NANETS-ENETS Webinar:

Virtual NET tumour board: Precision therapies and emerging strategies in NEN management

Wednesday, 10 December 2025,
12:00 – 13:30 EDT / 18:00 – 19:30 CET

Disclosure statement

The moderators have the following conflicts of interest to report:

Aman CHAUHAN, USA (NANETS):
Receipt of grants/research supports: Seneca Therapeutics, BMS, Clovis, EMD Serono, Nanopharmaceutics
Receipt of honoraria or consultation fees: Novartis, Crinetics, Curium, Lantheus, Exelixis, Ipsen, Tersera, Lexicon, Sanofi, Seneca Therapeutics, BI, ITM

Mairéad McNAMARA, GBR (ENETS):
Receipt of grants/research supports: Ipsen, Astra Zeneca, servier, NuCana
Participation in a company sponsored speaker's bureau: Astra Zeneca, AAA (Novartis)

The aim and concept

- ✓ Transferring research to education and teaching is a major goal at ENETS.
- ✓ Webinars are free of charge and can be accessed by all.
- ✓ All webinars will be recorded and made available on the ENETS website after the event.
- ✓ **This webinar is intended for HCPs qualified by law to prescribe medicine.**

CME accreditation by UEMS-EACCME®

- ✓ Accreditation by UEMS-EACCME® with **1.0 European CME Credits (ECMEC®)** is still pending.
- ✓ To receive CME credit, participants must **attend the live webinar** and complete a **feedback form**.
- ✓ Responses are anonymous.
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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

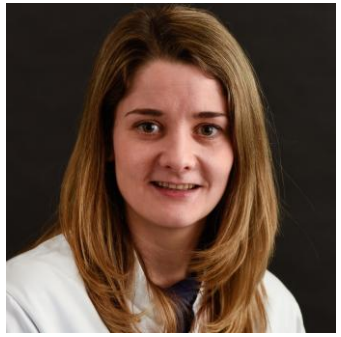
Aman CHAUHAN
NANETS Board of Directors

University of Miami
Florida, USA
Medical Oncology

Mairéad McNAMARA
ENETS Advisory Board Chair

The Christie NHS Foundation Trust
Manchester, United Kingdom
Medical Oncology

Tonight's faculty



Tessa BRABANDER

Erasmus MC
Rotterdam, the Netherlands
Nuclear Medicine

Beth CHASEN

University of Texas MD Anderson Cancer Center
Houston, Texas, USA
Nuclear Medicine

Maria DANIELI

European Institute of Oncology (IEO)
Milan, Italy
Surgical Oncology

Timm DENECKE

University Hospital Leipzig
Leipzig, Germany
Interventional Radiology

Tonight's faculty

Nicholas FIDELMAN

University of California
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Interventional Radiology

Aaron SASSON

Stony Brook University
Stony Brook, USA
Surgical Oncology

Suayib YALCIN

Hacettepe University Institute of Cancer
Ankara, Turkey
Medical Oncology

Tonight's agenda

Agenda:

12:00 - 12:05 EDT / 18:00 - 18:05 CET **Opening comments** – *Aman CHAUHAN, USA*

12:05 - 12:15 EDT / 18:05 - 18:15 CET **Case presentation: Advanced grade 2 pancreatic neuroendocrine tumour (PanNET)** – *Aman CHAUHAN, USA*

12:15 - 12:45 EDT / 18:15 - 18:45 CET **Panel discussion**

Panellists:

Medical Oncology: *Aman CHAUHAN, USA & Suayib YALCIN, TUR*

Surgical Oncology: *Maria DANIELI, ITA & Aaron SASSON, USA*

Nuclear Medicine: *Tessa BRABANDER, NED & Beth CHASEN, USA*

Interventional Radiology: *Timm DENECKE, GER & Nicholas FIDELMAN, USA*

12:45 - 12:55 EDT / 18:45 - 18:55 CET **Case presentation: Grade 2 small bowel or ileum NET (advanced/metastatic)** – *Suayib YALCIN, TUR*

12:55 - 13:25 EDT / 18:55 - 19:25 CET **Panel discussion** *(with moderators and panellists listed above)*

13:25 - 13:30 EDT / 19:25 - 19:30 CET **Closing comments** – *Mairéad McNAMARA, GBR*

Case presentation: Pancreatic NET

Aman Chauhan, MD

University of Miami
Florida, USA

DISCLOSURE

- Personal financial interests: Consultant for Novartis, Curium, BI, Exelixis, Lantheus, Sanofi, Tersera, Crinetics

- Institutional financial interests: Research Support: Novartis, BI, Crinetics

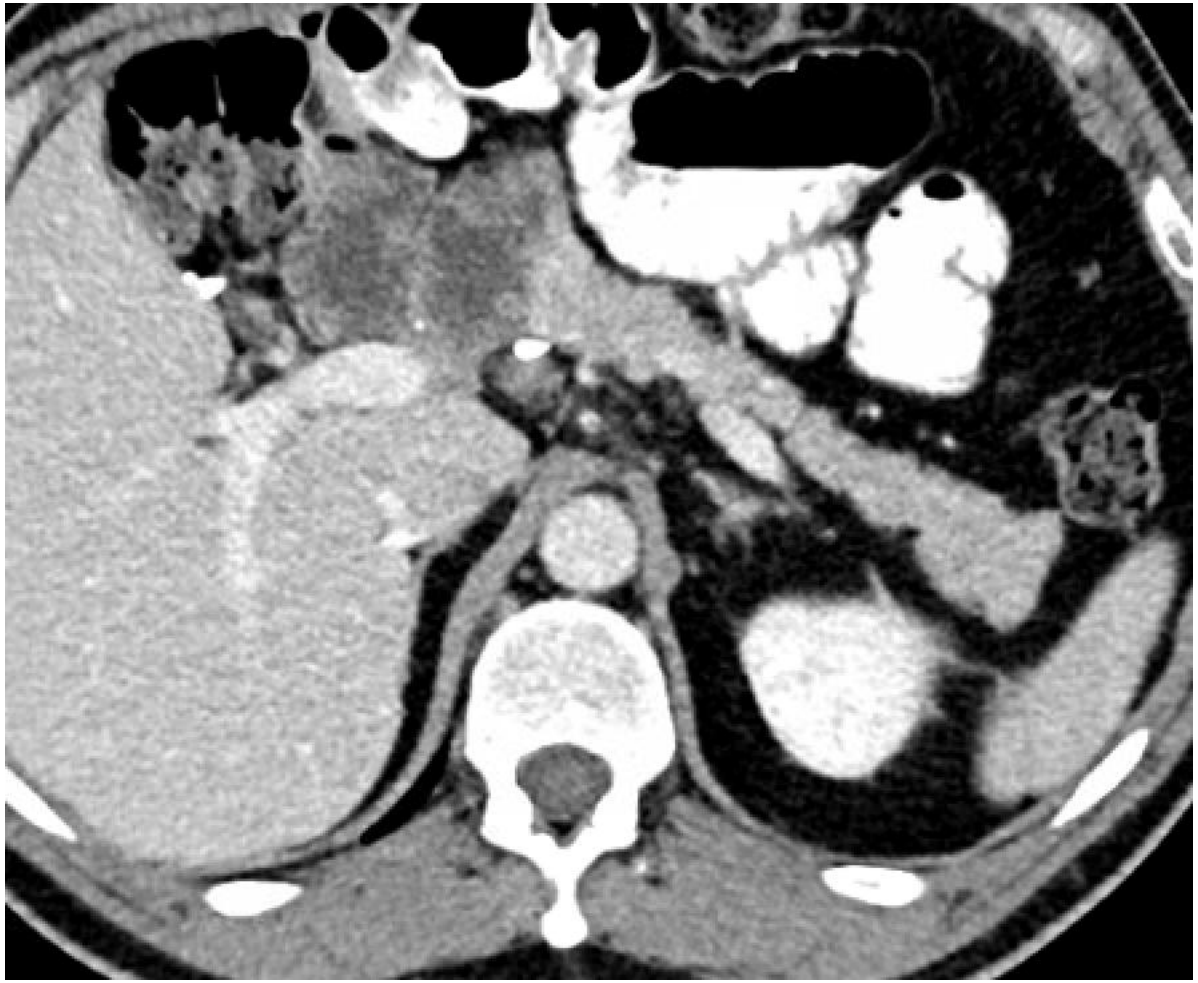
Case presentation

51 y.o. male adult, originally presented to a hospital on 03/2016 with complaints of pruritus, diarrhoea, weight loss and painless jaundice.

On admit total bilirubin was 9.9 and diagnostic CT scan revealed a pancreatic mass.

EUS reaffirmed pancreatic head mass which was biopsied and confirmed well differentiated neuroendocrine tumor of the pancreas.

A biliary stent was placed.



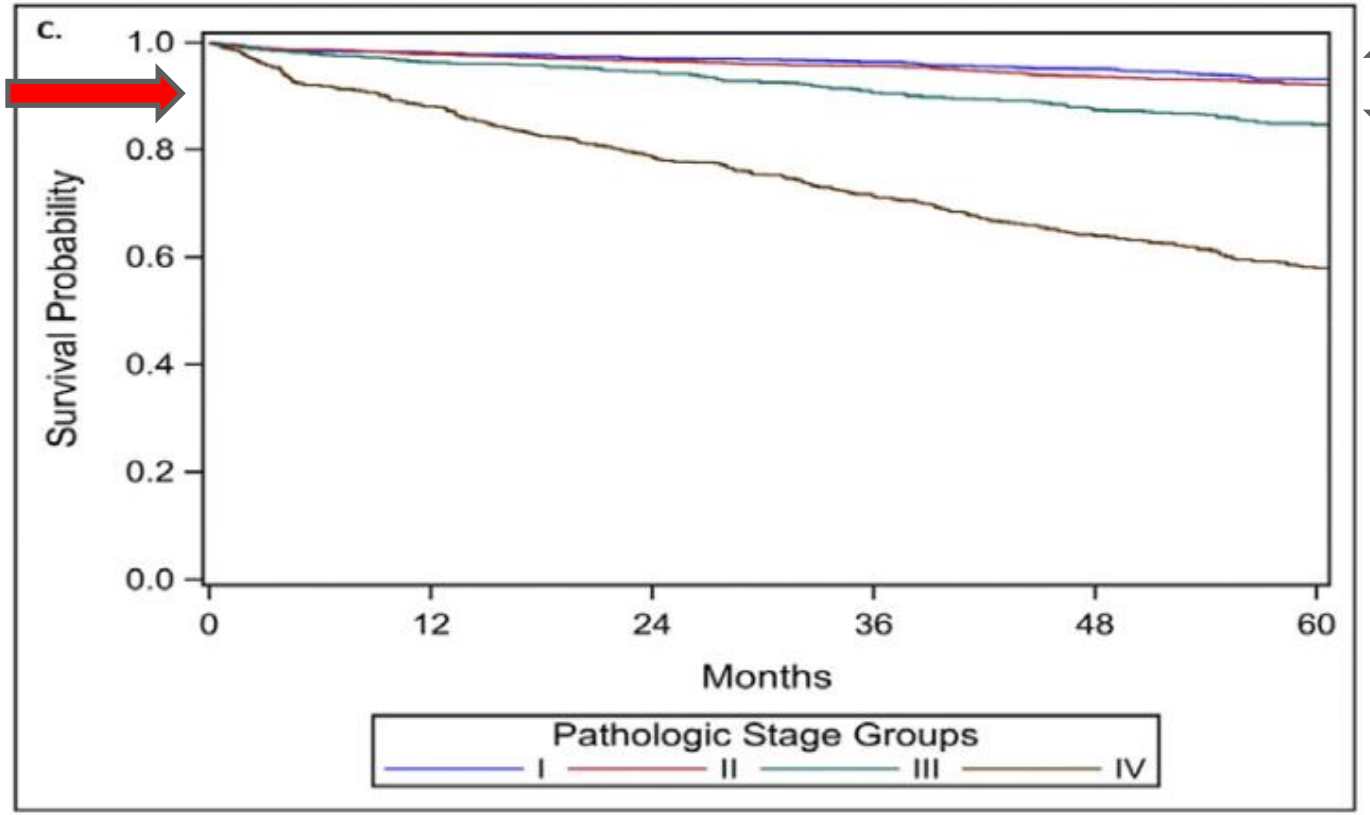
Next step in management

- Observation
- Surgery
- Chemo-Radiation
- PRRT

Next step in management

- Surgery

Fantastic 5-year survival with surgery in early-stage disease



	Stage I	Stage II	Stage III	Stage IV
Case number	1210	1453	705	680
5-year overall survival rate	92.98%	91.86%	85.18%	53.59%

Chauhan A. AJCC NET Guidelines. CA Jr of Clin 2024

Case presentation

Patient had Whipple surgery on March 2016.

The pathology showed invasive well differentiated neuroendocrine tumor of the pancreas (2.4 cm) involving the bile duct margin, all other margins clear, LVI and PNI identified, 3/10 lymph nodes positive, stains positive for pankeratin, chromogranin A and synaptophysin.

Ki 67 12%.

Next step in management

- Observation
- Adjuvant Chemotherapy
- Adjuvant SSA
- Clinical Trials

Next step in management

- Observation
- Clinical Trial

S2104: A Phase II Randomized Trial of Postoperative Adjuvant Capecitabine and Temozolomide versus Observation in High-Risk Pancreatic Neuroendocrine Tumors

Patients with resected WD grades 2/3 pNET *(Ki-67 ≤ 55%)* with high-risk features as defined as *Zaidi score* of ≥ 3.*

**N = 154*

**Patients with up to 5 liver metastases resected/ablated at the time of primary tumor resection will be eligible.*

2:1

RANDOMIZATION

- CAPTEM x4 months
- OBSERVATION

* Tumor assessment q6 months for the initial 3 years followed by q12 months for the subsequent 2 years

Stratification
Grade
Stage

Primary Endpoint*
3 years RFS

Correlatives
Blood and tissue will be banked
NETest will be performed in 3 time points

CAPTEM
Capecitabine 750mg/m2 PO BID days 1-14 and
Temozolomide 200mg/m2 PO QD days 10-14
Cycle q28 days

Heloisa Soares, MD, PhD

Syed Ahmad, MD

Mary Kay Washington, MD, PhD

Case presentation

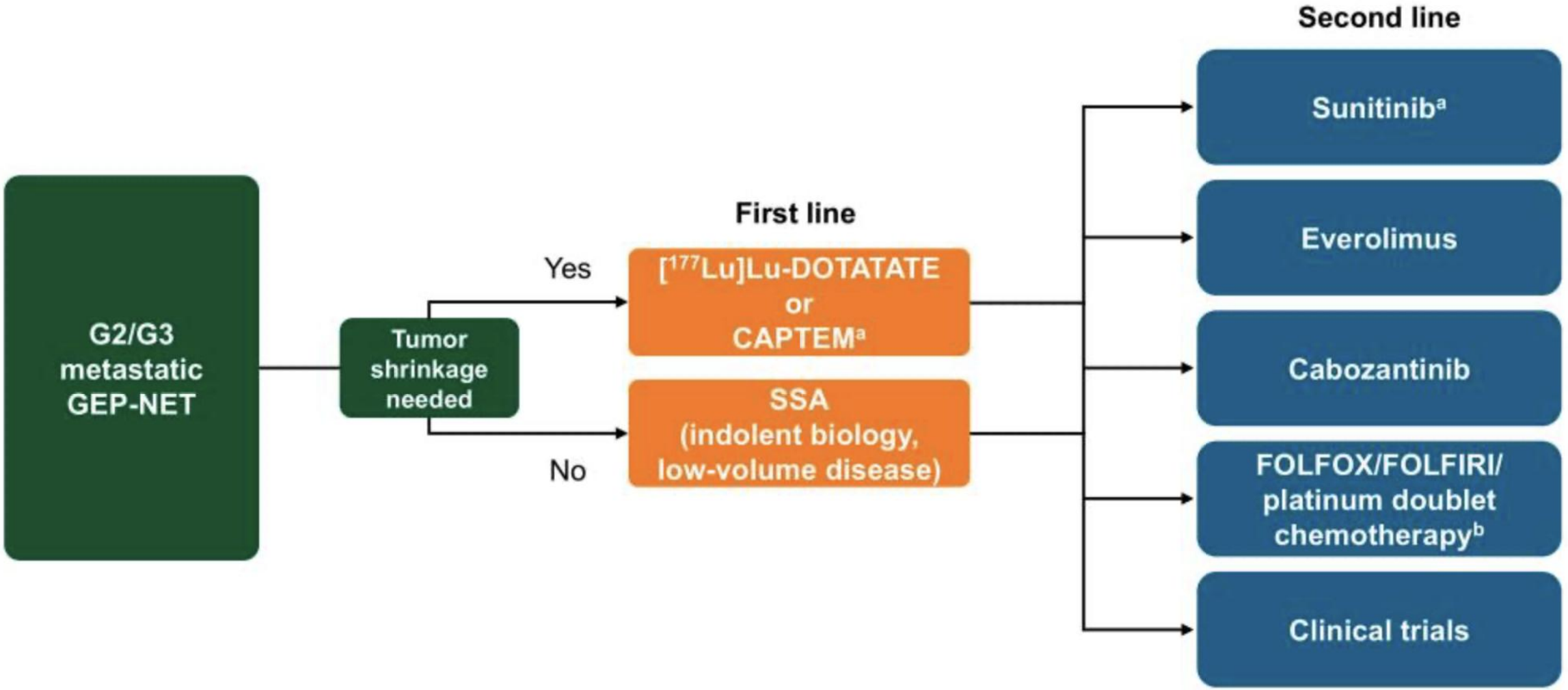
He followed with surveillance imaging and in **06/2020 metastatic recurrence was found on imaging**.

CT abdomen/pelvis showed hepatic mets. DOTATATE PET showed low volume SSTR +ve disease and biopsy confirmed G2 NET (Ki 67 12 %). Clinically asymptomatic

Chromogranin A trend: 259 → 369

Next step in management

- Observation
- Somatostatin Analog
- PRRT
- Everolimus



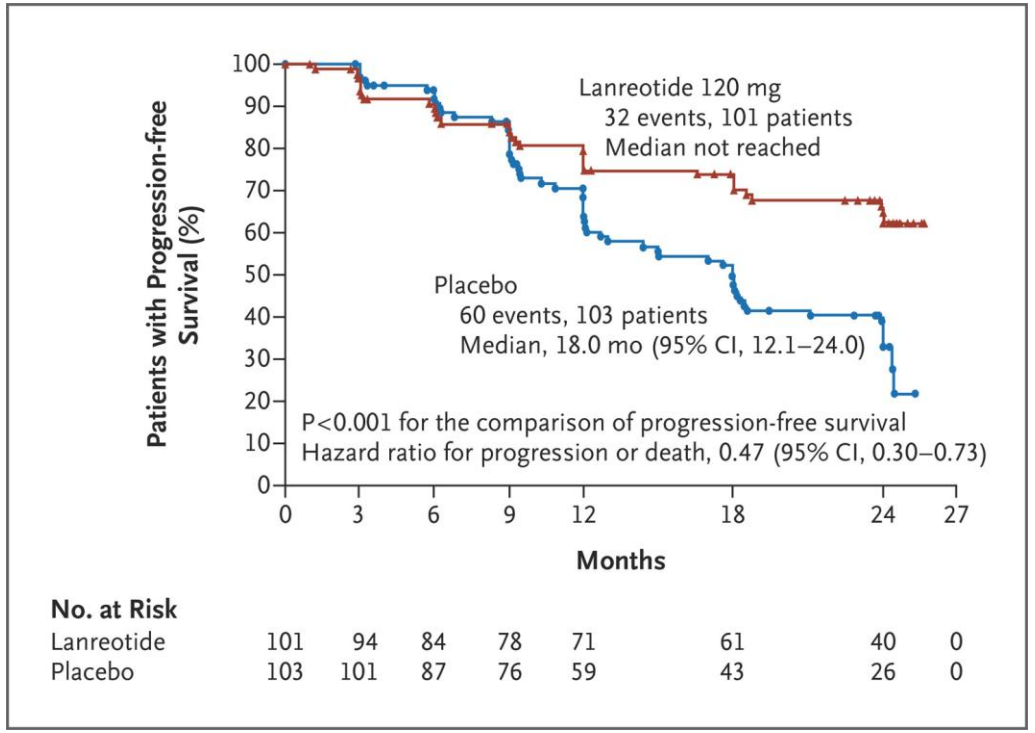
- Somatostatin Analog

Chauhan A. et. al. Cancers 2025

CLARINET: Lanreotide vs placebo for GI NETs

Lanreotide significantly prolonged PFS compared with placebo

Lanreotide Depot 120 mg	Placebo
n = 101	n = 103
Events[a]: 30 PD, 2 deaths	Events[a]: 58 PD, 2 deaths
18 withdrawals • Investigator decision (PD) n = 6 • AEs n = 3 • Withdrew consent n = 3 • Protocol violations n = 2 • Other reason n = 4	21 withdrawals • Investigator decision (PD) n = 9 • AEs n = 3 • Withdrew consent n = 5 • Protocol violations n = 2 • Other reason n = 2
53 completed the study without events	26 completed the study without events



Case presentation

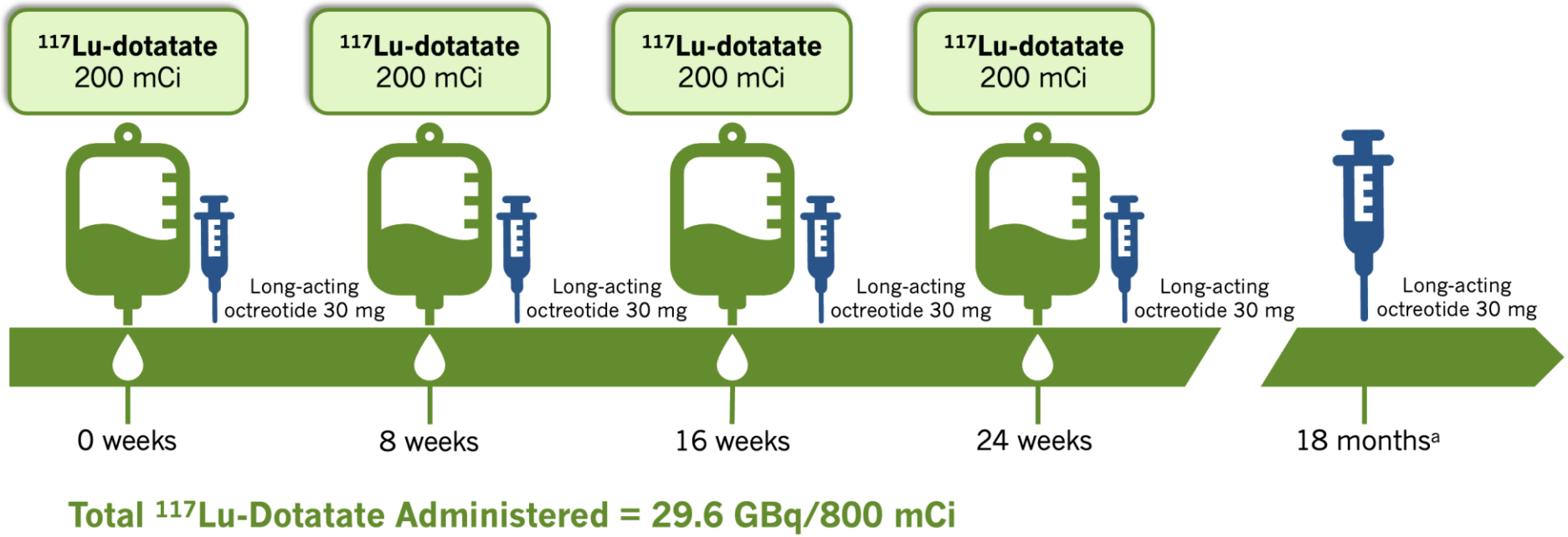
In Sept 2023 patient was found to have rapid progression in liver.

Liver biopsy confirmed Ki 67 20%.

DOTATATE PET revealed liver dominant SSTR positive disease.

Next step in management

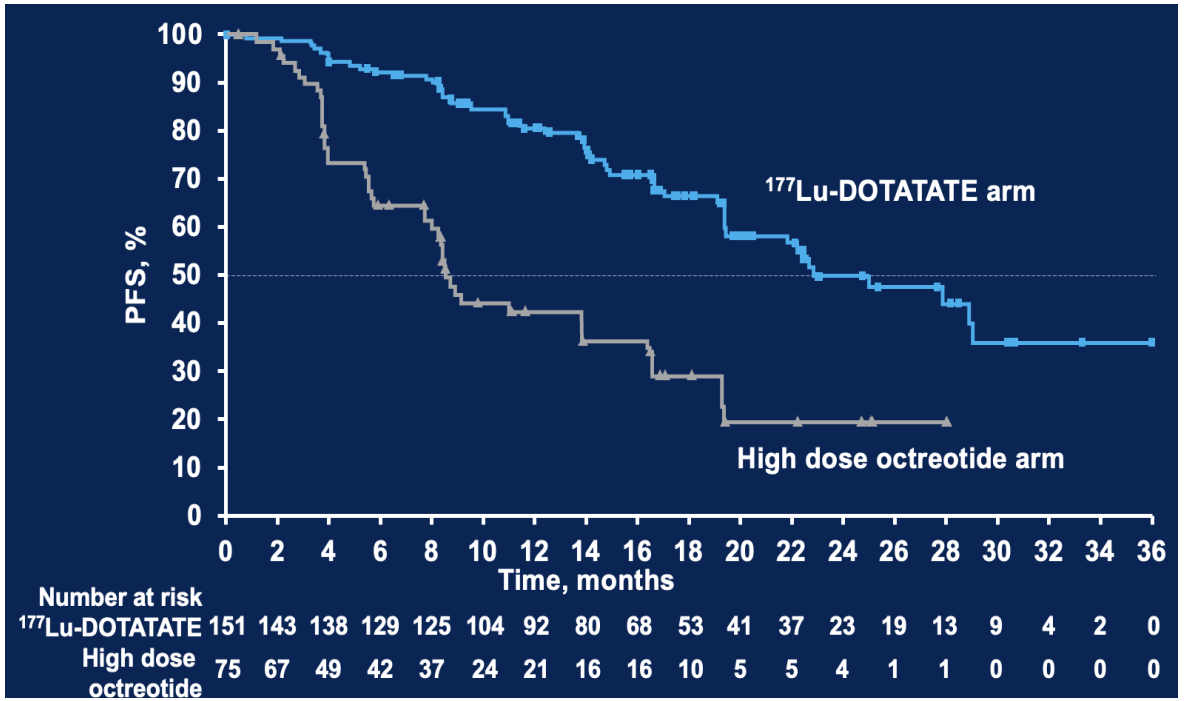
- Increasing dose of Somatostatin Analog
- PRRT
- Everolimus
- CAPTEM



Patient underwent Lu-177 dotatate plus DNA PK inhibitor treatment under Phase 1 trial protocol

NETTER-2: ^{177}Lu-Dotatate in WD GEP-NETs

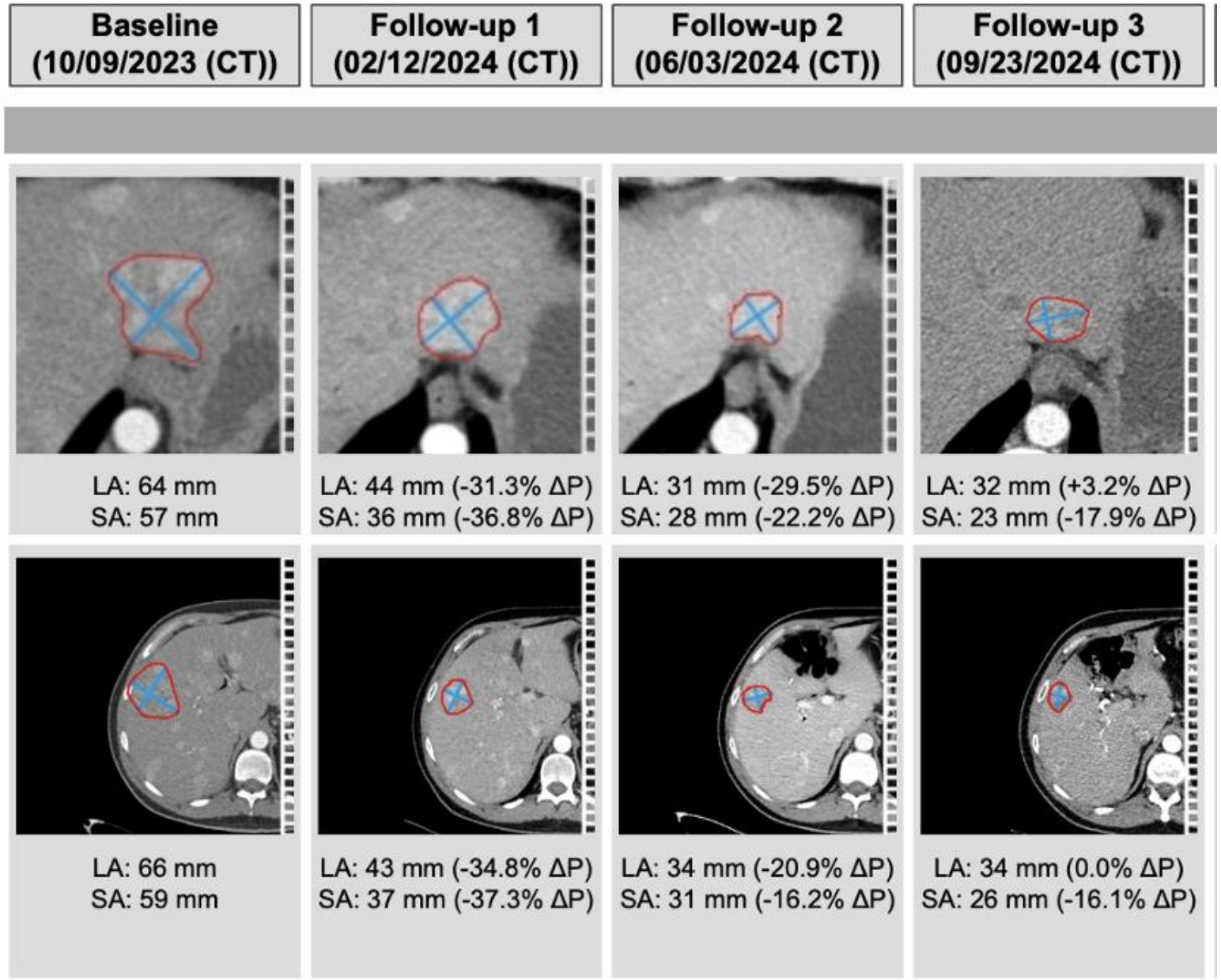
Efficacy



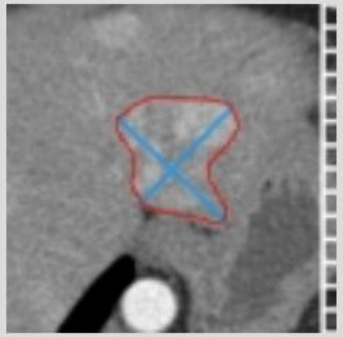
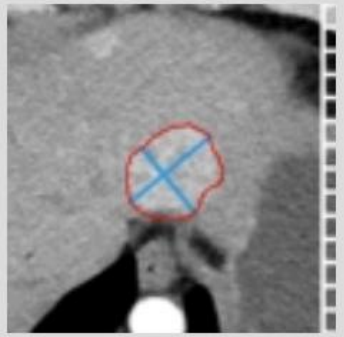
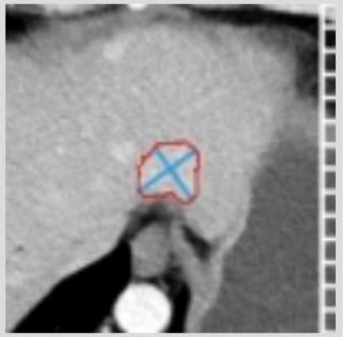
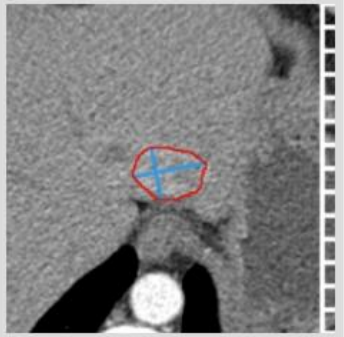
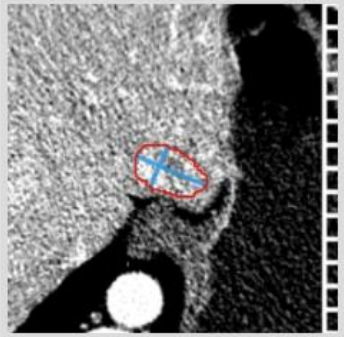
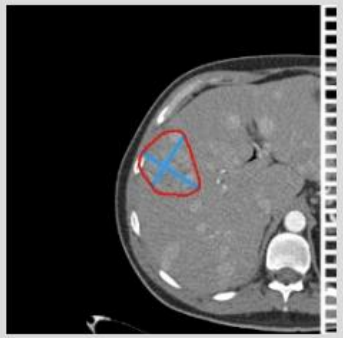
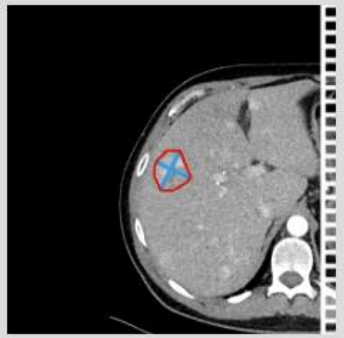
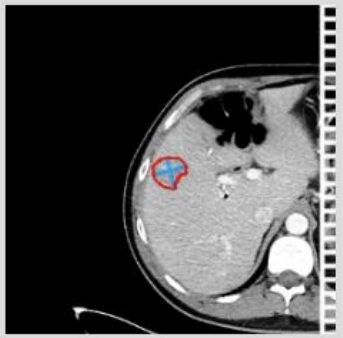
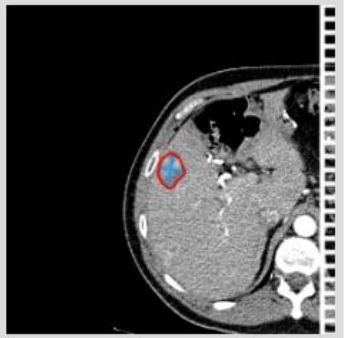
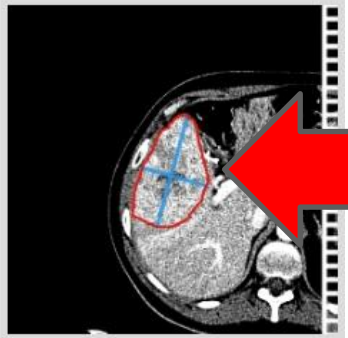
	^{177}Lu-Dotatate (n = 151)	High-Dose Octreotide (n = 75)
PFS median, months (95% CI)	22.8 (19.4, NE)	8.5 (7.7, 13.8)
Stratified HR (95%, CI) P value	0.276 (0.182, 0.418) <.0001	
Number of events Progression Death	55 (36%) 47 (31%) 8 (5%)	46 (61%) 41 (55%) 5 (7%)

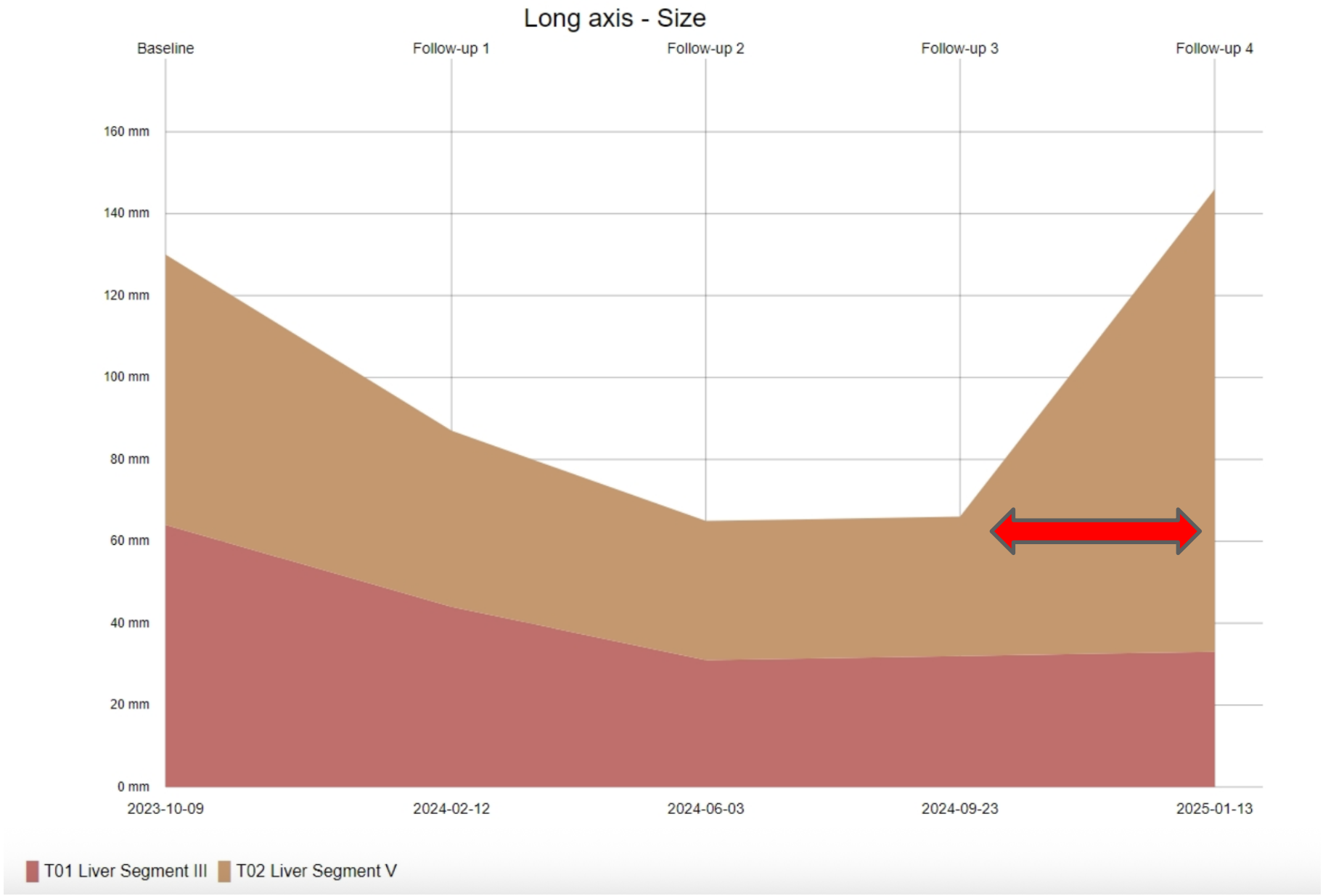
72% reduction in the risk of disease progression or death in the ^{177}Lu-dotatate arm vs the high-dose octreotide arm

- Partial response on the study.



- Roughly a year into the study patient had rapid progression

Baseline (10/09/2023 (CT))	Follow-up 1 (02/12/2024 (CT))	Follow-up 2 (06/03/2024 (CT))	Follow-up 3 (09/23/2024 (CT))	Follow-up 4 (01/13/2025 (CT))
				
LA: 64 mm SA: 57 mm	LA: 44 mm (-31.3% ΔP) SA: 36 mm (-36.8% ΔP)	LA: 31 mm (-29.5% ΔP) SA: 28 mm (-22.2% ΔP)	LA: 32 mm (+3.2% ΔP) SA: 23 mm (-17.9% ΔP)	LA: 33 mm (+3.1% ΔP) SA: 19 mm (-17.4% ΔP)
				
LA: 66 mm SA: 59 mm	LA: 43 mm (-34.8% ΔP) SA: 37 mm (-37.3% ΔP)	LA: 34 mm (-20.9% ΔP) SA: 31 mm (-16.2% ΔP)	LA: 34 mm (0.0% ΔP) SA: 26 mm (-16.1% ΔP)	LA: 113 mm (+232.4% ΔP) SA: 65 mm (+150.0% ΔP)


Long axis - Size
Baseline
Follow-up 1
Follow-up 2
Follow-up 3
Follow-up 4
160 mm
140 mm
120 mm
100 mm
80 mm
60 mm
40 mm
20 mm
0 mm
2023-10-09
2024-02-12
2024-06-03
2024-09-23
2025-01-13
T01 Liver Segment III
T02 Liver Segment V

Next step in management

- Cabozantinib
- CAPTEM
- PRRT Re-Treatment
- Everolimus

Biopsy now shows
Ki 67 of 37%

NET RETREAT study (CCTG-NE1)

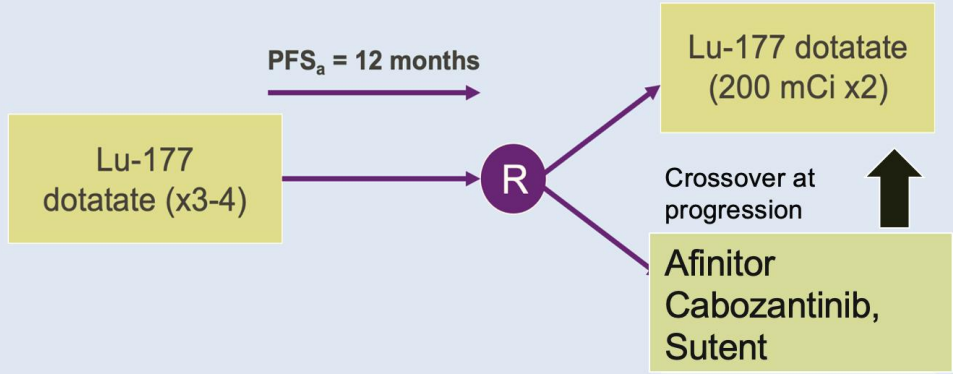
Open 06/05/2023

Key Inclusion/Exclusion Criteria:
- Metastatic Progressive GEPNET (Grade 1-2)
- No RECIST progression within 12 month from last dose of prior PRRT
  (3-4 prior PRRT doses)

Stratification:
- Use of SSA post initial PRRT
- Durable response >24 mo

Aman Chauhan, MD (SWOG) Simron Singh (CCTG)

NET RETREAT Study Design: Phase II RCT (2:1)



Primary Endpoint: Disease Free Survival

Secondary Endpoints: Safety/toxicity and Quality of Life assessment

Exploratory Endpoints: Novel predictive and disease monitoring biomarkers; NETEST and Plasma hPG80

Next step in management

- CAPTEM

Patient participated in CAPTEM plus Y-90 liver directed therapy under research protocol.

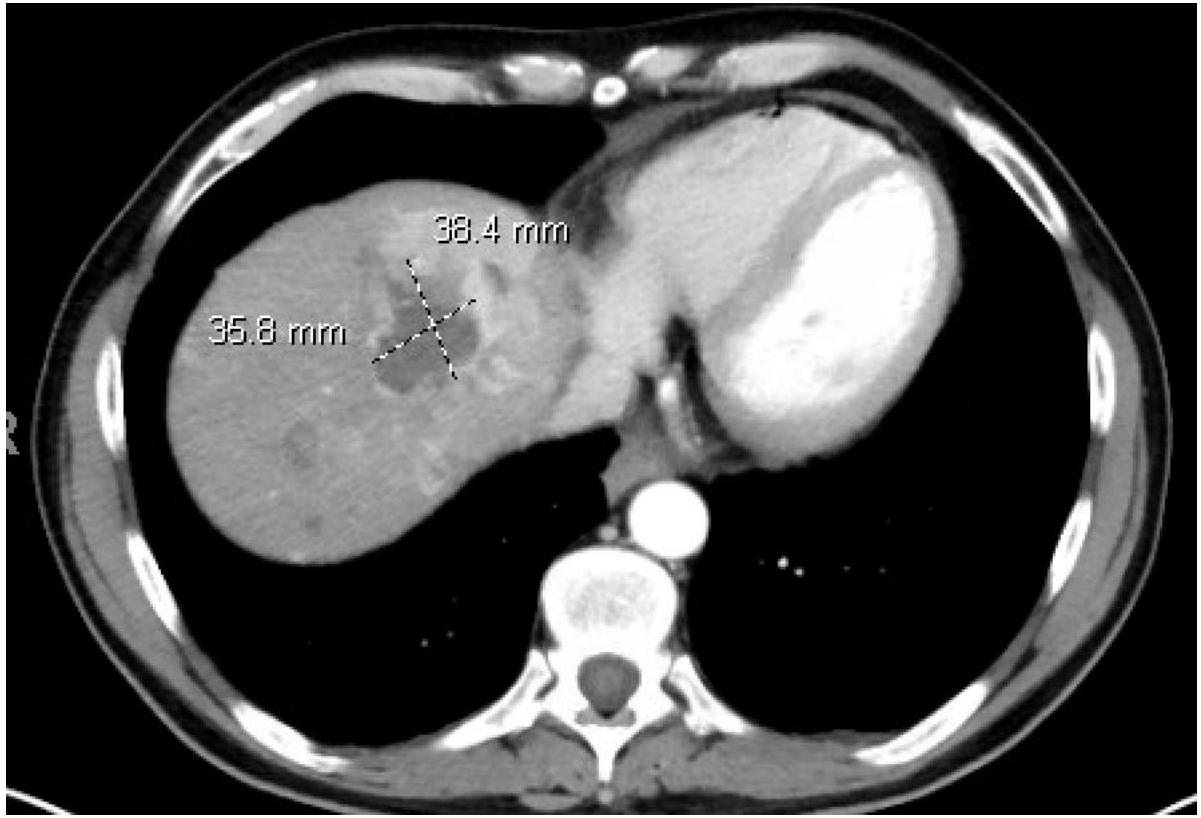
Unfortunately, 4 months in the study s/p 4 Cy of chemo and 1 Y-90 treatment patient had radiographic progression.

CT scan impression 6-2025

Interval development of a 4 x 4 cm area of nonenhancement at the dome of the right lobe of the liver corresponding to an ablation zone with interval development of surrounding enhancing tumor measuring approximately 7 x 5 cm extending towards segment 4.

Interval development of 7 x 5 cm area of nonenhancement involving segments 5 and 8 from ablation zone with continued surrounding enhancing tumor measuring up to 9 x 7 cm.

Multiple additional liver lesions noted, some of which are solid enhancing others are ring-enhancing distributed throughout the hepatic parenchyma involving both lobes, all segments, the largest in the left lobe measuring up to 5.2 cm (previously 3.8 cm and in the right lobe measuring up to 3.6 cm (previously 2.4 cm).



Next step in management

- Cabozantinib
- Carboplatin-Etoposide
- FOLFOX
- Everolimus

CABINET: Cabozantinib for advanced G1–3 NETs

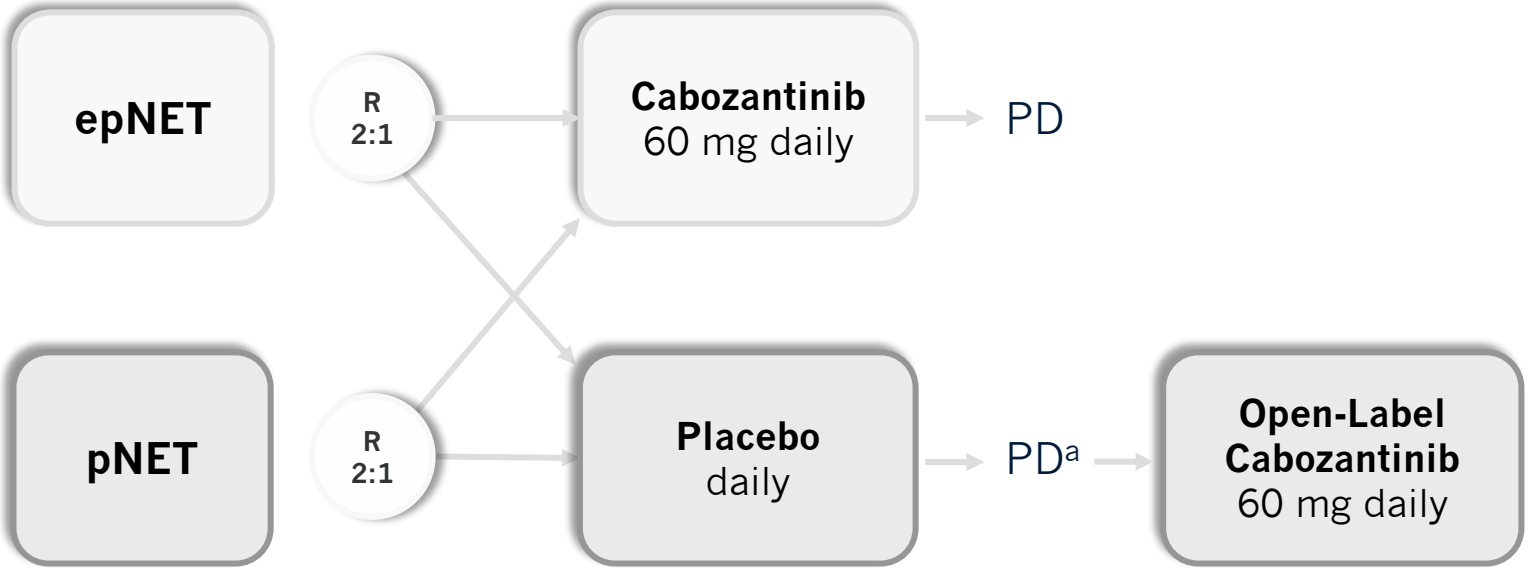
Study design

Key Inclusion Criteria

- Well- to moderately-differentiated NET, grades 1–3
- Disease progression by RECIST within 12 months prior to randomization
- Progression or intolerance of at least 1 prior FDA-approved systemic therapy, not including somatostatin analogues (SSA)
- Includes everolimus, sunitinib, or ^{177}Lu-dotatate for pNET
- Includes everolimus for lung NET
- Includes everolimus or ^{177}Lu-dotatate for GI-NET
- Concurrent SSA allowed provided stable dose for ≥2 months

Stratification Factors

- epNET: concurrent SSA and primary site (midgut GI/unknown vs non-midgut GI/lung/other)
- pNET: concurrent SSA and prior sunitinib

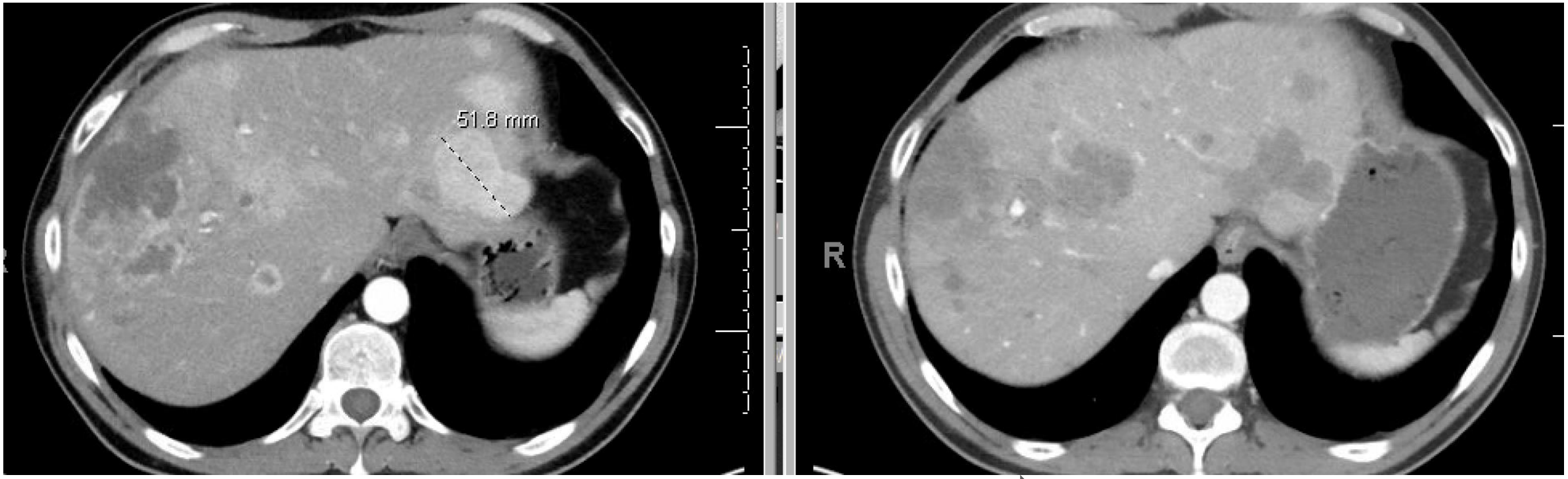


Primary Endpoint per Cohort

- Progression-free survival (PFS) by blinded independent central review

Secondary Endpoints per Cohort

- Overall survival (OS)
- Objective response rate (ORR)
- Safety and tolerability



BEFORE **AFTER**

CT Chest, abdomen and pelvis after 3 months on Cabozantinib reported good treatment response with decrease in size and less avid enhancement within the multifocal liver metastases.

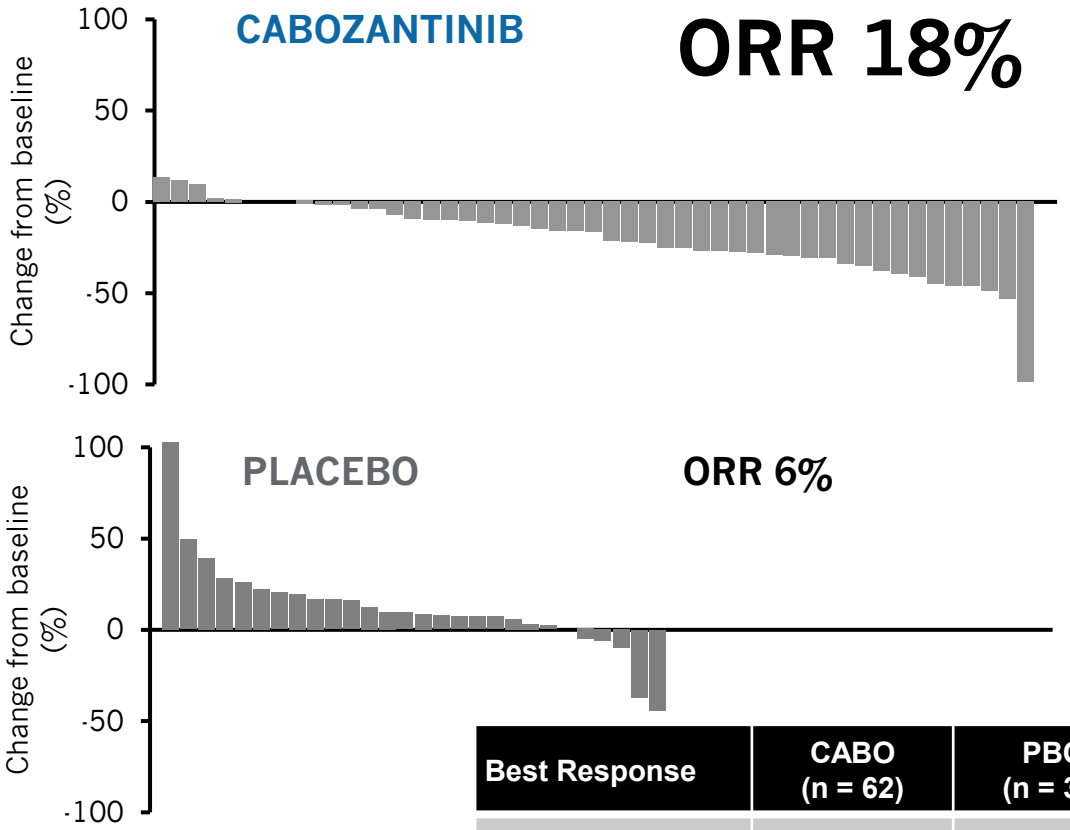
Currently patient is on Cabozantinib and is scheduled to get 6 month follow up scan later this month.

Clinically doing well on 40 mg Cabozantinib.

CABINET: Cabozantinib for advanced G1–3 NETs (cont.)

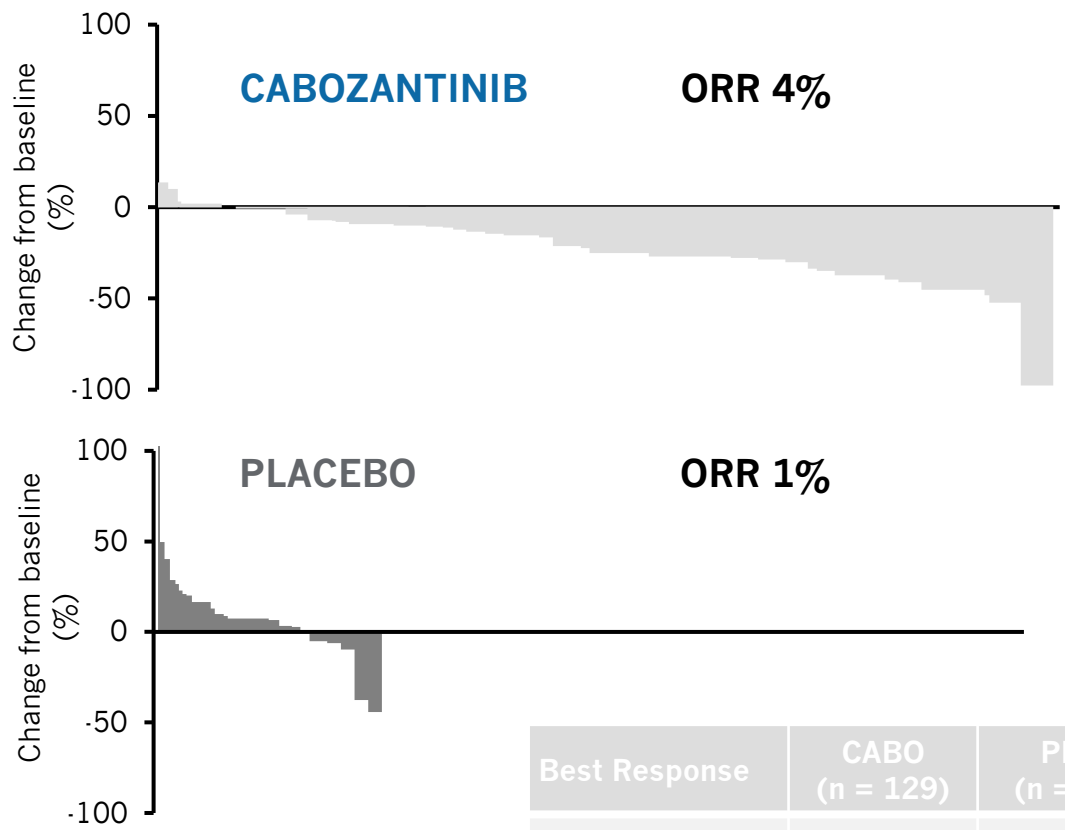
Best overall response (local review)

pNET Cohort



Best Response	CABO (n = 62)	PBO (n = 31)
PR	11 (18%)	2 (6%)
SD	36 (58%)	12 (39%)
PD	5 (8%)	14 (45%)
Not evaluable	10 (16%)	3 (10%)

epNET Cohort



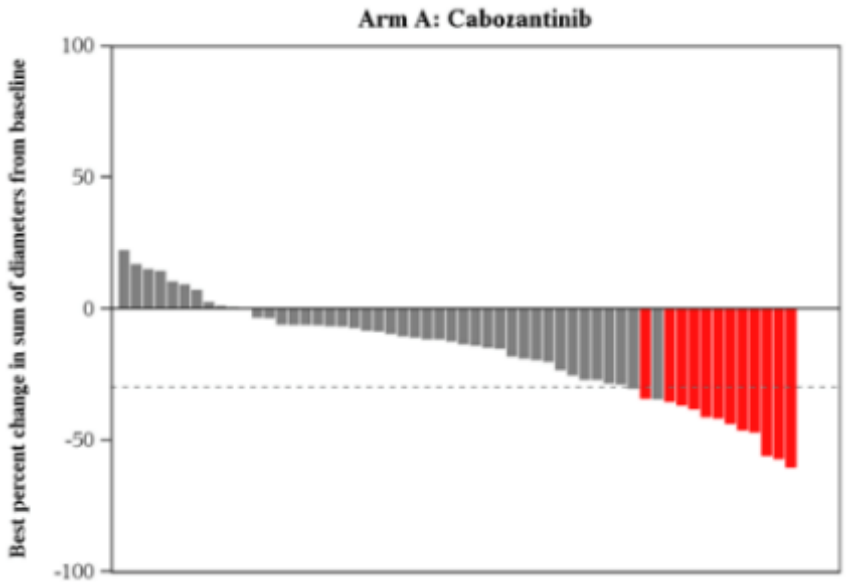
Best Response	CABO (n = 129)	PBO (n = 68)
PR	5 (4%)	1 (1%)
SD	78 (60%)	26 (38%)
PD	21 (16%)	29 (43%)
Not evaluable	25 (19%)	12 (18%)

CABINET: Subgroup analysis ASCO 2025

Efficacy in well differentiated grade 3 NETs

Table 2. Objective Tumor Response.*

Response	Extrapancreatic NET Cohort		Pancreatic NET Cohort	
	Cabozantinib (N=134)	Placebo (N=69)	Cabozantinib (N=64)	Placebo (N=31)
Objective response — % (95% CI)	5 (2 to 10)	0 (0 to 5)	19 (10 to 30)	0 (0 to 11)
Best overall response — no. (%)				
Partial response	7 (5)	0	12 (19)	0
Stable disease	87 (65)	37 (54)	39 (61)	17 (55)
Progressive disease	15 (11)	24 (35)	5 (8)	12 (39)
Not evaluable	25 (19)	8 (12)	8 (12)	2 (6)



G3: 24 pts had G3 NETs (16 CABO, 8 PB). Primary sites included pancreas (n=12); GI tract (n=7); unknown (n=3); lung/thymus (n=2).

Median PFS by blinded independent central review (RECIST 1.1) for pts treated with CABO was 7.9 months (95% CI, 5.6-NE) vs. 3 months with PB (95% CI, 1.5-NE) (HR 0.15, 95% CI, 0.04-0.57, 1-sided log-rank P=0.0007).

Confirmed overall radiographic response rate was 25% with CABO vs. 0% with PB

PNET cohort, any reduction in target lesions: 80% (45/56) and 24% (7/29) of the cabozantinib vs placebo groups, respectively

THANK YOU!

Panel discussion

Case presentation: Grade 2 small bowel or ileum NET (advanced/metastatic)

Suayib YALCIN, TUR

Hacettepe University Institute of Cancer
Ankara, Turkey

DISCLOSURE

I have no conflicts of interests to declare

De-novo metastatic grade 2 neuroendocrine tumor

- **Age /sex:** 32-year old, male
- **Chief complaint at diagnosis:** Diarrhoea, abdominal pain, flushing
  - The present findings had started 1.5 years before the referral.
- **Medical history:** None
- **Family history:** None
- **Social history:** Non-smoker, no alcohol misuse
- **Allergies:** No known drug allergies

De-novo metastatic grade 2 neuroendocrine tumor

Carcinoid Syndrome was noticed at the time of diagnosis.

- Findings
  - Flushing
  - Diarrhoea
  - Abdominal pain
- Laboratory
  - Baseline: Chromogranin-A – 724,3 ng/mL
  - Baseline: 5-HIAA (24h- Urine): 81.59 umol/d (N:10.46-36.61)

De-novo metastatic grade 2 neuroendocrine tumor

Diagnosis

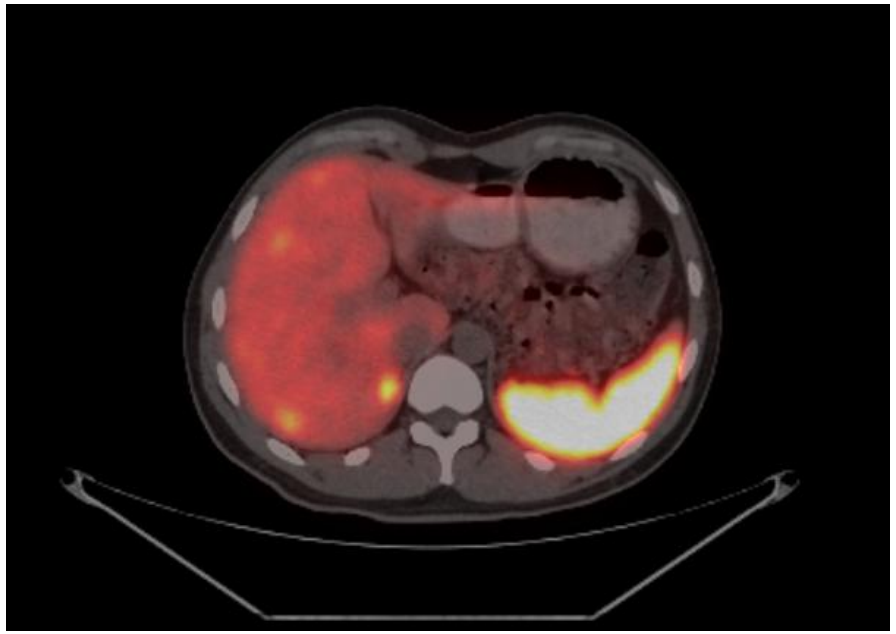
- January 2014 → Small intestinal mass (5cm x 1.5cm) + multiple liver metastases (+ Carcinoid Syndrome)

Treatment Plan

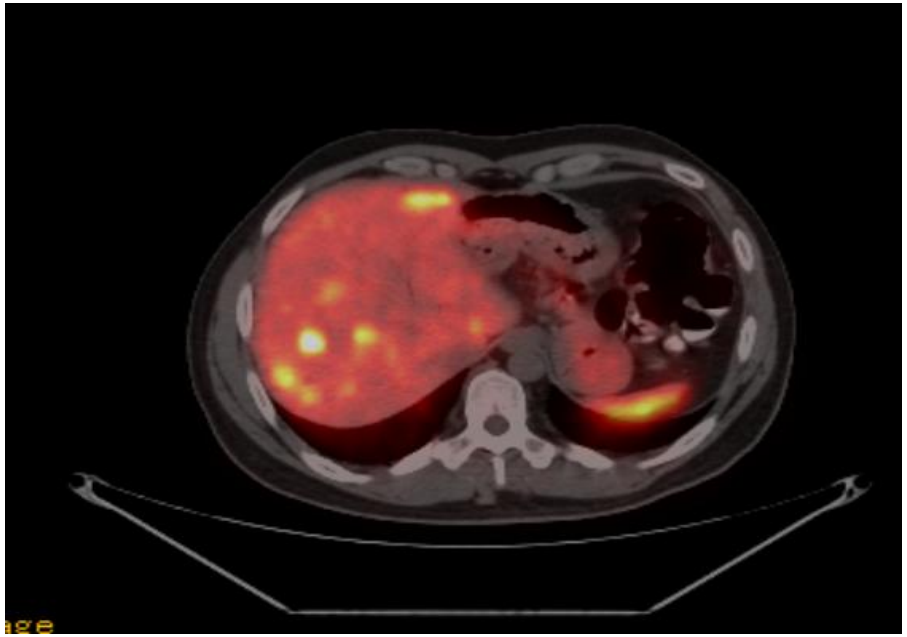
- Small intestinal mass excision performed by his local surgeons
- Referred to our center for further work-up and treatment plan
  - Pathology: Neuroendocrine tumor grade 1 Kİ-67 – 4%
  - Unresectable liver mets
  - Not suitable for ablative treatments
- Liver-directed local therapy for multiple hepatic lesions (Chemoembolization)
- February 2014 – November 2016 → Interferon (Interferon 5 million units/day 3 times a week) + Octreotide (Sandostatin 30 mg/day every 4 weeks)
  - Interferon was used due to carcinoid syndrome

De-novo metastatic grade 2 neuroendocrine tumor

- November 2016 → Progression at liver lesions
  - Chromogranin-A - 223,5 ng/mL (Nadir: 81)

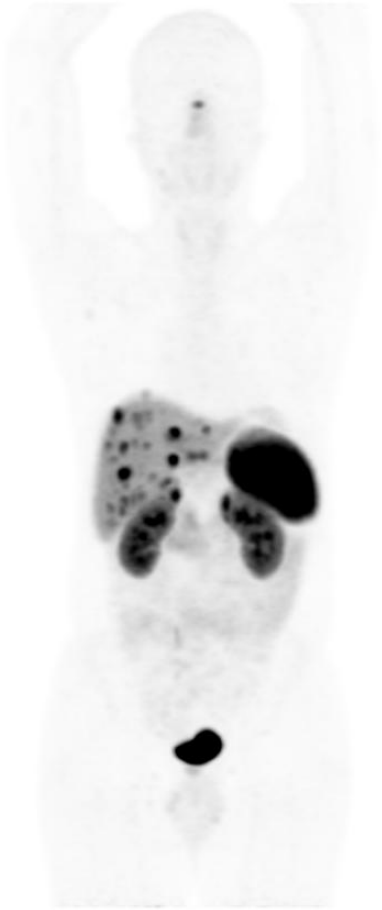


April 2016 Ga68-Pet

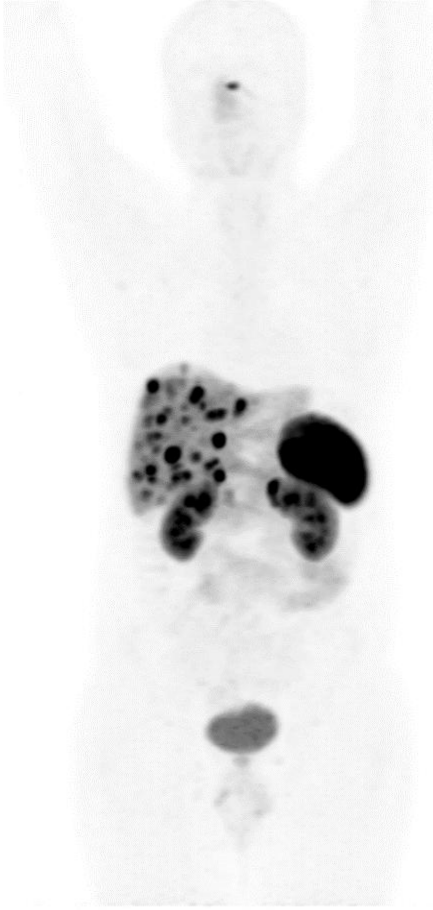


At the time of progression (Nov. 2016)

De-novo metastatic grade 2 neuroendocrine tumor



April 2016



November 2016

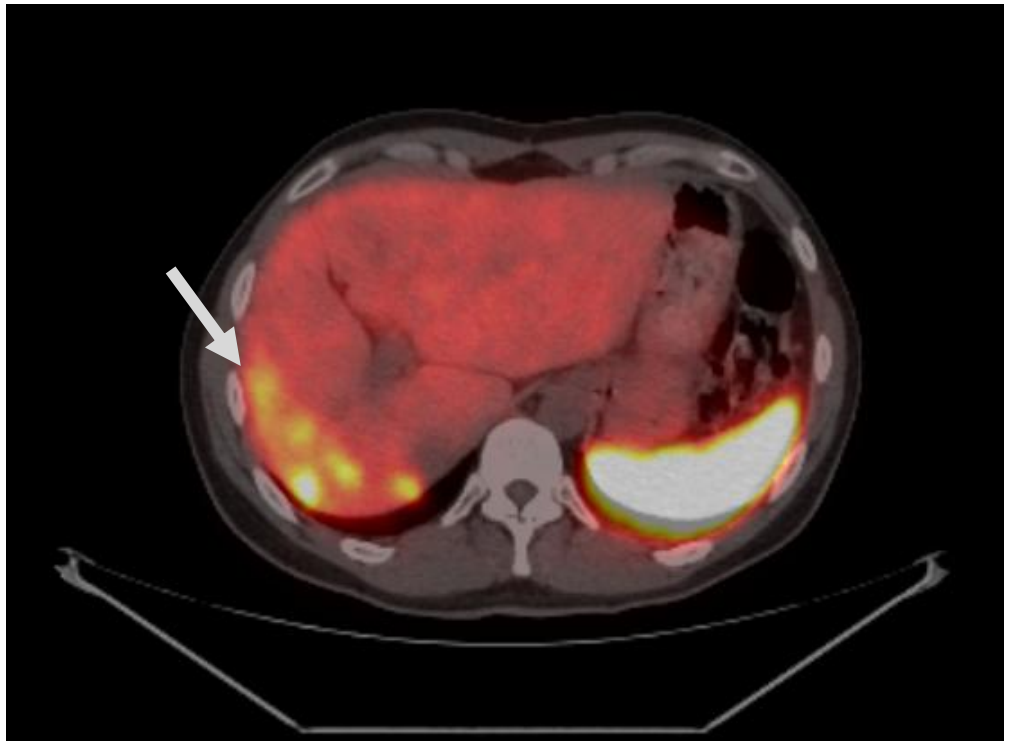
De-novo metastatic grade 2 neuroendocrine tumor

Treatment Plan

- November 2016 – May 2017 → 8 cycles Capecitabine (1500mg/m2) + Temozolomide (150mg/m2) + Lanreotide (Lanreotide 120 mg/day every 4 weeks)
- Lanreotide only between May 2017 – Nov 2018
- November 2018 → Y-90 microsphere therapy administered to the right lobe and left lobe segments 4 and 2-3
  - He was treated with intravenous antibiotics due to a cholangitic abscess following Y-90 microsphere treatment.
- November 2018 – December 2019 → Stable Disease, no carcinoid syndrome findings

De-novo metastatic grade 2 neuroendocrine tumor

December 2019 → Progression at the liver metastasis and aortocaval lymph node



Ga68- PET-CT At the time of Progression (Nov 2019)

Treatment Plan

- Everolimus 1x10mg + Lanreotide (Lanreotide 120 mg/day every 4 weeks)

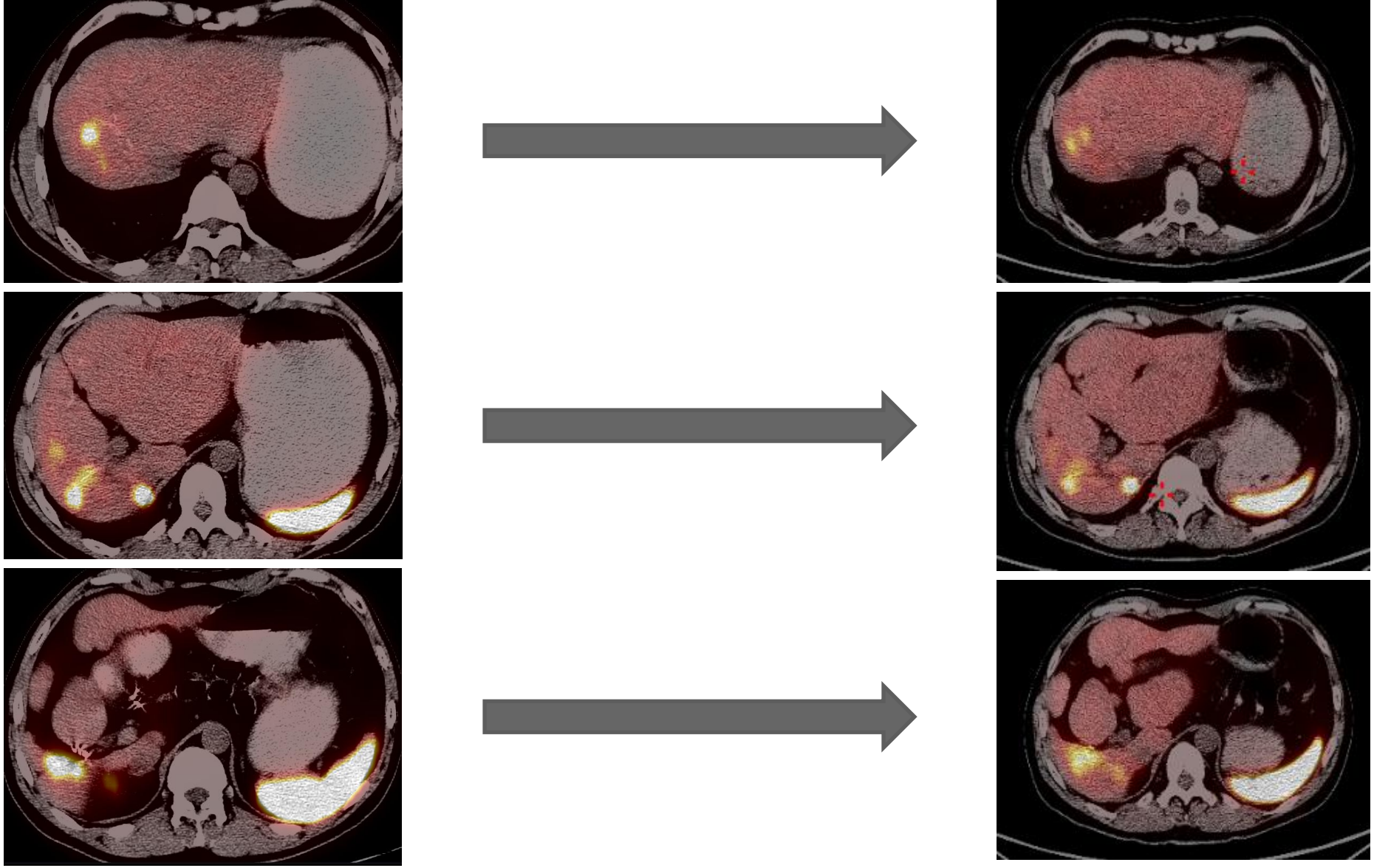
De-novo metastatic grade 2 neuroendocrine tumor

December 2019 – December 2023 → Stable Disease

Symptomatic relapse

Treatment Plan

December 2023 – September 2024 → 4 cycles 200 mCi Lu-177 DOTATATE + Everolimus (1x10mg)



December 2023

June 2024

Panel discussion

Closing comments

Take-home messages

- Multidisciplinary management of these patients is pertinent.
- Re-assessment at multidisciplinary meetings through-out treatment pathway is crucial.
- Consider re-biopsy if clinically appropriate.
- Clinical trials should be considered when available.

A BIG "Thank You" to

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- ✓ The ENETS Education Group
- ✓ YOU, our valued participants

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- **Simona GLASBERG (Lead)** | Endocrinology | Israel
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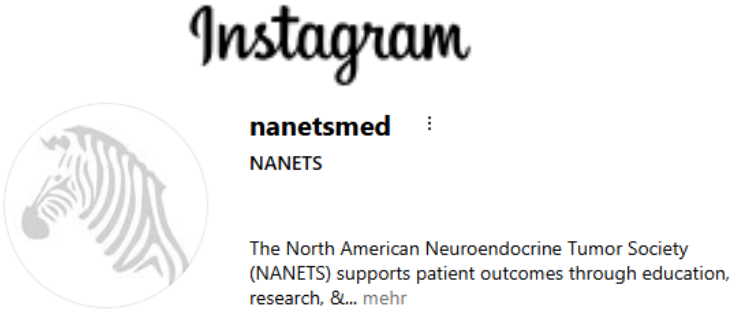

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