

SELNET MDT

20/9/2024

Coordination: Fondazione IRCCS Istituto Nazionale dei Tumori,
Italy

Case 1

Boris Itkin, Oman

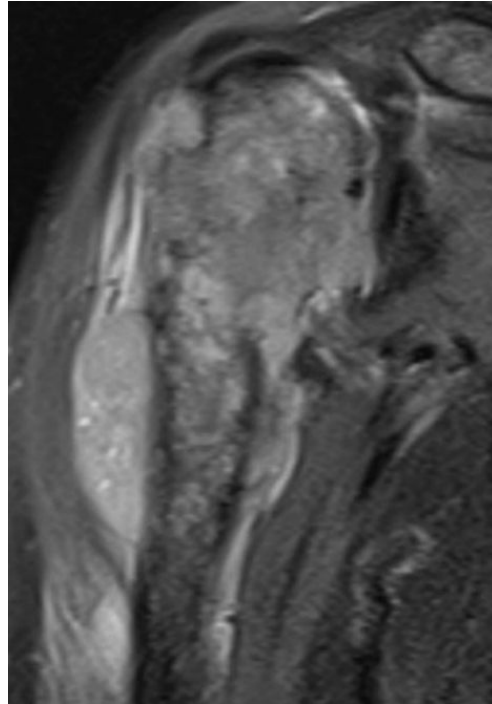
28 yo F

PMH and comorbidities: nil

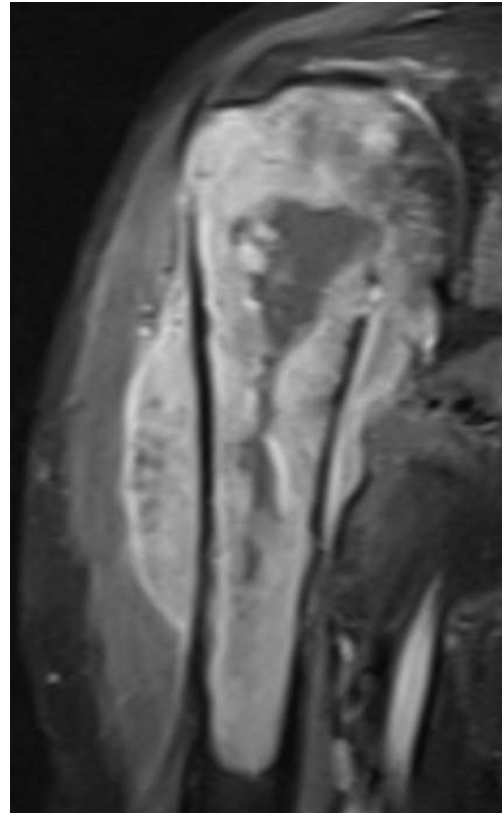
Present illness: 3 months history of right upper arm progressive swelling with moderate pain and decreased ROM in left arm.



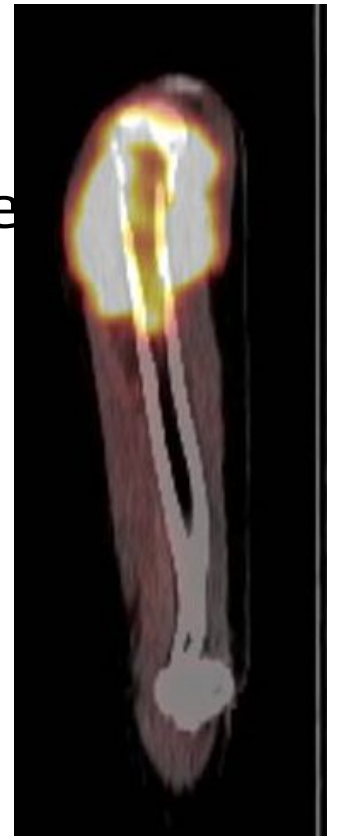
XR: Permeative changes with erosions and reduced density, soft tissue swelling, pathological fracture of neck of humerus



MRI: Contrast enhancing mass, 10.1 cm



7x10x7.6 cm
, SUVmax
12.8



PET/CT: large FDG avid right proximal humeral mass, involves intramedullary cavity and proximal meta-diaphysis with soft tissue component. Likely reactive ipsilateral axillary and supraclavicular nodes.

Biopsy:

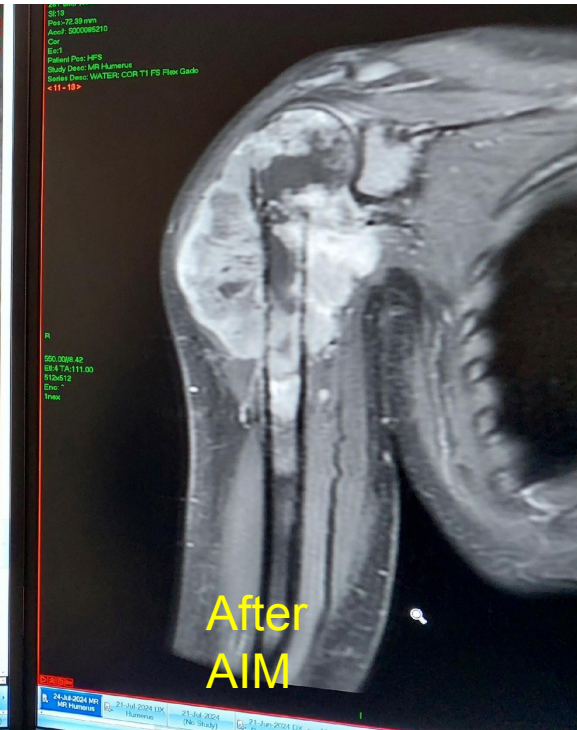
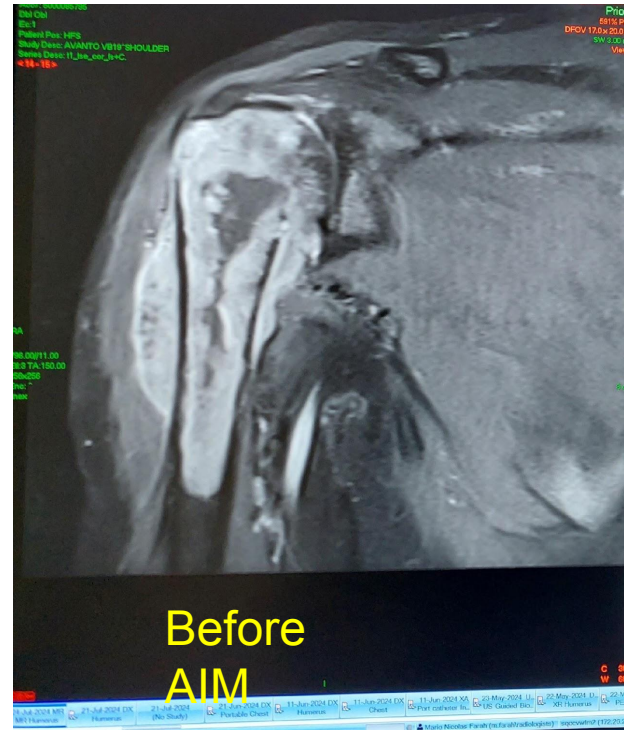
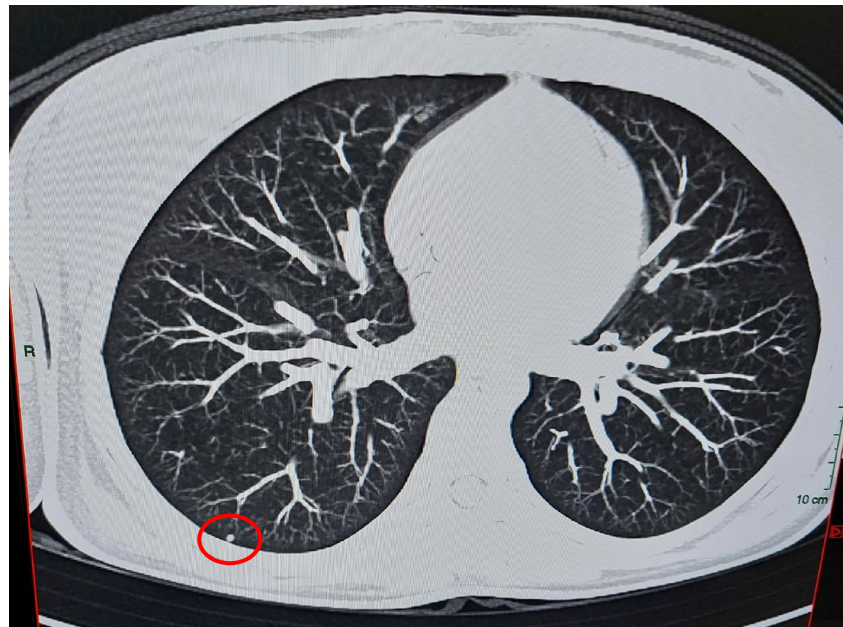
- Mildly to moderate cellular fascicles of spindle cells with moderate atypia embedded in fibrosclerotic stroma. Hyperchromatic, large nuclei. Foci of necrosis
- Positive: SMA strongly, S100 focally, TLE focally, H3KMe27 focally
- Negative: AE1/3, EMA, Desmin, Myogenin, MyoD1, CD3, WT1, MUC4, SOX10, BetaC

Pathology review:

- Neoplastic cells are positive for TLE1, SMA, H caldesmon with focal reactivity for BCL2.
- The cells show negative staining for MDM2, CDK4, CD99 and EMA
- Diagnosis: Spindle cell sarcoma, high-grade. FNCLCC Grade: 3

She received **3 cycles of AIM** with radiological progression and underwent complete resection.

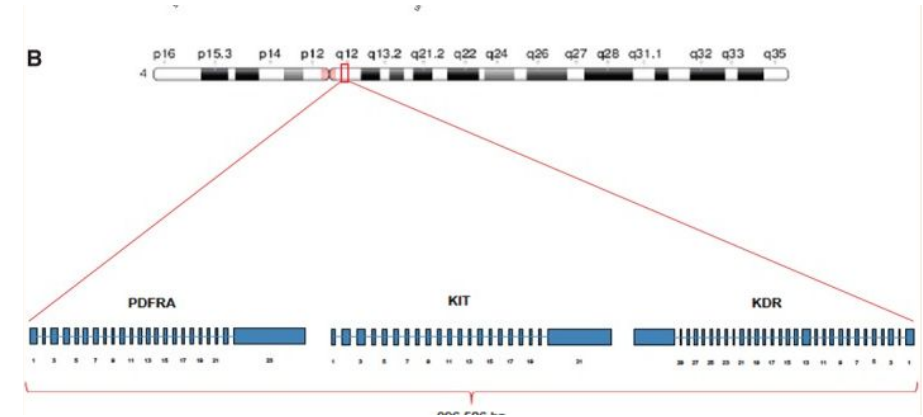
Restaging images showed



WETS: co-amplification of VEGFR2, KIT, PGFRA, MAP2K4: probable 4q12amp

Genes Tested with Pathogenic or Likely Pathogenic Alterations

Gene	Method	Analyte	Variant Interpretation	Protein Alteration	Exon	DNA Alteration	Variant Frequency
KDR (VEGFR2)	CNA-Seq	DNA-Tumor	Amplified	-	-	-	-
KIT	CNA-Seq	DNA-Tumor	Amplified	-	-	-	-
MAP2K4	CNA-Seq	DNA-Tumor	Amplified	-	-	-	-
PDGFRA	CNA-Seq	DNA-Tumor	Amplified	-	-	-	-



Disel U, The Pan-Cancer Landscape of Coamplification of the Tyrosine Kinases KIT, KDR, and PDGFRA. *Oncologist*. 2020 Jan;25(1):e39-e47. doi: 10.1634/theoncologist.2018-0528. Epub 2019.

Table S2: All four known 4q12amp cases with response to TKIs. four cases with response to TKIs are listed here, which are the three index cases newly reported in this series, as well as the best responder from Ho et al. The predominant type of response is stable disease, and average duration of response across cases 1,2, and 4 was 20+ months, with case 3 excluded as mortality was due to non-neoplastic causes.

Index Case	Disease as Diagnosed by Treating Team	Age/Sex	TKI	Best Response	Response Duration
1	MPNST	44/F	Pazopanib	SD	>3 years
2	Ameloblastoma	58/F	Imatinib	SD	>24 months
3	Adnexal Carcinoma	42/M	Imatinib	Clinical Benefit (Suppl Figure 3)	6 week*
4	Adenoid Cystic Carcinoma (Ho et al, PMID: 27566443)	NA	Axitinib	SD	>21 months

*Patient 3 had mortality from non-neoplastic causes-- Supplemental Table 3

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Table S4: Inhibitory coefficients for various TKI's against KIT, KDR, and PDGFRA.

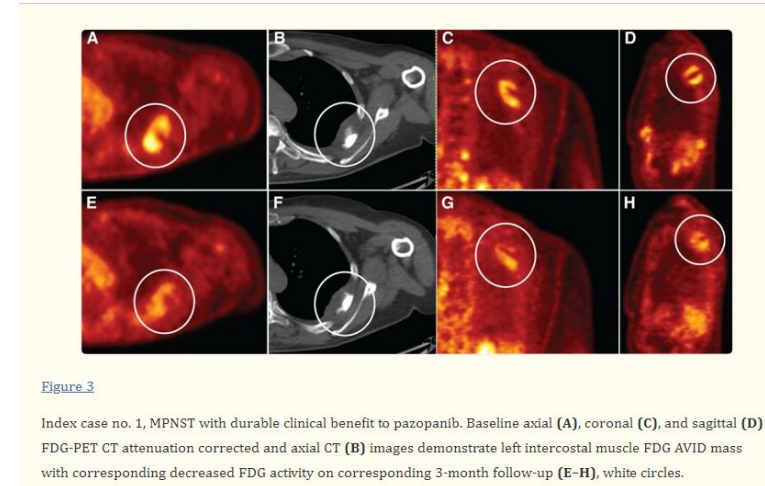
	KIT	KDR	PDGFRA
Imatinib	2 nm Ki	>1um	18 nm (IC50)
Pazopanib	2.3 nm Kd	8 nm Kd	4.9 nm Kd
Axitinib	0.49 nm Kd	0.02 nM Ki	0.51 nm Kd

Question to the board:

- What is the diagnosis?
- What is the next treatment? Postop cytotoxic chemo?
- Sunitinib, Axitinib, Pazopanib, or Imatinib were reported to be effective against 4q12amp tumors. In our case, if the lung nodule will grow, is here a role for TKIs?

4q12amp

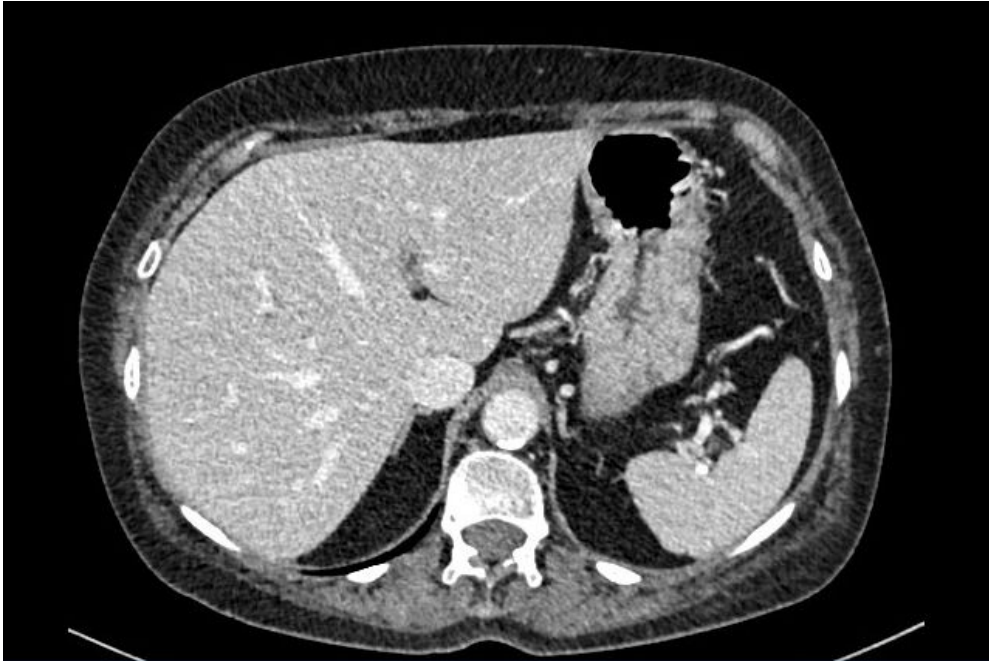
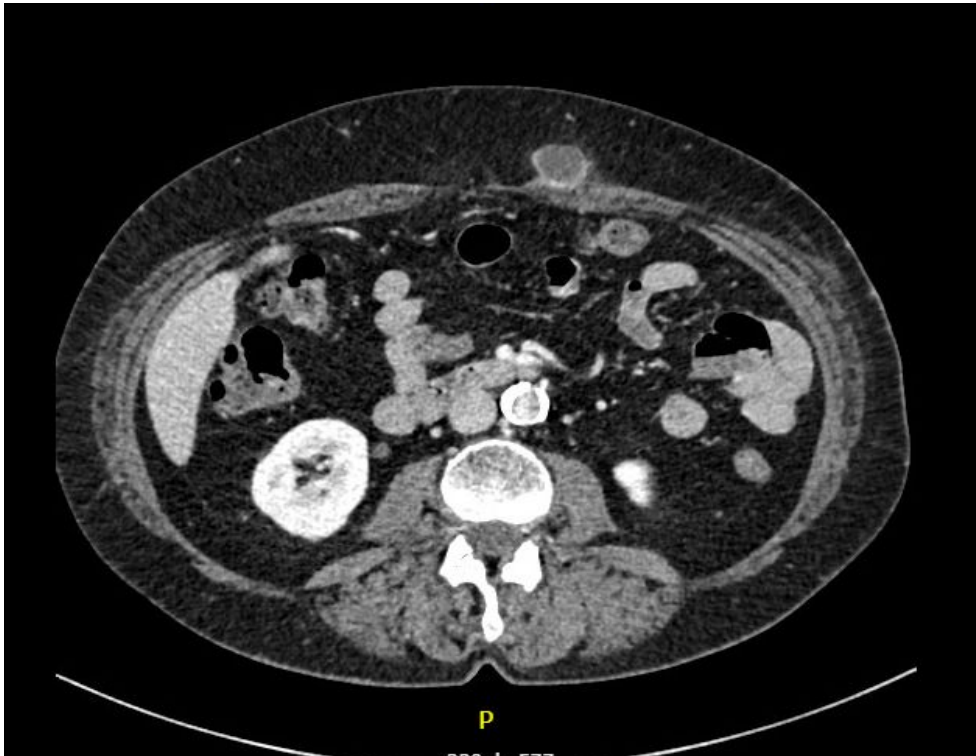
- 0.65% of all cancers (740/114,200),
- Median copy number == 10,
- 4.8% of GBM
- 0.83% of lung cancers
- 0.77% of breast cancers
- **1.9%** of sarcomas
- **In sarcomas:** 7.1% of osteosarcomas (26/367) and 2.8% of soft tissue sarcomas NOS (22/780) harbored 4q12amp.
- Of 4q12amp lung cancer cases, the supramajority (86%) did not harbor known oncogenic drivers of NSCLC (alterations of EGFR/HER2/MET, ALK/ROS/RET fusions, or BRAF V600E).
- Cases of durable responses to pazopanib and imatinib will be described in undifferentiated sarcoma, synovial sarcoma, and head and neck/ salivary cancers.



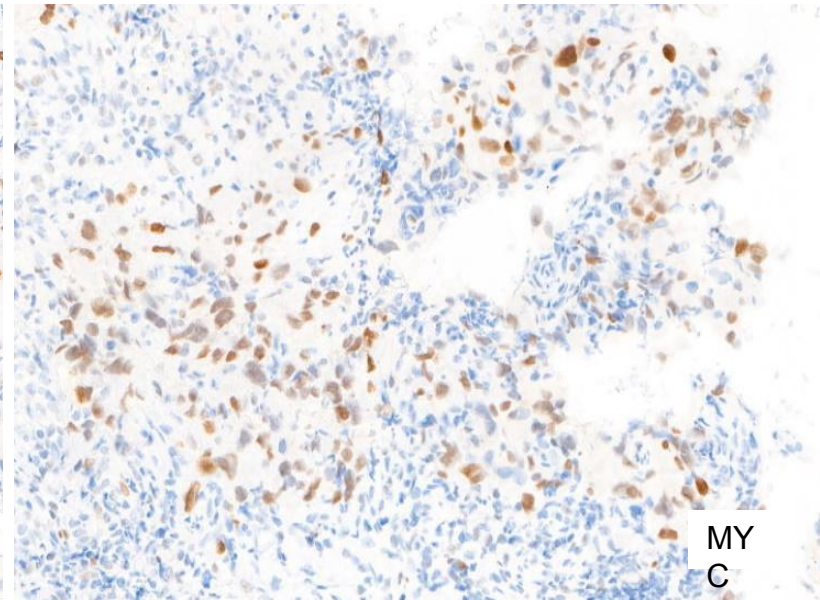
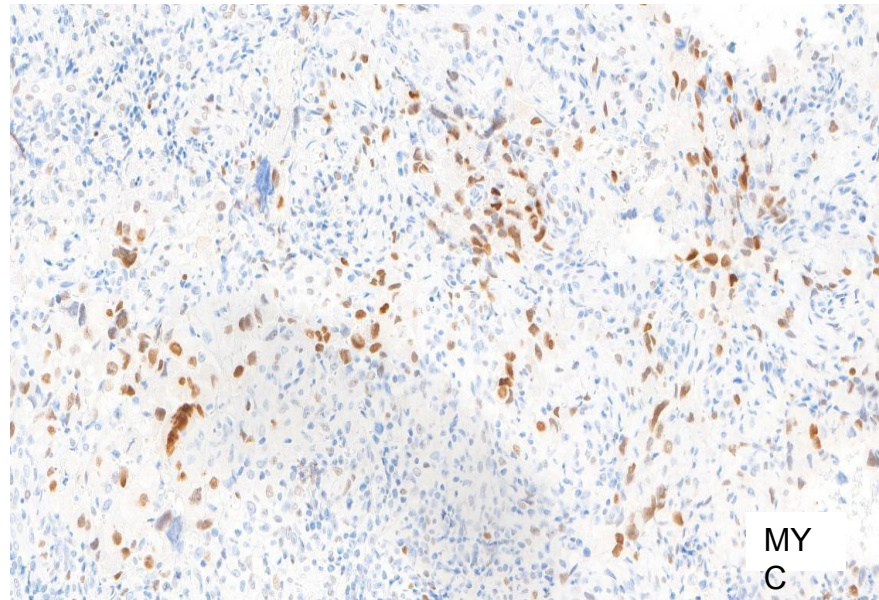
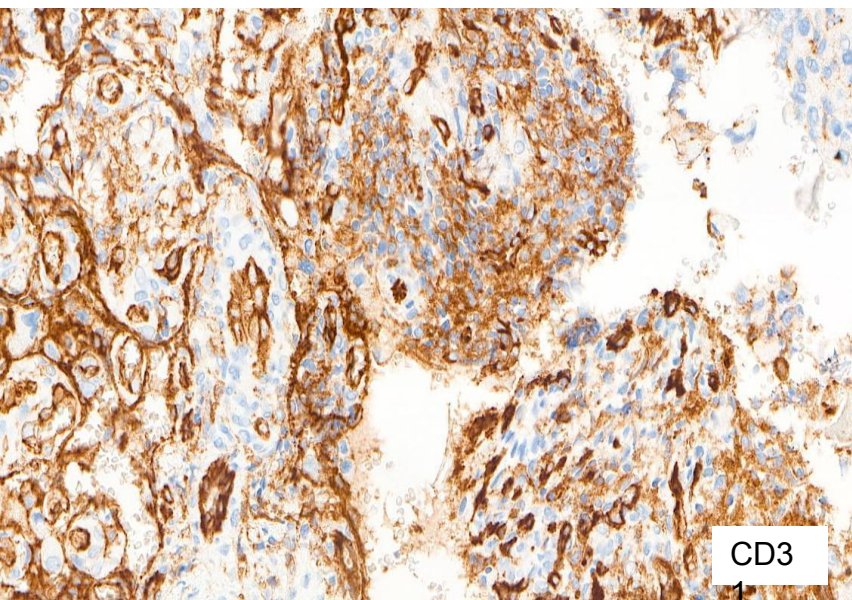
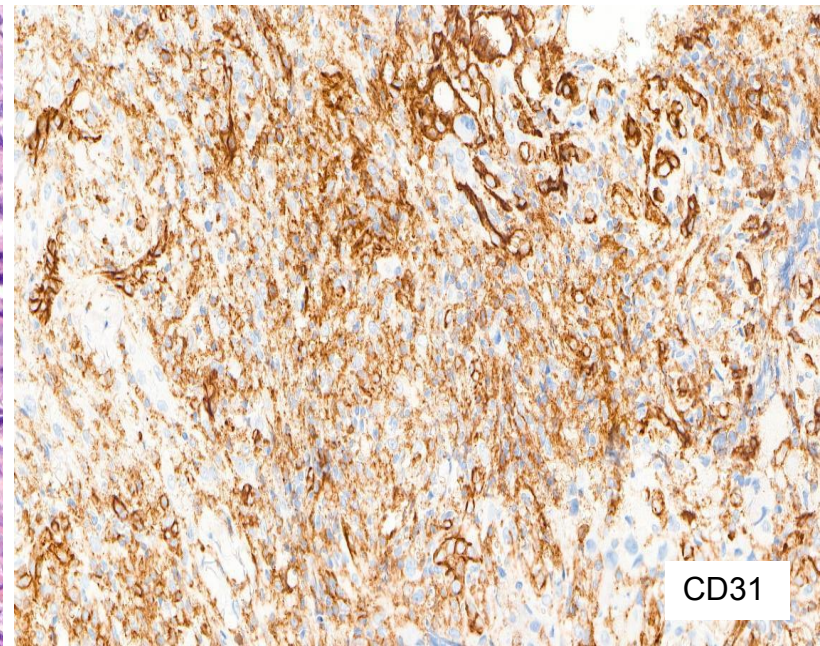
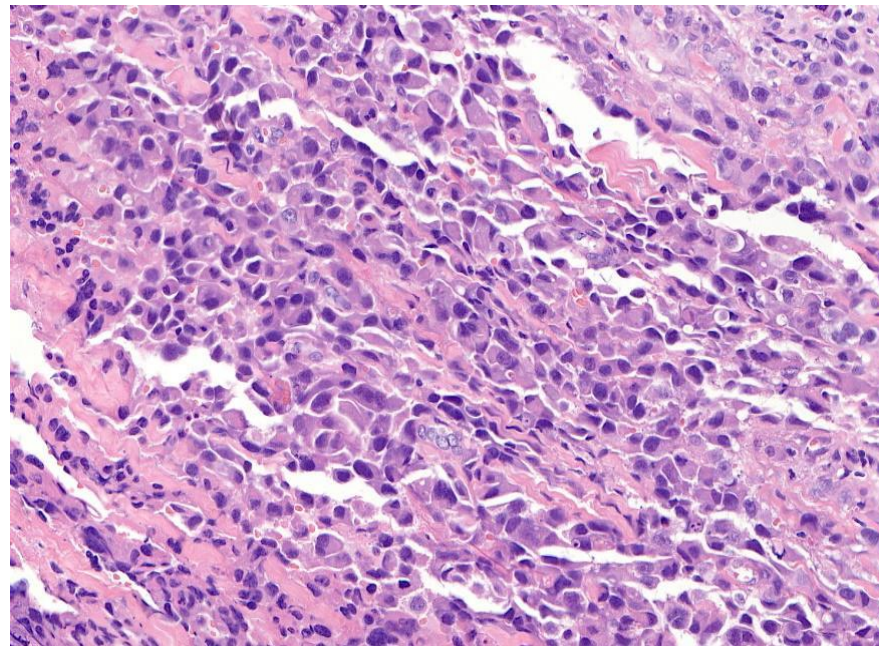
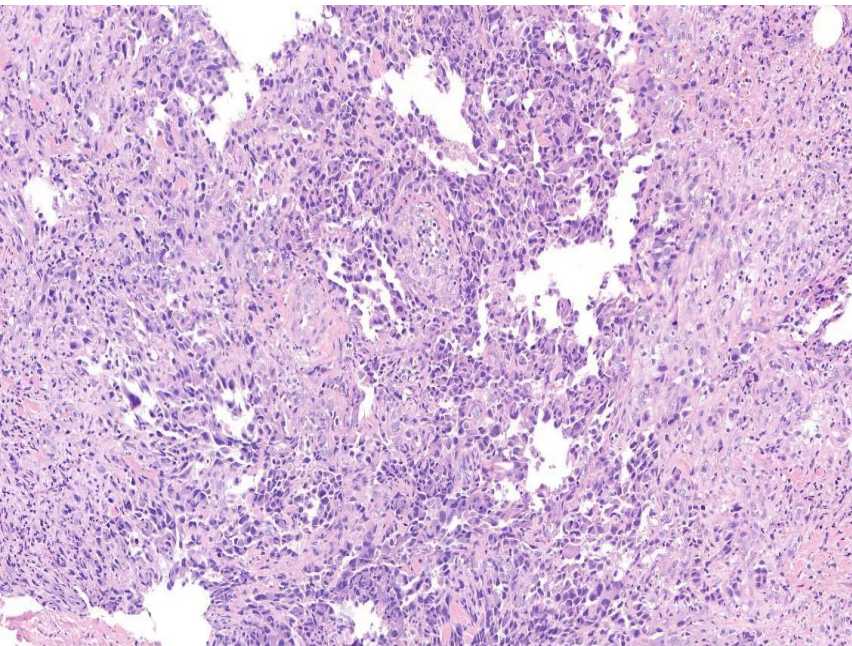
Case 2

Isidro Machado Puerto, Hector Aguilar, Reyes Claramunt - Spain

61 y/o/woman abdominal wall tumor. Surgical resection in external institution.
Pathology Report: Primary Angiosarcoma

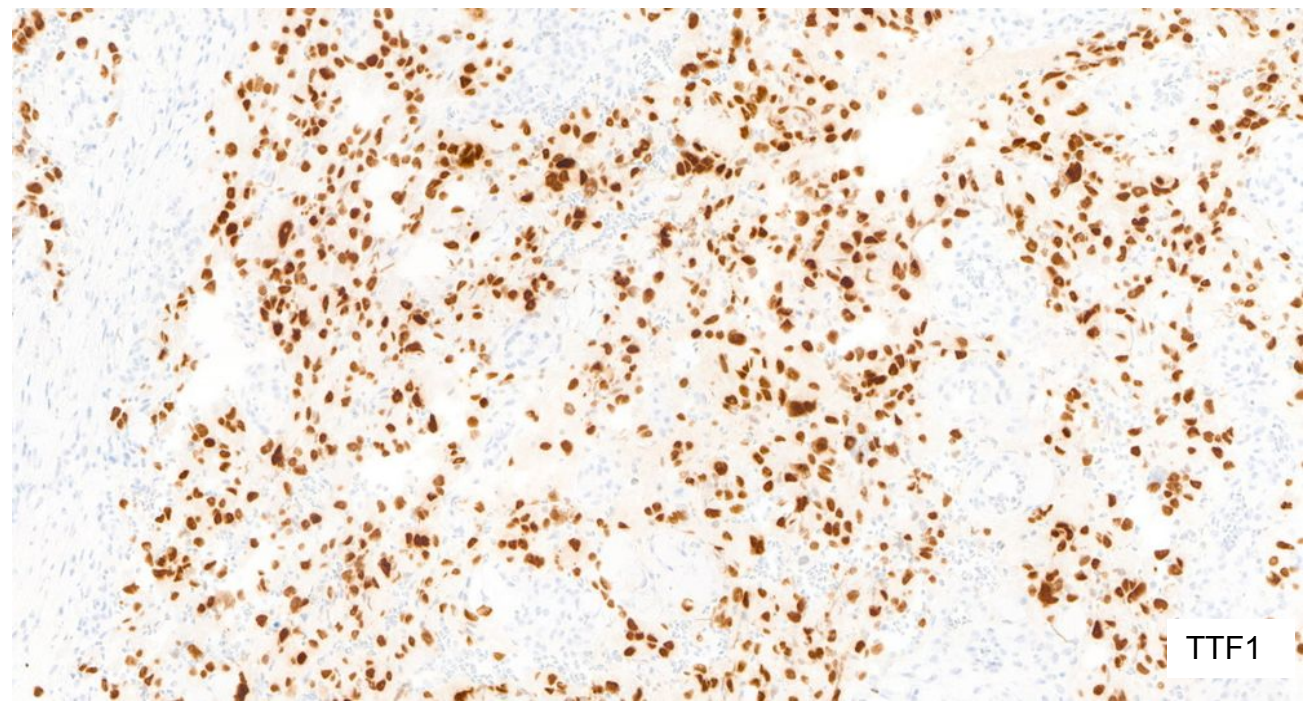
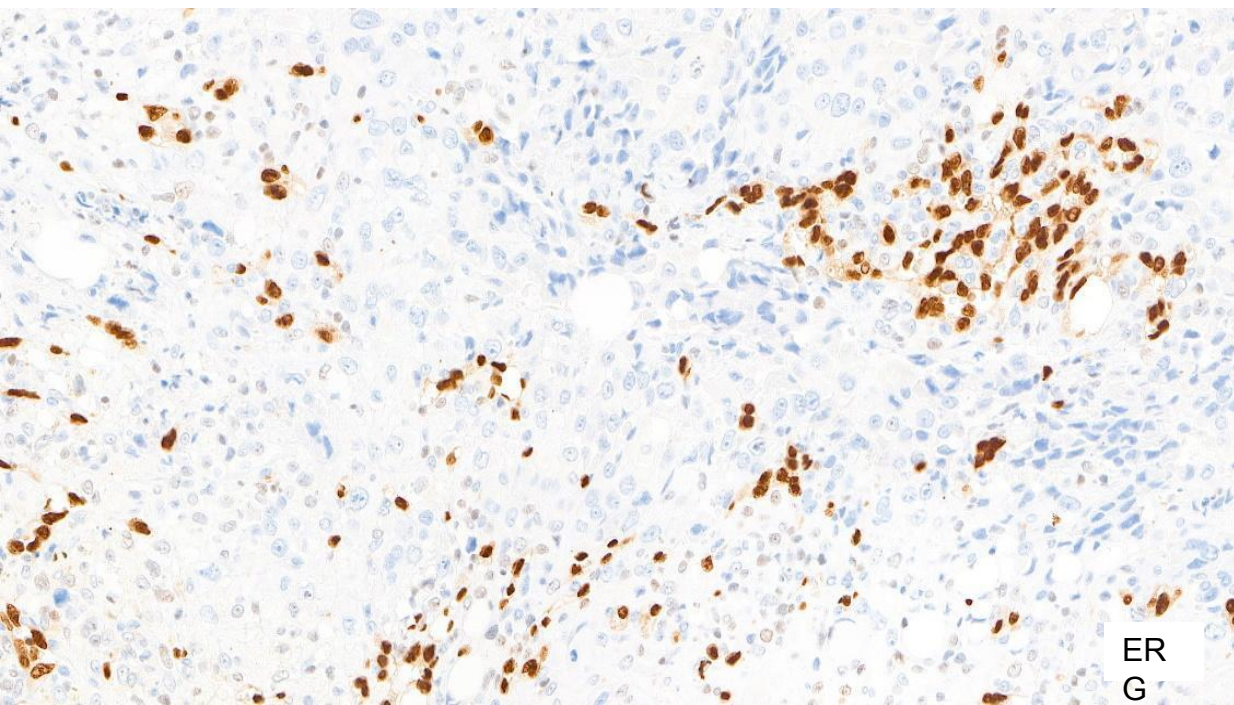
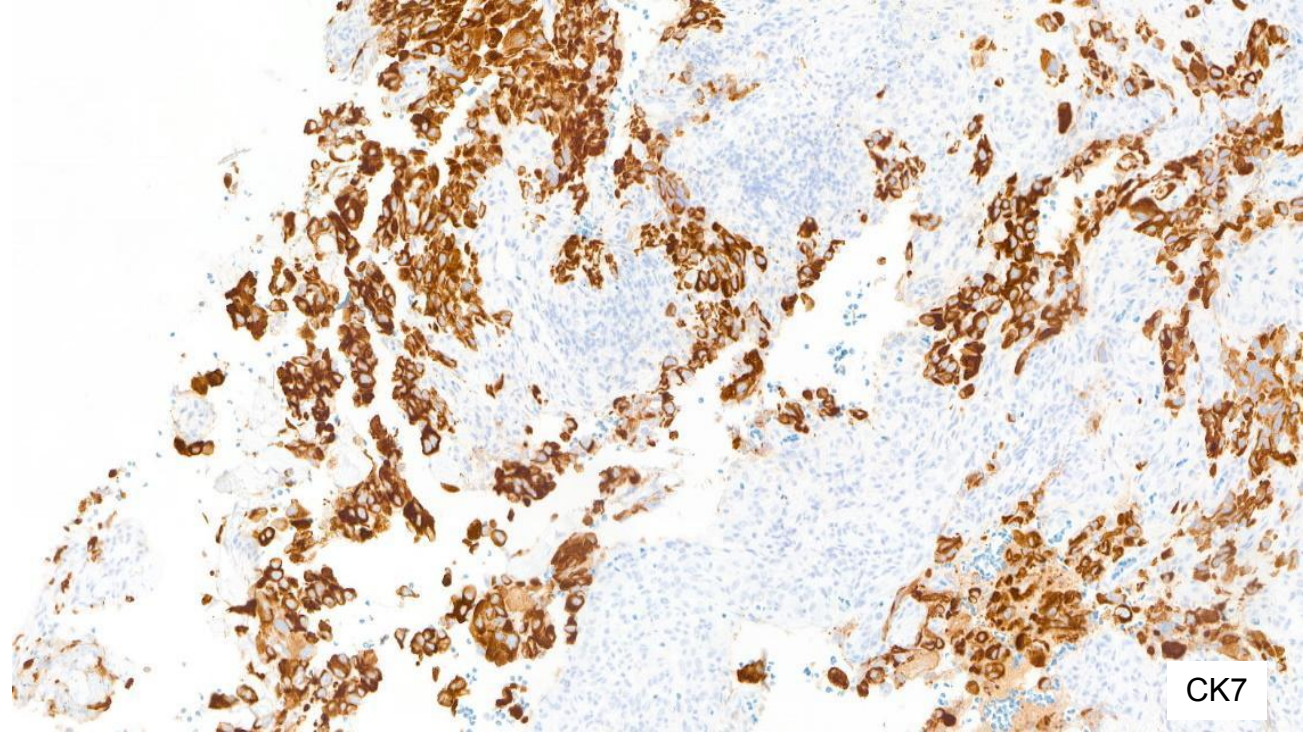
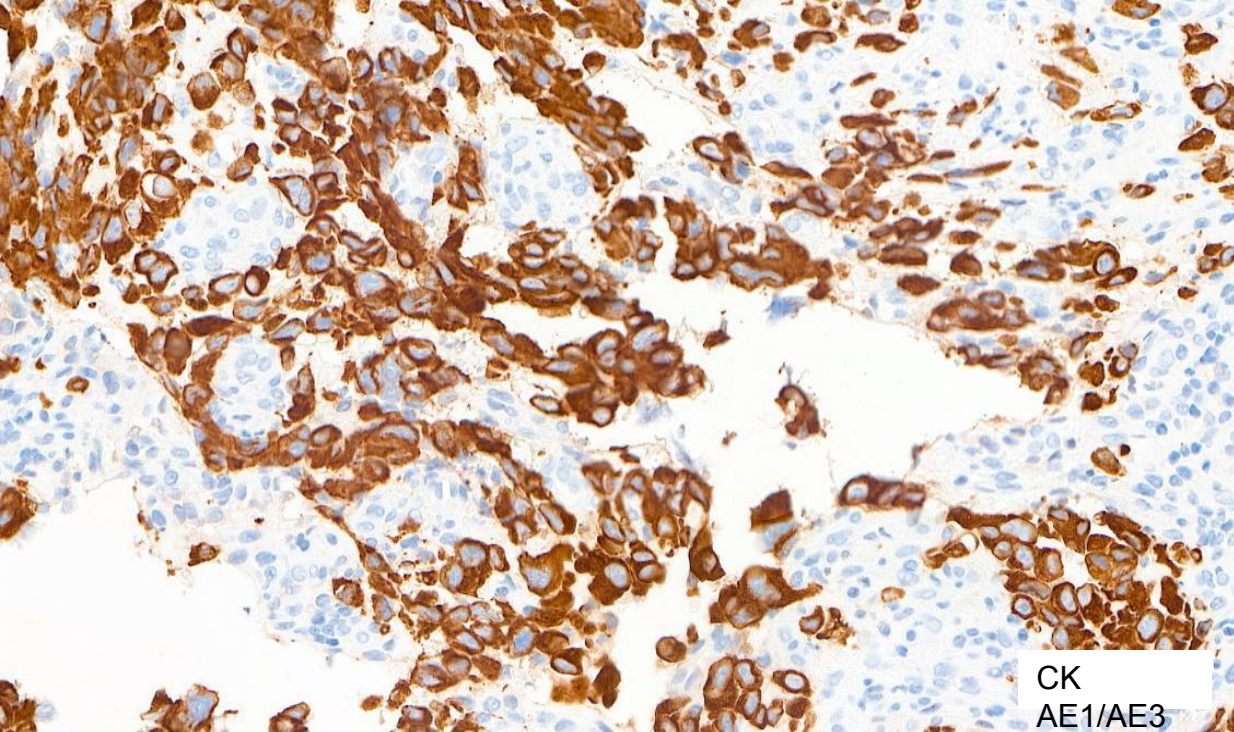


SELNET Session September. IVO. Valencia.
Isidro Machado, Hector Aguilar, Reyes Claramunt



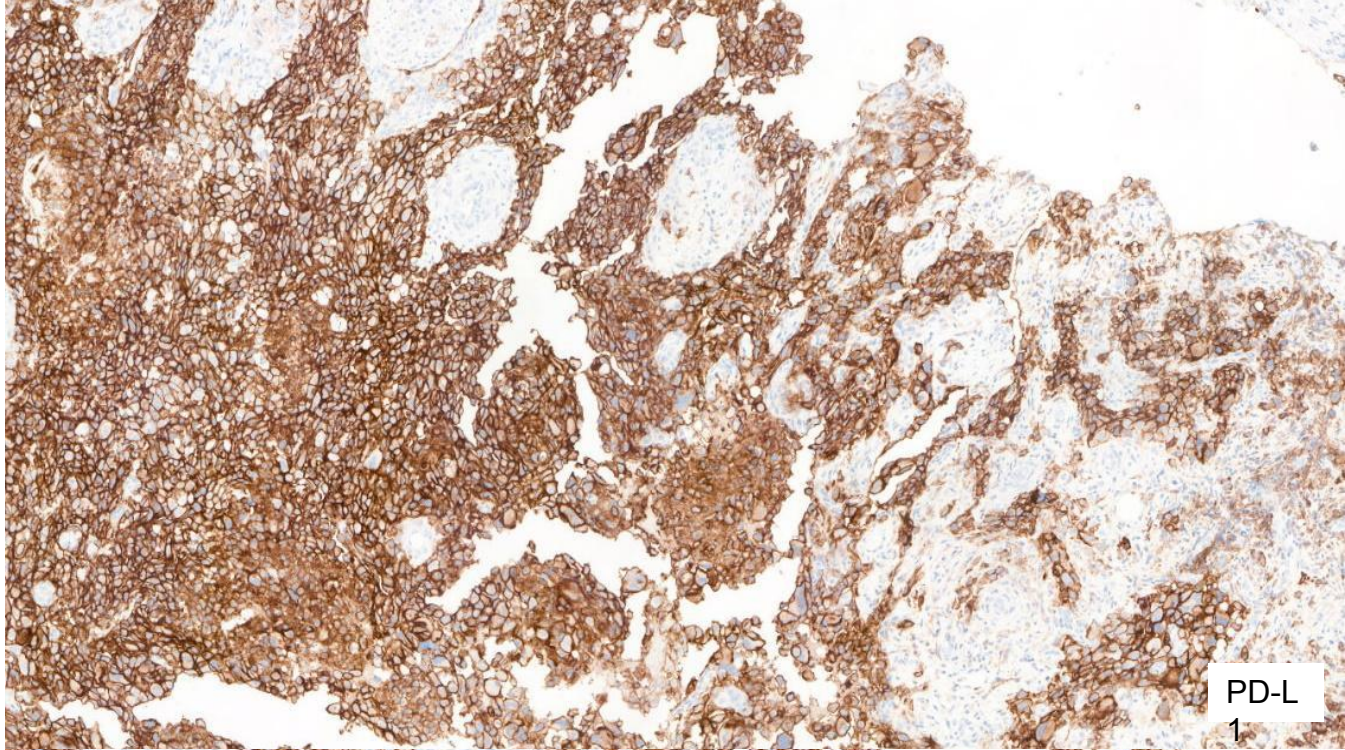
Pathology Report (External Hospital):

Pathology Review in IVO

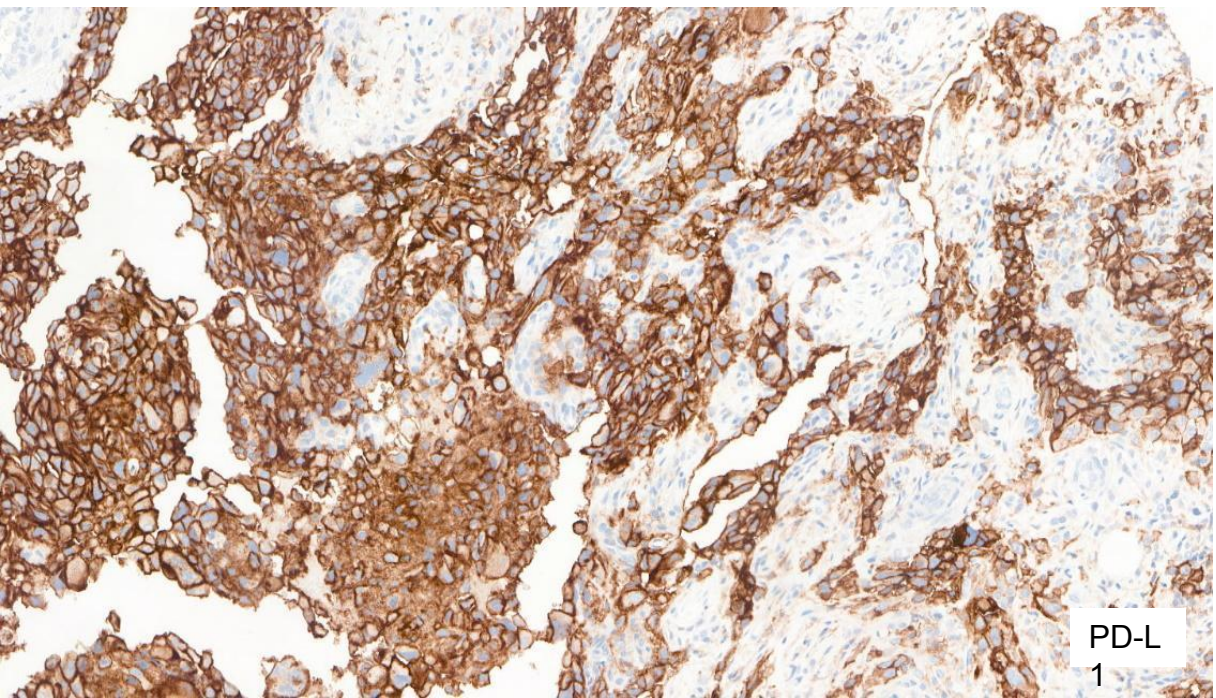




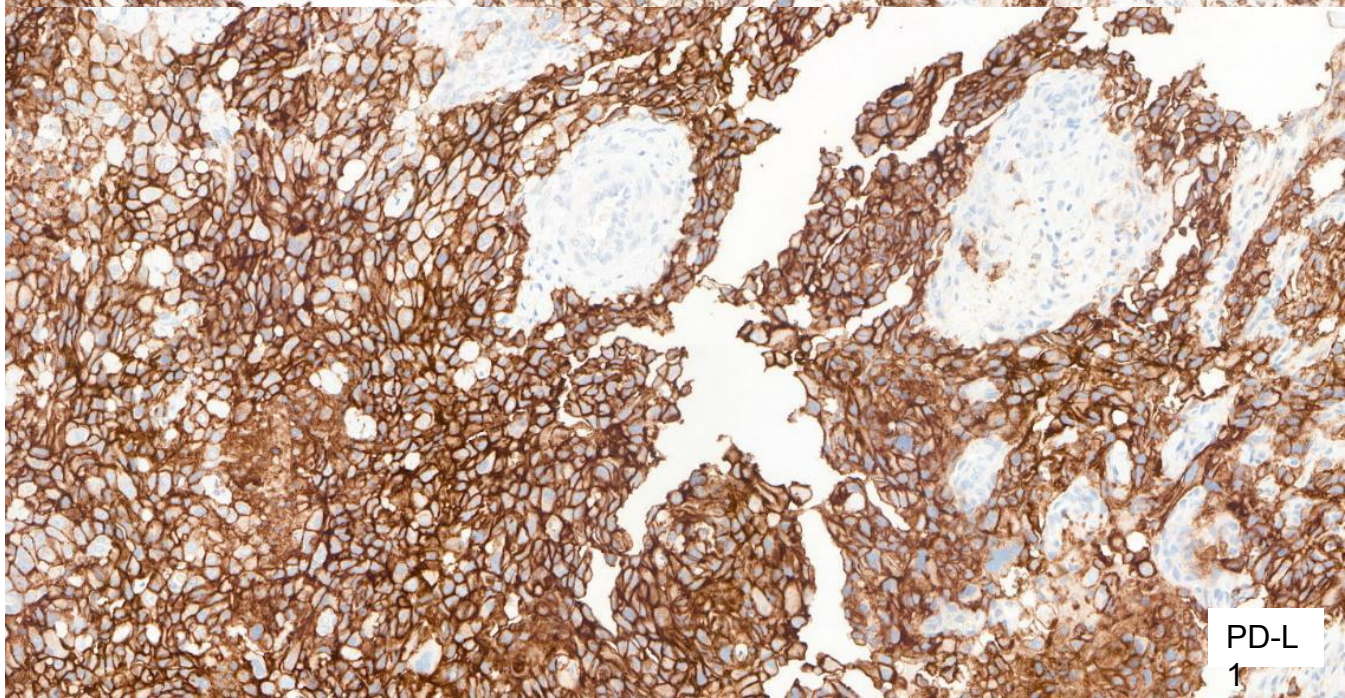
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PET after AS diagnosis review



- New subcutaneous nodules.
- Pembrolizumab monotherapy PD-L1>50%
- Evident clinical response after first cycle with disappearance of skin nodules pending of new follow up PET/TAC

Review

Atypical Histopathological Aspects of Common Types of Lung Cancer—Our Experience and Literature Review

Angela-Ştefania Marghescu ^{1,2,*}, Diana Gabriela Leonte ³, Alexandru Daniel Radu ¹, Elena Doina Măgheran ³, Adrian Vasiliţă Tudor ³, Cristina Teleagă ¹, Mirela Țigău ¹, Livia Georgescu ¹ and Mariana Costache ^{2,4}

Medicina 2024, 60, 112

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Table 1. Rare histopathological features of lung carcinoma—literature review (2013-present).

No.	Rare Histopathological Features of Lung Carcinoma	Keywords	Total Number of Articles	Number of Relevant Articles
1	Acantholytic	acantholytic, carcinoma, lung, pulmonary	8	5
2	Pseudoangiosarcomatous	pseudoangiosarcomatous, lung, pulmonary, carcinoma	2	1
3	Signet ring cell	signet ring, lung, pulmonary, carcinoma, squamous cell carcinoma, adenocarcinoma	11	5
4	Clear cell	clear features, lung, pulmonary, carcinoma, squamous cell carcinoma, adenocarcinoma	38	2

Molecular biology

Fusion plex lung. No fusion
BRAF mutation
HRAS, *TP53*, *PIK3CA*
mutation
EGFR, *KRAS*: WT

Case 3

Rodrigo Vasquez - Chile

- Male, 74 years old, engineer, working, ECOG 0
- Medical history:
 - Hypertension / Pre-diabetes.
 - Prostatic cancer Gleason 7, prostatectomy 2021, in follow-up, latest PSA (0.9, upwards).
 - 7 mm sylvian bifurcation cerebral aneurysm (considered high risk by neurosurgery), in follow-up .
 - Spironolactone, amlodipine, bisoprolol.
 - Allergies: (-).
- Mass in left forearm, up to 3cm.
- MRI November 2023: Heterogeneous solid nodule, undetermined etiology.

Q1: Need for biopsy?

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 - Hypertension / Pre-diabetes.
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Q1: Need for biopsy?

- Surgery December 26th 2023, Cl. Avansalud: 3cm tumor, myogenic sarcoma, high grade. Ki67 50%, S100 weakly (+), SOX 10 (-), calretinin (-), desmin (+), myo D1 (-), vimentin intensely (+).
- Bp review Cl. Alemana: Leiomyosarcoma G3. FNCLCC 7 (diff 2, mit 3, necr 2), Ki67 60%.
- PET January 25th, 2024 vs PSMA PET November 20th, 2020: Renal nodule with slight increase, 12 vs 8mm. 5mm lung nodule vs 4mm. Other nodules stable.
- Re-excision (surgical margins expansión) February 29th, 2024 Cl. Alemana: bp (-).

Q2: Need for adjuvant RT and/or ChT?

- No subsequent RT.
- Local recurrence May 2024. June 10th 2024 transradial amputation: Bp: 5.4x4cm tumor, Leiomyosarcoma G3. (FNCLCC score 6), negative margins, ILV and IPN (-).
- PET CT August 22th, 2024: right renal nodule 14 vs 12 mm. Mild cardiomegaly, stability of pulmonary nodule. Echocardiogram: LVEF 63% , strain OK, concentric remodeling. Creat 1.16, glycemia 175.
- One oncologist recommends “adjuvant” ChT, the other does not, due to comorbidities and age.

Q3: Utility of Sarculator? 10-year OS 49%

Q4: Adjuvant ChT?. Epi/doxo + ifo x 3c?, doxo + DTIC?