

# SELNET MDT

19/12/2024

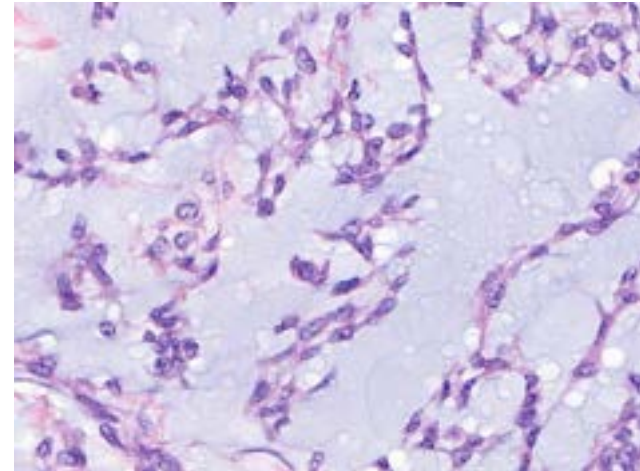
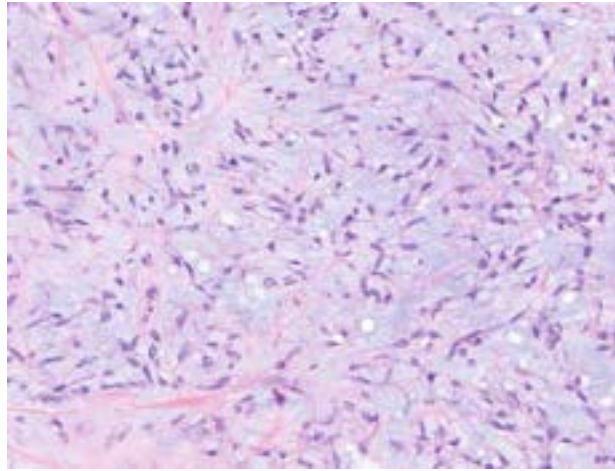
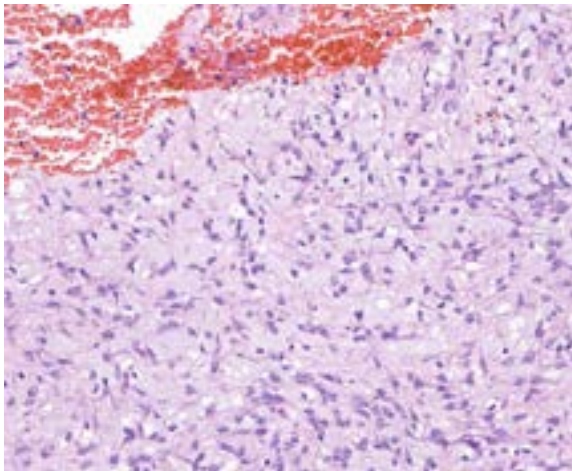
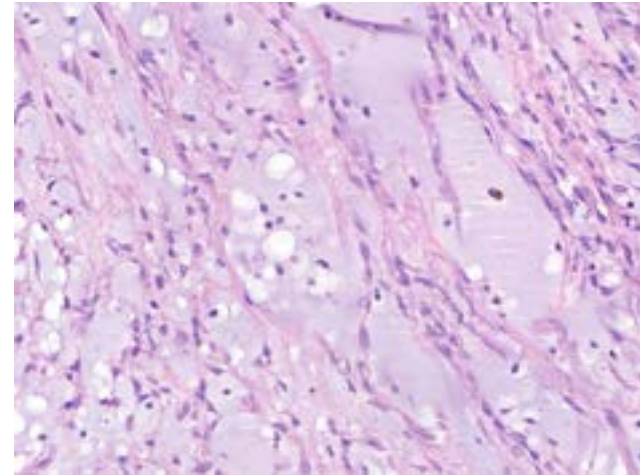
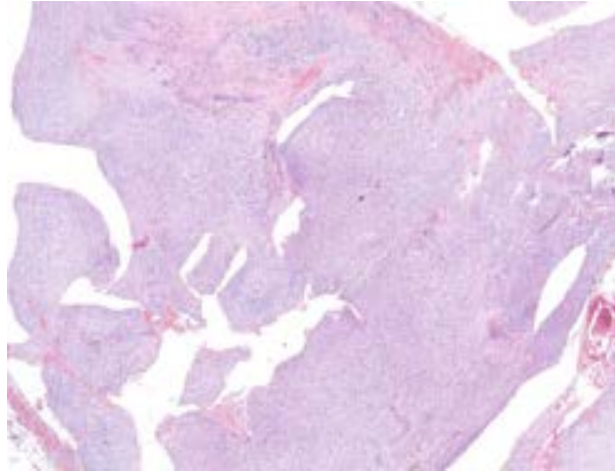
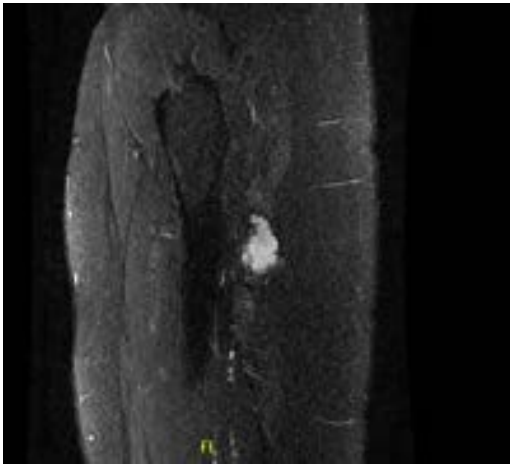


# CASE 1

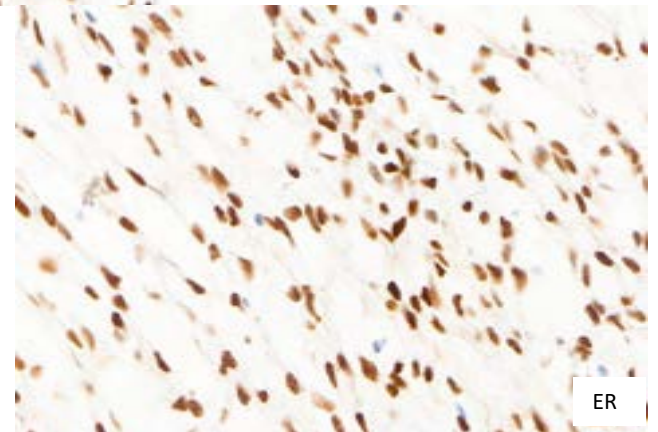
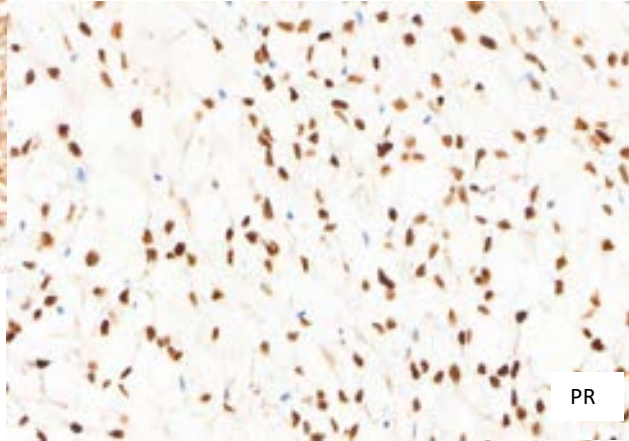
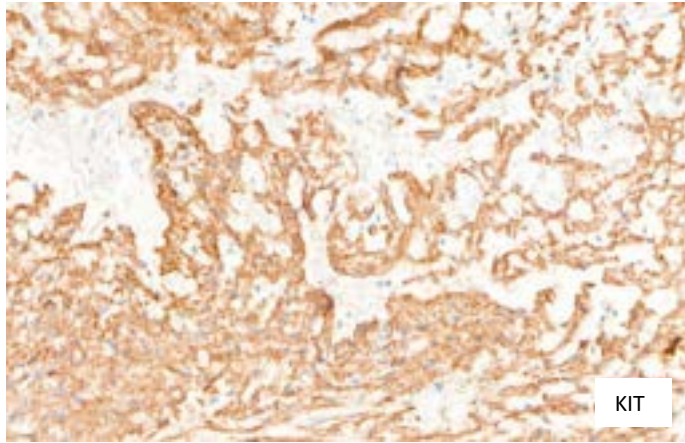
Isidro Machado- Spain



45 y/o/w. Gluteal tumor: The radiology report suggests a vascular neoplasm or malformation.

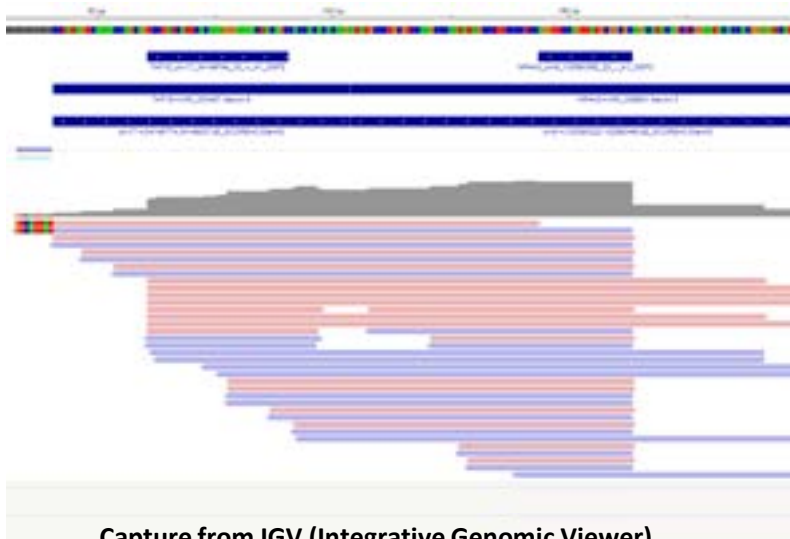


December SELNET meeting. IVO (Isidro Machado, Reyes Claramunt, Héctor Aguilar)





Capture from Archer Analysis software versión 7.2.0-1



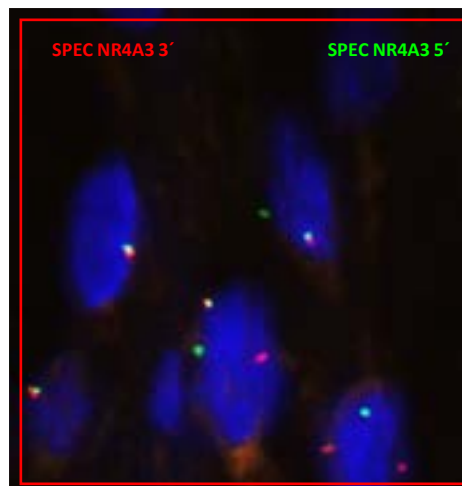
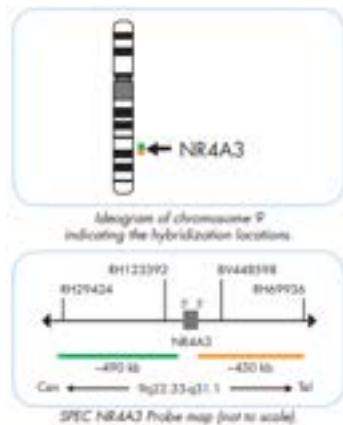
Capture from IGV (Integrative Genomic Viewer)

The percent depth of this structural variation (9.33%) is below the established threshold (10%).

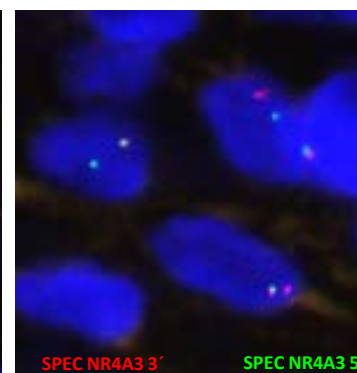
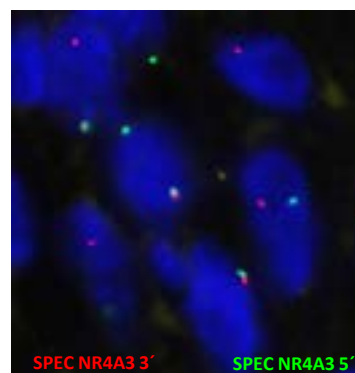
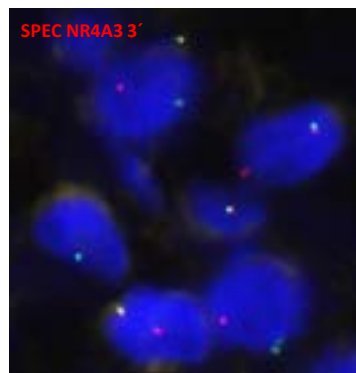
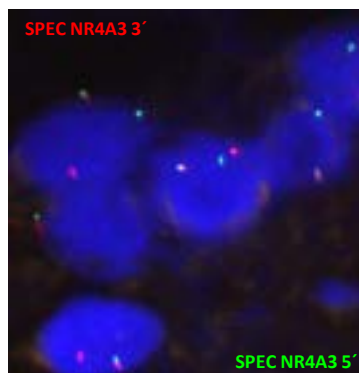
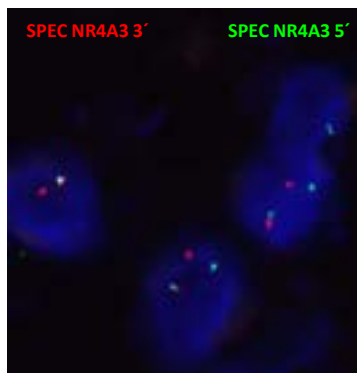


Estructure of the fusion *TAF15::NR4A3*

ZytoLight® SPEC NR4A3 Dual Color Break Apart Probe



63X



68% Rearrangement

Received: 7 November 2022 | Revised: 9 March 2023 | Accepted: 4 April 2023  
DOI: 10.1002/jcr.23144

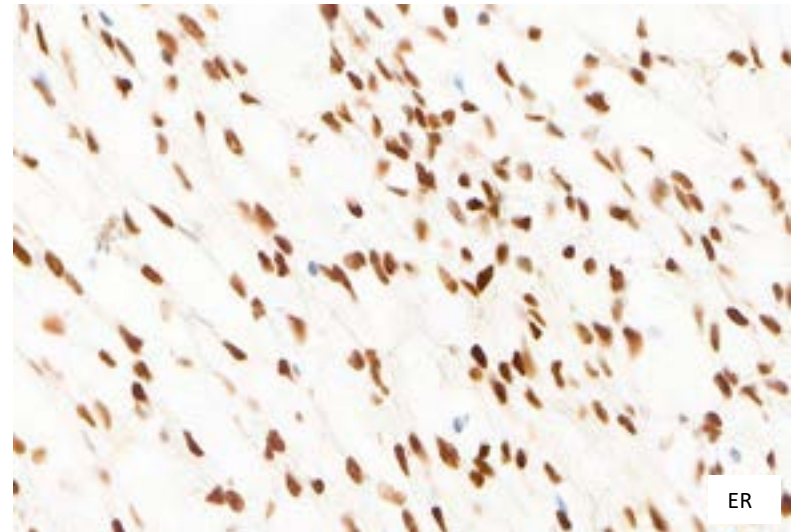
RESEARCH ARTICLE

WILEY

# TAF15::NR4A3 gene fusion identifies a morphologically distinct subset of extraskeletal myxoid chondrosarcoma mimicking myoepithelial tumors

Laura M. Warmke<sup>1</sup> | Wei-Lien Wang<sup>2</sup> | Daniel Baumhoer<sup>3</sup> | Vangelita Andrei<sup>3</sup> | Baptiste Ameline<sup>3</sup> | Michael L. Baker<sup>4</sup> | Darcy A. Kerr<sup>4</sup>

Estrogen receptor expression is rare in EMC but is not exclusively found in PGR::NR4A3 tumors, and it may represent a potential target for therapy.



## Identification of Novel PGR-NR4A3 Fusion in Extraskeletal Myxoid Chondrosarcoma and Resultant Patient Benefit From Tamoxifen Therapy

H. Catherine Wilbur, MD<sup>1,2</sup>; Dan R. Robinson, PhD<sup>1,2</sup>; Yi-Mi Wu, PhD<sup>1,2</sup>; Chandan Kumar Sinha, PhD<sup>1,2</sup>; Arul M. Chinnaiyan, MD, PhD<sup>1,2</sup>; and Rashmi Chugh, MD<sup>3</sup>

JCO Precis Oncol 6:e200038. © 2022 by American Society of Clinical Oncology

# CASE 2

Emy Estefany García- Mexico





# CLINICAL CASE

Speakers: **Emy Estefany García Guillén, MD.**  
Medical Oncology

**Haydee Caro, MD**  
Oncologic Pathologist

**National Cancer Institute, Mexico City.**  
December 19th, 2024.



## Medical history:

**Male, 30 yo, without remarkable medical background or risk exposure**

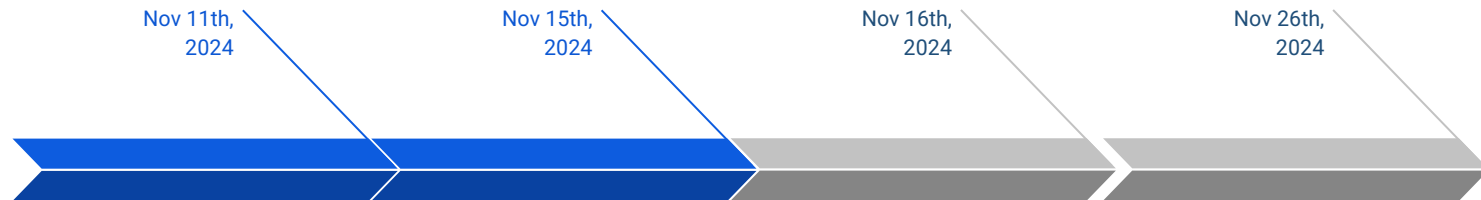
Pain on right leg which causes abnormal gait during the last 10 months.

**Foot X ray:** lytic lesion on navicular bone and med. and lat. cuneiform bones.

**Physical examination:** Pigmented lesion in 1st and 4th fingers of the right foot. No enlarged lymph nodes



# TIMELINE



## Bx 1st finger

Pseudomyogenic hemangioendothelioma 10 mitosis per HPF, no LVI, with PNI. Tumour in contact with border.



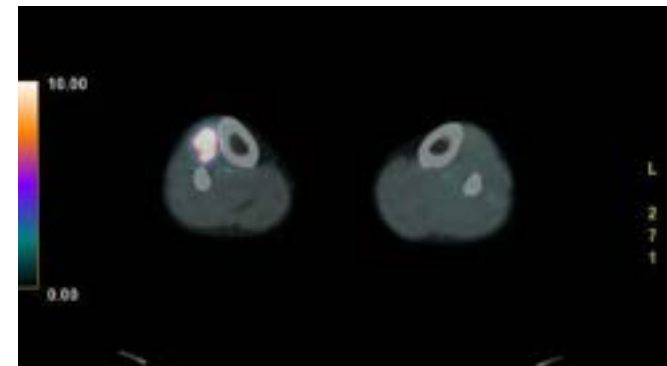
## RMI

Multiple, hyperintense lesions in talus, calcaneus, navicular and cuneiform bones, with soft tissue involvement



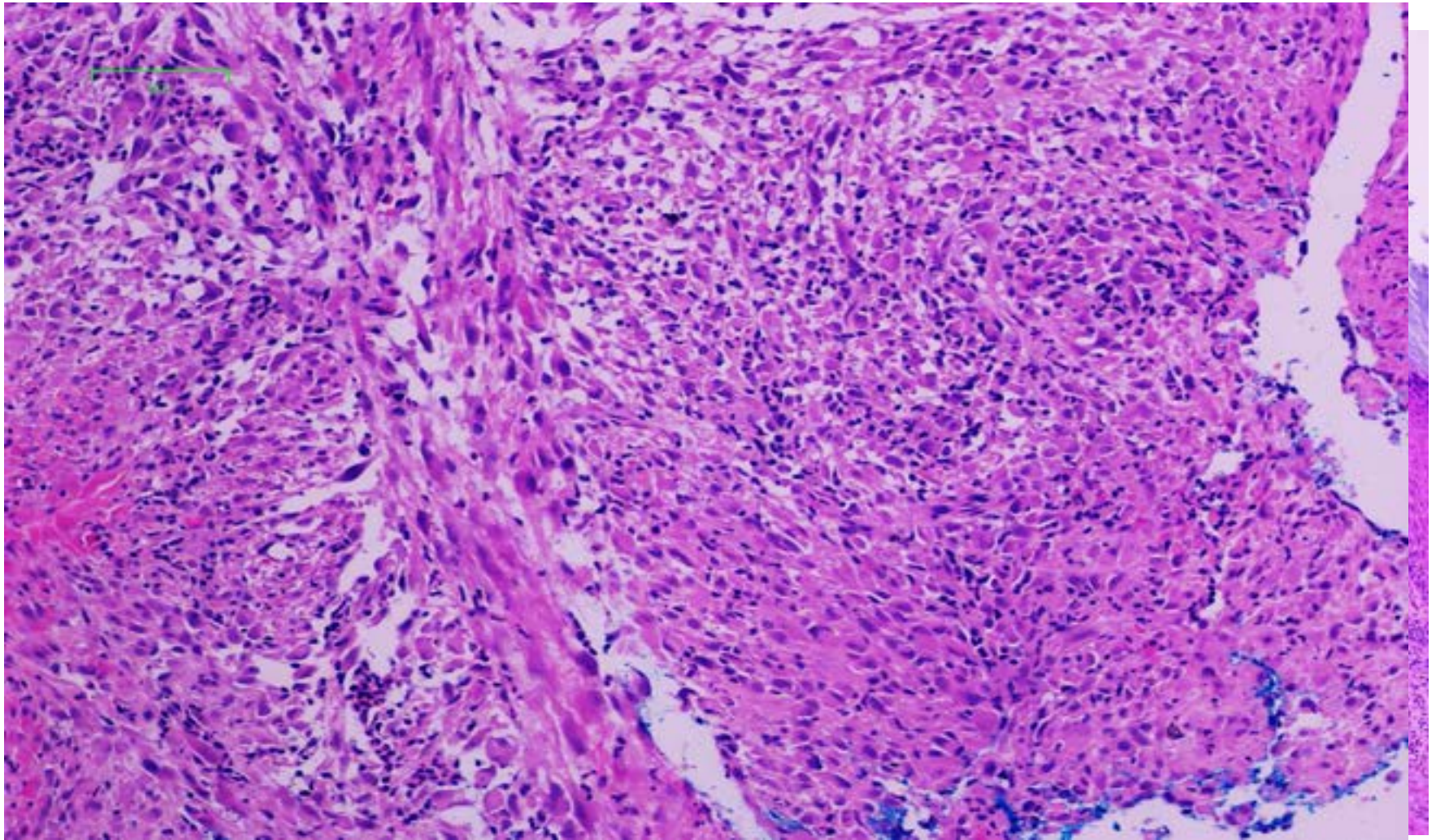
## PET CT 18 FDG

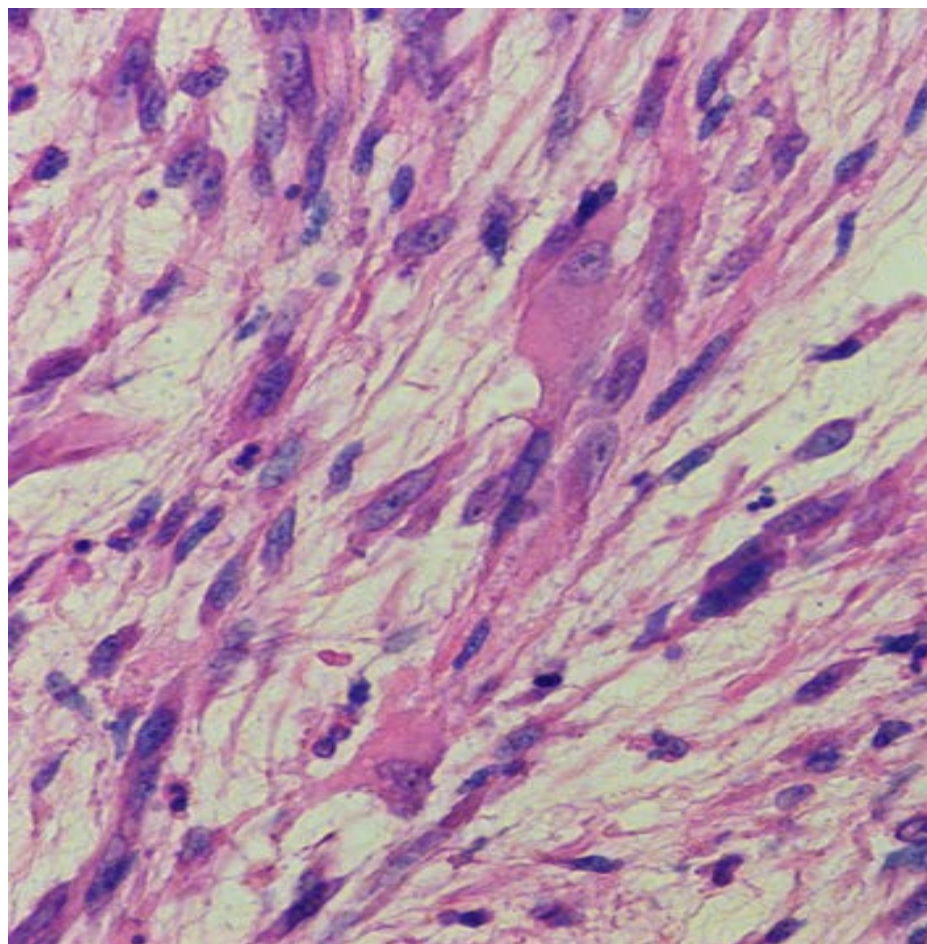
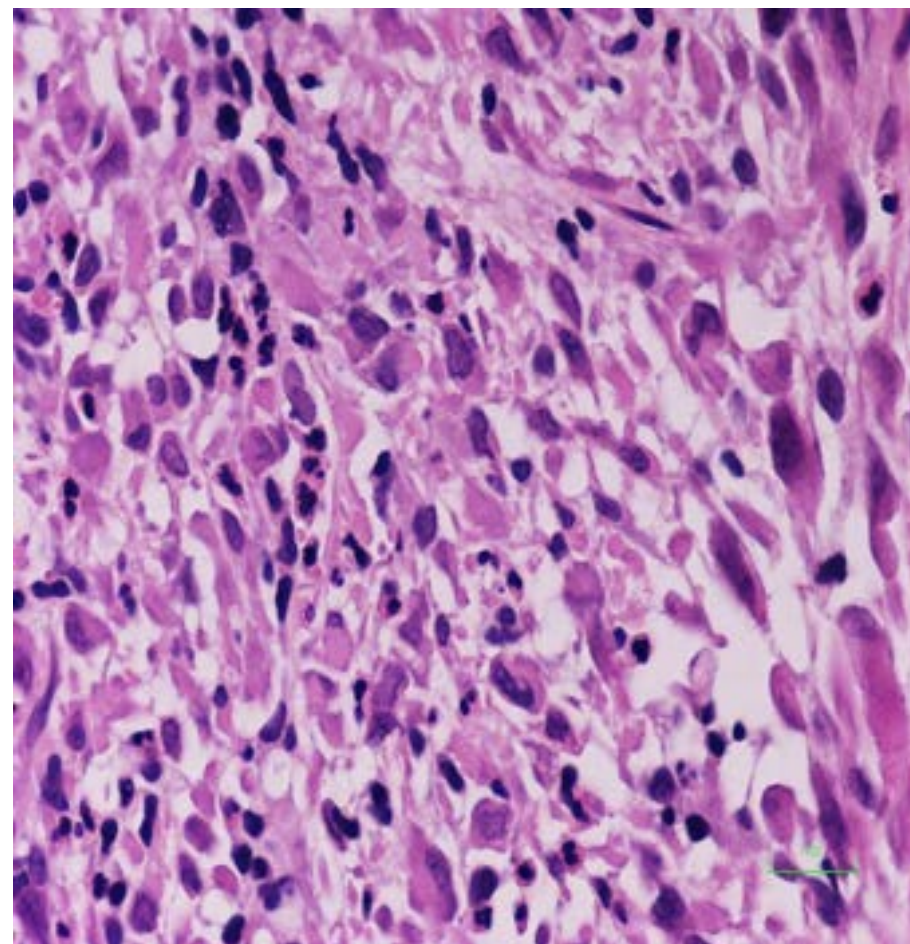
Multiple hypermetabolic lesions on foot bones, soft tissue in proximal third of right leg lungs with multiple, non hypermetabolic micronodules.



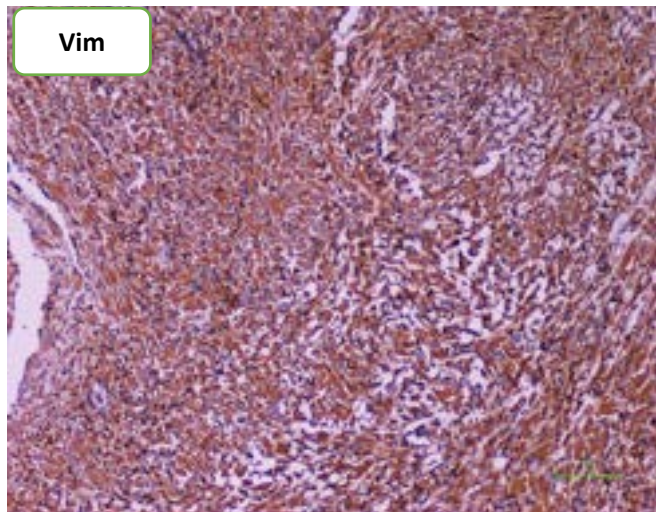
## Blood test

All within normal range

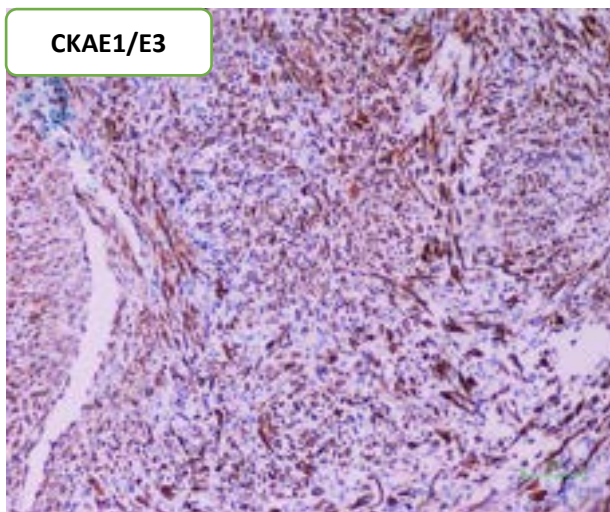




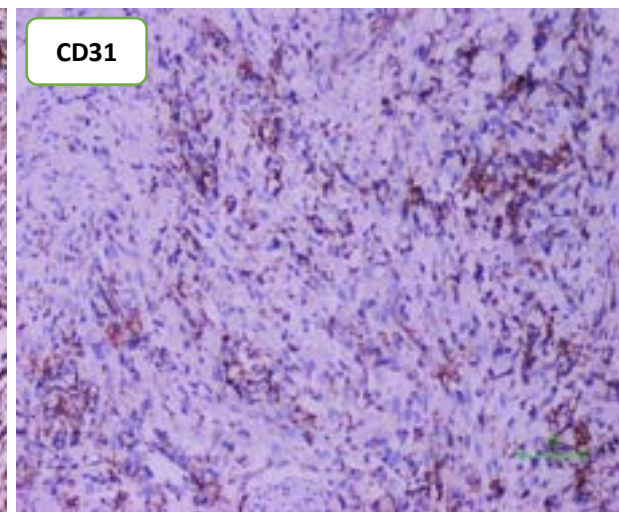
**Vim**



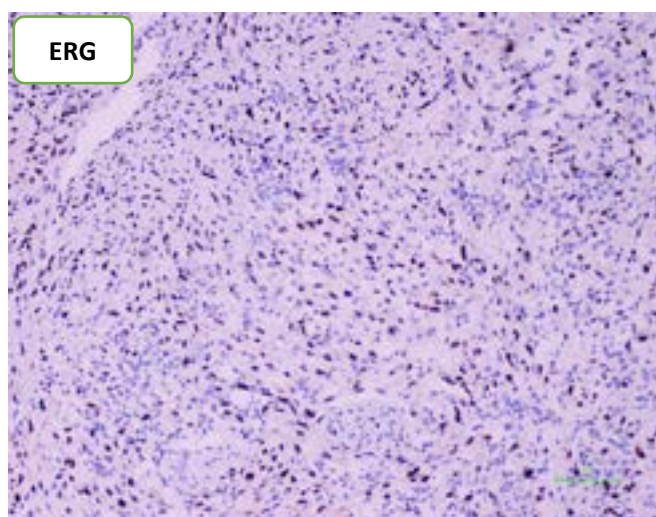
**CKAE1/E3**



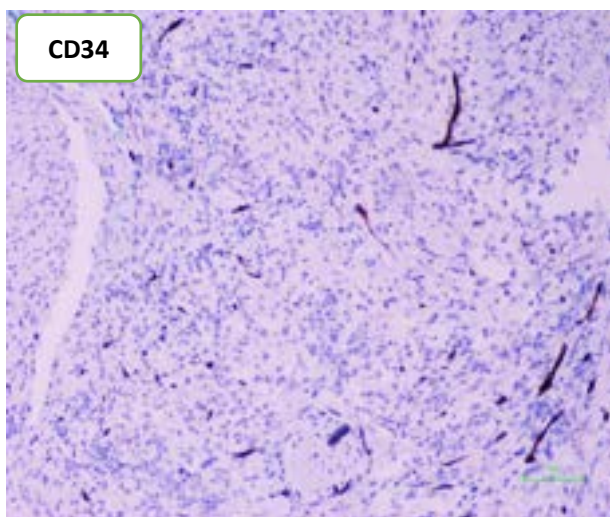
**CD31**



**ERG**



**CD34**



**Positive**

- ERG
- CD31 (focal)
- CKAE1/E3
- CK7
- Vimentin

**Negative**

- INI-1 (non mutated)
- HMB45, MELAN-A, SOX10
- CD34
- CK20
- EMA
- Actin
- P63

# Questions

- 1.- What is your **experience in the management** of these kind of tumors, since these are rare?
- 2.-What would be your **first line treatment**? Would you choose an antiangiogenic or anthracycline?
- 3.-What do you think about **palliative radiotherapy** to the limb?



@emyeeg



# CASE 3

Carlos López - Spain



# SELNET Virtual MDT

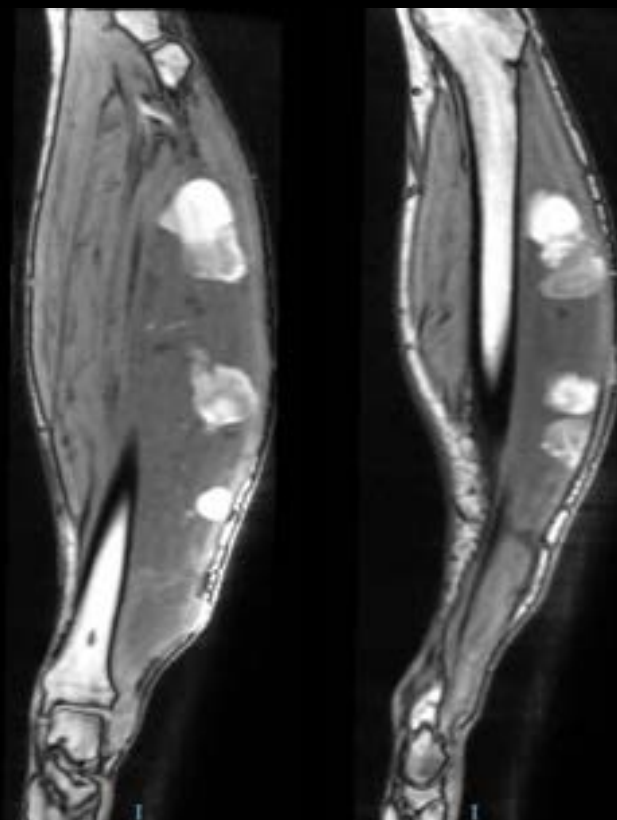
19th December 2024

Carlos López Jiménez

Fundación Jiménez Díaz University Hospital  
Madrid, Spain

- **Male, 20 years old**
- **June 2021** → Tumor on the left leg.
- **MRI** → 3.2 x 7.2 cm mass involving the **anterior, lateral, and posterior compartments** of the left leg. The mass contains **cystic** and/or **necrotic** areas as well as intralesional **hemorrhagic** components. It is dependent on the anterior tibialis, extensor digitorum longus, peroneus longus, and posterior tibialis muscles.
- **TRU-CUT BIOPSY** → High-grade malignant neoplasm composed of spindle cells arranged in short fascicles. Nuclei show mild atypia and scant cytoplasm.
  - **IHC profile:** TLE1 focally positive, BCL2 focally positive; STAT6 negative (cytoplasmic staining only), ERG positive in vessels.
  - **Grade of differentiation:** 3.
  - **Mitotic index:** 2 (6 mitoses identified per 1 mm<sup>2</sup>).
  - **Tumor necrosis:** 1 (approximately 10% tumor necrosis identified).
  - **Molecular:** SS18:SSX1 fusion.
  - **Diagnosis:** FNCLCC grade 3 monophasic synovial sarcoma.
- **THORACIC CT** → At least six **pulmonary metastases** identified.
- **DIAGNOSIS** → **G3 metastatic synovial sarcoma (pulmonary metastases, multi-compartmental neurovascular tumor involvement).**
- **FIRST TREATMENT** → **Doxorubicin** 60 mg/m<sup>2</sup> on day 1, plus **ifosfamide** 3000 mg/m<sup>2</sup> for 5 days, administered every 21 days for six cycles (July 2021 to January 2022). Best response: **STABLE DISEASE.**

**JUNE 2021**



- Local symptoms.
- **MRI** → Intramuscular mass (7,5 x 9,2 x 29 cm) in the lateral region of the left leg with extensive areas of **necrosis**, infiltrating the **musculature** of the lateral and deep compartments, and involving more than 50% of the anterior tibial neurovascular bundle.
- The patient refuses amputation.
- **SECOND LINE TREATMENT** (February/2022)

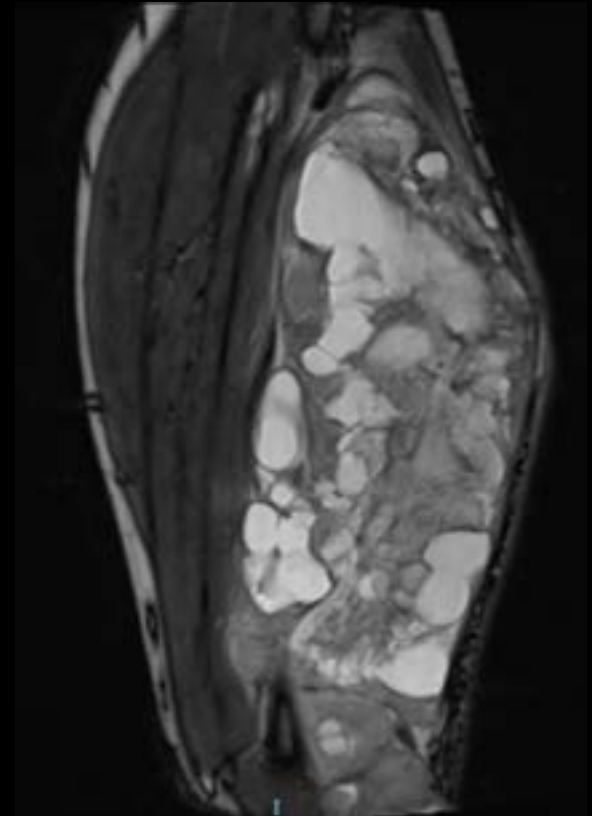
**Trabectedin**  
(1.5 mg/m<sup>2</sup> every 21 days)

+

**Radiotherapy**  
(45Gy in 25 fractions)

Immediate goal of symptom control.

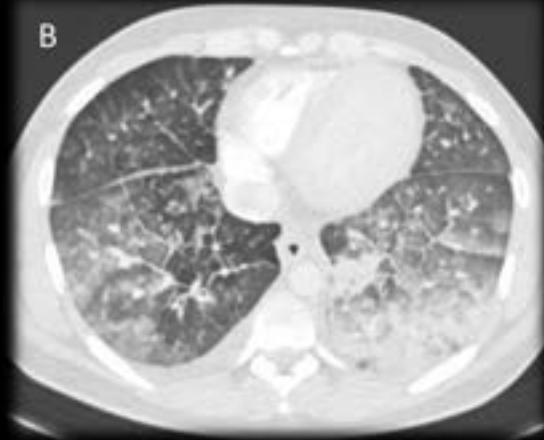
**JANUARY 2022**



## Second cycle of trabectedin (14th March 2022)

- The patient presented to the emergency room with universal jaundice, nausea, and fever.
- **LABORATORY TESTS**  
G2 thrombocytopenia + G1 neutropenia + G3 hypertransaminasemia + G3 hyperbilirubinemia.
- Infection and other differential diagnoses were ruled out, and **TRABECTEDIN TOXICITY** was raised as the primary diagnostic possibility.
- **INITIAL TREATMENT** → Dexamethasone 4 mg every 12 hours, plus IV fluid therapy.
- **48 hours after admission** → Respiratory function worsened (85% oxygen saturation). Thoracic CT showed bilateral patchy infiltrates, compatible with **TOXIC PNEUMONITIS / ACUTE RESPIRATORY DISTRESS SYNDROME**. No signs of an infectious origin.
- **IV METHYLPREDNISOLONE** was administered at a dose of 1 mg per kg. No high-flow oxygen was required.





**A:** CT scan performed at the day of emergency room admission.

**B:** CT scan performed at the day of ICU admission.

**C:** CT scan performed 10 days after hospital discharge with complete resolution of lung toxicity.

- Complete recovery of hepatic and hematological function occurred after 5 days of treatment. The patient was discharged 11 days after admission.
- Consumption of inadvertent toxins or drugs was reassessed to explain the unexpected toxicity despite receiving standard doses of trabectedin.



Consumption of daily hibiscus flower infusion (4-5L)  
during the 5 days prior to admission

**CYP3A4 and P450 cytochrome inhibitor!**

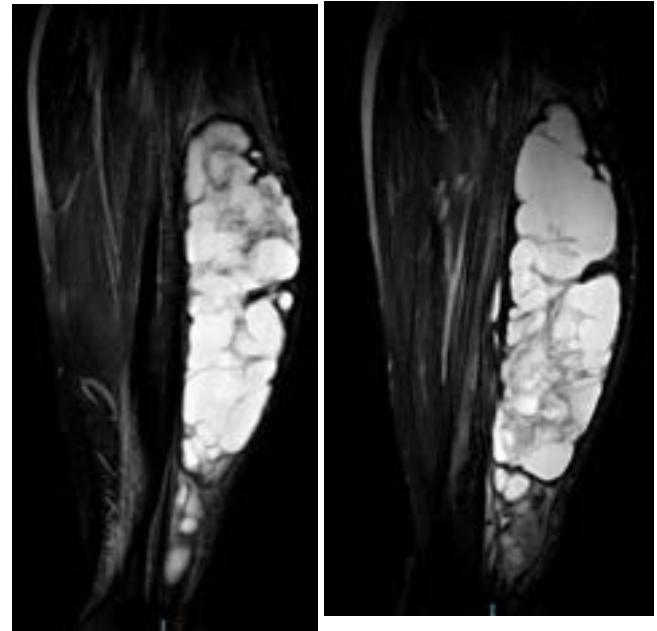
- After 3 cycles, the patient fulfilled a **MAJOR PARTIAL RESPONSE**. He completed 5 cycles of treatment until June/2022.

- Surgery of amenable pulmonary lesions.

DECEMBER 2022

- Primary tumor surgery (excision) in January 2023:

- Stereotactic Body Radiation Therapy for lung metastases (x5),



# Relevant questions for discussion

- Pharmacological interactions and trabectedin toxicity profile.

Hibiscus sabdariffa (*Jamaica flower*) as a CYP3A4 and P450 inhibitor.

Subsequent severe trabectedin toxicity.

FAS-mediated hepatotoxicity and acute respiratory distress syndrome.

- Trabectedin in rearranged-sarcomas.

From amputation to limb salvage surgery.

THANK YOU, GRACIAS, OBRIGADO,  
DANKE, *GRAZIE*, MERCI

