5th Milan NET Conference

A live and web multimodal meeting among active Italian NET Centers

Wednesday June 12th, 2019
Fondazione IRCCS Istituto Nazionale dei Tumori
Milano

Session 3: Web Multimodal Tumor Board

Tumor Board 1

Case1

Retroperitoneal Pheochromocytoma

C.F. 33 yo

BMI 25
PS (ECOG) 0

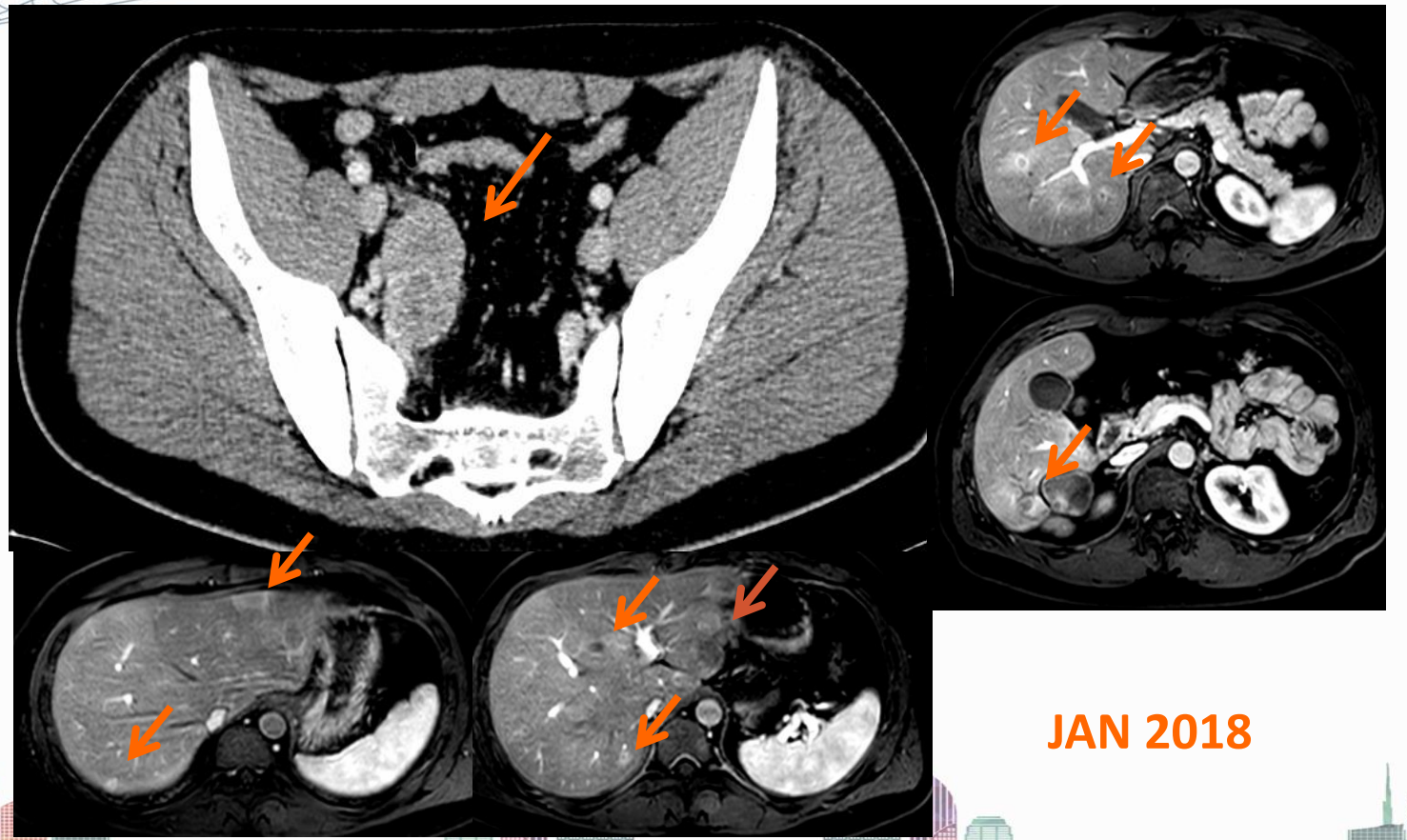
Medical history

Orthopedic surgery
Cryptorchidism

In other Center…

2017
Hypertransaminasemia and hypertensive crisis

JAN 2018
CT scan: on the liver multiple bilateral localizations. In the pelvis: 47x30 mm parenchymatous lesion close to the right iliac vessels
18FDG PET scan: Intense enhancement in pelvis and inhomogeneous hepatic hypermetabolism



JAN 2018

In other Center…

FEB 2018
Liver biopsy: NET G1 (WHO2010) Sinapto+, CgA+, Ki67: 1%

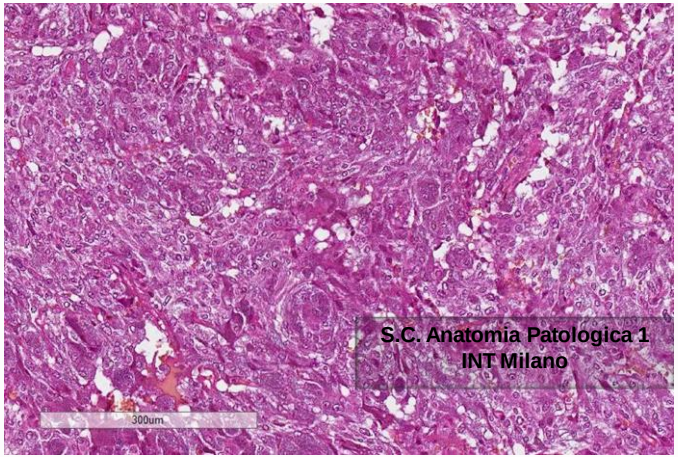
MAR 2018
Sandostatina LAR 20 mg/28

JUN 2018
CT scan *SD* → **PRRT in LUTHREE protocol**

SEP 2018
Metanephrine **2923** (nv<320),
normetanephrine **3622** (nv<390),
vanilmandelic acid **20.8** (nv<6/24h)

IN INT (TUMOR BOARD DISCUSSION SEP 2018)

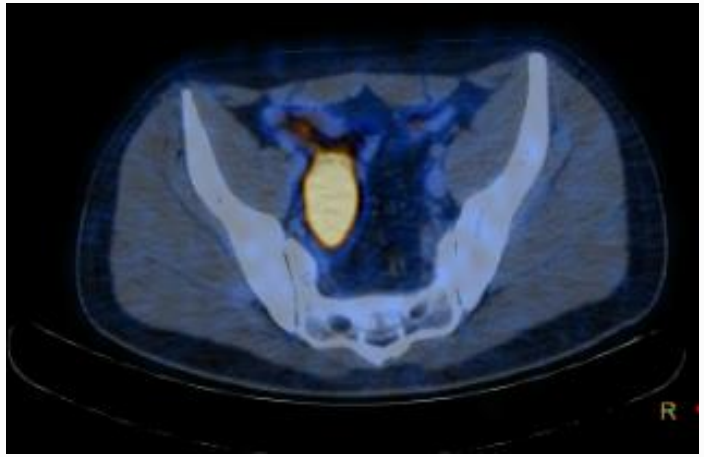
OCT 2018 ***68GaPET*** *"…* intense enhancement in **pelvis**, inhomogeneous **hepatic** hypermetabolism and suspected enhancement at **the left scapula spine** …"



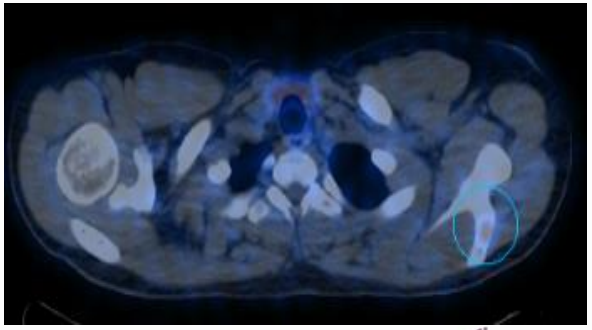
NCI hystological evaluation NET G1 (WHO 2010) Mitotic index: 1/10 / HPF Chromogranin-A: + Synaptophysin: + CDX-2: - TTF1: - Islet -1: + Vimentin: + Citocheratin cam 5.2: -

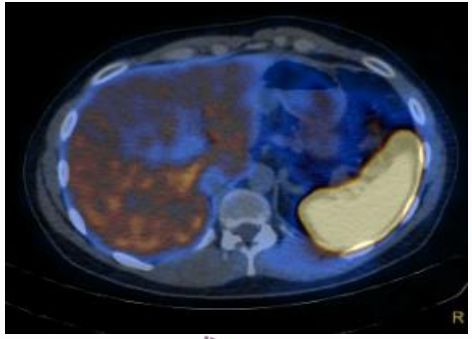
MIB-1 / Ki- 67: 0.5%

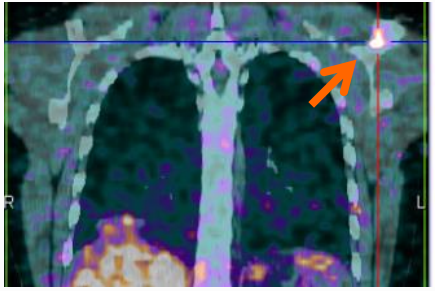
The immunophenotypic picture suggests to evaluate also the origin from paraganglia system.



OCT 2018



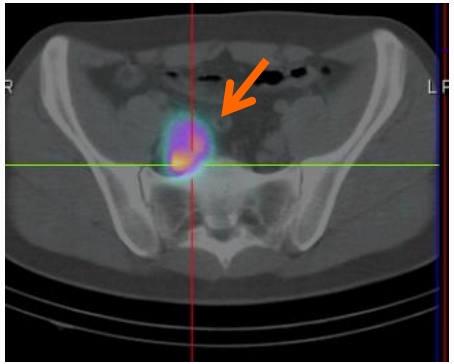


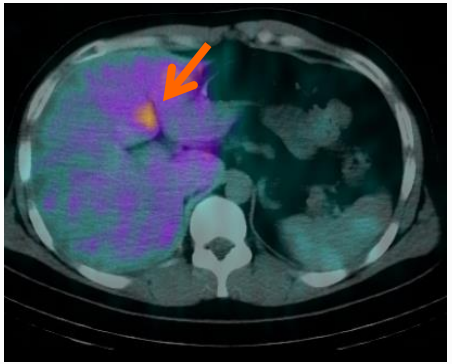


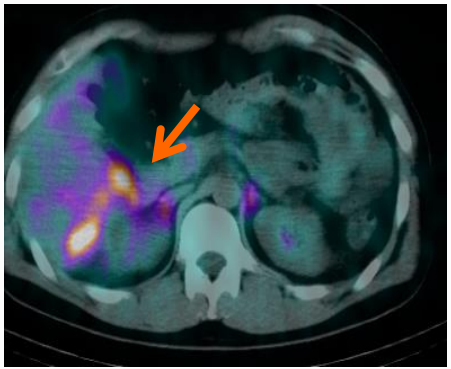
In INT

DEC 2018 ***mibg Scintigraphy***

intense enhancement in pelvis, left hepatic lobe, on the liver segment 5 and enhancement at the left scapula spine







FEB 2019

Pelvic lesion resection and liver IOUS

<u>In order to treat important hypertensive crises</u>

At Pathology: Paraganglioma.
Mitotic index: 1/10 / HPF
Synaptophysin: + Citocheratin pool: - Chromogranin-A: + Vimentin: +
MIB-1 / Ki-67: 0.2%
Epitheliomorphic alveolar architecture
PASS score: not assessable

RET mutations on peripheral blood: no mutations

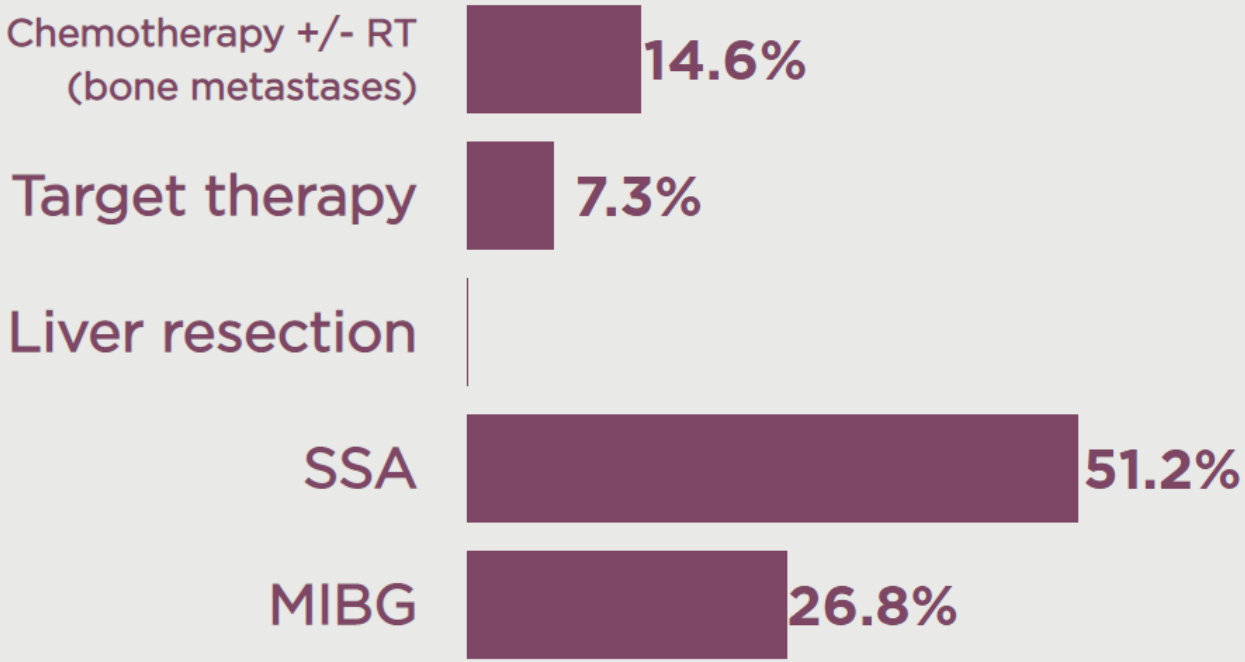
APR 2019

Metanephrine **667** (from 2923) (nv<320),
normetanephrine **617** (from 3622) (nv<390)

Which treatment would you propose next?

1. Chemotherapy +/- RT (bone metastases)
2. Target therapy
3. Liver resection
4. SSA
5. MIBG

Which treatment would you propose next?



Session 3: Web Multimodal Tumor Board

Tumor Board 1

Case 2

Therapy-resistant Insulinoma

Male, 50 y.o.
PS (ECOG): 0

Past medical history

negative

Oncological history

Apr 2016:
abdominal pain and increasing of lipase.
Abdominal-US: pancreatic body hypoechogenic lesion

Diagnostic Work-up

APR 2016

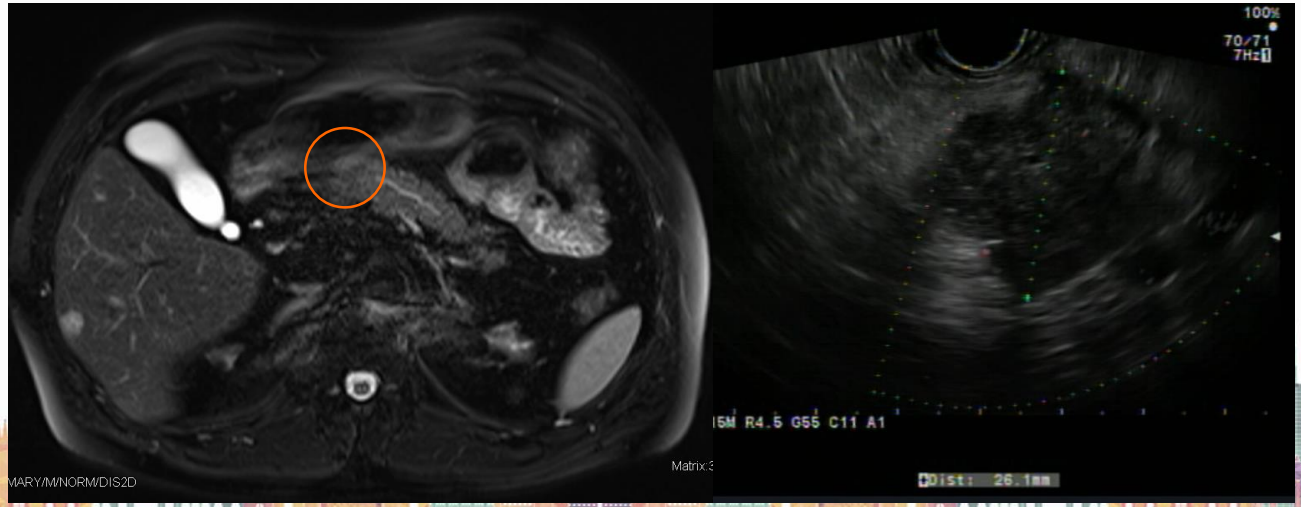
CT-scan: pancreatic inhomogeneity

Abdominal MRI: nodular lesion (Ø15 mm) in the pancreatic isthmus. S6 lesion referable to angioma even if with not completely typical characteristics

JUN 2016

EUS: hypoechoic solid focal area at the body-tail of the pancreas (Ø26 mm).

Biopsy report: the overall framework is strongly suspected by neoplasia with acinical differentiation.



Surgery and 1st disease progression

SEP 2016

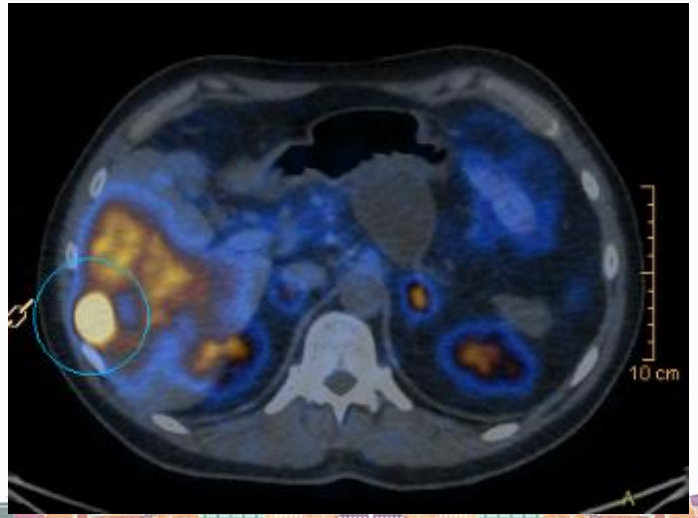
VLS Distal spleno-pancreatectomy and locoregional lymphadenectomy.
Intraoperative ultrasound: S6 lesion (Ø 20 mm) highly vascularized with angiomatous features. No biopsy done

At pathology: **pNET G2 pT3N1 (1/8) R0 Ki 67: 13%**

NOV 2016

CT-scan: nodular hepatic lesion in S6 (Ø 25 mm)

Ga68-PET: focal uptake of the tracer (SUV 60) in S6



Multidisciplinary approach

DEC 2016

Start treatment with somatostatine analogue (SSA): **Octreotide LAR 30mg 1vl/monthly.**

Tumor Board discussion: indication to liver resection.

FEB 2017

VL atypical liver resection of S6.

At Pathology: **pNET R0 Ki 67 7.5%**

MAR 2017

Tumor Board discussion: stop treatment with SSA and indication to follow up.

Relapse

MAY 2018

CT-scan: multiple metastatic liver lesions.

Ga68-PET: multiple liver lesions with high tracer uptake.

JUN 2018

Restart: **Octreotide LAR 30 mg 1 vl monthly**

SEP 2018 - NOV 2018

Onset of dizziness, shakiness, hunger, weight gain.

Start treatment with **diazoxide 100 mg 1 tabx3/day.**

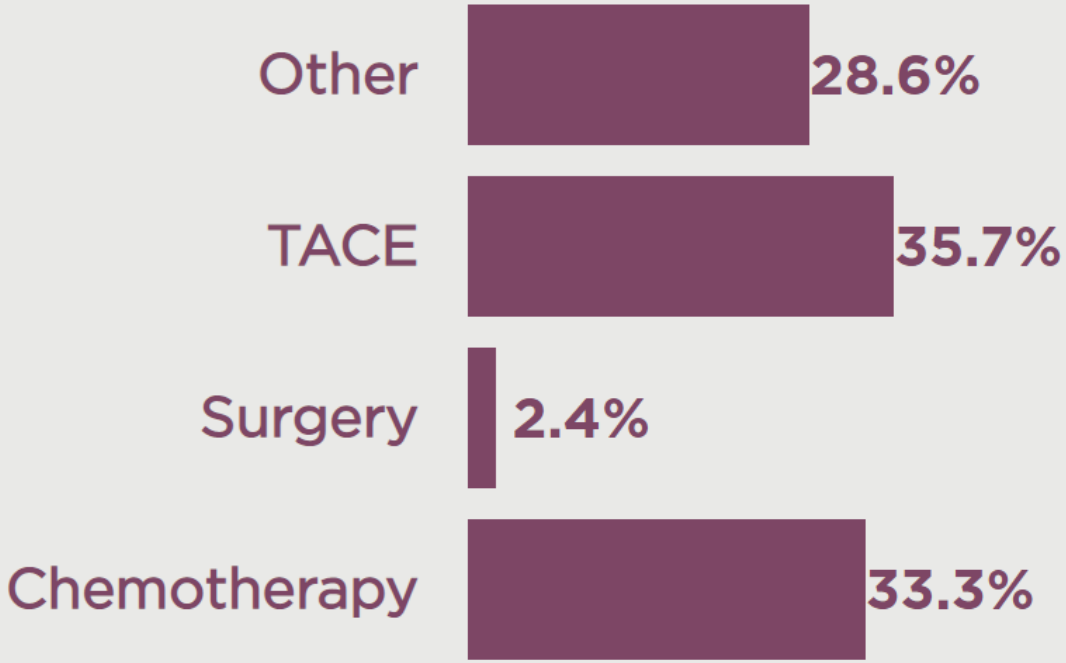
CT-scan: progression of hepatic lesions

Glycemia	25 mg/dL
Insuline	104.9 µU/mL
C Peptide	9.1 ng/mL

Which treatment would you propose next?

1. Chemotherapy
2. Surgery
3. TACE
4. Other

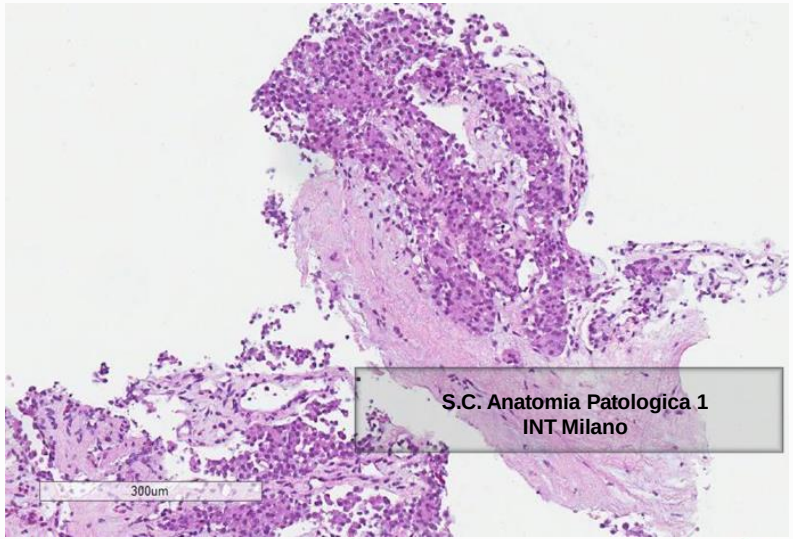
Which treatment would you propose next?



NOV 2018

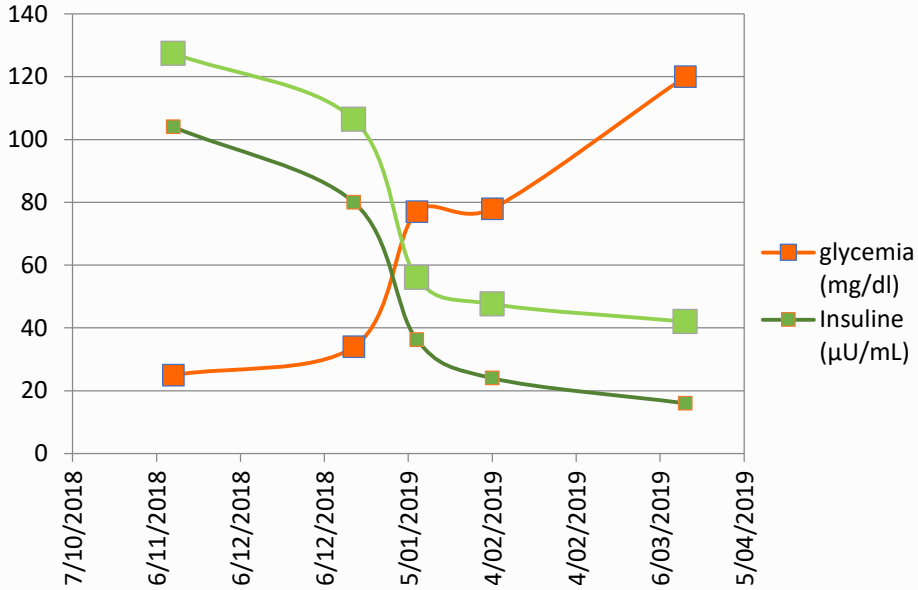
TACE: unsuccessful attempt for anatomy inaccessibility.

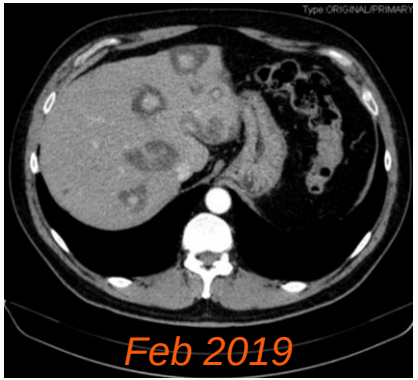
Liver biopsy: **pNET Ki 67 5%. IHC: insuline positive**

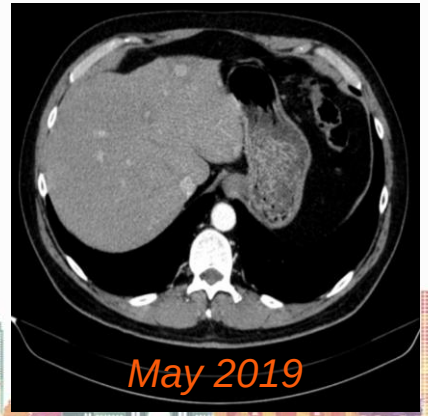


Last follow up

Start chemotherapy with **FOLFOX** regimen (cycle 10 on May 25th)







Session 3: Web Multimodal Tumor Board

Tumor Board 1

Case 3

pNET Liver Metastases

Female, 37 y.o.
PS (ECOG): 0

Past medical history

ocular angiomatosis

Oncological history

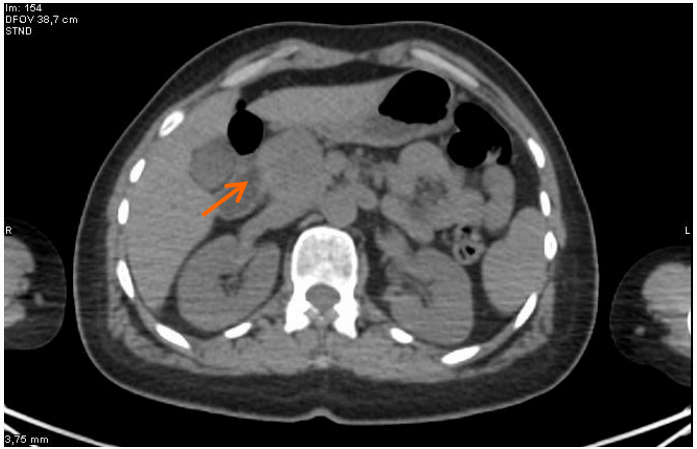
2012

resection of endolymphatic sac tumor

Diagnostic Work-up

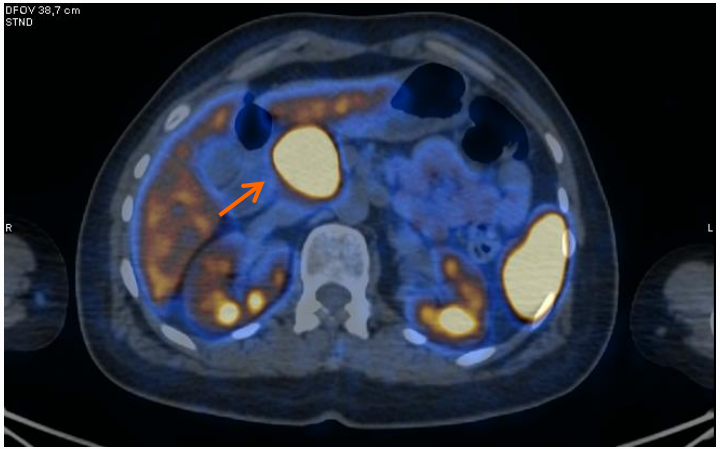
JUL 2014

CT-Scan: 4 solid pancreatic lesions



AUG 2014

Ga68 PET: pancreatic pathological uptake

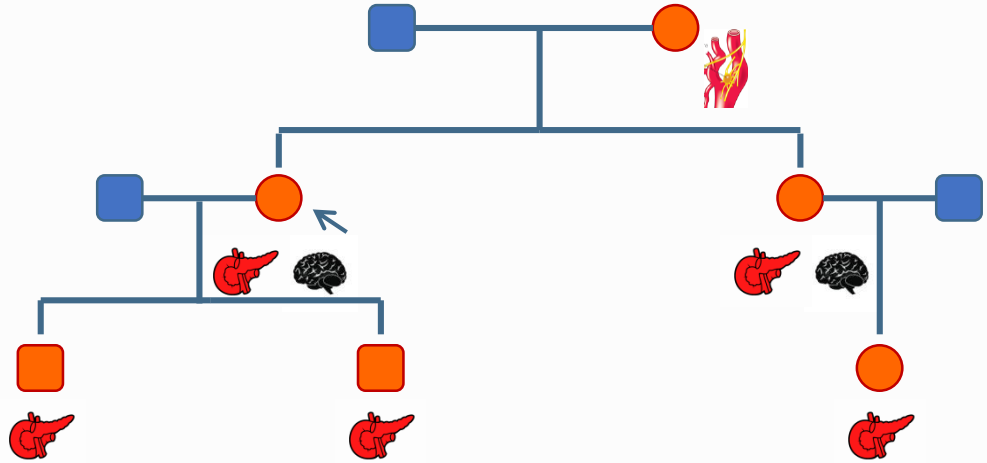


OCT 2014 Whipple's procedure.

At Pathology: *one nodule **NET G3 Ki 67 30%;** 3 nodules **NET G2 Ki 67 2.7%** and **5.9%*** **pT3 N0 (0/23)**

Beginning of follow-up

Family History

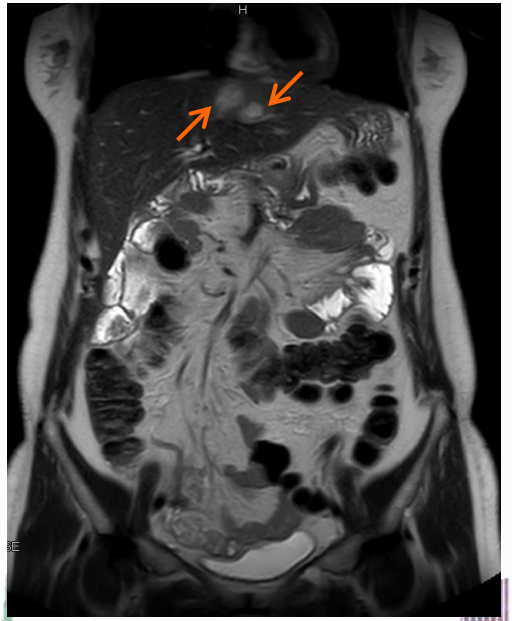


von Hippel Lindau syndrome

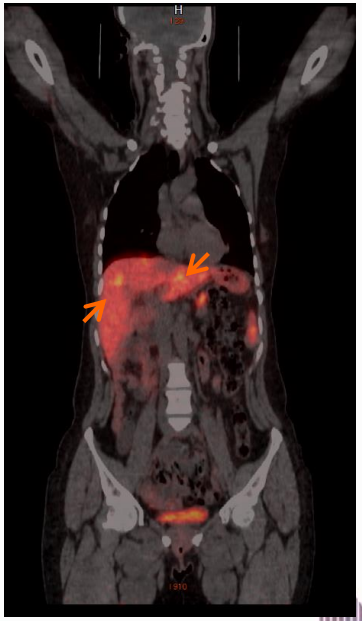
VHL mut P86A

Recurrence

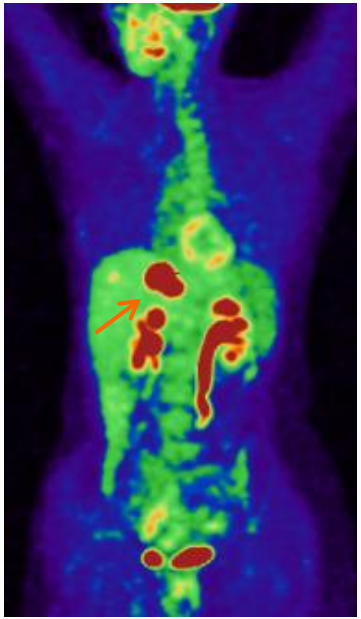
OCT 2018
MRI-Scan: multiple bilobar liver metastases (3.5 and 2 cm)



NOV 2018
Ga68 PET: hepatic pathological uptake



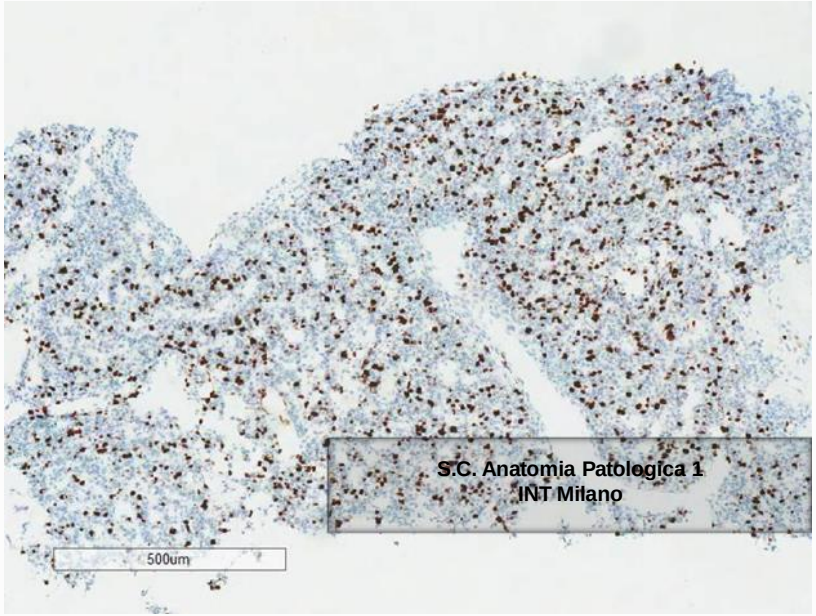
NOV 2018
FDG PET: hepatic pathological uptake



FEB 2019

Liver biopsy

At Pathology: NETG3 Ki 67 30%

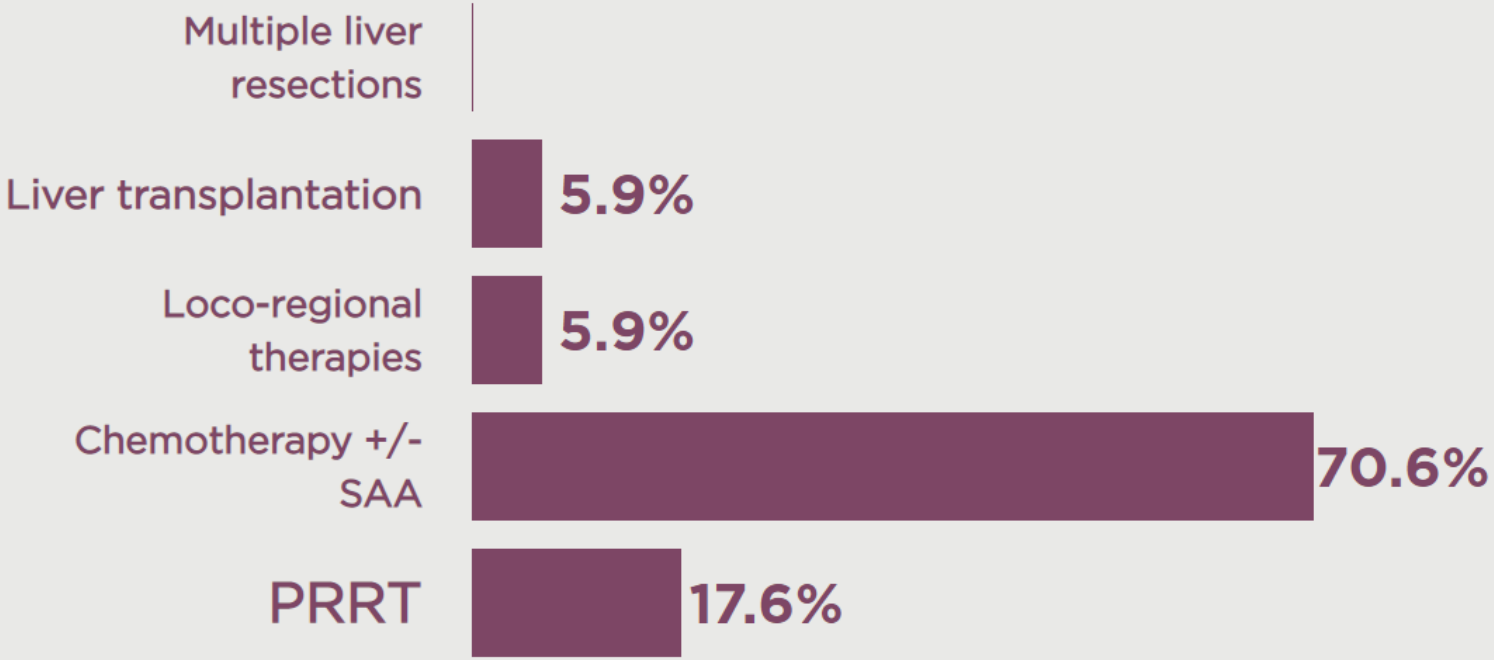


Start **lanreotide** 120 mg q28

Which treatment would you propose next?

1. Multiple liver resections
2. Liver transplantation
3. Loco-regional therapies
4. Chemotherapy/target therapy +/- SAA
5. PRRT

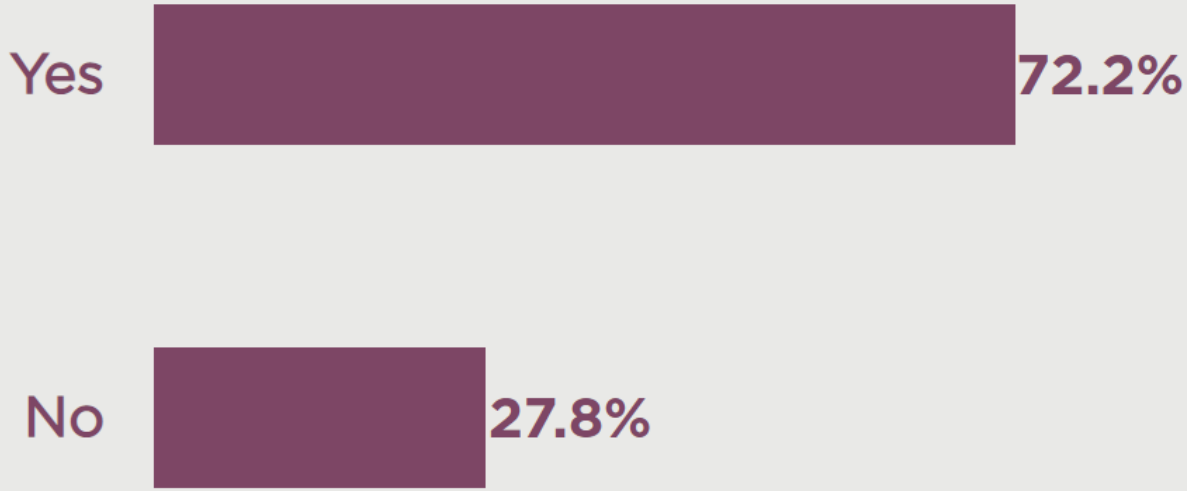
Which treatment would you propose next?



Does the VHL syndrome change our choice?

1. Yes
2. No

Does the VHL syndrome change our choice?



Session 3: Web Multimodal Tumor Board

Tumor Board 1

Case 4

Paraneoplastic syndrome in lung carcinoid

Female 73 yo

PS (ECOG) 0

Medical history

Active smoker (1 pack/year)

1998

left breast conserving surgery and axillary dissection for IDC G2 pT1N0M0 → RT/HT (tamoxifen)

Diagnostic Work-up

JAN 2017

Exeresis of cutaneous lesion of the scalp

At Pathology: dermal localization of well differentiated neuroendocrine tumor consistent with atypical carcinoid of the lung;

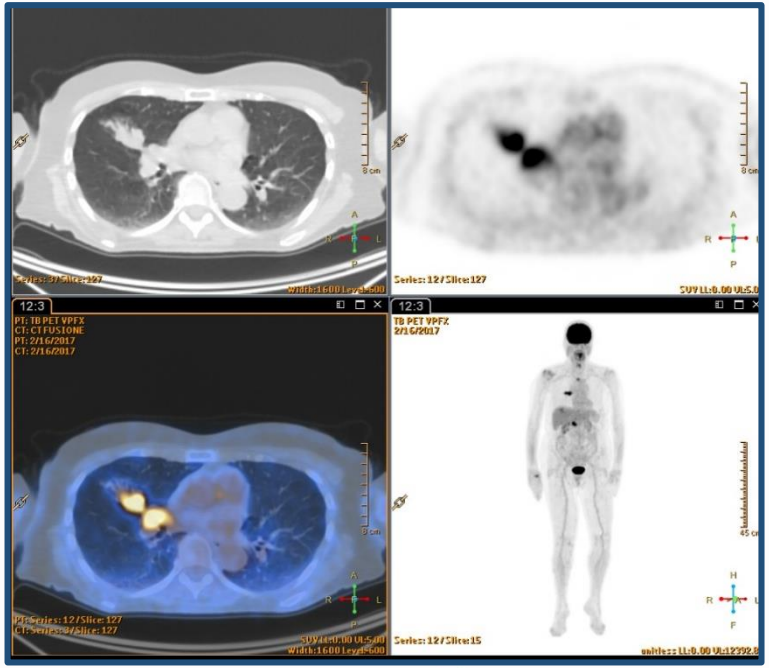
3 mitoses/mm2; Ki67: 18%.

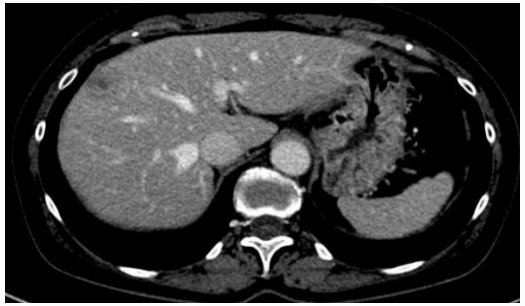
Immunophenotype:

- CK7+, AE1-3+, TTF-1+, synaptophysin +, CgA+ EMA+;
- CK20-,PAX8-,CDX2-, SOX10-, CD34-,HMB45-, S100-

CT scan/18-FDG PET: pulmonary, nodal, liver, pancreatic and bone localizations

68-GaPET: lung and skeleton uptakes





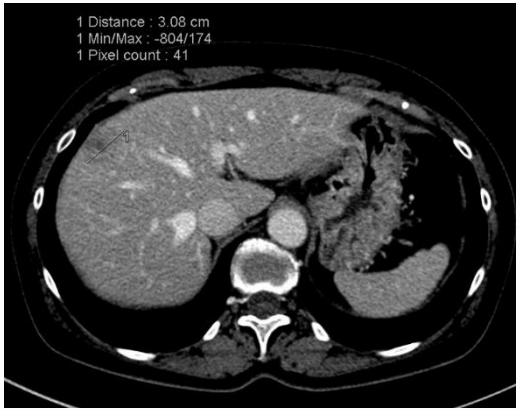
Liver biopsy:

well-differentiated neuroendocrine malignancy (immunophenotype consistent with that of the cutaneous lesion)

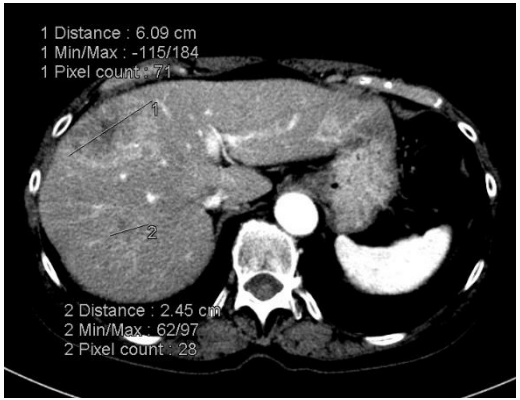
Treatment

MTB discussion: **first line systemic treatment with SSA**

MAR 2017 - SEP 2017: **Lanreotide 120 mg q28d**



FEB 2017



SEP 2017

OCT 2017

MTB discussion: **Second line therapy with everolimus 10 mg/day**

Best response: stable disease

MAR 2018

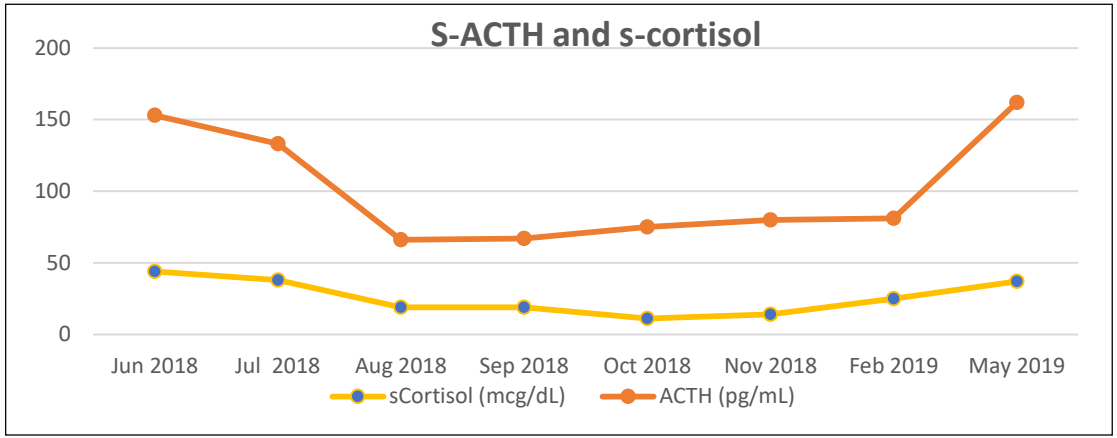
gradual onset of bilateral leg oedema, hirsutism, skin pigmentation, hyperglicaemia, fatigue, proximal limb muscle hypotrophy

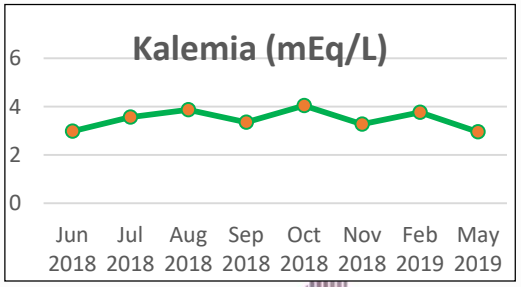
Test	Value
sACTH	109 ng/L (UNL 46)
24h Urinary cortisol	1082 mcg/24h (UNL 320)
Testosteron	0.48 ng/mL (UNL 0.48)
Delta-4-androstenedione	2.7 ng/mL (UNL 2.3)
DEHAS	2219 ng/mL (UNL 300)
Nugent Test	No cortisol suppression
CRH Test	Negative for ACTH/cortisol increment

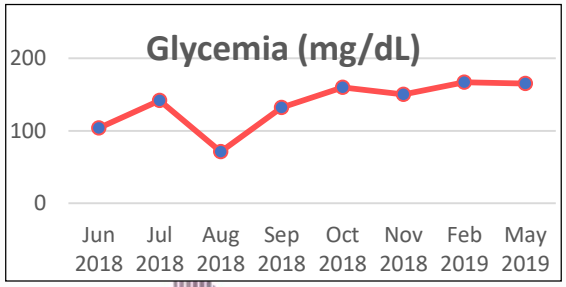
Diagnosis of paraneoplastic Cushing syndrome
Ectopic ACTH secretion

JUN 2018

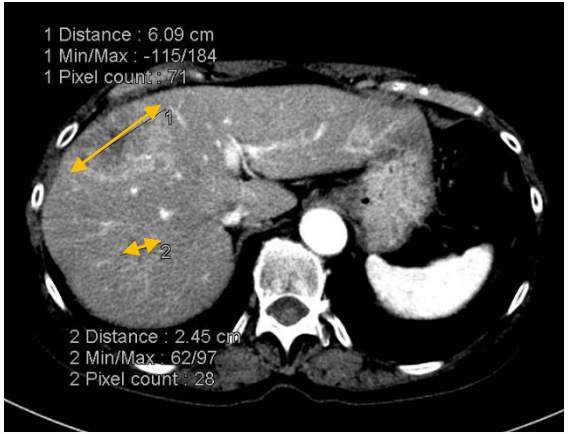
Treatment with metirapone (11-β-hydroxilase inhibitor)



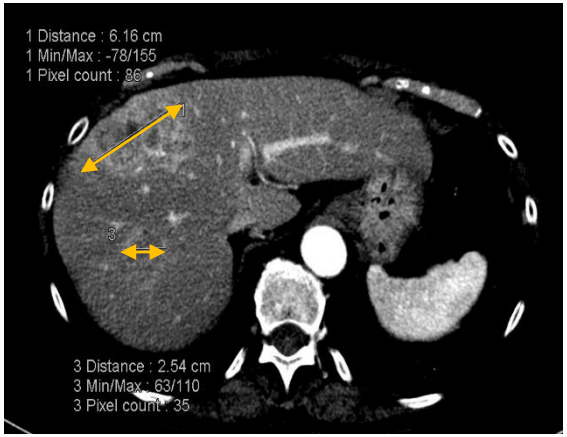




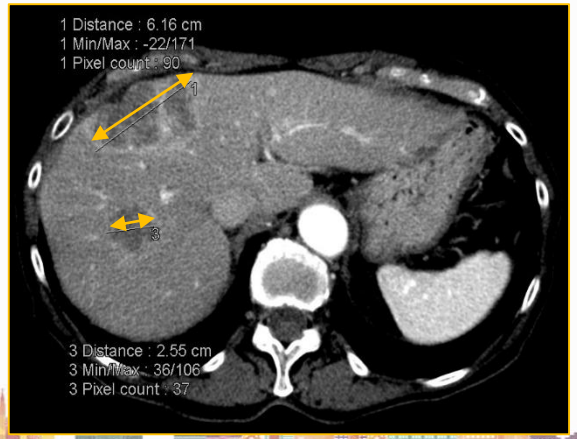
SEP 2017



FEB 2018



MAR 2019



Everolimus ongoing toxicities:

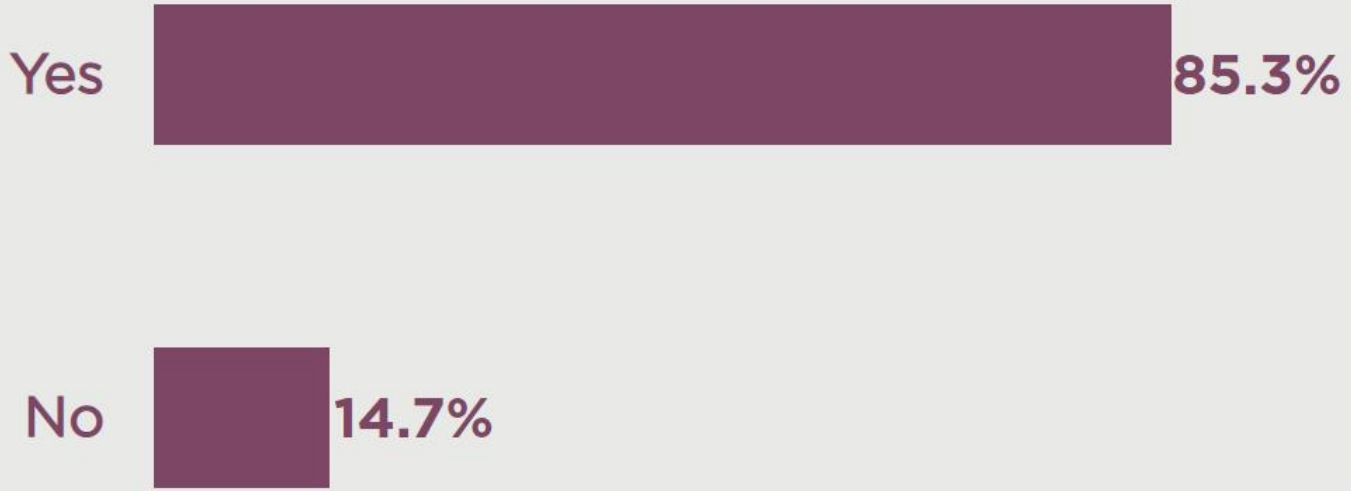
Dyslipidemia G1

Stomatitis G1

May the onset of paraneoplastic syndrome be considered as disease progression?

1. Yes
2. No

May the onset of paraneoplastic syndrome be considered as disease progression?



How shoud we treat paraneoplastic ACTH hyperproduction?

1. SSAs (+ everolimus)
2. Chemotherapy
3. PRRT
4. Surgery (bilateral adrenalectomy)
5. Tapering of symptomatic treatment

How shoud we treat paraneoplastic ACTH hyperproduction?