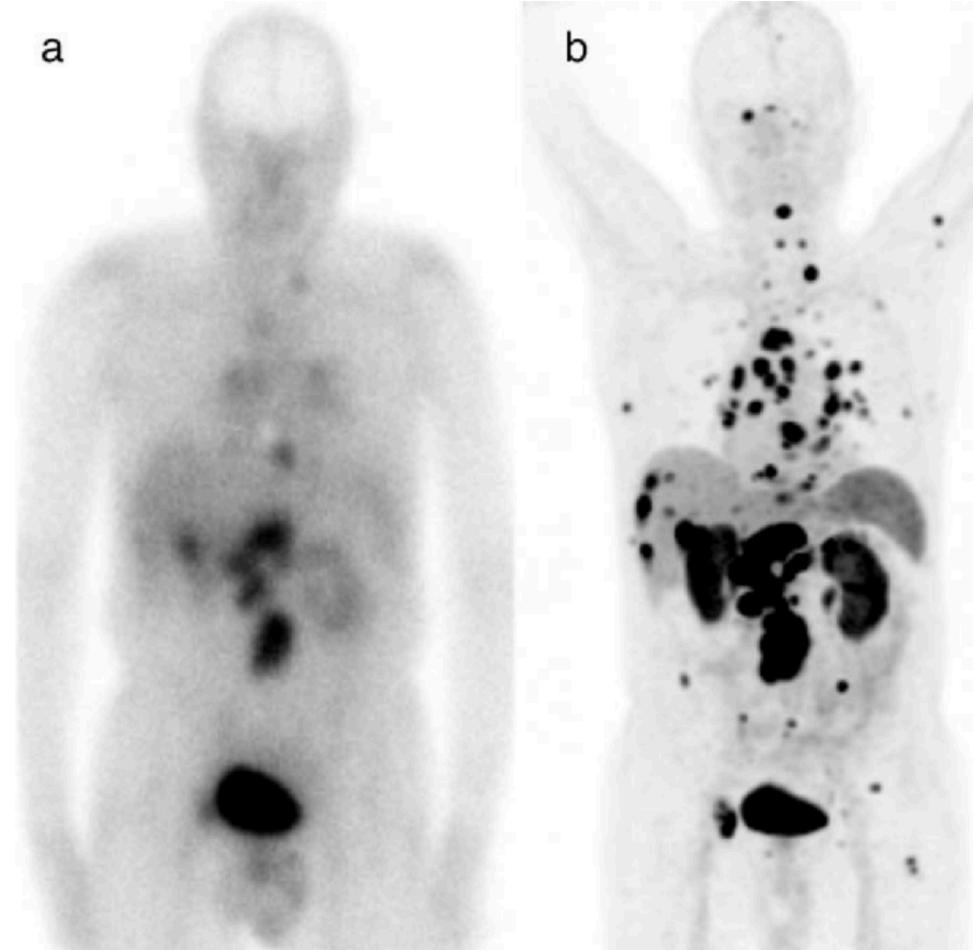
~~cancer.~~



- ✓ We realized we were in front of an extremely heterogenous disease
- ✓ **Improved diagnostic and follow-up techniques**

Head-to-head comparison of ^{111}In -pentetreotide SSRS and ^{68}Ga -DOTATATE PET/CT

~~cancer.~~



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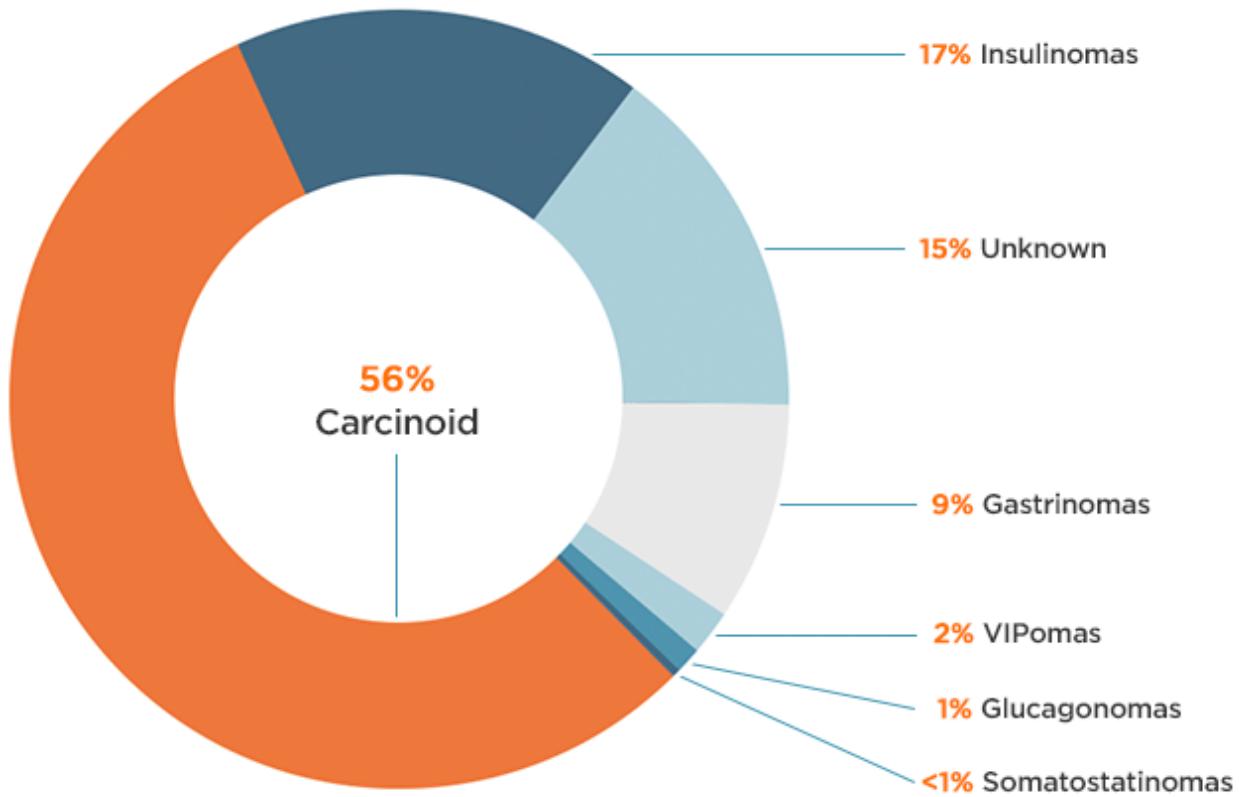
~~cancer.~~



- ✓ We realized we were in front of an extremely heterogenous disease
- ✓ Improved diagnostic and follow-up techniques
- ✓ **Improved symptoms control**

Hormone-release syndromes

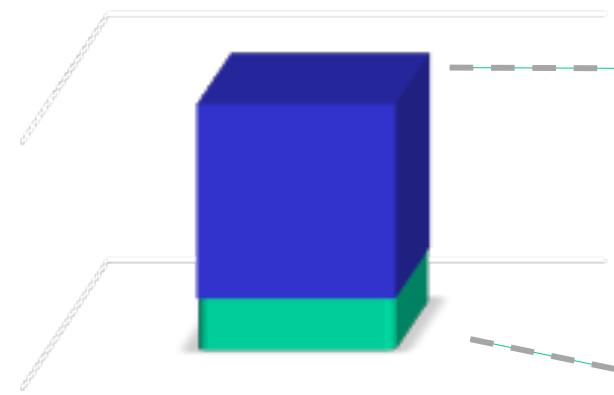
~~cancer.~~



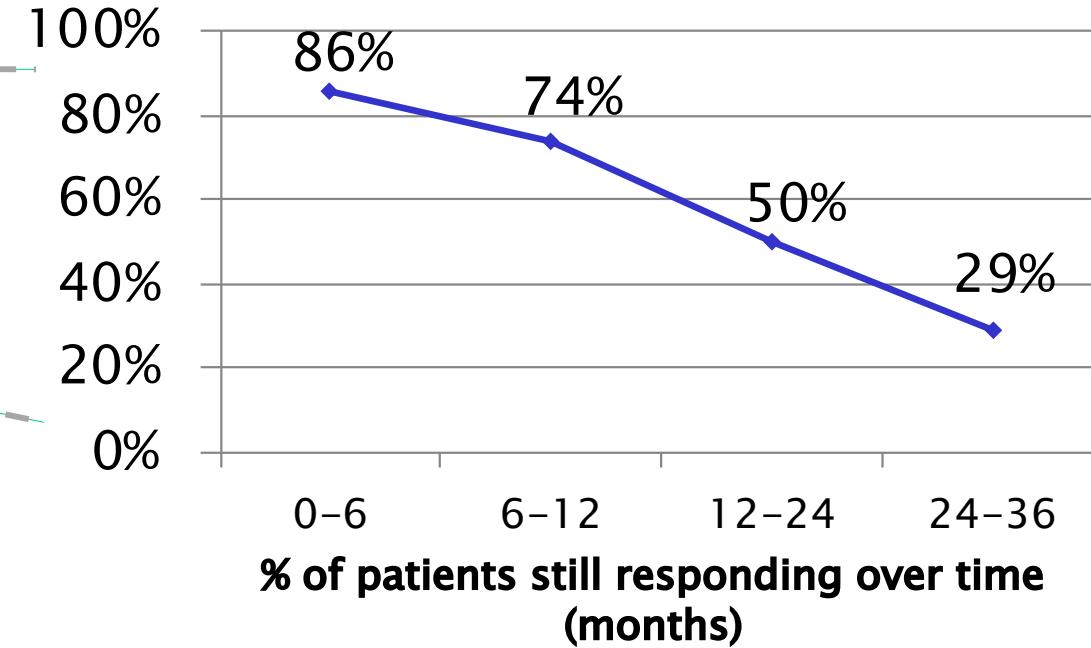
79% of patients are eventually not adequately controlled on SSAs after 2-3 years in the ‘Real World’

~~Cancer~~

SSAs fails to adequately control carcinoid syndrome within 36 months for 71% of patients



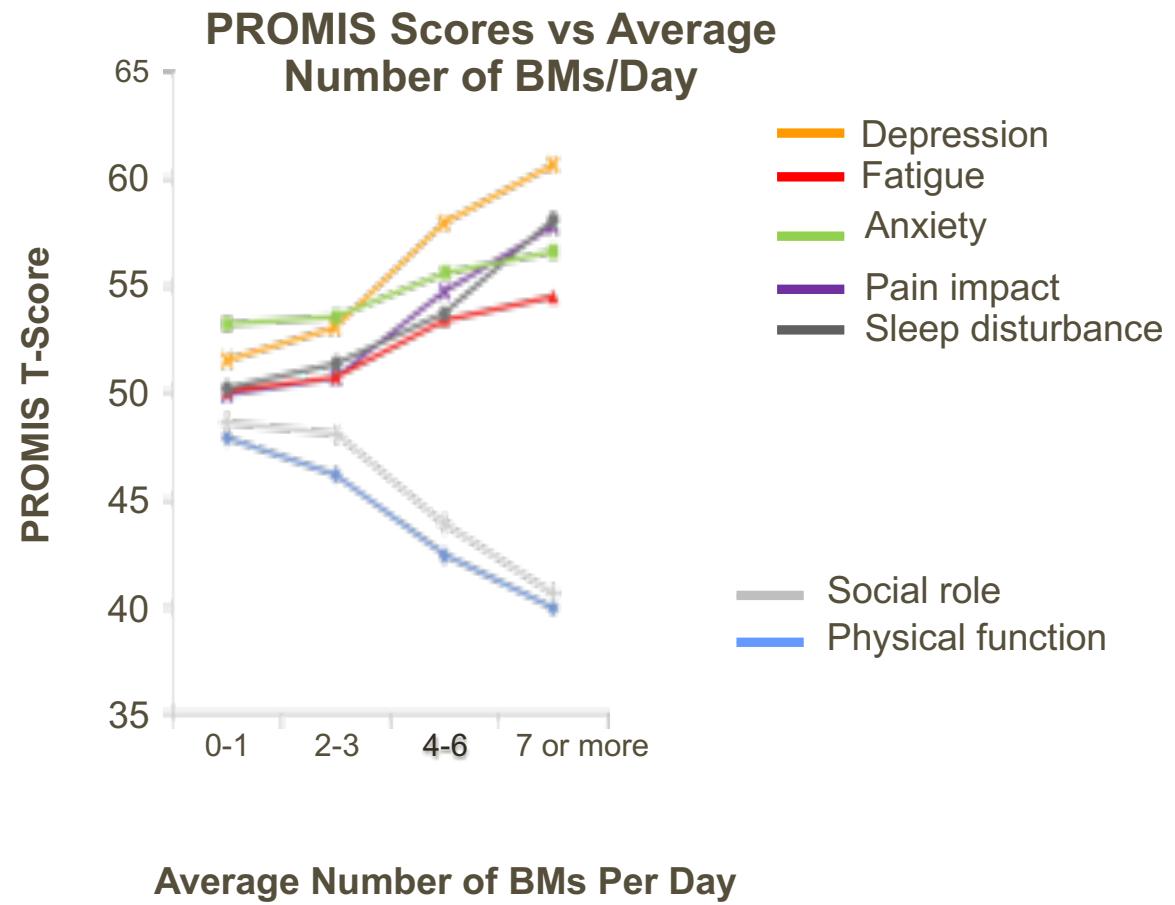
■ % eventually not controlled
■ % controlled



Quality of Life vs Carcinoid Syndrome

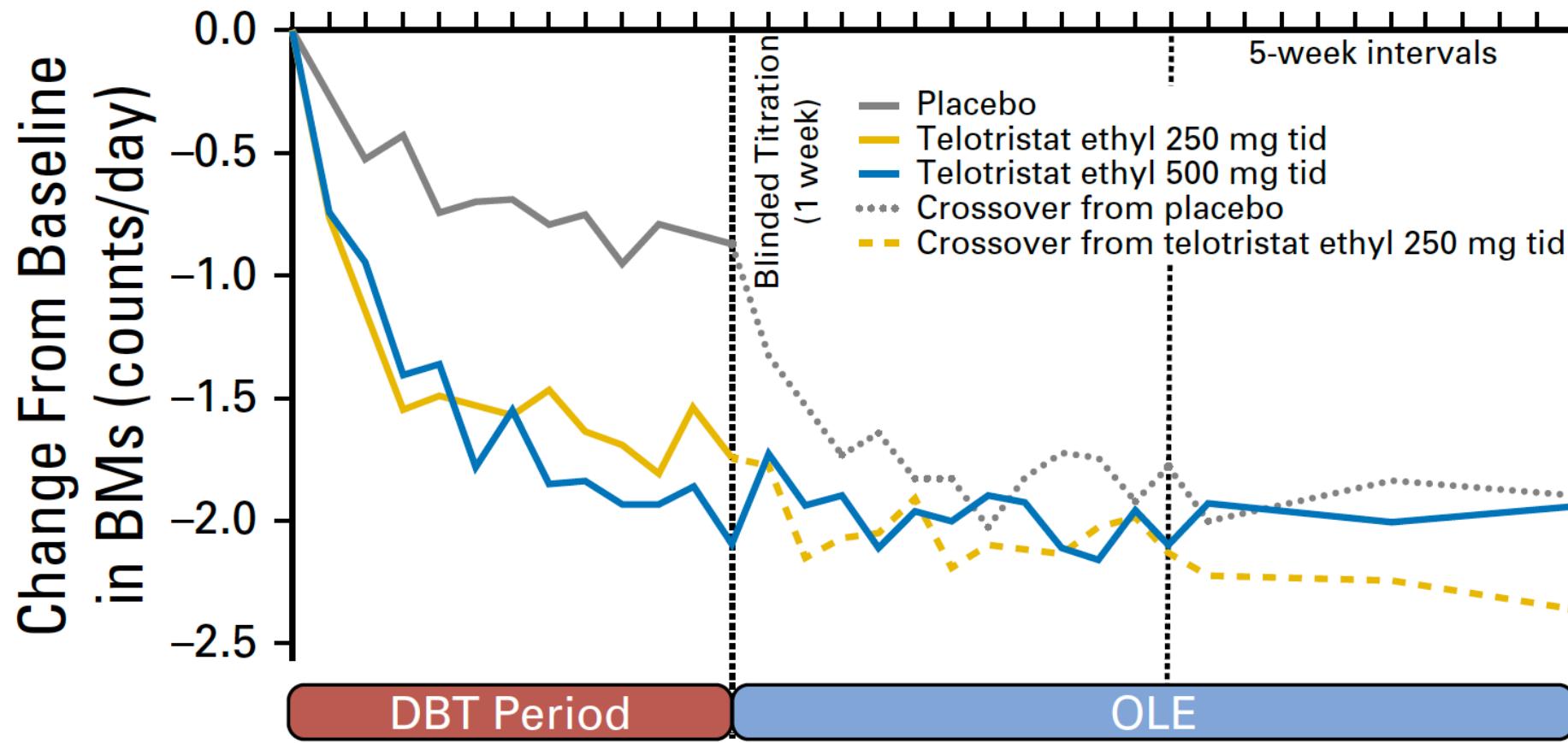
~~Cancer~~

- NET-related symptoms such as diarrhea and flushing are associated with reduced QoL
- Optimal management of NET and carcinoid syndrome may significantly improve HRQL among patients with NETs.



TELESTAR: Reduction in Daily Bowel Movement Frequency Averaged Over Double-blind Treatment Phase

~~cancer~~



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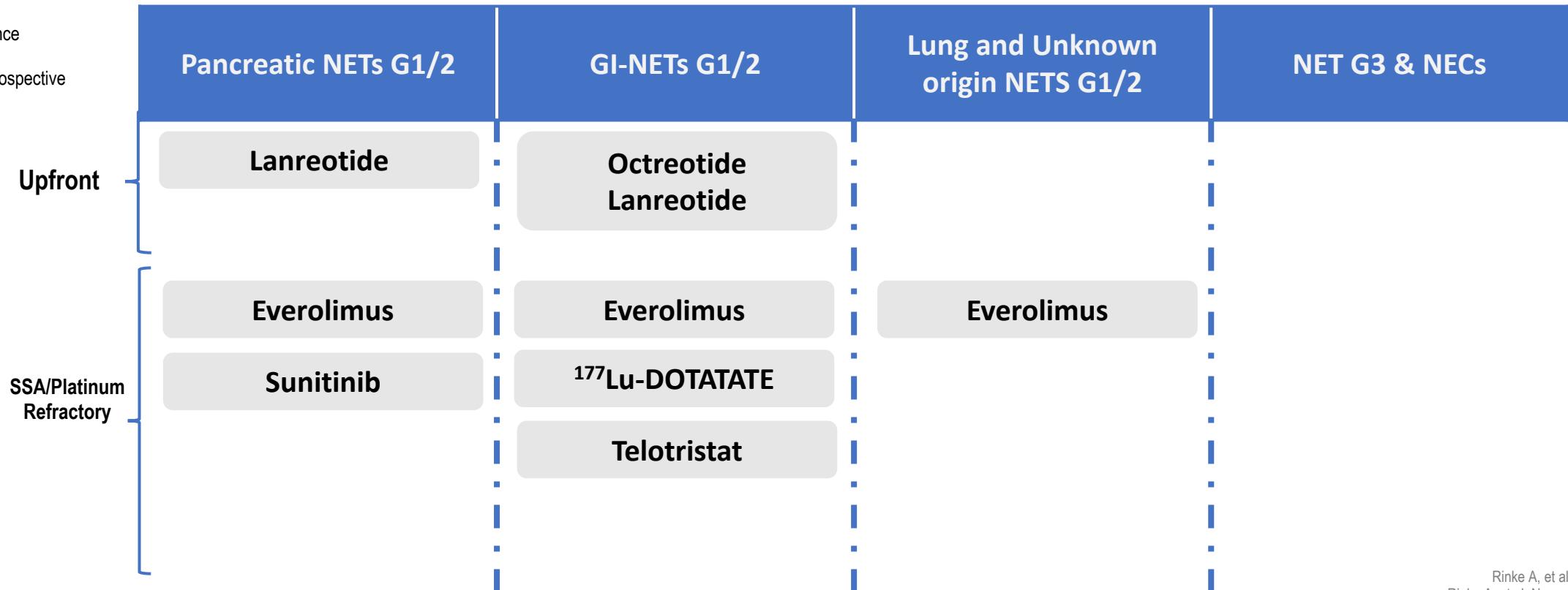


- ✓ We realized we were in front of an extremely heterogenous disease
- ✓ Improved diagnostic and follow-up techniques
- ✓ Improved symptoms control
- ✓ **Improved tumor growth control and learnt to sequence treatments**

Treatment of NETs at a Glance (Phase 3 evidence)



Phase 3 evidence
Phase 2 or retrospective



Rinke A, et al. J Clin Oncol 2009

Rinke A, et al. Neuroendocrinology 2017

Caplin ME, et al. N Engl J Med 2014

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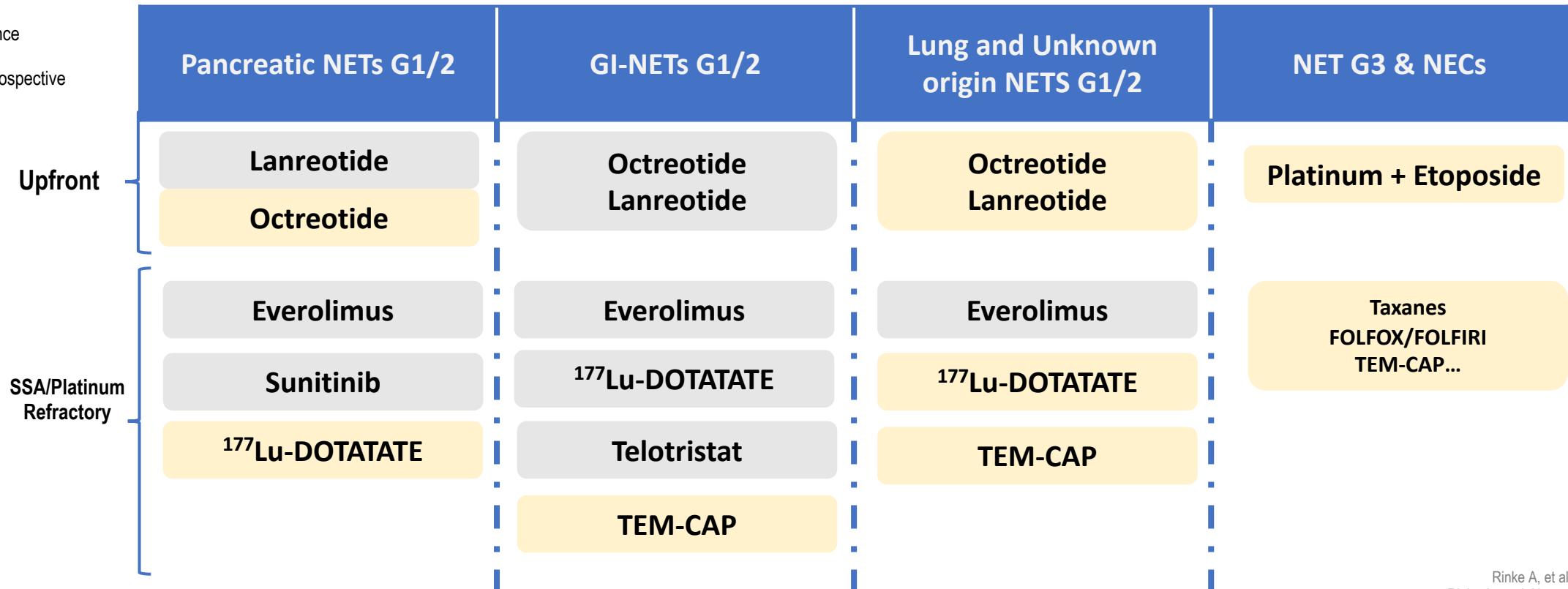
Kulke MH, et al. J Clin Oncol 2017

García-Carbonero R, et al. Neuroendocrinology 2016

Treatment of NETs at a Glance (Daily practice)



Phase 3 evidence
Phase 2 or retrospective



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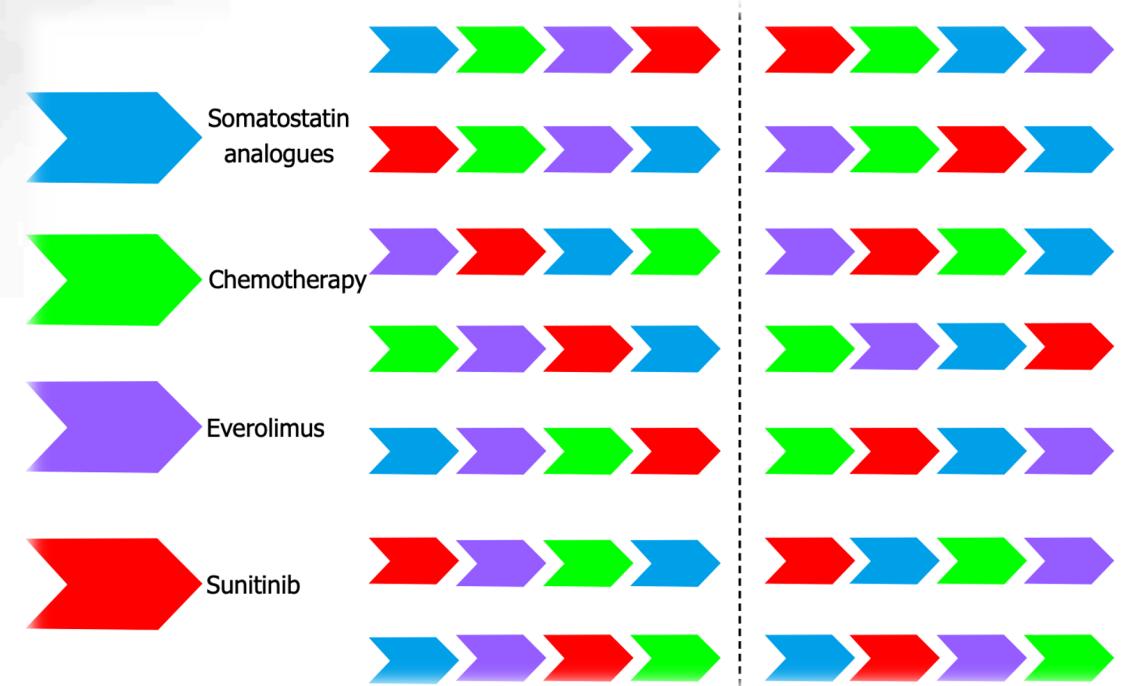
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The key role of the multidisciplinary team

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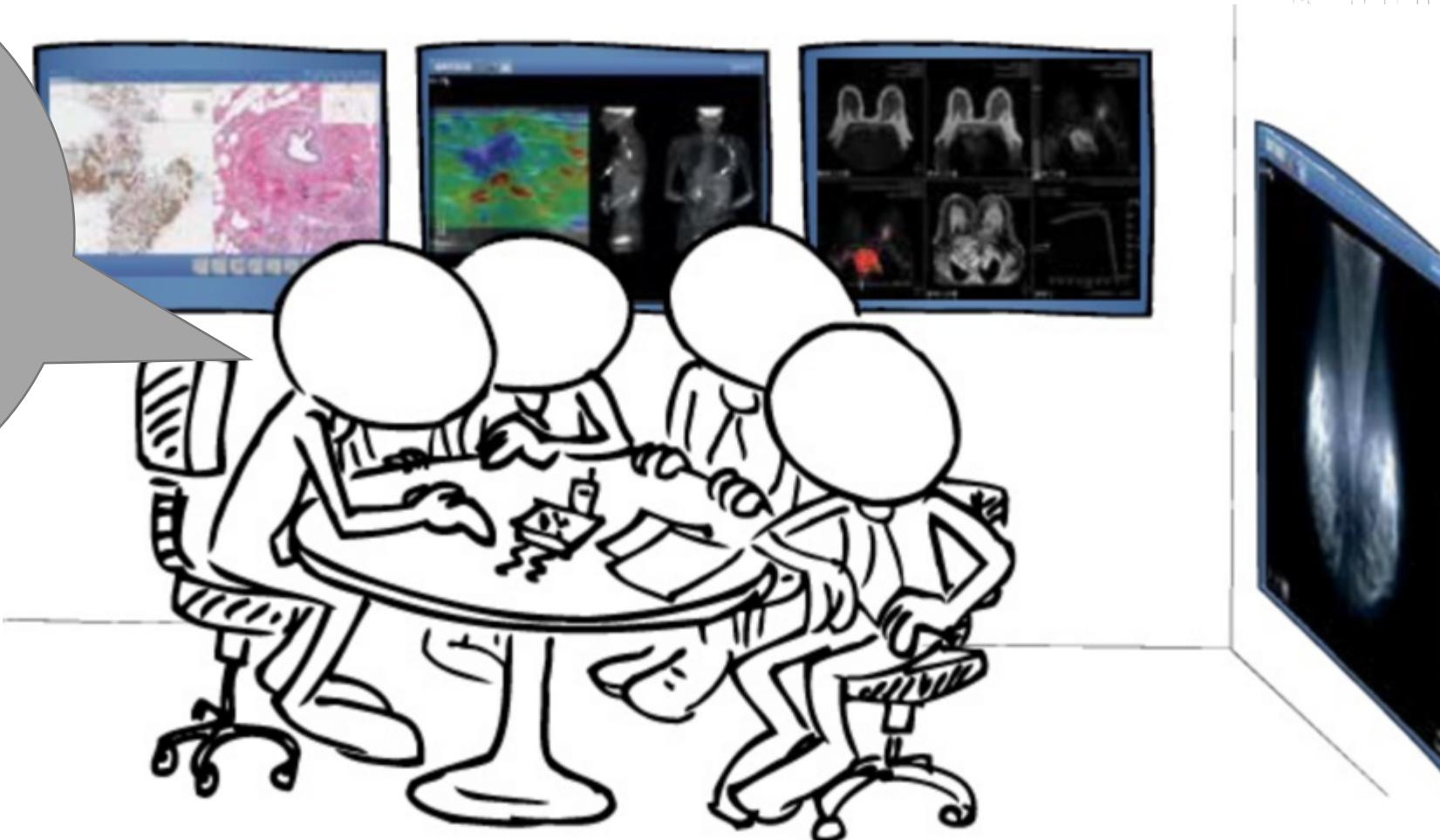


- ✓ We realized we were in front of an extremely heterogenous disease
- ✓ Improved diagnostic and follow-up techniques
- ✓ Improved symptoms control
- ✓ Improved tumor growth control and learnt to sequence treatments
- ✓ **We need to work as a team**

The key role of the multidisciplinary team

~~cancer.~~

Loco-regional
techniques (RFA,
embolization...)
Liver
transplantation,
radiosurgery,
surgery,
palliative care...

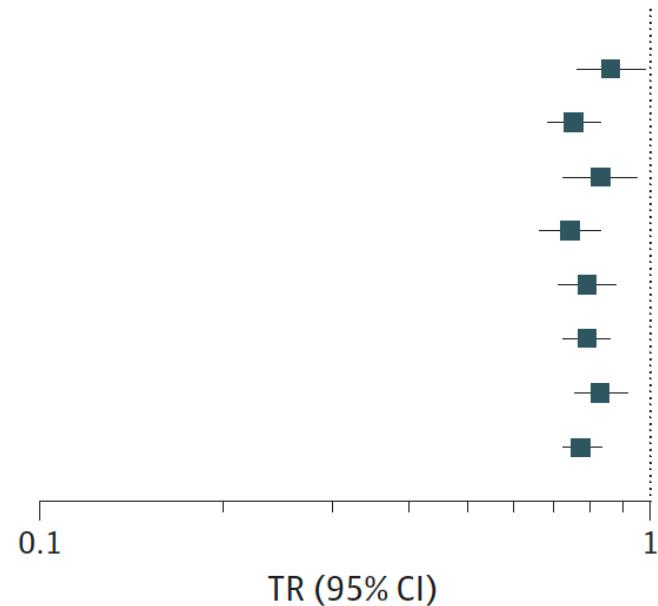


*Source: Newman, E.A., et al., *Cancer*, 2006., Lim, H.K. et al., *ANZ J Surg*, 2014. Whelles SA et al, *Otolaryngol Head Neck Surg*. 2010, Wiggins MG et al, *HPB Surg*. 2013, van Hagen P et al, *Int J Clin Oncol* 2013, Santoso JT et al, *Int J Gyn Cancer* 2004.

Survivorship at Affiliate Hospitals Compared With Top-Ranked Hospitals

~~cancer.~~

Procedure	TR (95% CI)
Esophagus	0.86 (0.76-0.98)
Colon	0.75 (0.68-0.83)
Rectal	0.83 (0.72-0.95)
Gastric	0.74 (0.66-0.83)
Pancreas	0.79 (0.71-0.88)
Lung	0.79 (0.72-0.86)
Bladder	0.83 (0.75-0.92)
All procedures	0.77 (0.72-0.83)



The models were adjusted for year, age category, insurance type, Charlson-Deyo group, income category, sex, pathological stage, grade, receipt and timing of chemotherapy, receipt and timing of radiation therapy, sequence, and, for relevant procedures, whether they involved extended resections or not. Boxes indicate time ratio (TR), and whiskers, 95% CI. A total of 886 patients (0.7%) did not have a precise date of diagnosis and were excluded from survival results.

Cancer

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PARTNETS

Partnership in Neuroendocrine Tumors

23NOV2020