ENETS-NANETS Webinar:

Multidisciplinary management of pancreatic NET – A discussion on symptom burden, surgical versus medical management, and treatment sequencing

Thursday, 28 August 2025, 18:00 – 19:10 CEST

Disclosure Statement

The moderators
Simona GLASBERG, ISR (ENETS) and **Alexandra GANGI, USA (NANETS)**
have NO potential conflicts of interest to report.

The Aim and Concept

- ✓ Transferring research to education and teaching is a major goal at ENETS.
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Live poll question: Getting to know the audience

In which medical discipline are you trained or currently working?

Tonight's moderators

Simona GLASBERG
ENETS EC Member

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Endocrinology

Alexandra GANGI
NANETS Board of Directors

Cedars-Sinai Medical Center
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Tonight's faculty

Udhayvir SINGH GREWAL

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Oncology

Delphine CHEN

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Nuclear Medicine

Vera MEGDANOVA

University Hospital
Queen Yoana – ISUL
Sofia, Bulgaria
Oncology

Christophe DEROOSE

University Hospitals
Leuven, Belgium
Nuclear Medicine

Tonight's agenda

Agenda:

18:00 – 18:05	**Opening comments –** *Simona GLASBERG, ISR (ENETS)*
18:05 – 18:15	**Case presentation 1: Stage 4 metastatic, functional grade 2 pancreatic NET** – *Udhayvir SINGH GREWAL, USA*
18:15 – 18:30	**Discussion on symptom burden, surgical versus medical management, and treatment sequencing** ***Panelists:*** *Alexandra GANGI, USA / Simona GLASBERG, ISR / Udhayvir SINGH GREWAL, USA / Vera MEGDANOVA, BUL / Delphine CHEN, USA / Christophe DEROOSE, BEL*
18:30 – 18:45	**Case presentation 2: Advanced grade 3 well-differentiated pancreatic NET** – *Vera MEGDANOVA, BUL*
18:45 – 19:00	**Discussion**
19:00 – 19:10	**Closing comments** – *Alexandra GANGI, USA (NANETS)*

Metastatic G2 Functional pNET

Udhayvir Singh Grewal, MD

Assistant Professor of Medical Oncology
Winship Cancer Institute of Emory University
Atlanta, GA, USA

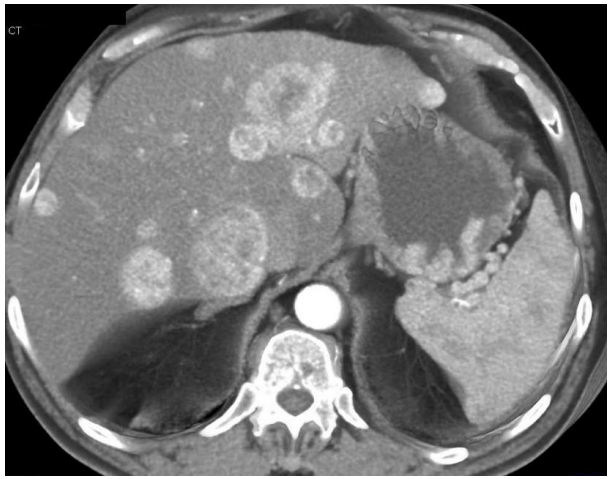
DISCLOSURE INFORMATION

- I have no relevant disclosures.

Clinical Presentation

✓ **Initial Presentation:**

- 51 year old male with no significant PMHx presented with a 4-month long history of fever, diarrhea and night sweats. Night sweats occured less frequently for a few months before. Also endorsed having slowly lost 50 lbs over 5 years.
- Performance status: ECOG PS 0. No recent medication changes. No S/S of infection.
- Social history: Occasional EtOH, never smoker. Family history: Negative for FDR.



✓ **Initial lab investigations:** CA 19-9 239 [reference range:]. Glucose: 220 mg/dl [reference range:]

✓ **Imaging (1/2017)**- CT Abd and Pelvis: There is a large heterogeneous mass within the body/tail of the pancreas with a multi-lobular border in the areas of low attenuation and calcification, measuring approximately 5.6 x 7.2 x 7 cm with multiple liver metastases.

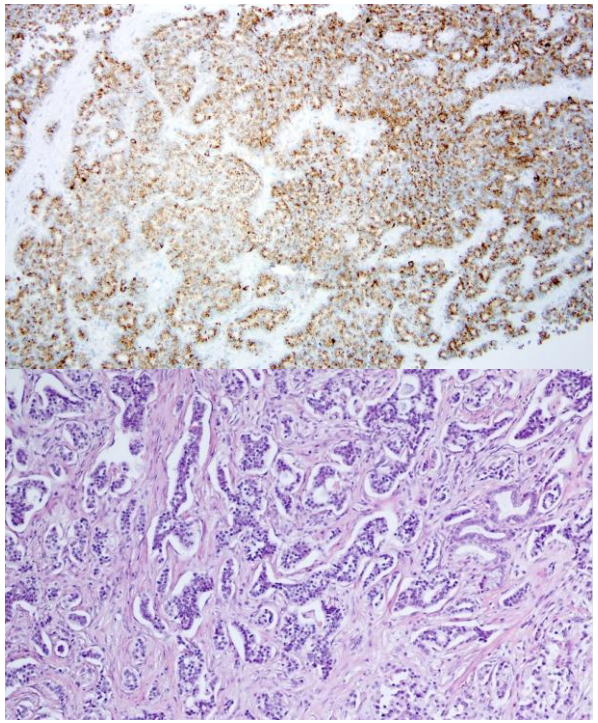
Contd Diagnosis/Clinical Course

✓ **Biopsy:**

- Image-guided liver biopsy was done which showed a well-differentiated neuroendocrine tumor, consistent with origin from the pancreas. Chromogranin+, Synaptophysin+, Ki67 6% (WHO G2)
- **CT Chest:** No evidence of metastatic disease.

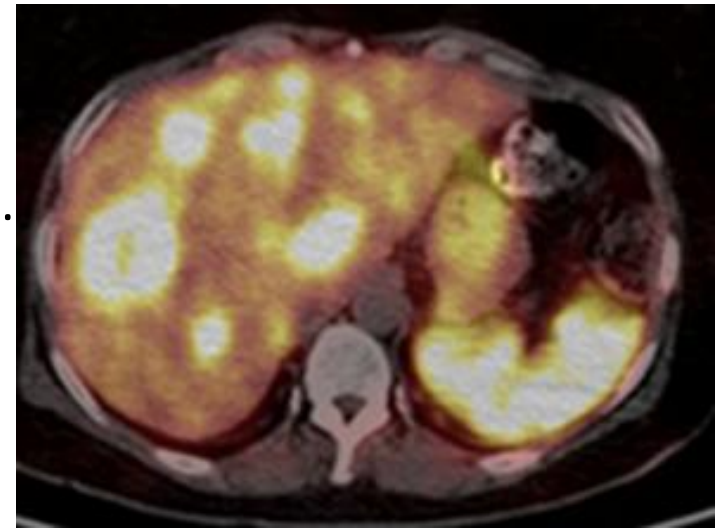
✓ Patient seen by local medical oncologist who discussed initiation of therapy with CAPTEM and octreotide LAR. This was initiated 2/2017.

✓ Blood sugars running in 400s-500 mg/dl range. HbA1c 10% (metformin, glipizide). **Continued on CAPTEM for 7 cycles**– only mild reduction in size of pancreatic primary and liver metastases however dramatic improvement in symptoms. Diarrhea and night sweats resolved completely by cycle 6 and weight stabilised and finally started improving. No abdominal pain. Initiated on maintenance with Octreotide LAR alone.



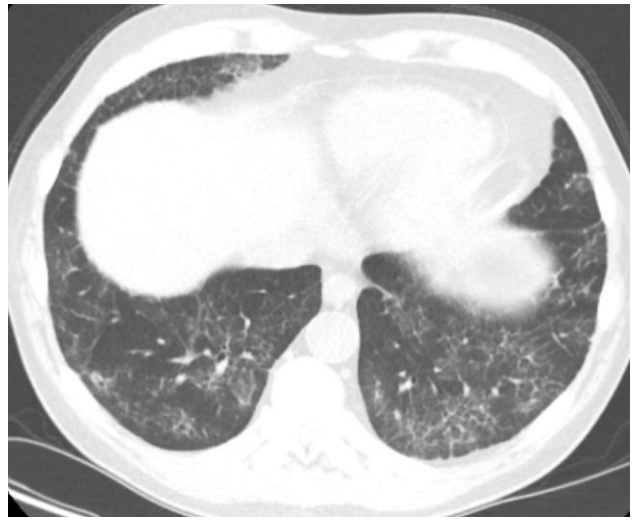
Management Continued

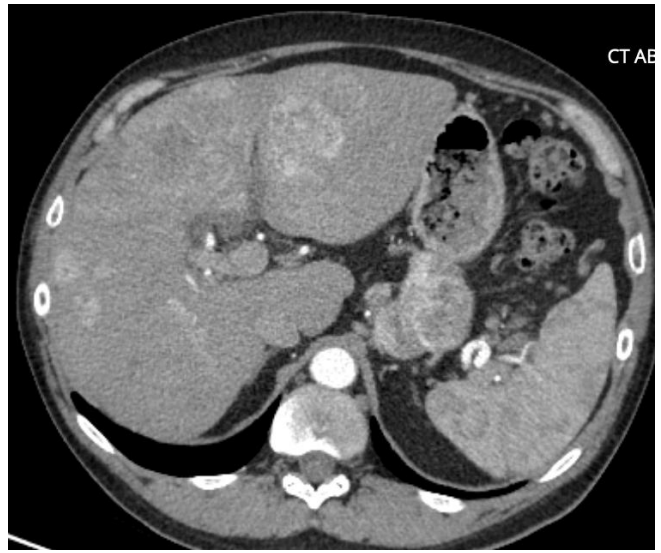
- ✓ **Successive scans-** continued to show progression, new areas of metastatic disease in intra-abdominal LNs.
- ✓ 11/2022 **Copper dotatate PET/CT** uptake in the pancreatic tail, bilobar hepatic lesions and retroperitoneal lymph nodes.
- ✓ Several options discussed, Lutathera recommended. (Lu177 Dotatate).
- ✓ 3/2023 - 8/24/2023: **Lutathera (4 cycles, 200 mCi, 8 weeks apart).** Blood sugars better controlled and taken off of anti-diabetic medications. Post-Lutathera restaging imaging: stable disease.
- ✓ 12/2024: Worsening hypoglycemic episodes, anti-diabetic meds discontinued.
- ✓ 1/2025- 3 hypoglycemic episodes per night, symptomatic. Admitted for insulinoma work-up.
- ✓ With glucose 48 mg/dl, C-peptide: 6.8 ng/mL [1.1-4.4 ng/mL], Pro-insulin: 665 pmol/L [reference range: 0-10 pmol/L], Insulin: 28.5 uIU/mL [reference range: 2.6-24.9 uIU/mL]. Positive glucagon response. **c/w diagnosis of Insulinoma**.



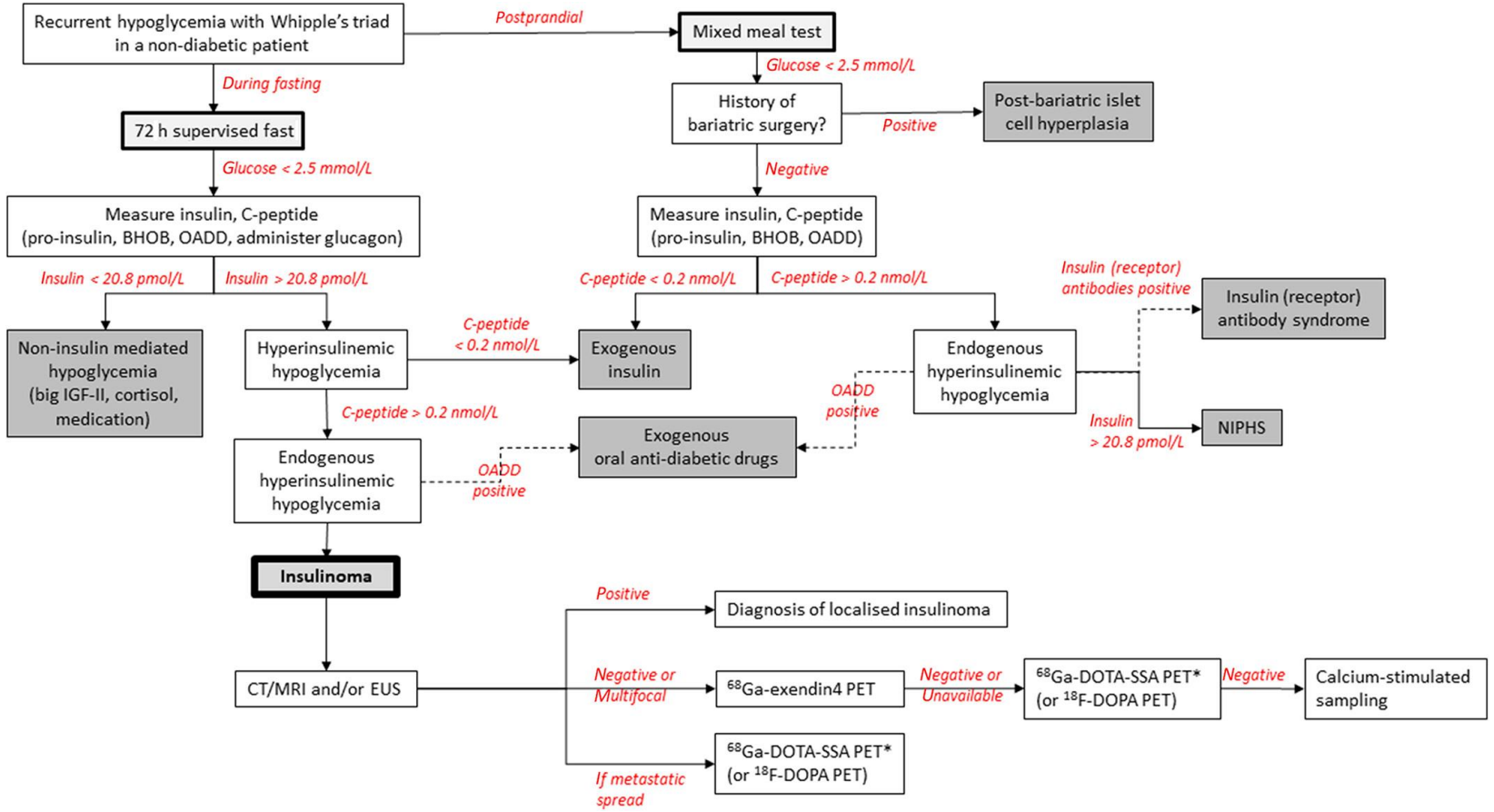
Management continued

- ✓ Octreotide LAR discontinued. **Everolimus 10 mg daily initiated 2/2025.**
- ✓ 4/2025- Hypoglycemia resolved, hyperglycemia noted. Clinically better.
- ✓ 6/2025- Worsening shortness of breath, dyspnea on exertion and cough.
- ✓ CT Chest- new GGO, with patchy consolidation c/w pneumonitis. **Everolimus held** and oral steroids initiated. Symptomatic improvement.
- ✓ As steroids tapered off- recurrent hypoglycemic episodes. Re-iniated on octreotide LAR and diazoxide (3 mg/kg/day) added by endocrinologist.
- ✓ 8/2025- Restaging CT CAP with IV contrast- worsening in size and number of liver metastases. c/w disease progression.





A few thoughts on diagnostic algorithm for insulinoma



ENETS guideline on functional pNETs. *J Neuroendocrinol*. 2023

Thank You!

Questions for discussion

- ✓ What next lines of therapy would you discuss with the patient?
- ✓ What additional strategies can be used to manage insulin-mediated hypoglycemia in patients with insulinoma (in addition to disease control)?
- ✓ Does therapy sequencing matter in the care of patients with functional pNETs?
- ✓ Should biochemical functional testing be performed in all patients with a new diagnosis of pNET? Role for serial testing? (tranformation to insulinoma is very real)*

**Endocrinol Diabetes Metab Case Rep*. 2015;2015:150032.

DISCUSSION

Advanced well-differentiated G3 pNET- A case presentation

Vera Megdanova-Chipeva, MD, PhD

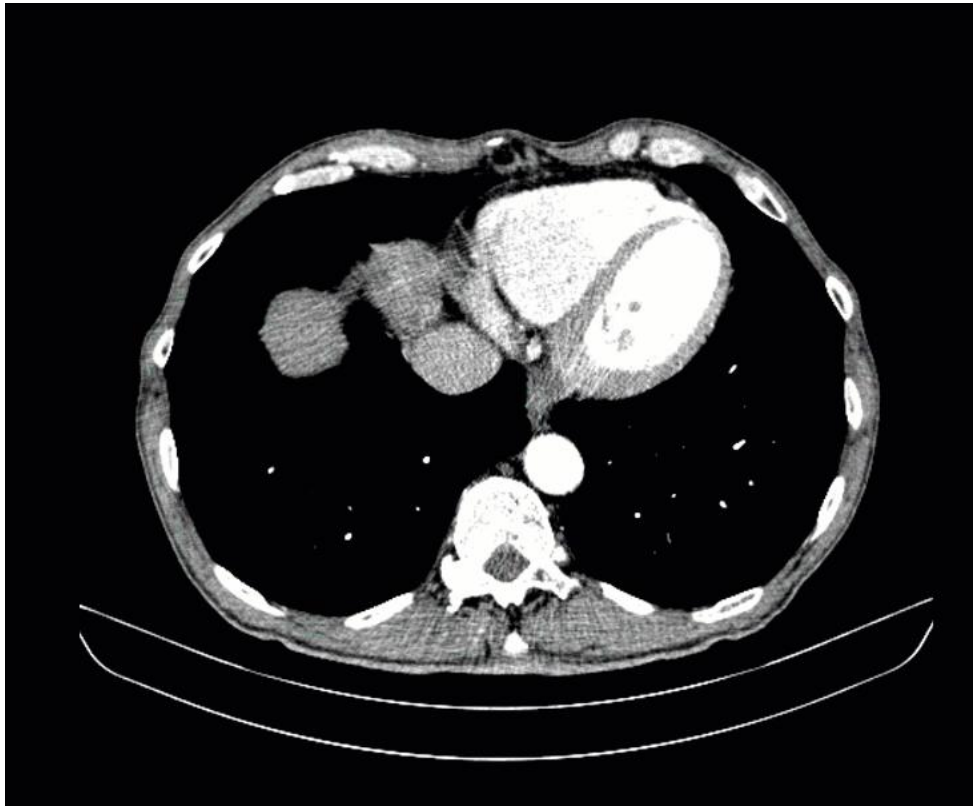
Medical Oncology Department,
University Hospital Queen Yoana-ISUL,
Sofia, Bulgaria

DISCLOSURE INFORMATION

no conflicts/disclosures to declare

Step 1 – initial diagnosis of the patient

- ✓ 69 male, no comorbidities, no family history
- ✓ **Initial symptoms** – loss of weigh, loss of appetite for 3 months newly diagnosed >> levels of blood sugar, abdominal pain, no diarrhoea, flushes or shortness of breath
- ✓ **Gastroenterology** department m12.2022 – 01.2023
- abdominal echo, contrast enhanced – multiple bilobar liver lesions
- Gastroscopy – pangastritis
- Colonoscopy – diverticulosis in sigmoid and descendent colon, internal haemorrhoids
- CT TAP – multiple liver mets up to 7,5/9 sm in 2seg, thickening up to in dorsal part of pancreatic body and tail, no enlarged LN

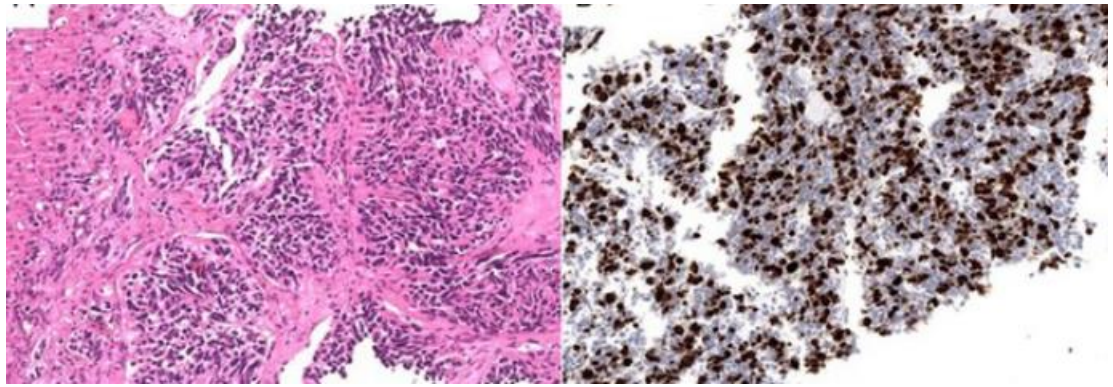


Step 1 – initial diagnosis of the patient

- ✓ **Liver biopsy /m01.23/Histology + IHC** – Synaptophysin (+), Chromogranin (+), Ki 67 – 30% - **Metastasis of well differentiated pancreatic NET G3**
- ✓ **Octreoscan /m01.23/–** increase metabolic activity in all liver lesions and in the focus of pancreatic body/tail
- ✓ **Chromogranin A /m01.23/** - >900ng/ml

Diagnosis: Metastatic Non-Functioning pNET G3

- ➢ **Difficult differentiation b/n pNETG3 and pNEC**[1]
- ➢ NETG3 with favourable and with unfavourable biological behaviour – Ki67, TGR, SSR+ on imaging
- ➢ Functional activity in NET G3 is rare (5-41%)



NB! ENETS Guidelines
Diagnostic work-up for NF-PanNET[2]
- ➢ CT/MRT
- ➢ SST-PET/CT
- ➢ FDG- PET/CT in case of SSR(-)neg lesions

1-Jie Chen, J Pancreat. 2024; 2-Beata Kos-Kudła, NJE, 2023

1-st line treatment

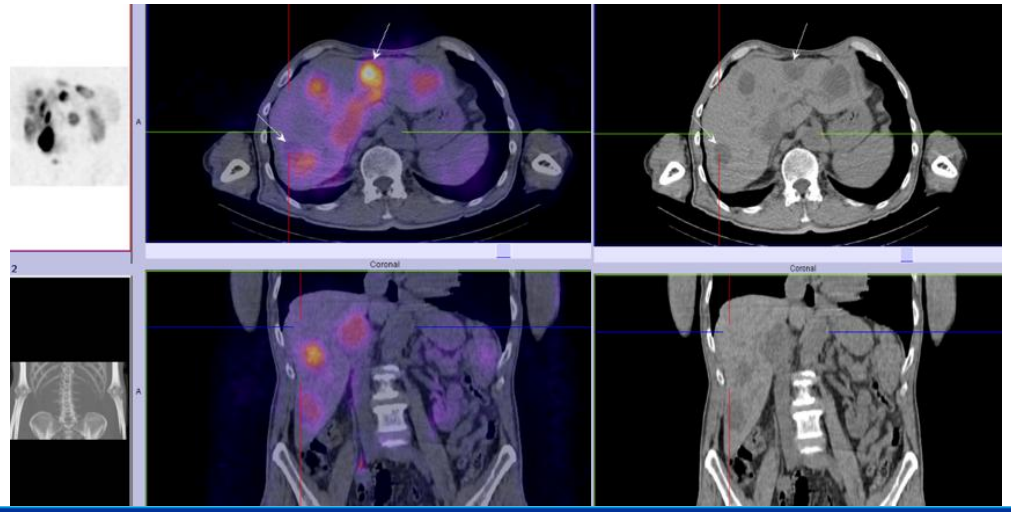
- ✓ **<u>Octreotide LAR 30mg initiated m01.2023</u>**
- ✓ No side effects
- ✓ **Control imaging CT m04.23** –

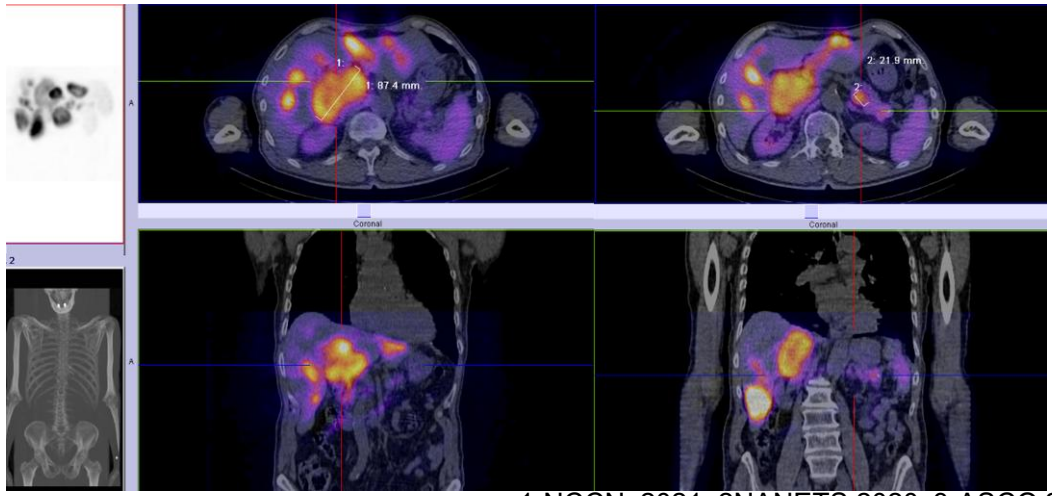
Partial morphological response (33% reduction in tumour size) of all liver metastases, reduction in size in the pancreatic lesion

- ✓ **Octreoscan /m06.23/** – Partial morphological and metabolic response in liver and pancreas

pNET G3 with favourable biological behaviour (Ki67 <55%, low tumour growth and SSR+ on imaging) may be treated with SSA according to NCCN, NANETS, ASCO Guidelines [1,2,3]

- ✓ **Octreoscan /m12.23/ -** no dynamics in size and metabolic activity of the primary, increase in size of liver mets, new peripancreatic metabolically active LN





1-NCCN. 2021; 2NANETS,2020, 3-ASCO 2023

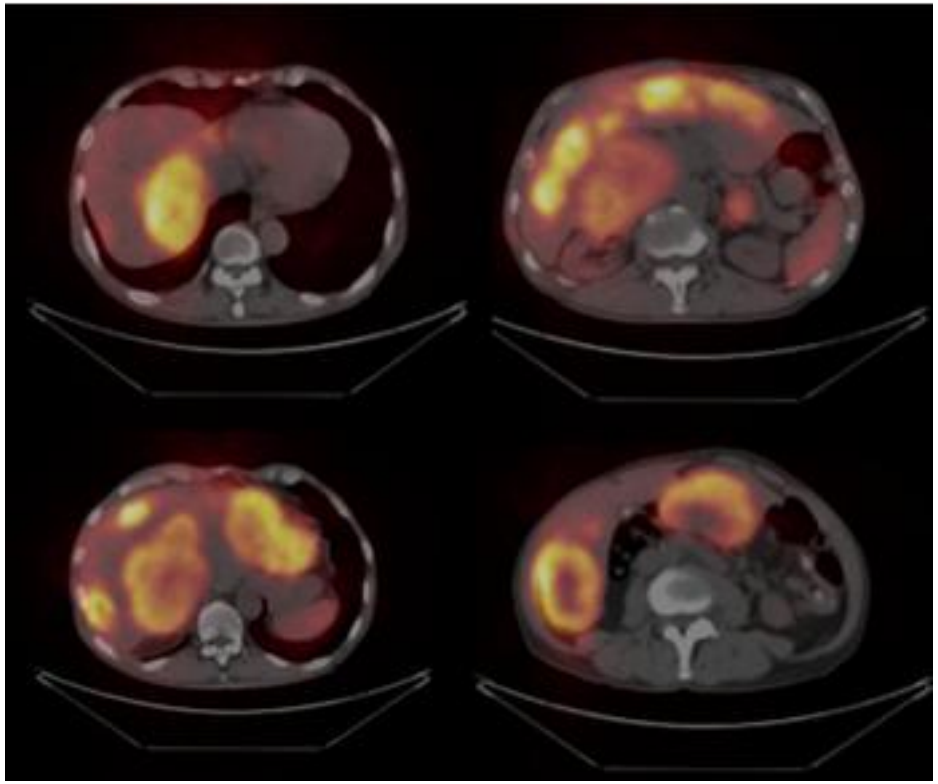
2nd line treatment

- ✓ **Octreotide LAR 60mg initiated m01.2024**

- ✓ **Ga^{68}DOTATOC m04.24 – PD**
  - **52% increase in size of all liver mets and retropancreatic LN,**
  - **no morphological diff. in size of primary,**
  - **all metabolically active (SUVmax up to 48 in liver, 24 in LN, 10,8 in primary)**

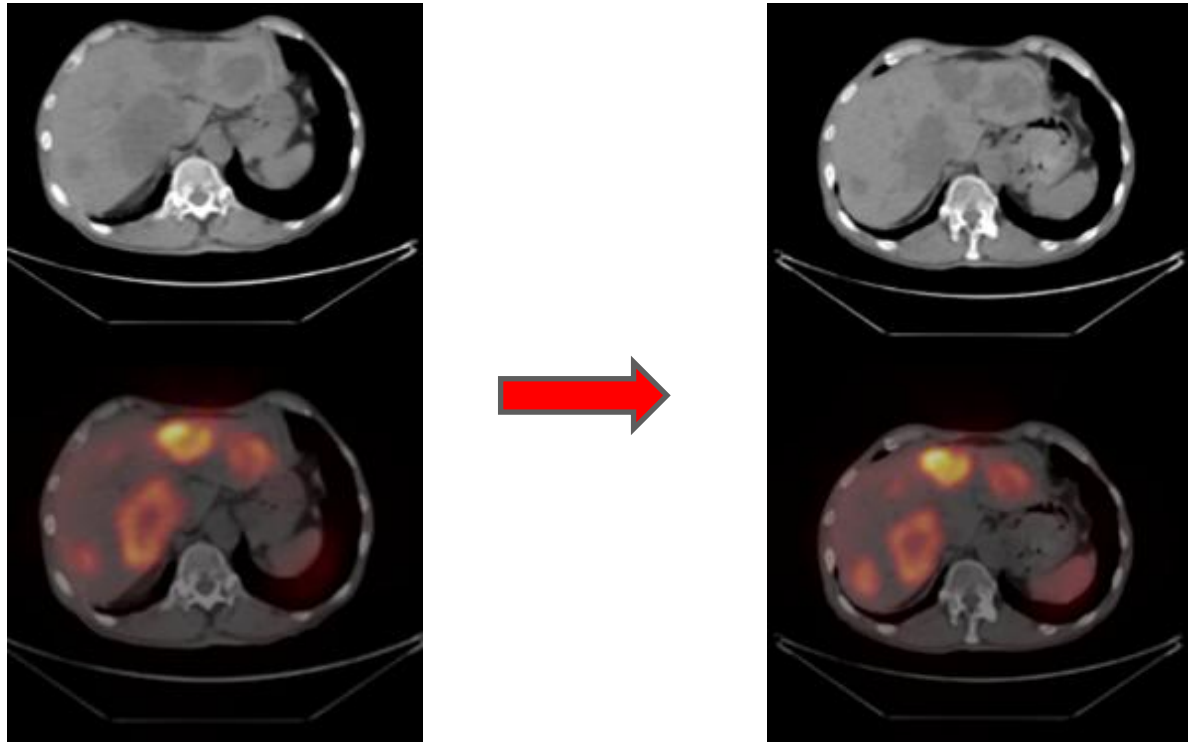
- ✓ **Chromogranin A /m06.24/** - >900ng/ml

Options for 2nd line after SSA:
- High dose SSA (NCCN)
- Eve/Sun
- CAPTEM



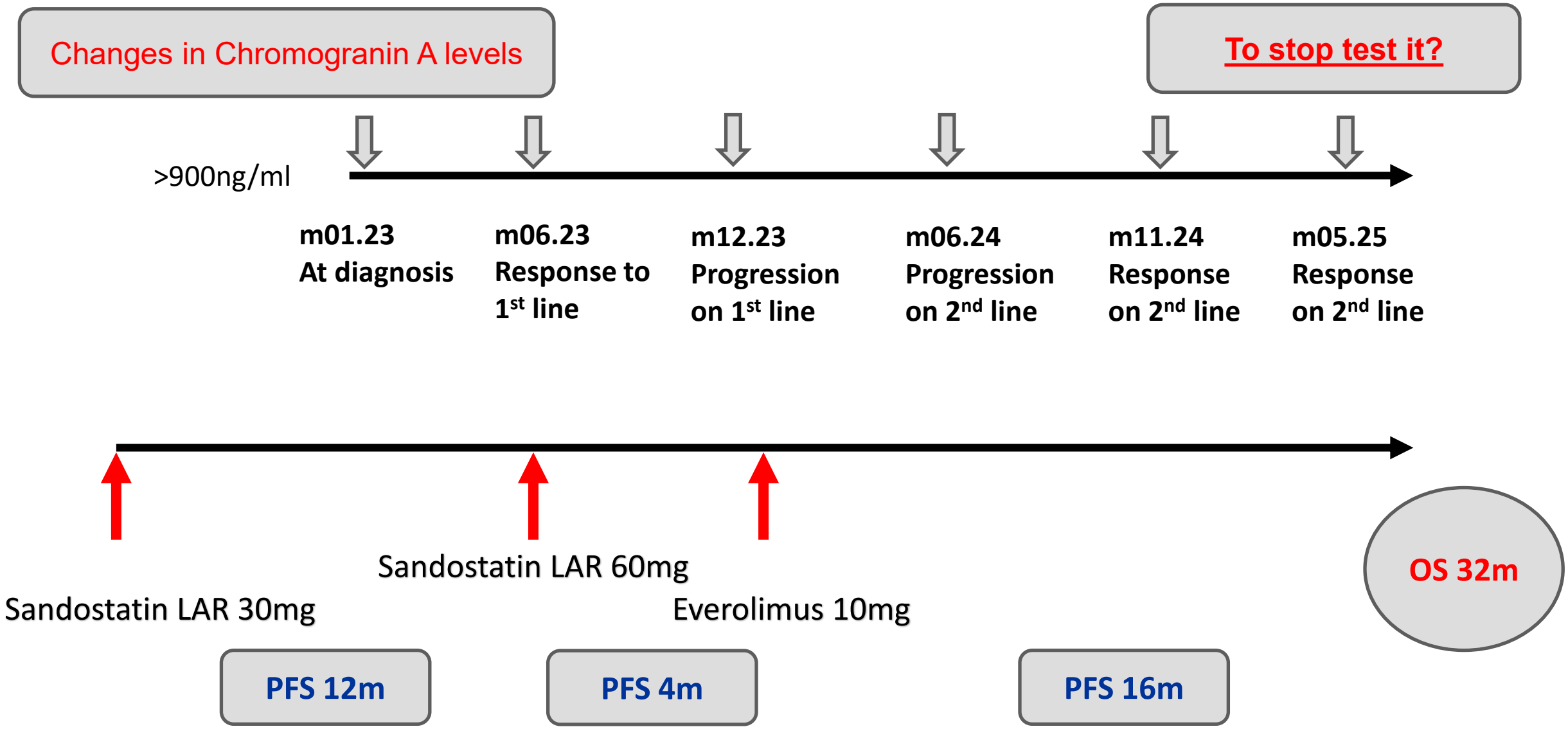
3rd line treatment

- ✓ **<u>Everolimus 10mg initiated m05.2024</u>**
- ✓ **Very good tolerability**
- ✓ **Side effects –** hyperglycemia G1-2, anemia G1



- ✓ **Ga^{68}DOTATOC m11.24 – PR**
  - 39% reduction in size of all liver mets and retropancreatic LN,
  - - << metabolically activity
  - no morphological diff. in size of primary

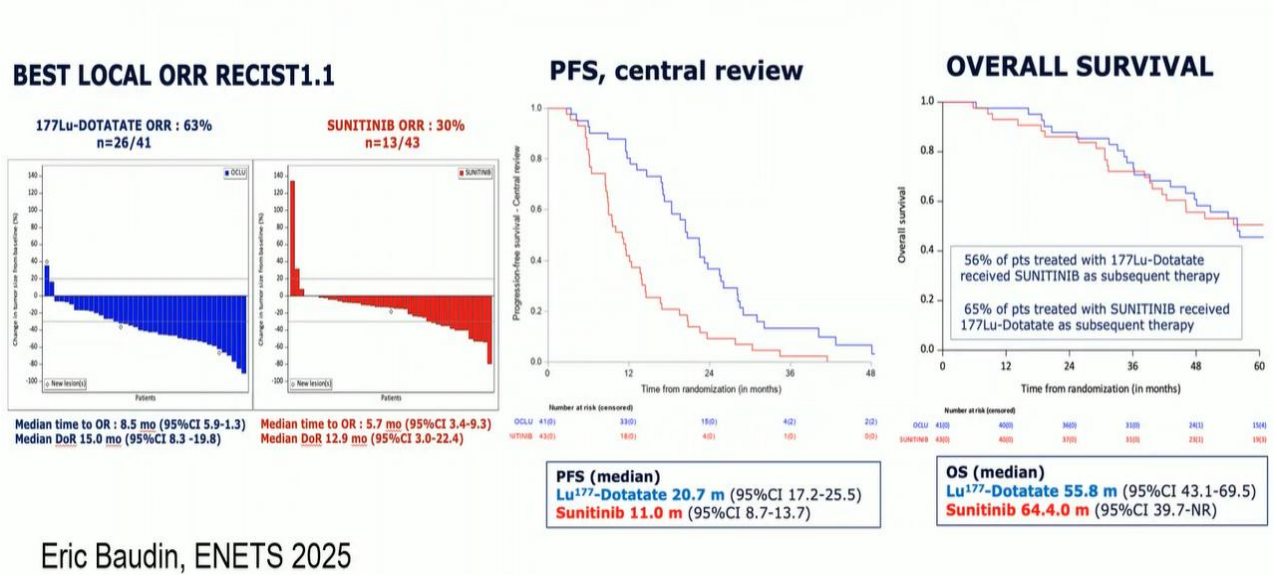
- ✓ **Ga^{68}DOTATOC m04.25 – PR**
  - 15% more reduction in size of all liver mets
  - persistence of metabolically activity
  - no morphological diff. in size of primary


Changes in Chromogranin A levels
To stop test it?
>900ng/ml
m01.23
At diagnosis
m06.23
Response to
1st line
m12.23
Progression
on 1st line
m06.24
Progression
on 2nd line
m11.24
Response
on 2nd line
m05.25
Response
on 2nd line
Sandostatin LAR 30mg
Sandostatin LAR 60mg
Everolimus 10mg
OS 32m
PFS 12m
PFS 4m
PFS 16m

In case of progression..

- ✓ **PRRT -** Lu^{177} **….soon**
- ✓ **Chemo** – CA~~P~~EM, Cis/Carbo +Etoposide, ST~~Z~~5Fu, CA~~P~~X, FOLFOX,
- ✓ **Targeted therapy** – Sunitinib, Cabo~~z~~tinib
- ✓ **Immunotherapy** – Pemb~~ro~~izumab
- ✓ **Local treatment** in case of oligoprogression
- ✓ **Clinical trial**

OCLURANDOM – PhII academic trial, >2prior lines, G2-3 NET



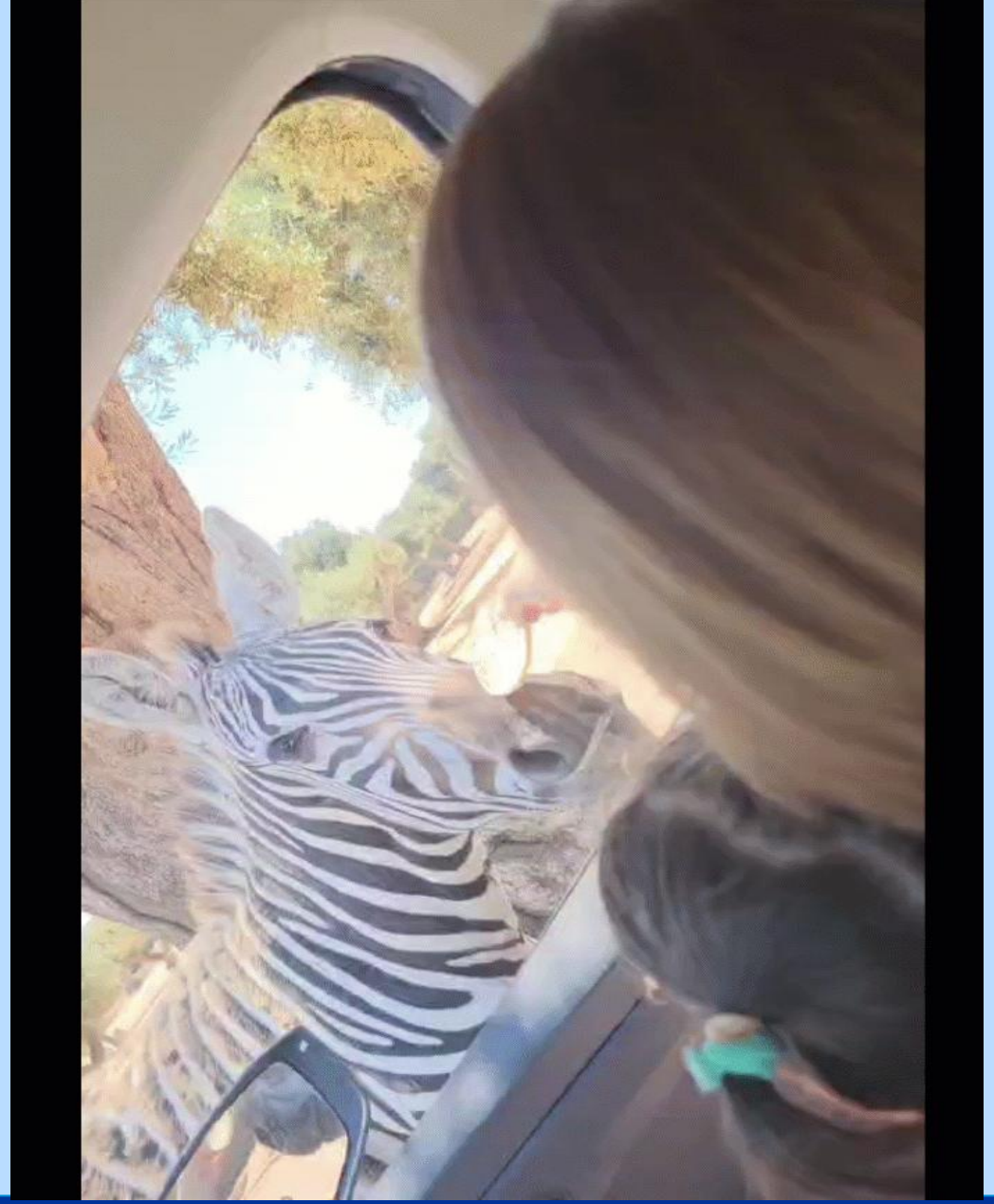
Eric Baudin, ENETS 2025

Conclusion

- ✓ Advanced pNET G3 is a heterogenous group
- ✓ ENETS, NANETS, ESMO, NCCN, ASCO guidelines – similarities and differences
- ✓ Clinical behaviour, tumour growth rate, tumour burden, Ki67 %, SSR (+) are crucial for decision of treatment strategy

Questions to discuss:

? In case of F-pNET G3 – are there some hormones more commonly secreted?
? May you consider watch and wait in some cases?
? PRRT – optimal place, N of cycles, dose, interval b/n cycels, new ligands, isotopes, targets
? Immunotherapy - already option outside clinical trial?



Thank you for your attention!

DISCUSSION

Closing comments

A BIG "Thank You" to

- ✓ Our speakers and moderators
- ✓ The ENETS Office team: Leah MATTHEWS, Ulrike KNELL, and Martina FLESCHEN
- ✓ The NANETS Office Team: Cassandra CLEARE
- ✓ The ENETS & NANETS Education Groups
- ✓ YOU, our valued participants

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