SELNET MDT – July 18th, 2024

Coordinator: Brazilian Team

AGENDA:

- Case 1 – Gisela German (AR)
- Case 2 – Isidro Puerto (SP)
- Case 3 – Brois Itkin (OM)
- Case 4 – Franklin Castillero (PN)
- Case 5 – Luciana Auresco (BR)
- Case 6 – Nadia Hindi (SP)

Case 1

Gisela German - Argentina

SELNET

VIRTUAL MDT BOARD

SECOND PRESENTATION CASE UPDATE

HOSPITAL ONCOLÓGICO

Unidad de Tumores Musculoesqueléticos de la Provincia de Córdoba

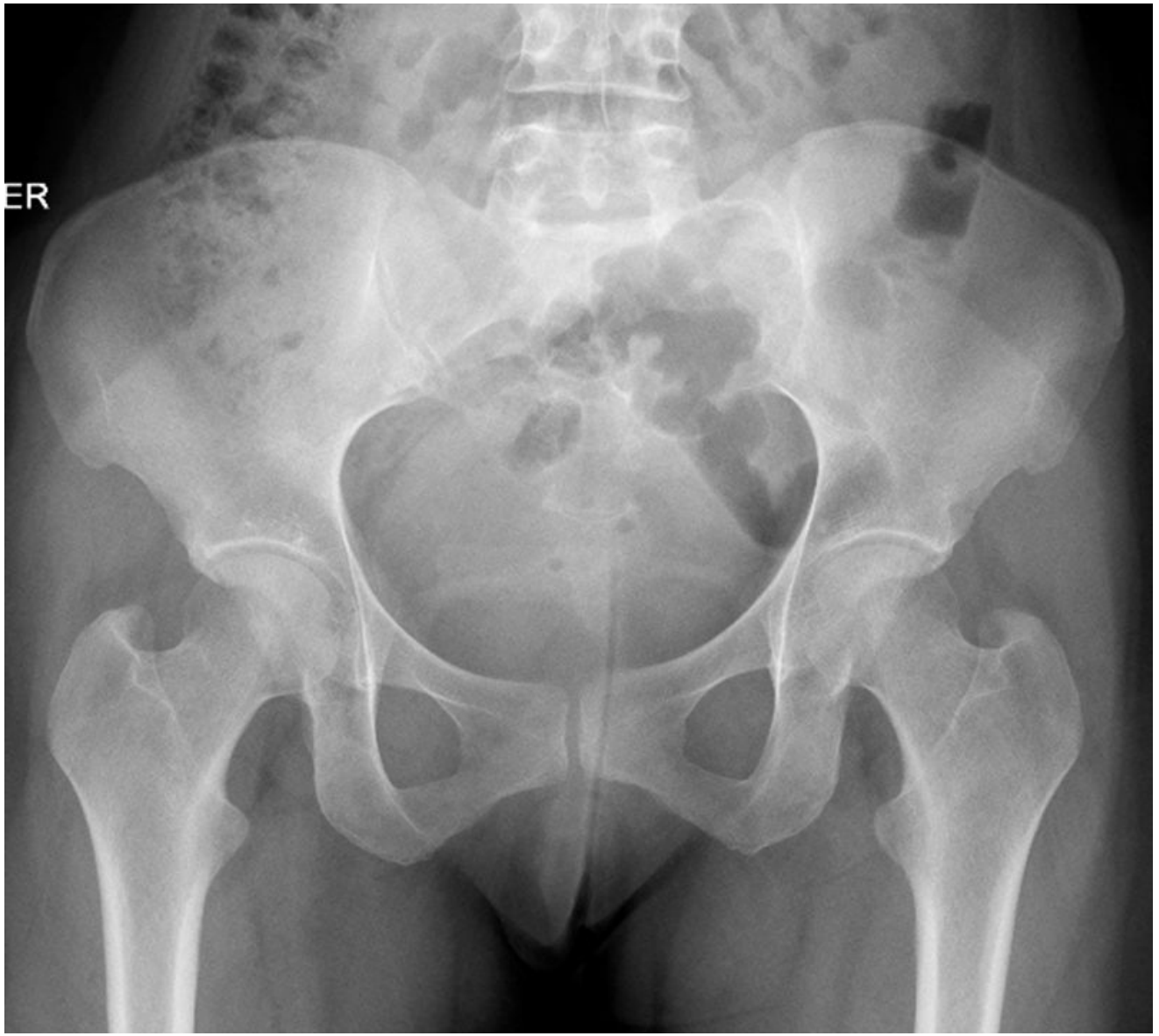
GASPAR

Grupo Argentino de Sarcomas de Partes blandas y óseos

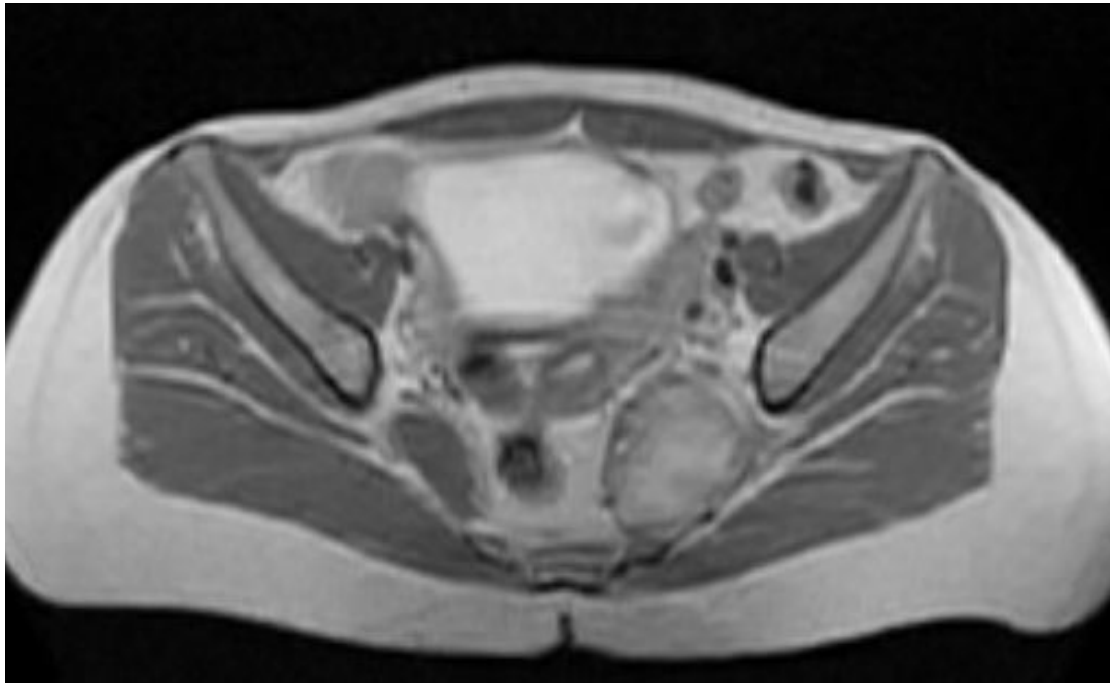
35 years old female patient.

Without pathological history.

Multiple consultations due to pain in the left lumbosacral región.

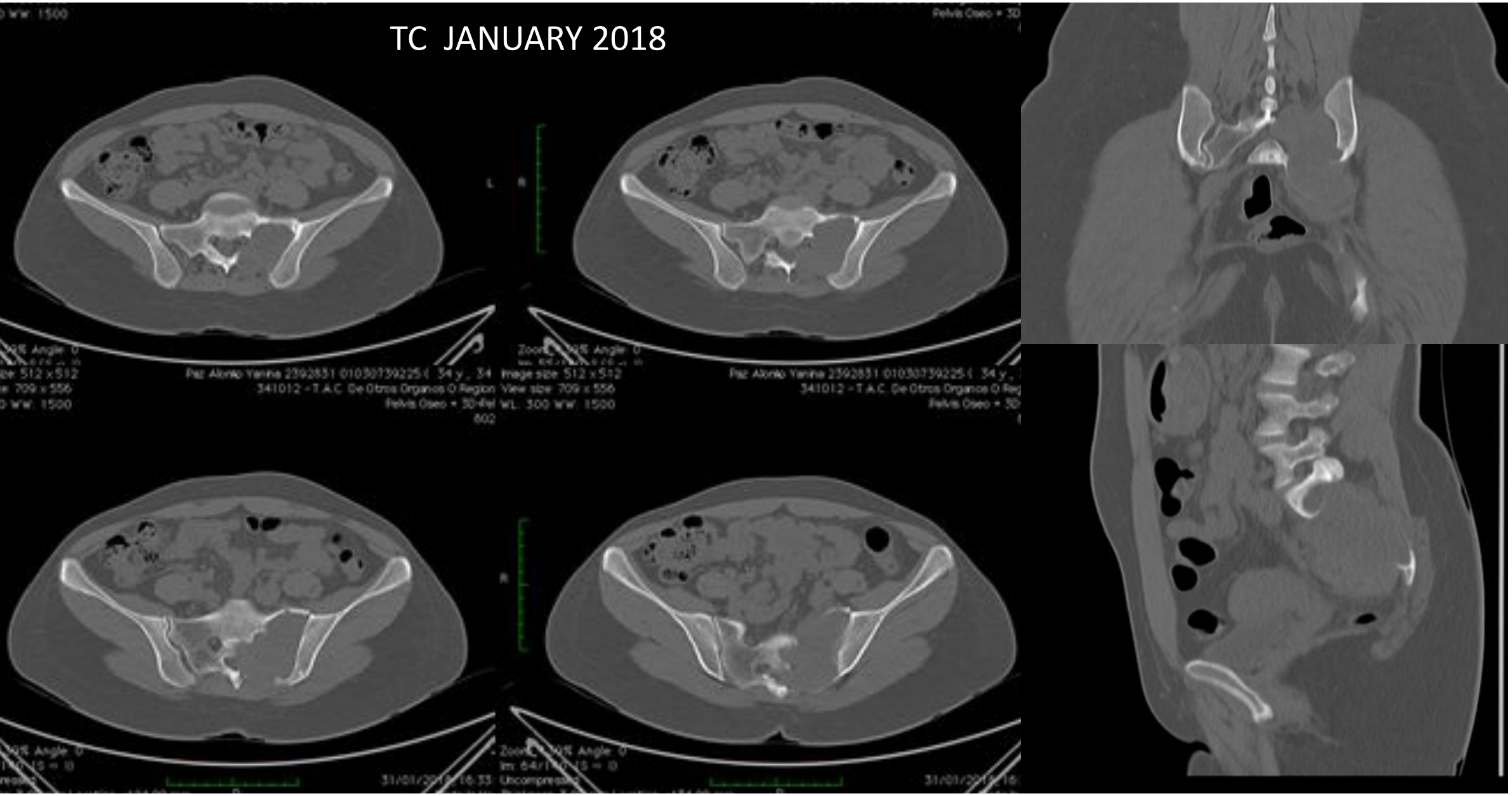


PELVIS MRI PERFORMED JAN 26th 2018:

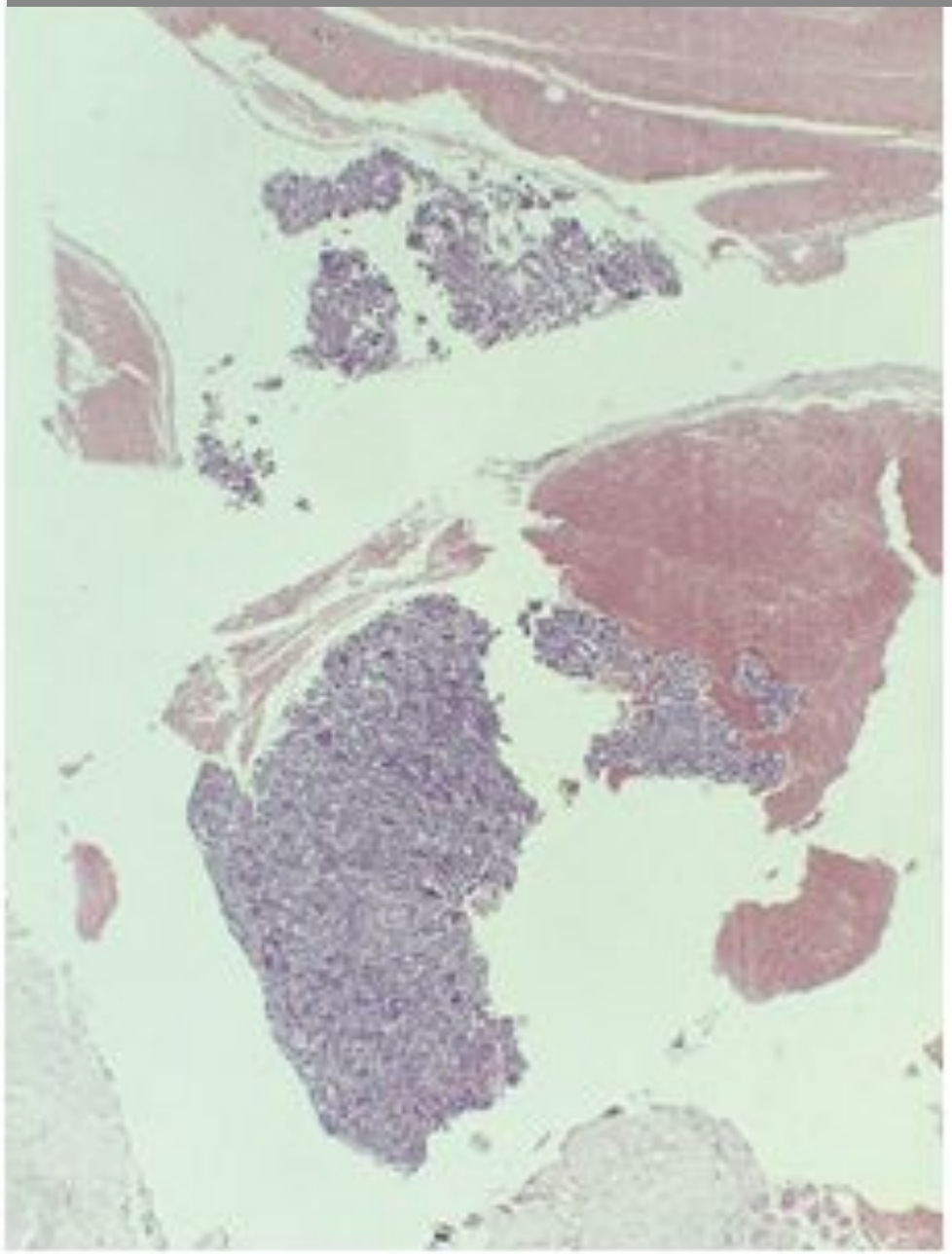


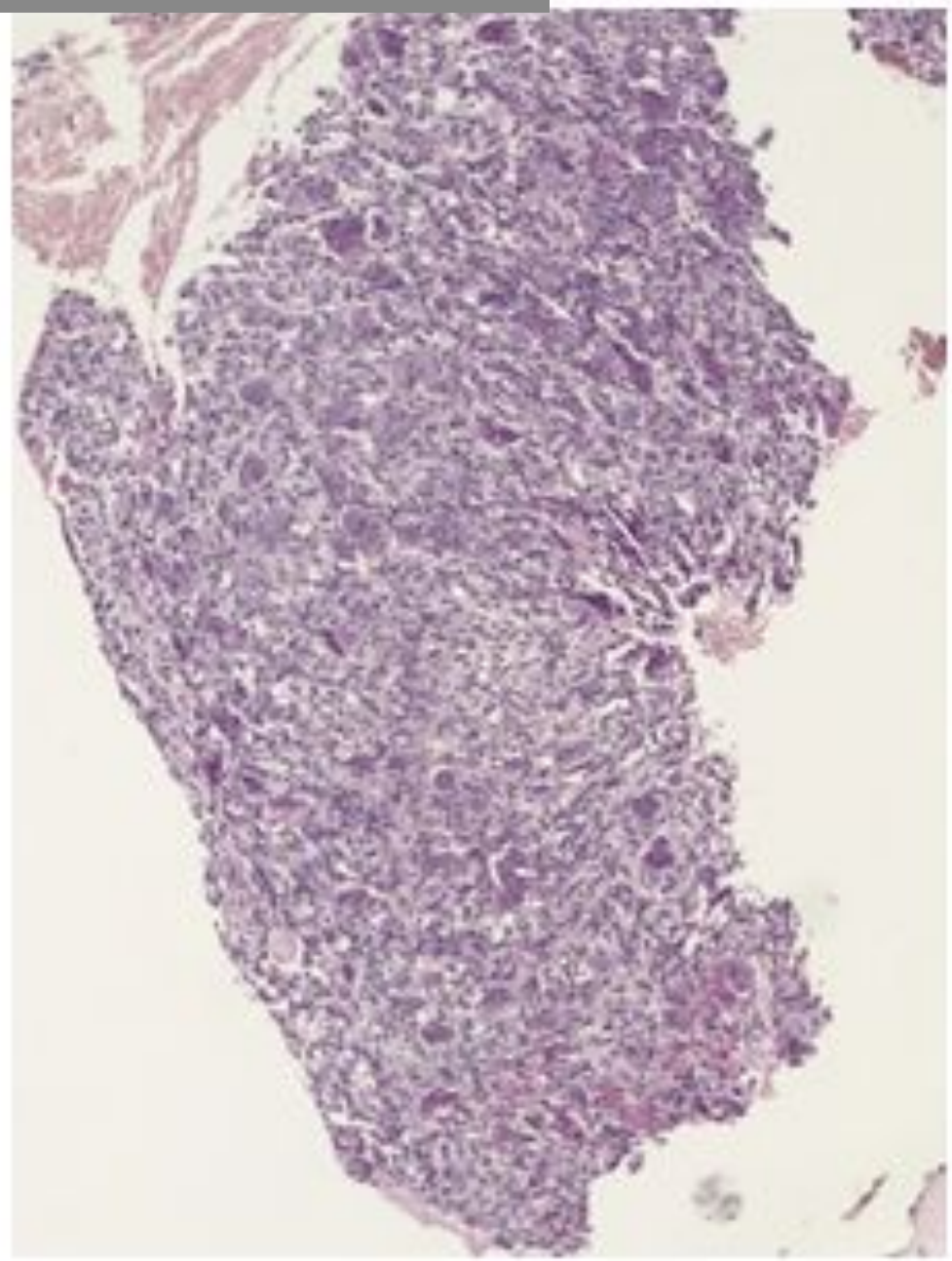
In left sacra region heterogenic image is observed. Hyperintense in STIR and T2 sequences, hypointense in T1, with heterogeneous caption to contrast.
It presents apparent involvement of the left iliac bone in the inferior articular region.
Presents ventral and caudal extension that displaces adjacent soft tissues, with a diameter greater than 67mm.

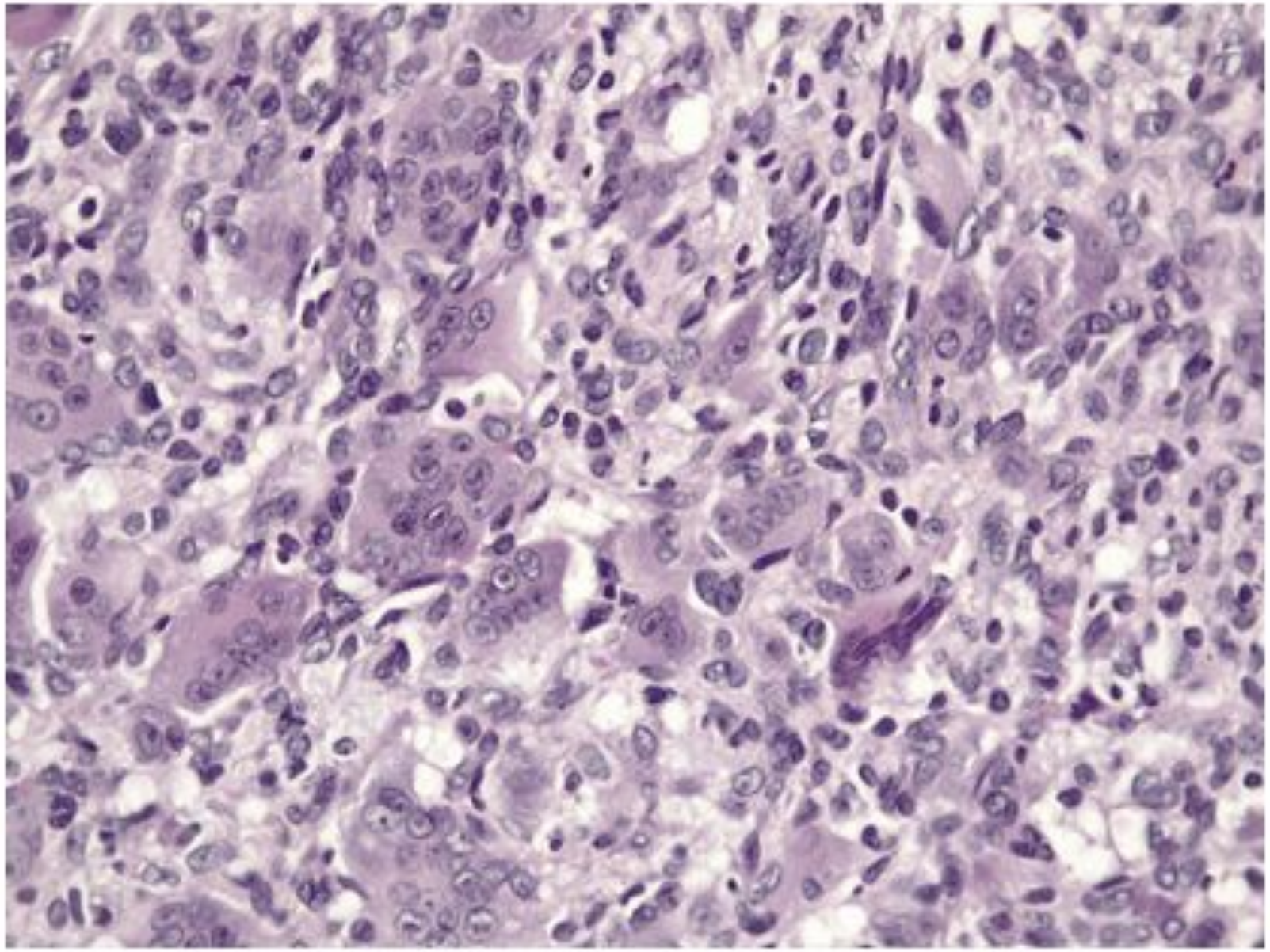
TC JANUARY 2018



CT-guided biopsy was performed on February 1st, 2018.







DIAGNOSTIC:
Fragment of dense fibrous tissue, periosteum, hyaline cartilage and compact bone tissue, with numerous multinucleated osteoclast-like giant cells.

GIANT CELL TUMOUR

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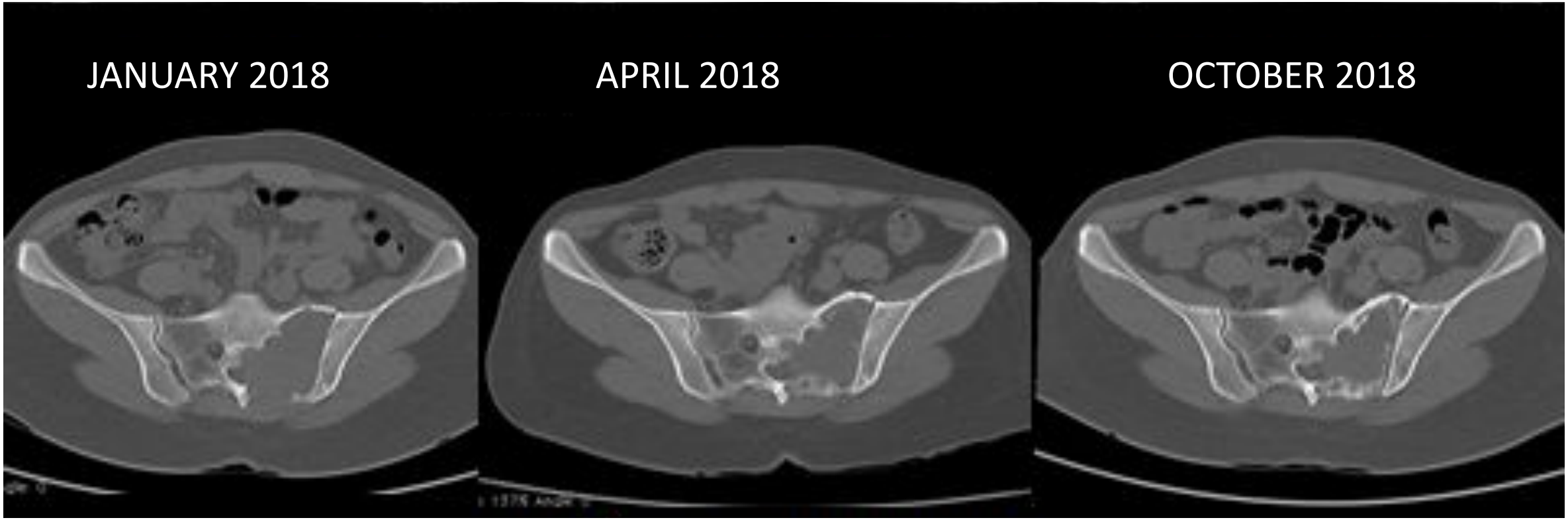
Unidad de Tumores Musculoesqueléticos de la Provincia de Córdoba

GASPAR
Grupo Argentino de Sarcomas de Partes blandas y óseos

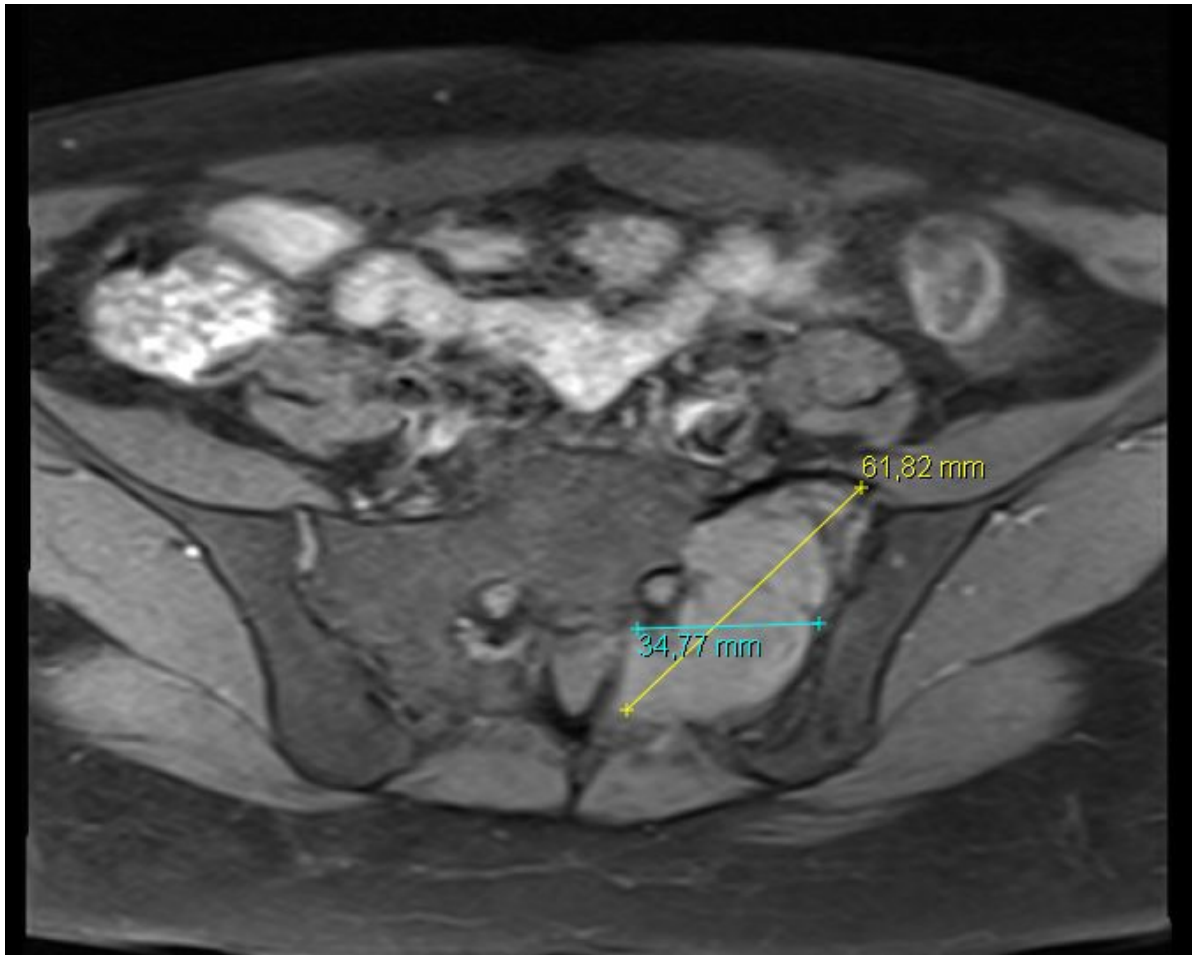
TREATMENT WITH DENOSUMAB WAS STARTED FROM MARCH 2018 TO MARCH 2019.
SHE WAS TREATED ON A MONTHLY BASIS, WITH GOOD CLINICAL RESPONSE, IMPROVEMENT IN PAIN WITHOUT REQUIRING ANALGESIA, NO FUNTIONAL LIMITATION.

SINCE MARCH 2019 CONTINUED WITH QUARTERLY TREATMENT UP NOVEMBER 2021

TC COMPARATIVE IMAGES

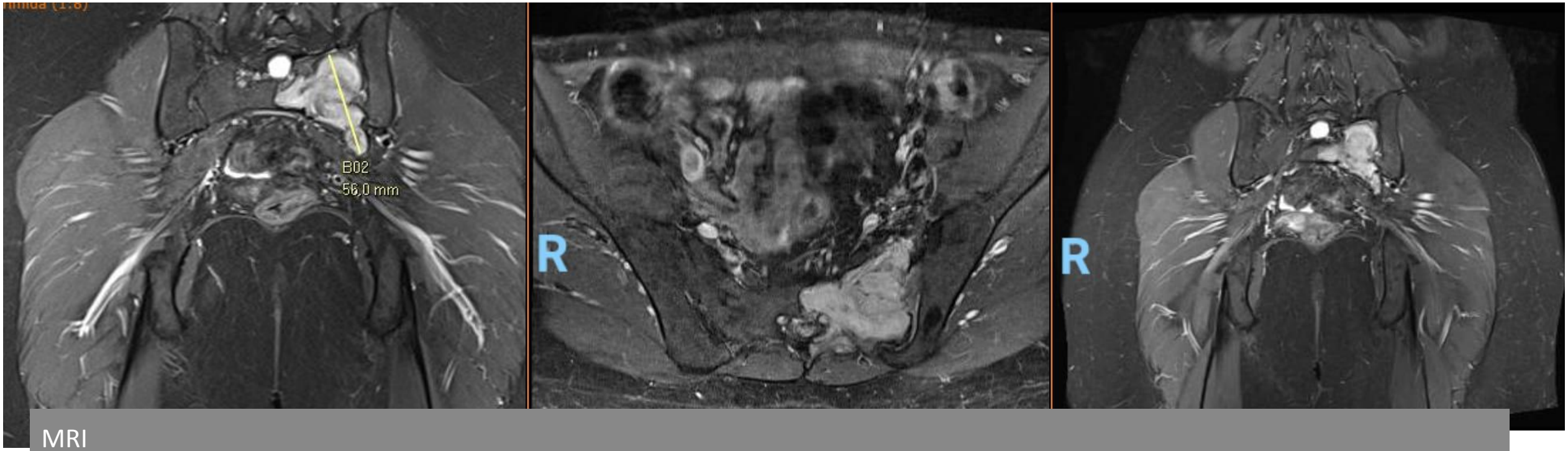


IN MAY 2019 (14th months of treatment) MRI WAS PERFORMED WITH ANGIOGRAPHY OF THE TUMOR, WITH THE INTENTION OF EMBOLIZATION, WHICH WAS DISCARDED.



IN OCTOBER 2021 (22 applications of denosumab) WITHOUT PHARMACOLOGICAL COMPLICATIONS AND ASYMPTOMATIC.

THE PATIENT EXPRESSES DESIRE FOR PREGNANCY



MRI

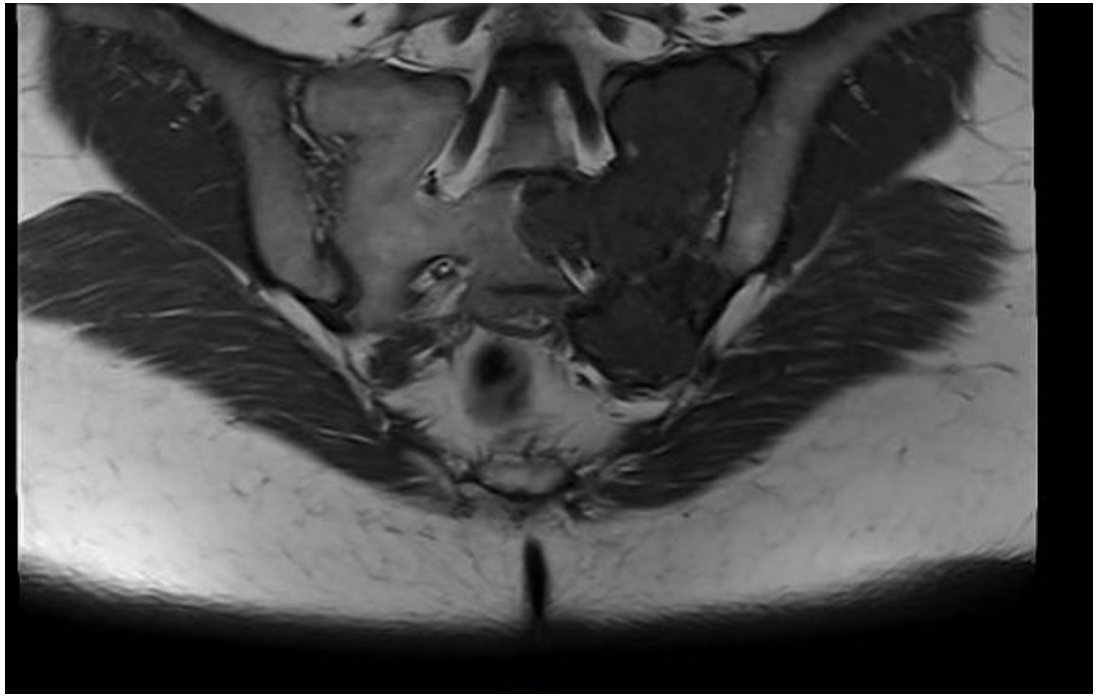
Imaging stability of the lesion located at the level of the left sacral aileron, which presents morphology and signal similar to the previous examination. It currently measures 56 mm cranio-caudally by 52 mm transversely by 46 mm anteroposteriorly.

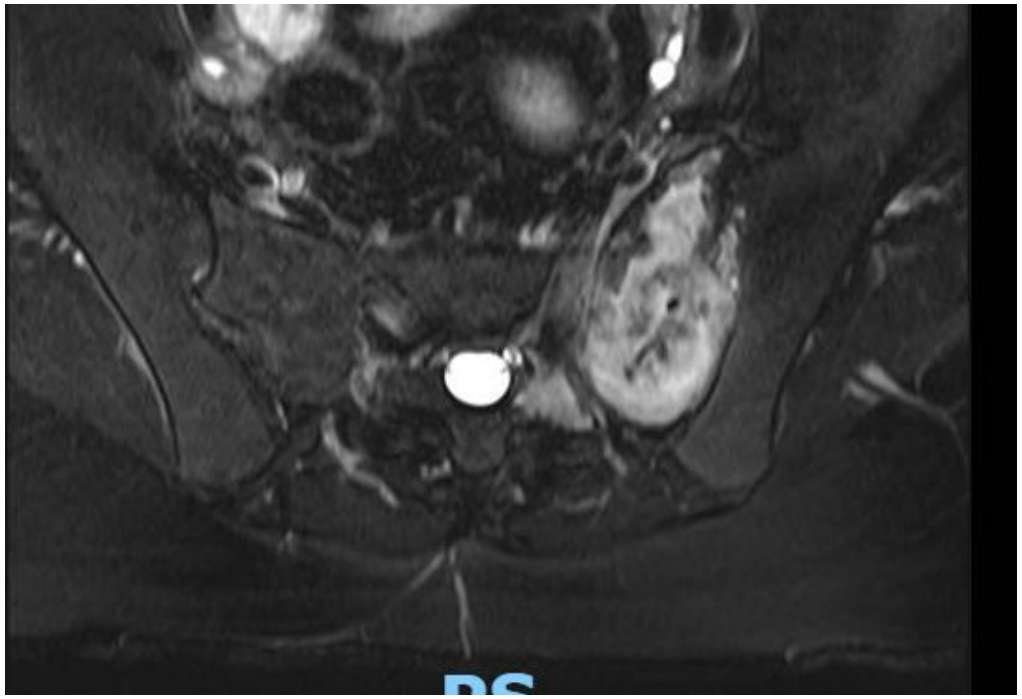
-In the post Gadolinium injection sequence presents a moderate and homogeneous enhancement of the lesion without changes with respect to previous study.

-The ADC coefficient measurement shows similar values to those of his previous examinations, with values of 1.4, 1.2 and 1.1 x 10^{-3} mm^2/sec in the upper, middle and lower thirds.

She stop denosumab and had uncomplicated twin pregnancy 17/06/23

MRI 18/04/24 Imaging stability 16/09/2022





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Extensive replacement of the bone marrow of the sacral aileron and in relation to vertebral bodies S1, S2, S3 and S4, which behaves hypointense on T1 and hyperintense on T2 Stir, showing cortical insufflation, without significant disruption.

Tenuous areas of diffusion restriction are observed, presenting an ADC coefficient of 1.1x10-³ mm²/s.

SELNET

QUESTION FOR THE TUMOR VIRTUAL MDT BOARD

DENOSUMAB SHOULD BE RESTARTED ?

HOSPITAL ONCOLÓGICO

Unidad de Tumores Musculoesqueléticos de la Provincia de Córdoba

GASPAR

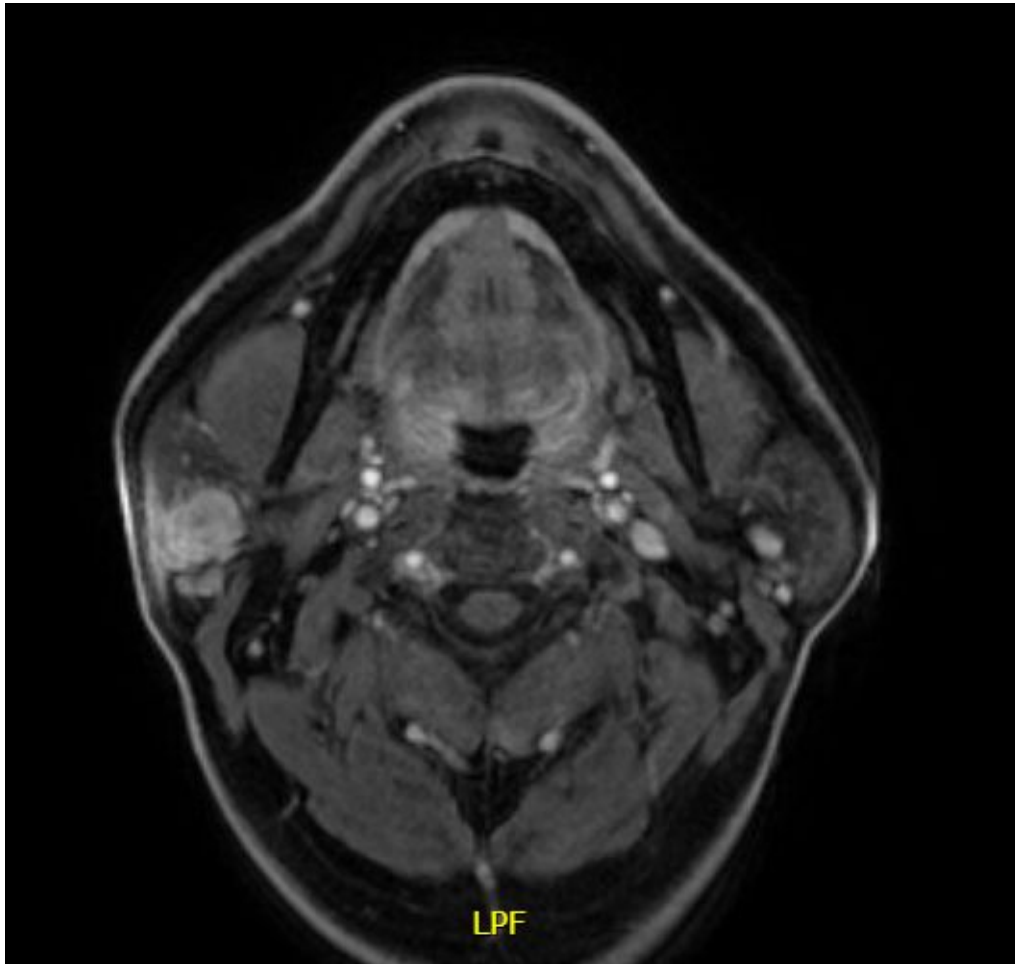
Grupo Argentino de Sarcomas de Partes blandas y óseos

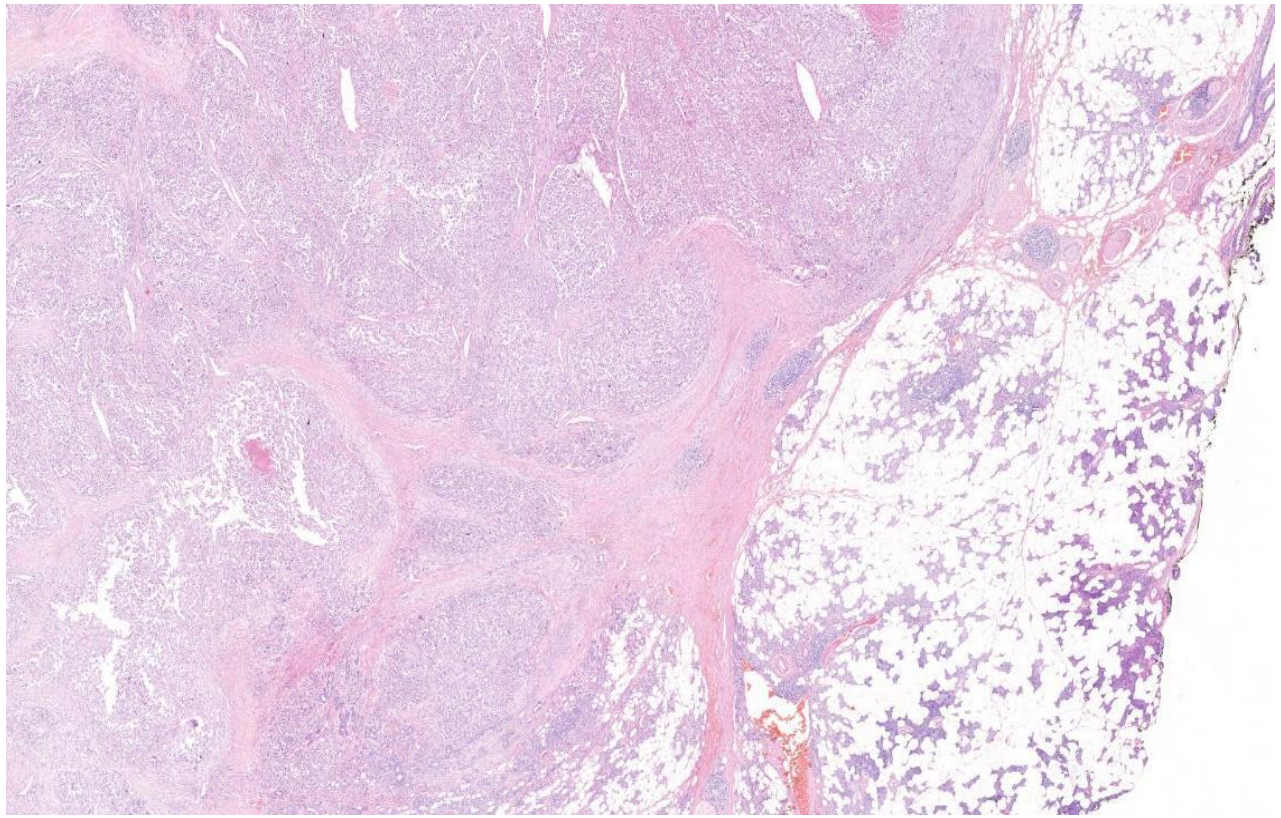
Case 2

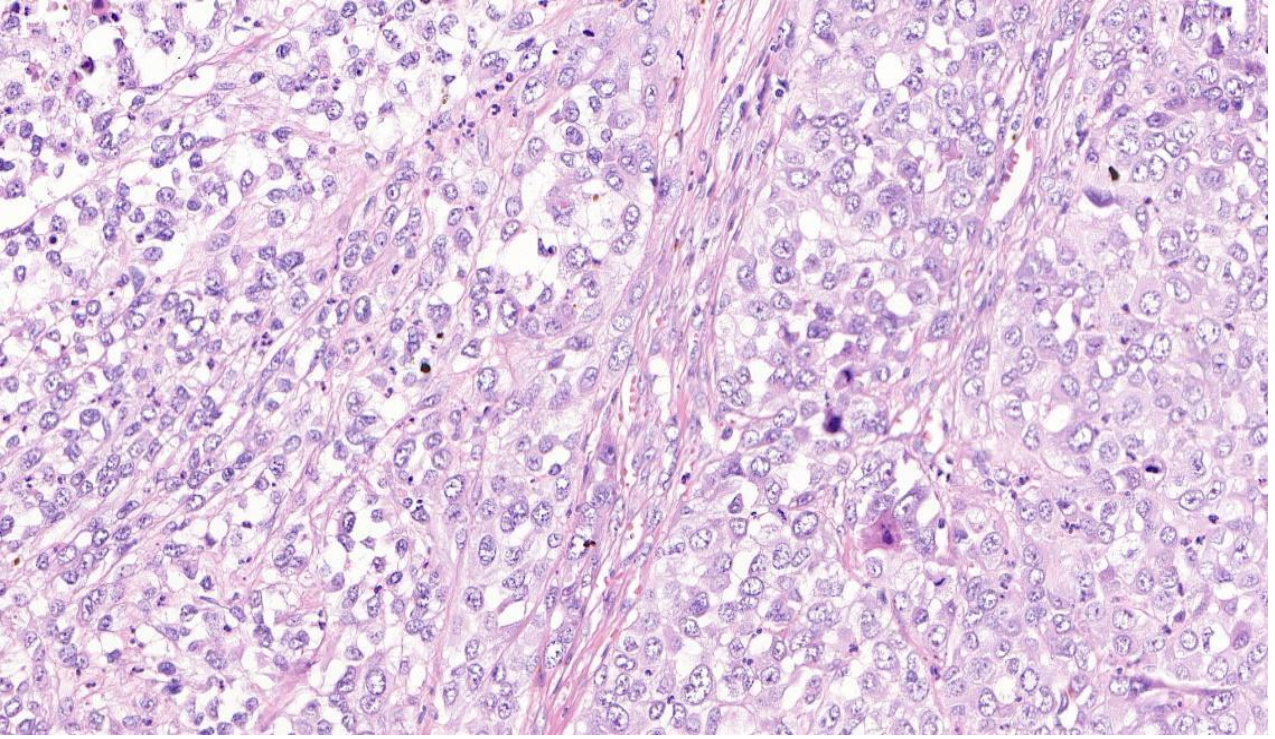
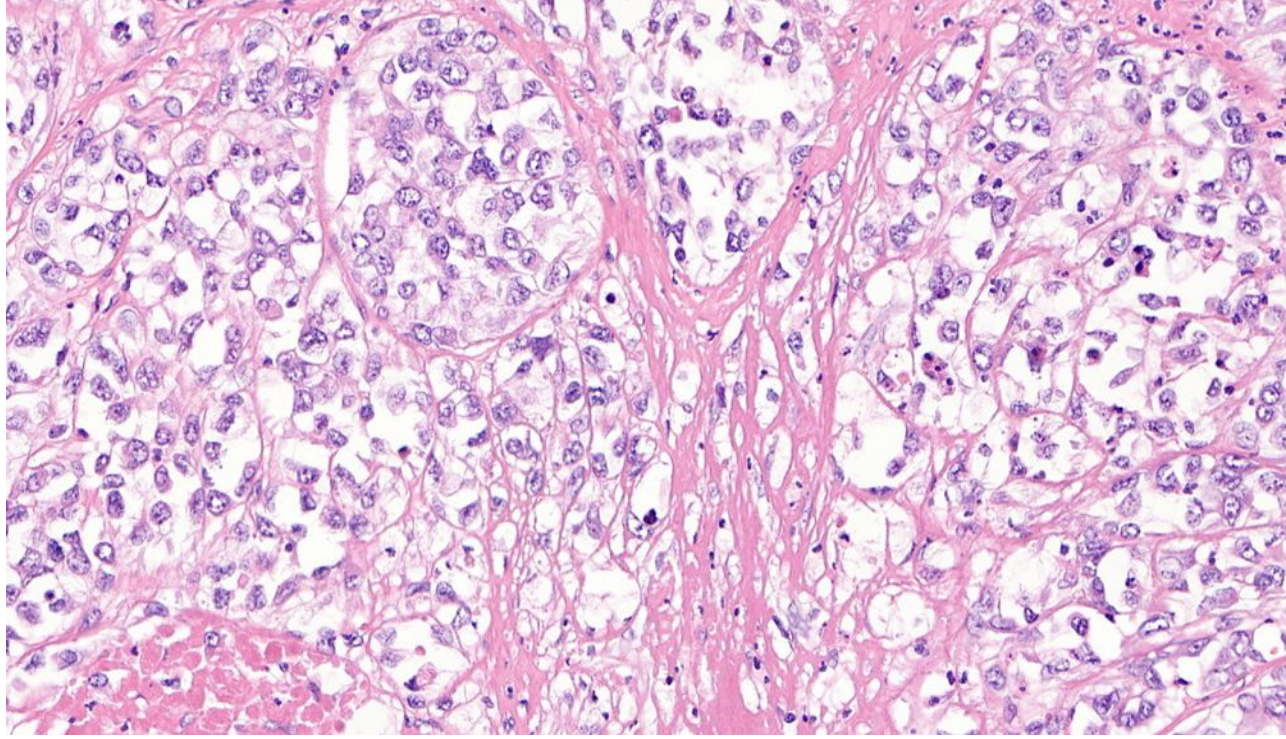
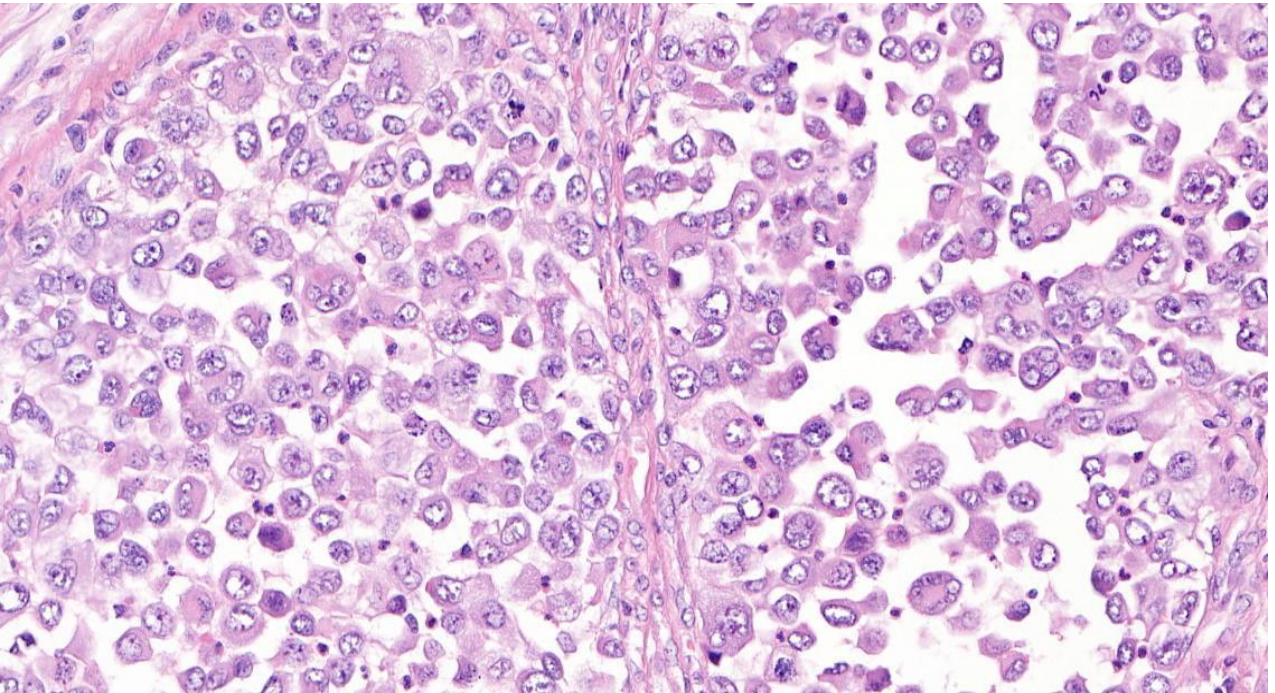
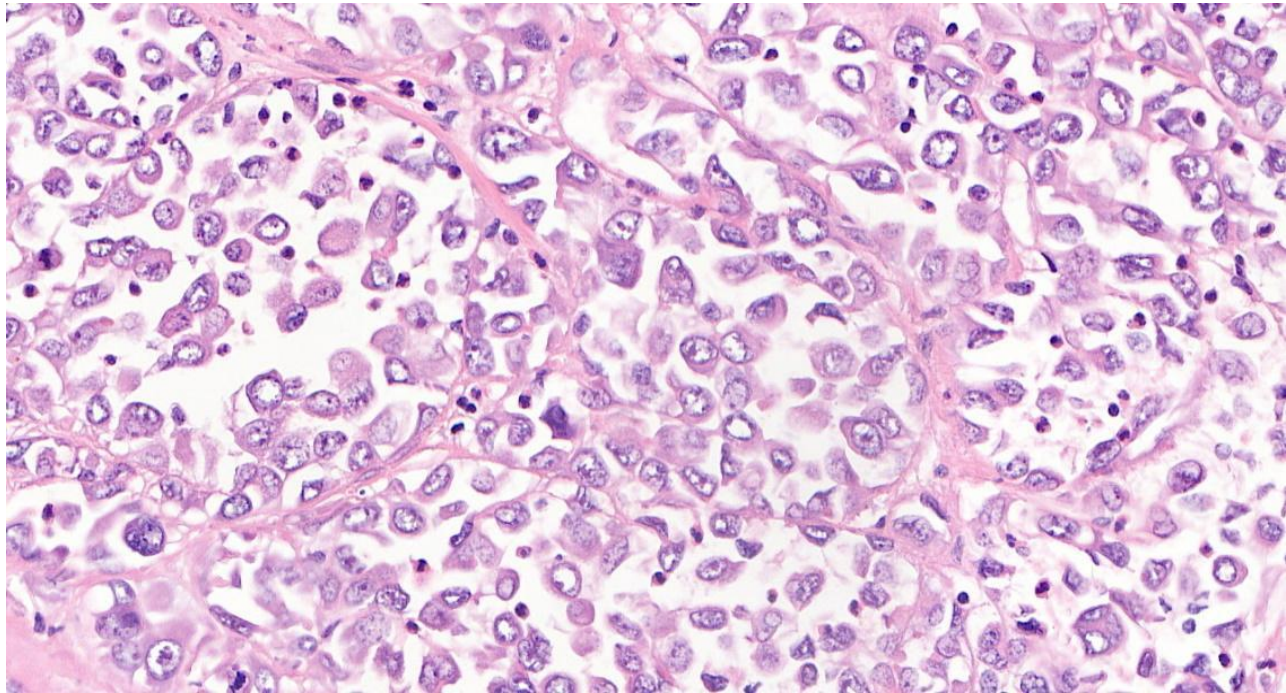
Isidro Puerto - Spain

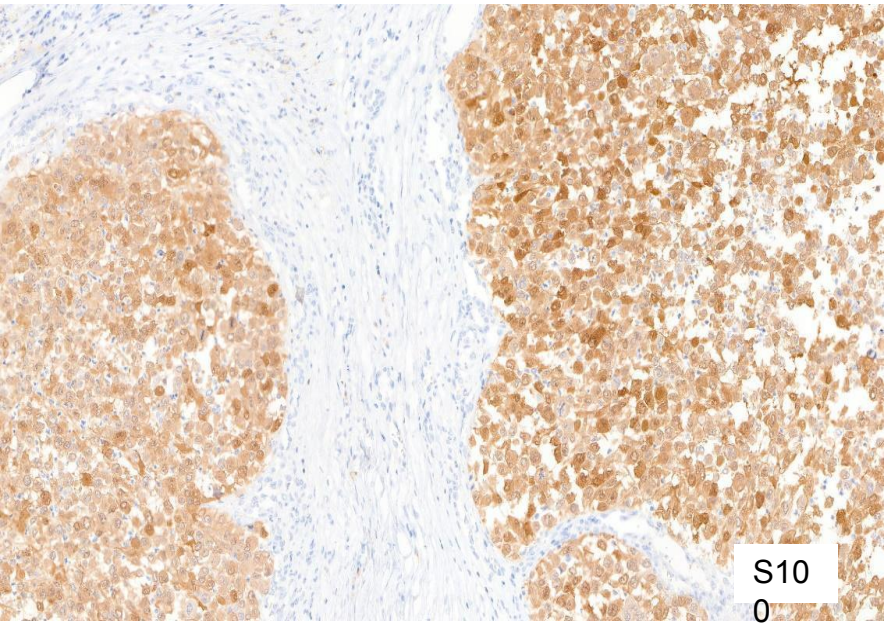
SELNET Session. Instituto Valenciano de Oncología (IVO). Valencia. Spain.
Isidro Machado, Reyes Claramunt, Hector Aguilar.

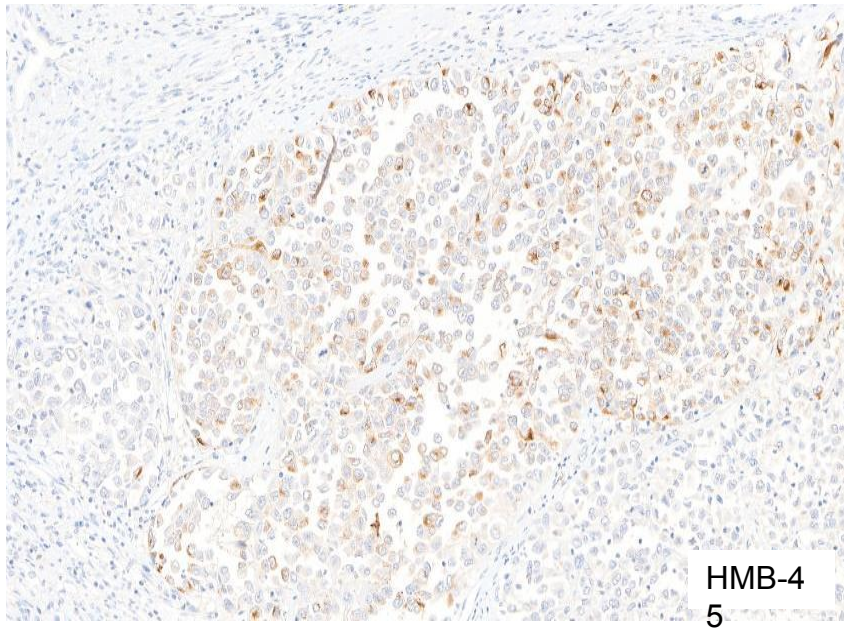
59 y/o male. Previous history of prostatic ADC. Parotid gland tumor with lymph nodes enlargement, FNAB (Milan VI, malignant). Surgical resection. Epithelioid tumor with locoregional lymph node metastasis. CT scan and PET: no significant findings (no distant metastasis).

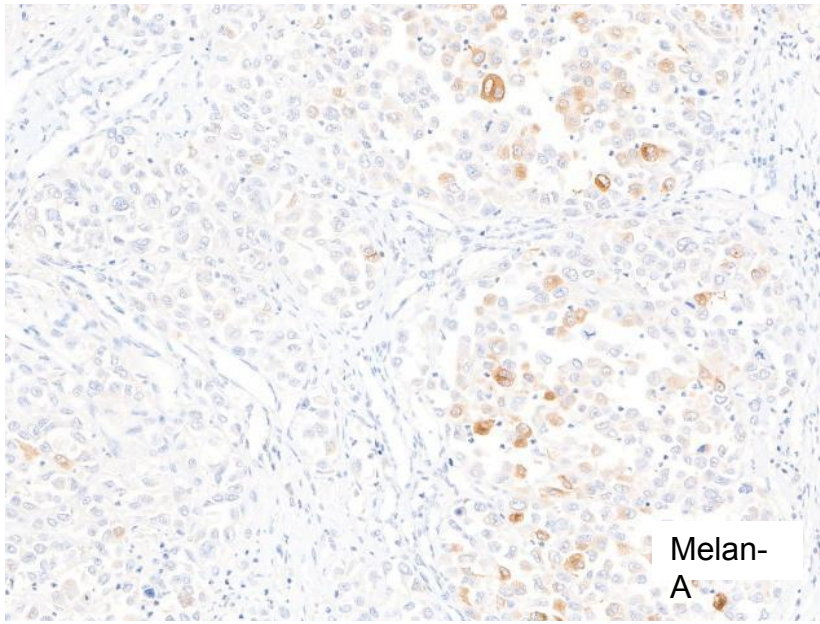


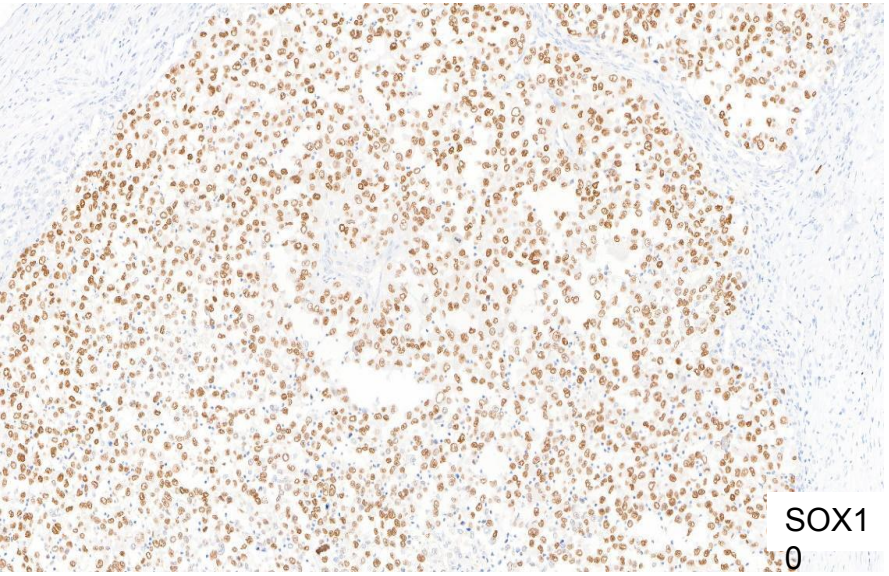


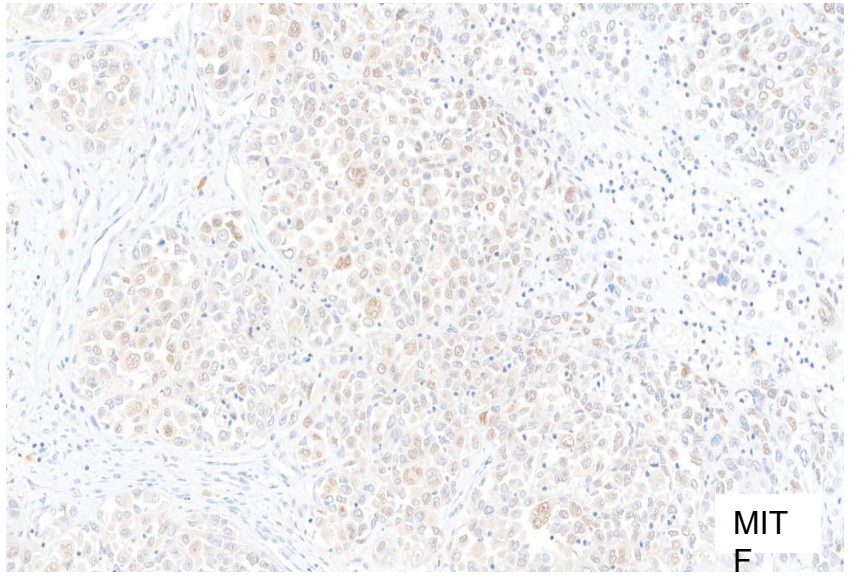






S10
0


HMB-4
5


Melan-
A


SOX1
0


MIT
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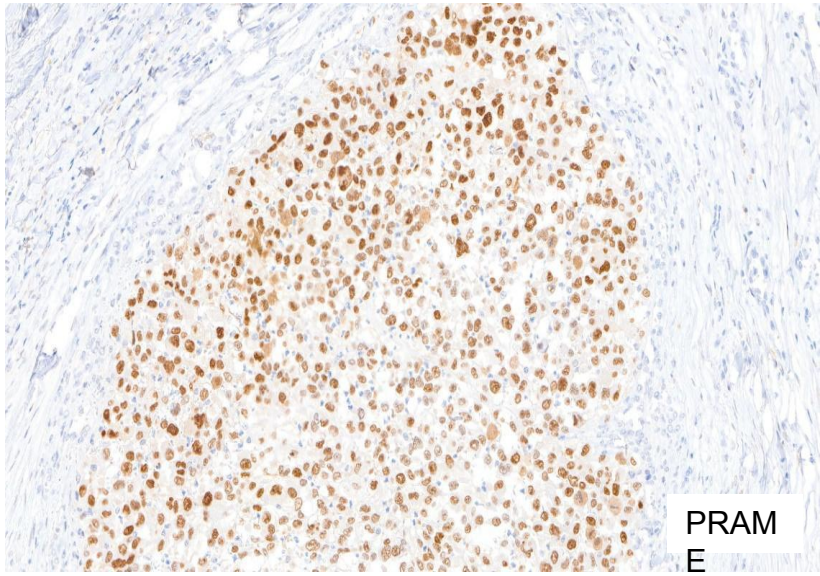
PRAM
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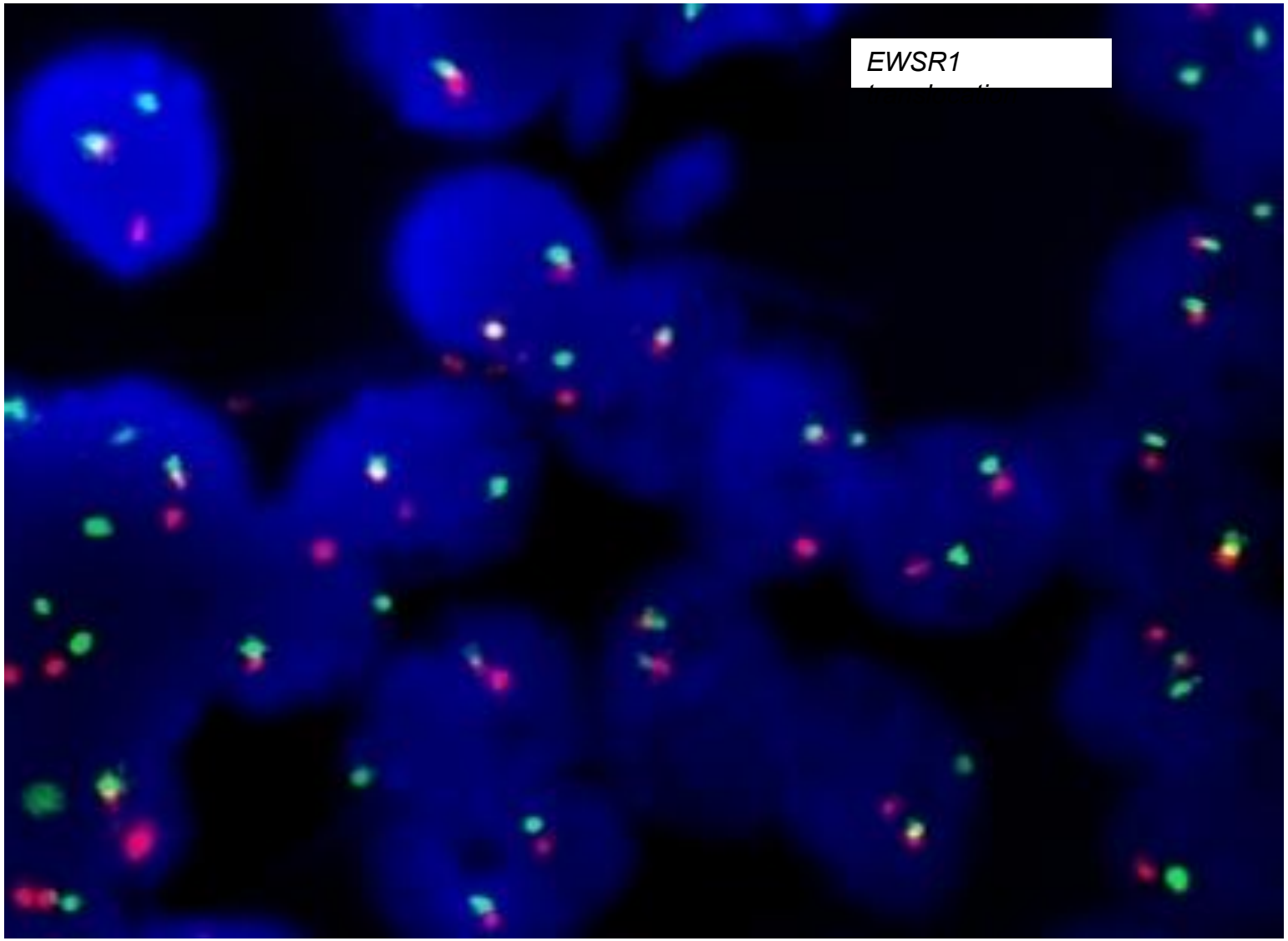


STS NGS panel: *BRAFV600E* and *TERT* mutation
Fusion panel Archer: no fusion

-Manoel EM, et al. Clear cell sarcoma of the parotid region. Braz J Otorhinolaryngol. 2012;(5):135.

-Poignonec S, et al. Clear cell sarcoma of the pre-parotid region: an initial case report. Acta Otorhinolaryngol Belg. 1994;(4):369-73.

-Park BM, et al. Two cases of clear cell sarcoma with different clinical and genetic features: cutaneous type with BRAF mutation and subcutaneous type with KIT mutation. Br J Dermatol. 2013;(6):1346-52.

-Protsenko SA, et al. BRAF-mutated clear cell sarcoma is sensitive to vemurafenib treatment. Invest New Drugs. 2015;(5):1136-43.

-Hyman DM, et al. Vemurafenib in Multiple Nonmelanoma Cancers with BRAF V600 Mutations. N Engl J Med. 2015 20;(8):726-36.

4 months of follow-up, NED

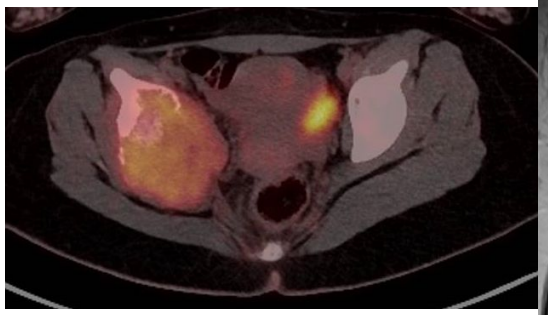
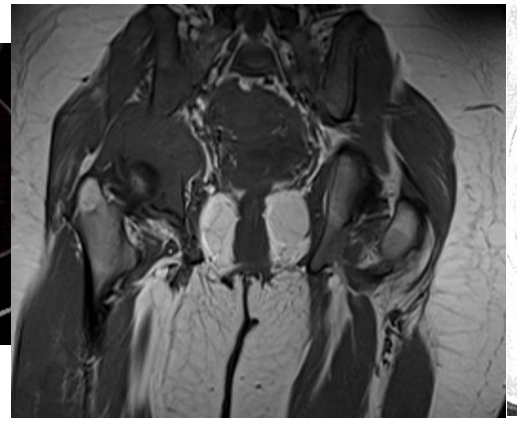
Case 3

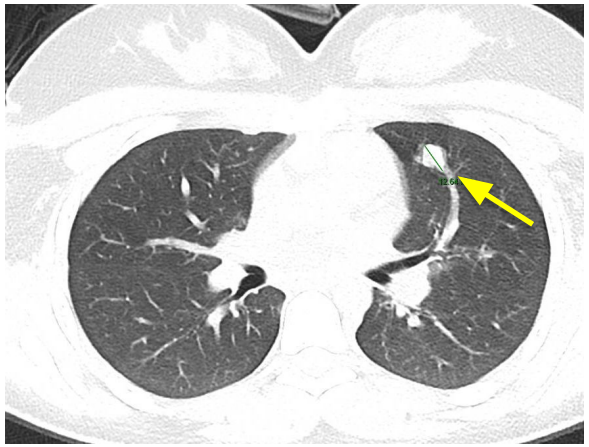
Boris Itkin - Oman

Sultan Qaboos Comprehensive Cancer Care and Research Center

15-years-old, young lady without any significant PMH

Diagnosis: De novo metastatic Ewing sarcoma of the right pelvis with involvement of acetabulum and lung metastases since August 2023



A mildly avid nodular lesion is seen in left upper lobe, appears continuous with vascular branches and measures approximately 1.0 X 1.2 cm in size with SUV max 2.6

Subcentimeter-sized nodule along the left oblique fissure with no uptake

No other lesions consistent with metastases were observed outside of the lung

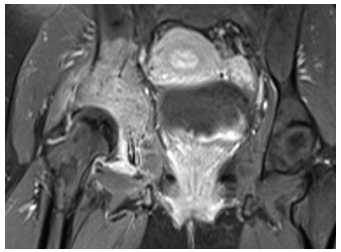
Treatment

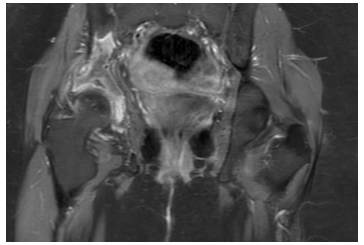
- VDC/IE chemotherapy for 14 cycles (COG AEWS 1031 Arm A protocol up to14 cycles)
- Definitive RT (VMAT, 57.6 Gray in 30 fractions) to the pelvic lesion was administered concurrently with cycles 7, 8, and 9 (VC-IE-IE)
- End of treatment == 15.05.2024

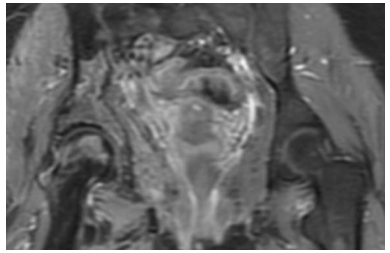
Baseline

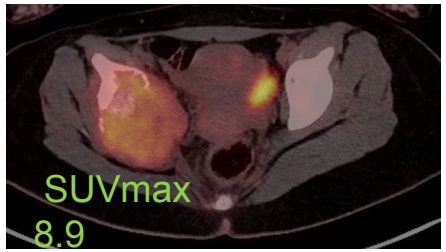
After #6

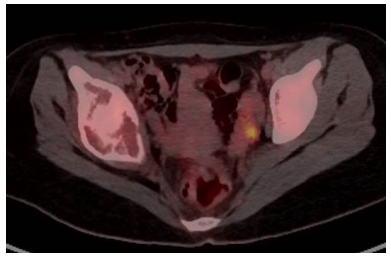
End of treatment

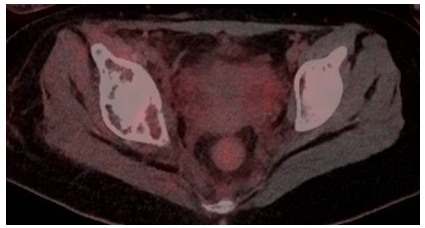


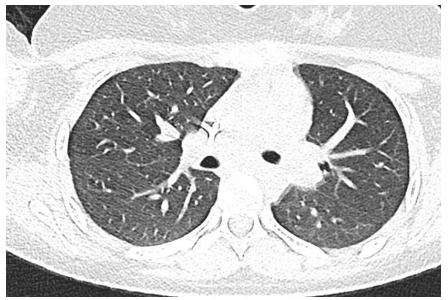












Summary

- Pelvic Ewing with acetabulum invovment and isolated lung metastases after the completion of VDC/IE #14 and definitive RT to the primary

Questions to the board:

- Was the initial staging correctly done or biopsy was necessary?
- How to continue?
  - Surveillance?
  - Surgery of the primary +/- Whole lung irradiation?
  - Whole lung irradiation. If no systemic disease, consider the resection of the primary?
  - Maintenance
  - Others

Case 4

Franklin Castillero R. - Panamá

Centro Hemato Oncológico

Clinical data: male, 35y old, salesman

- January, 2024: right upper arm neuropathic pain. MRI: cervicothoracical paravertebral tumor of 66 cm, with anterior displacement of right carothid, yugular vein and trachea.
- Biopsy: atypical fusocelullar high grade neoplasia
- February 5, 2024: patient started induction chemotherapy with ADR – IFO, completing 4 cycles on april.
- CT-Scan: tumor reduction in about 16%, however, with irresectability criteria (brachial plexa infiltration and scalenus muscle)
- June, 2024: The patient completed 35 sesions of 70gy IMRT

Pathologic assessment

INFORME HISTOPATOLOGICO

HISTORIA CLÍNICA: Masa cervical en estudio, dolor y parestesias en miembro superior derecho.

DIAGNÓSTICO CLINICO:	**TIPO DE MUESTRA:**
NEOPLASIA MESENQUIAL E/E	BIOPSIA LESION CERVICAL - MEDIASTINO

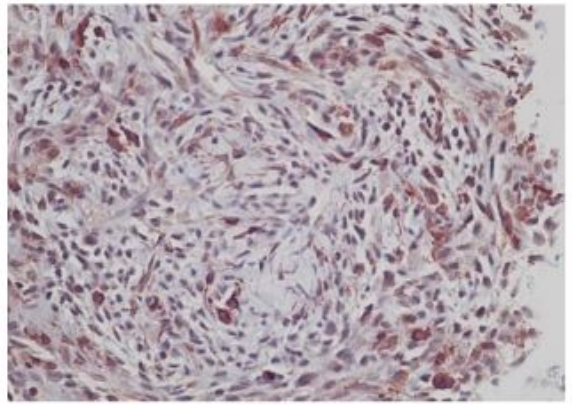
ESTUDIOS DE INMUNOHISTOQUÍMICA:

- **SMA:** **POSITIVO FOCAL**
- **BCL-2:** **POSITIVO FOCAL**
- **CD34:** **NEGATIVO (0%)**
- **S100:** **NEGATIVO (0%)**
- **KI-67:** **POSITIVO (10%)**

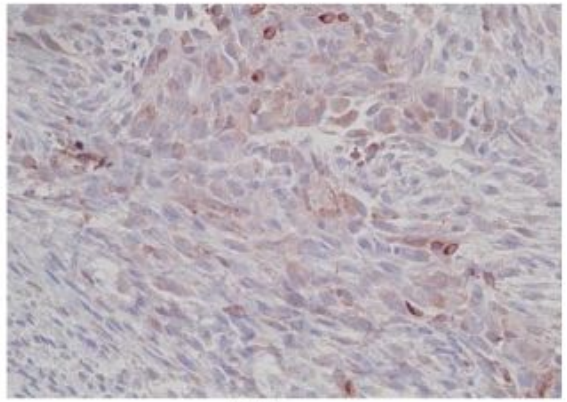
DIAGNÓSTICO FINAL: REGION CERVICAL- MEDIASTINO, BIOPSIA PERCUTÁNEA:

- **NEOPLASIA FUSOCELULAR MALIGNA COMPATIBLE CON SARCOMA, NOS.**
- **LA EXPRESIÓN DE SMA Y BCL-2 SE OBSERVA EN DIFERENTES NEOPLASIAS FUSOCELULARES, NO ES ESPECÍFICA, PERO ORIENTA A UN ORIGEN MIOFIBROBLASTICO.**
- **LA NEGATIVIDAD DE S-100 NO ME DESCARTA UN TUMOR MALIGNO DE LA VAINA DE NERVIO PERIFERICO.**
- **NO CUENTO CON CD99 NI TLE-1 QUE AYUDAN A CONFIRMAR UN SARCOMA SINOVIAL.**
- **SUGIERO LA EVALUACIÓN DE ESTOS MARCADORES (CD99, TLE-1, CKAE1/AE3) DURANTE LA RESECCIÓN DEL TUMOR. ADEMAS DE UN BUEN MUESTREO DE ESTA NEOPLASIA POR SI EXISTE OTRO COMPONENTE NO OBSERVADO EN ESTA BIOPSIA.**

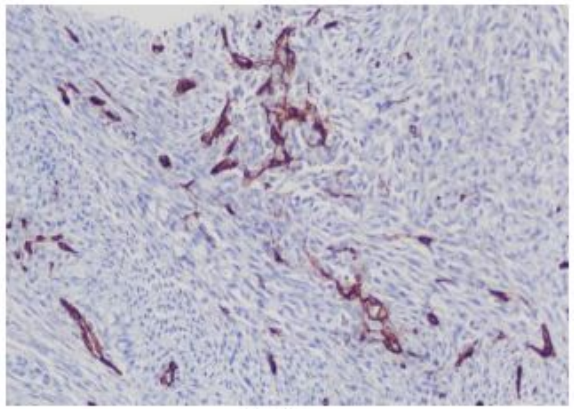
CPT: 88342



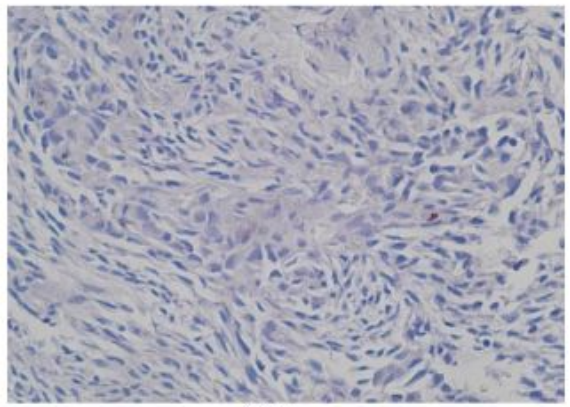
SMA



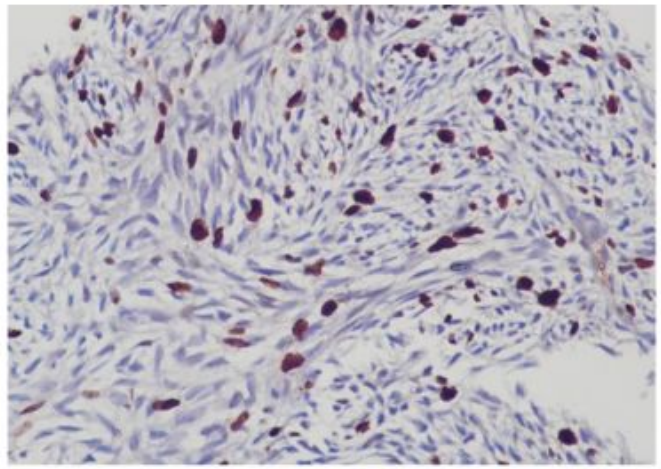
BCL-2



CD34



S-100



KI-67

NGS: Tempus xt+ xr analysis

GENOMIC VARIANTS

Potentially Actionable / Biologically Relevant

No reportable pathogenic variants were found.

Tumor / Normal Matched Analysis (Potential Germline)

No normal sample was received, therefore tumor/normal matched analysis was not performed.

IMMUNOTHERAPY MARKERS

Tumor Mutational Burden

2.1 m/MB | 18th percentile

Microsatellite Instability Status

Stable | Equivocal | High

TREATMENT IMPLICATIONS

No reportable treatment options found.

VARIANTS OF UNKNOWN SIGNIFICANCE

Gene	Mutation effect	Variant allele fraction
NOTCH1	c.410C>T p.S137L Missense variant NM_017617	68.8%
ALK	c.1918G>A p.G640R Missense variant NM_004304	49.9%
FLCN	c.1654_1709dup p.P572fs Frameshift NM_144997	12.9%
SETD2	c.361G>A p.G121S Missense variant NM_014159	10.2%

Institution
CENTRO HEMATOONCOLOGICO PANAMA (CHOP)

TEMPUS | RNA
Transcriptome

EXPRESSION DETAILS

ERBB3 Overexpressed

CDKN2B Underexpressed

GENOMIC VARIANTS

Potentially Actionable

SS18-SSX1 Chromosomal rearrangement

ADDITIONAL INDICATORS

Diagnostic

NCCN, Consensus, Synovial Sarcoma
SS18-SSX1 Chromosomal rearrangement

We were unable to determine whether treatments on this report were previously prescribed for this patient.

Which is the most appropiate step

- Follow up
- Try the surgical resection (at least a debulking surgery)
- Start a HER 3 inhibitor given the ERB3 mRNA overexpression
- Any other recommendation?

Case 5

Luciana Auresco - Brazil

Clinical Case Discussion

Luciana Campi Auresco, MD
Mirella Nardo, MD – Sarcoma Unit Director

São Paulo, Brasil

Clinical Case

Men, 50 years old, ECOG-OS 0
Medical history:

- **Possible NF1 mutation (phenotype)**
  - **At age 42: duodenal GIST pancreaticoduodenectomy**
  - **2022: Myocardial Infarction**
  - **April/2024: Ischemic stroke**

Family History: Father died of a MPNST around age 40

Feb/ 2024

Patient felt a mass growing on the inside of his left thigh; Due to his past history, a PET-CT was performed and showed a mass of 14,8x6,3x5,5cm with a max. SUV of 16,9.

Mar/ 2024

Dedicated MRI: Voluminous expansive formation in inter/intramuscular planes in the posteromedial region of the proximal and middle thirds of the thigh; Possible high- grade lipossarcoma
Brain MRI: NED but showed an ischemic area that was further investigated and resulted in a delay to perform the biopsy.

Clinical Case

02/2024 PET-CT

Mass mesures 14,8x6,3x5,5cm
Max. SUV 16,9

April/2024 Core Biopsy:

- High grade pleomorphic sarcoma
- Mitotic Index : 10/10 CGA

IHC:

CD34 Positivo focal	**Postive (focal)**
Desmin	**Negative**
S100 Negativo	**Negative**
Caldesmon	**Negatve**
Beta-catenin 1	**Positive**
EMA	**Negative**
AE-1AE-3 Negativo	**Negative**
CD99	**Positive**
Actin (smooth muscle)	**Negative**
TLE-1 Negativo	**Negative**
Sox10	**Negative**

Clinical Case

May 2024

Pathology review:

- Histone H3 positive

Due to his clinical history and IHC □ pathology reported as a **MPNST**

June/24

New systemic evaluation: NED

Neoadjuvant RT:
50/54Gy in 25 fractions

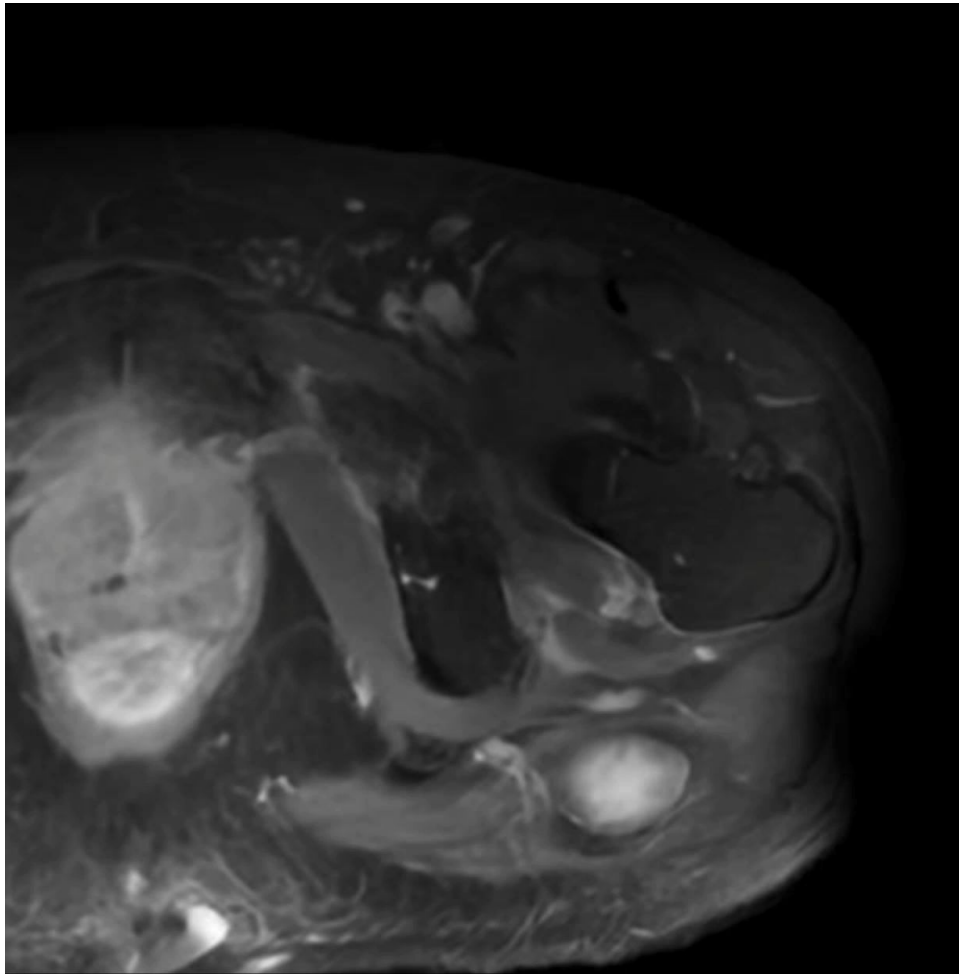
Jul/24

Echocardiogram: Ejection fraction 40%, mild diastolic dysfunction due to impaired left ventricular relaxation

Clinical Case

Jul/2024 Sagital Stir

Axial FatT1



Clinical Case

Questions:

- **Neoadjuvant IE vs Upfront surgery**
- **Anthracycline-based CT?**

Case 6

Nadia Hindi - Spain

Long survivor metastatic angiosarcoma

Dr. Carlos López Jiménez/Dra Nadia Hindi

HU Fundación Jiménez Díaz, Madrid, Spain

- 66 yo women. No relevant medical history.

- **August/2018**

Fast-growthing tumor in the medial region of right thigh (2 cm).

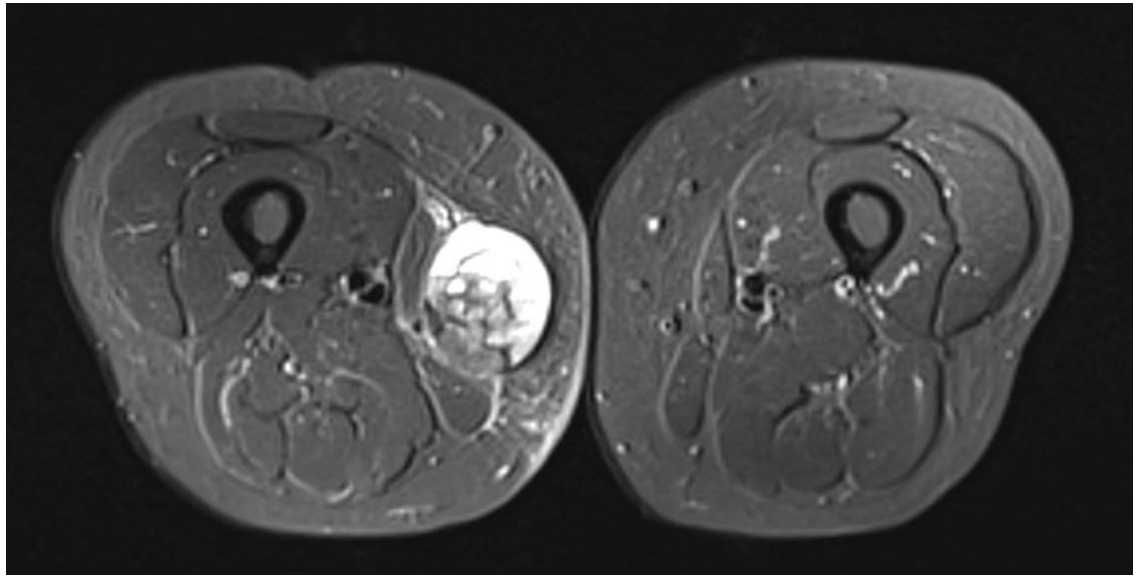
- **October/2018**

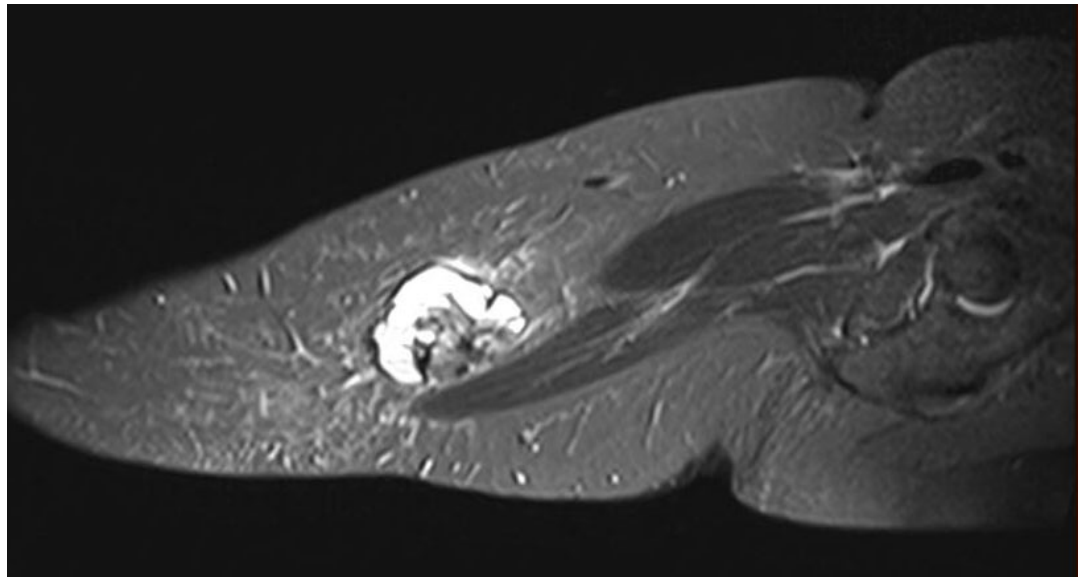
10 cm lesion, adhered to a deep plane, hard consistency.

RMI:
65 x 40 x 51 mm lesion.
Heterogeneous solid portion on its posterior and inferior margins, with restriction of diffusion and *heterogeneous enhancement* after the administration of intravenous contrast.

No other lesions in CT or bone scan.

Biopsy: High grade sarcoma (impossible to filiate differentiation due to scarce material in the sample).





65 x 40 x 51 mm lesion.
Heterogeneous solid portion on its posterior and inferior margins, with restriction of diffusion and heterogeneous enhancement after the administration of intravenous contrast.

- **December/2018**

  Wide resection of the lesion + reconstruction

- **Pathology report:**
  - Grade 3 **ANGIOSARCOMA**
  - 11 mitosis/10 HPF.
  - 20% necrosis.
  - Vascular invasion.
  - Resection margins not affected.

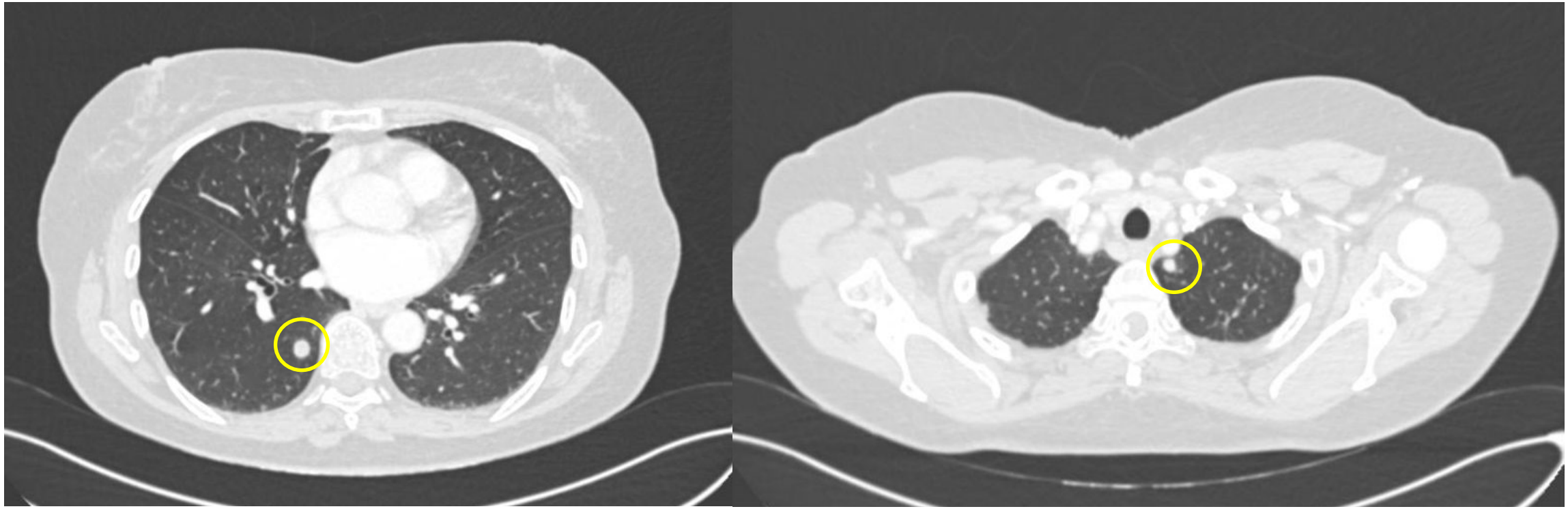
- **<u>SARCULATOR</u>: High grade sarcoma, >5 cm**
  - **37%** 5-YEARS OS
  - **22%** 10-YEARS OS.

- **February/2019**
  - **ADYUVANT CHT** (Epirrubicin 60 mg/m2 + Ifosfamide 3 mg/m2, x3)
  - Ifosfamide discontinuation from the second cycle due to volume overload and microhematuria.
  - **ADYUVANT RT** (50 Gy + boost -64 Gy- in the nearest resection margin).

-
-

7.2 mm

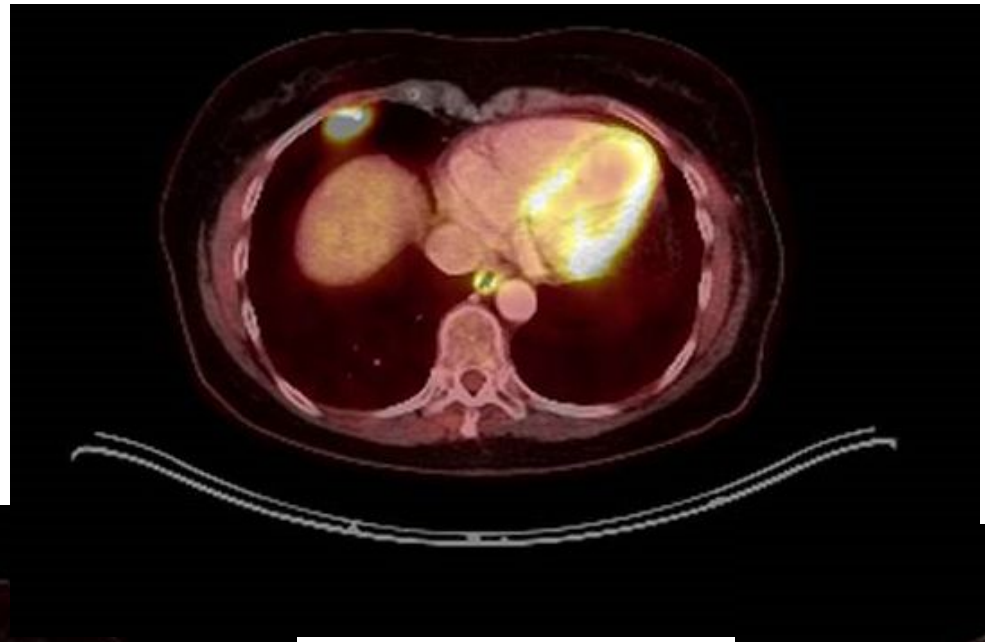
9.5 mm



- Pulmonar metastasectomy is proposed.

- December/2019: **Atypical segmentary resection** (upper left lobe metastasis).

- PET-TC January/2020: Suggestive of **secondary mediastinal adenopathic, pulmonary and right subpleural involvement**.



First Line Treatment: Weekly Paclitaxel

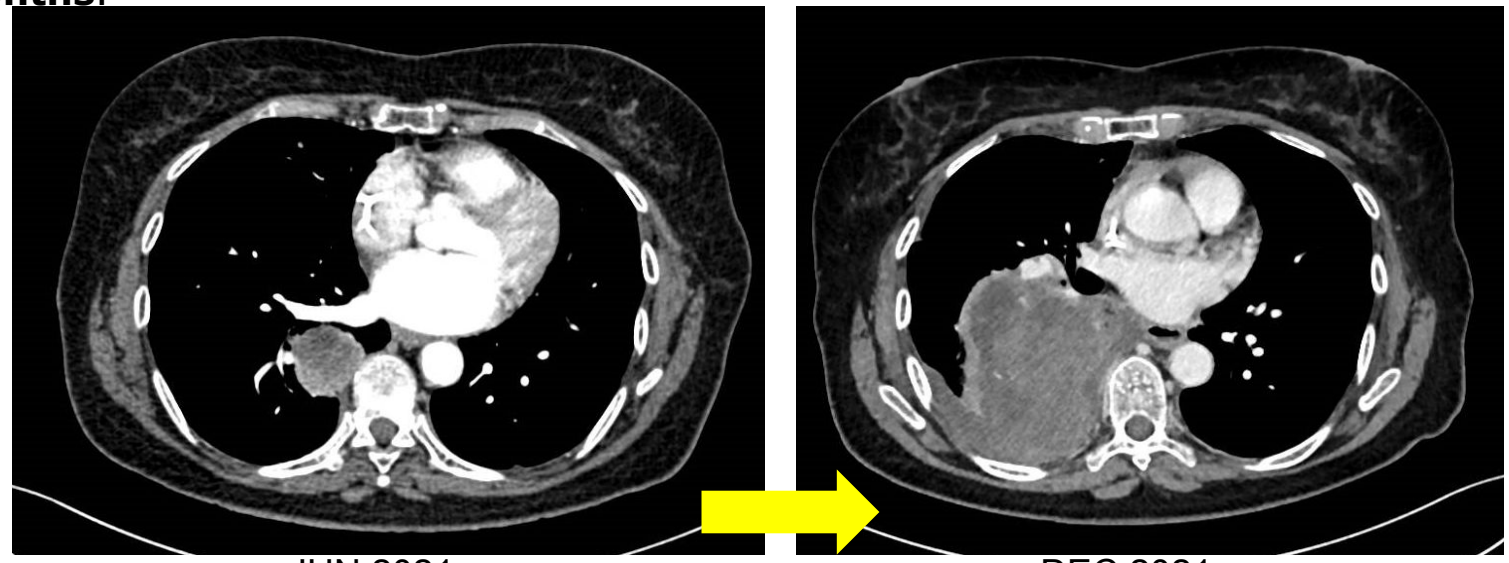
- From february/2020 to september/2020.
- First reevaluation in mayo/2020: **PARTIAL RESPONSE**.
- Dose reduction due to neuropathy G2.
- September/2020: **PROGRESSION DISEASE** (increased size of known lung metastases).
- PFS: **8 months**

Second Line Treatment: Pazopanib

- From september/2020 to june/2021.
- February/2021: **STABLE DIASEASE**.
- Toxicity: High blood pressure G1 and diarrhea G1.
- June/2021: **PROGRESSION DISEASE** (lung disease: right lower lobe and left lower lobe).
- PFS: **10 months**.

Third Line Treatment: IMMUNOSARC2

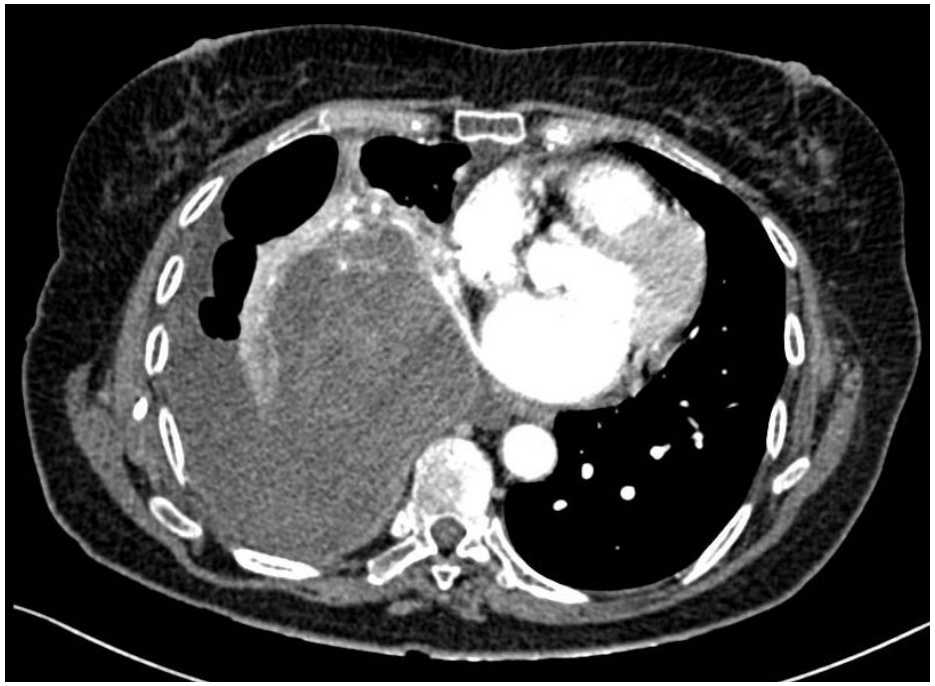
- Sunitinib + Nivolumab.
- From june/2021 to december/2021.
- Best response (november/2021): **STABLE DISEASE (with dimensional increase)**
- Toxicity: Asthenia G1.
- December/2021: **PROGRESSION DISEASE** (lung metastases, pleural invasion and effusion).
- PFS: **7 months**.

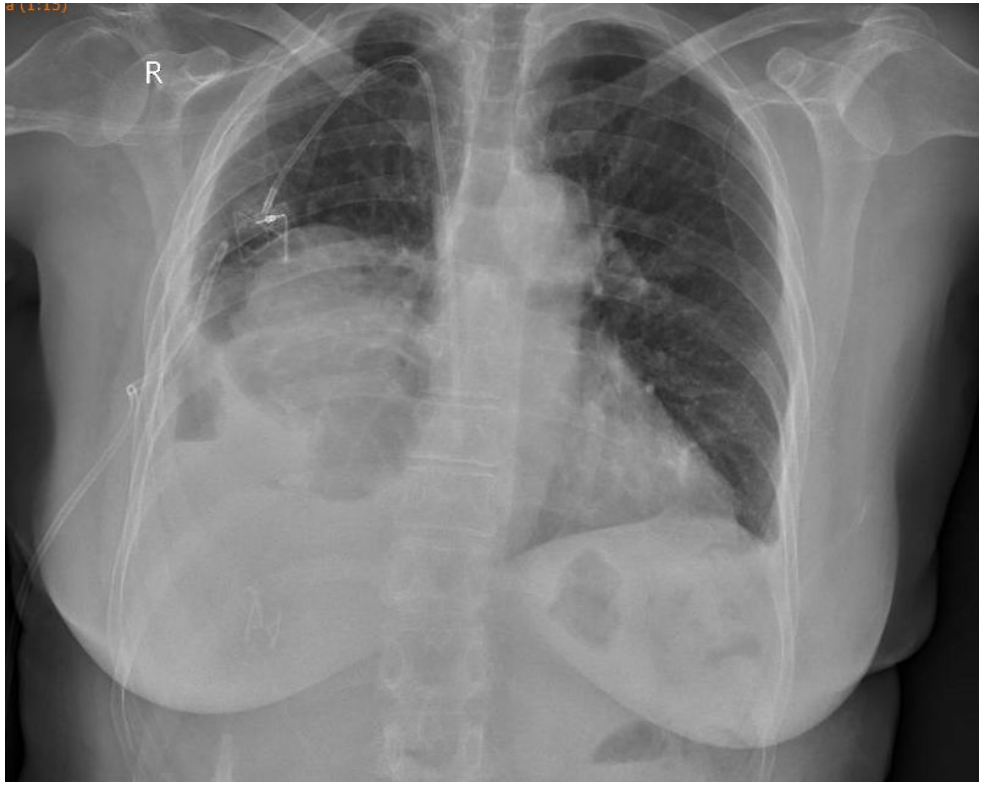


JUN 2021 DEC 2021

Fourth Line Treatment: Gemcitabine + Docetaxel

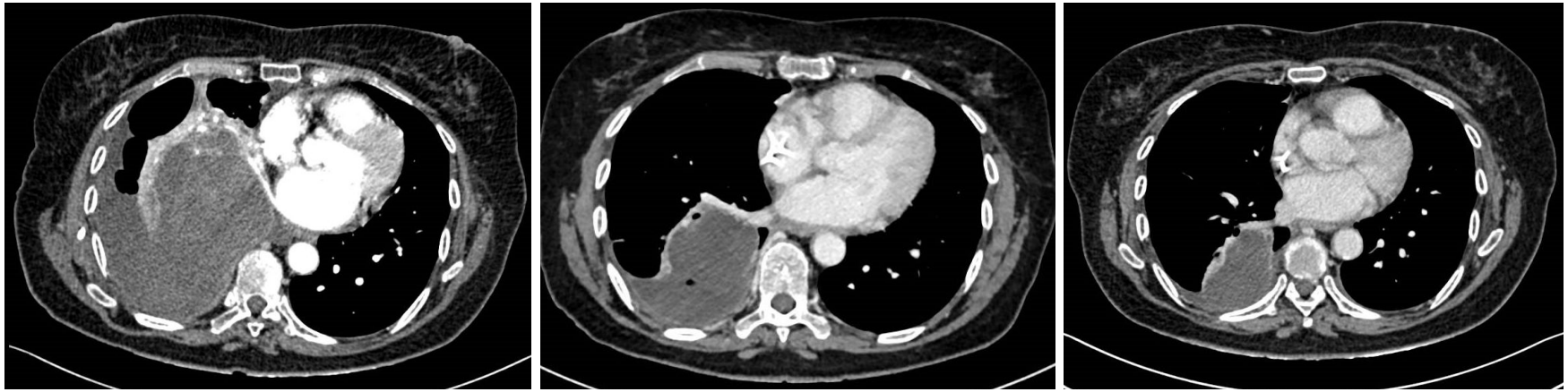
- January 2022: Admission due to symptomatic pleural effusion, with hemothorax thoracic dreinage. Chemo administration





Fourth Line Treatment: Gemcitabine + Docetaxel

- From January 2022 to september/2023 (30 CYCLES - NO PROGRESSION)
- After 4 cycles: **PARTIAL RESPONSE**.



Jan 2022 March 2022 Aug 2022

- Discontinuation of treatment after **30 cycles** in september/2023 (accumulated toxicity and therapy break needed).

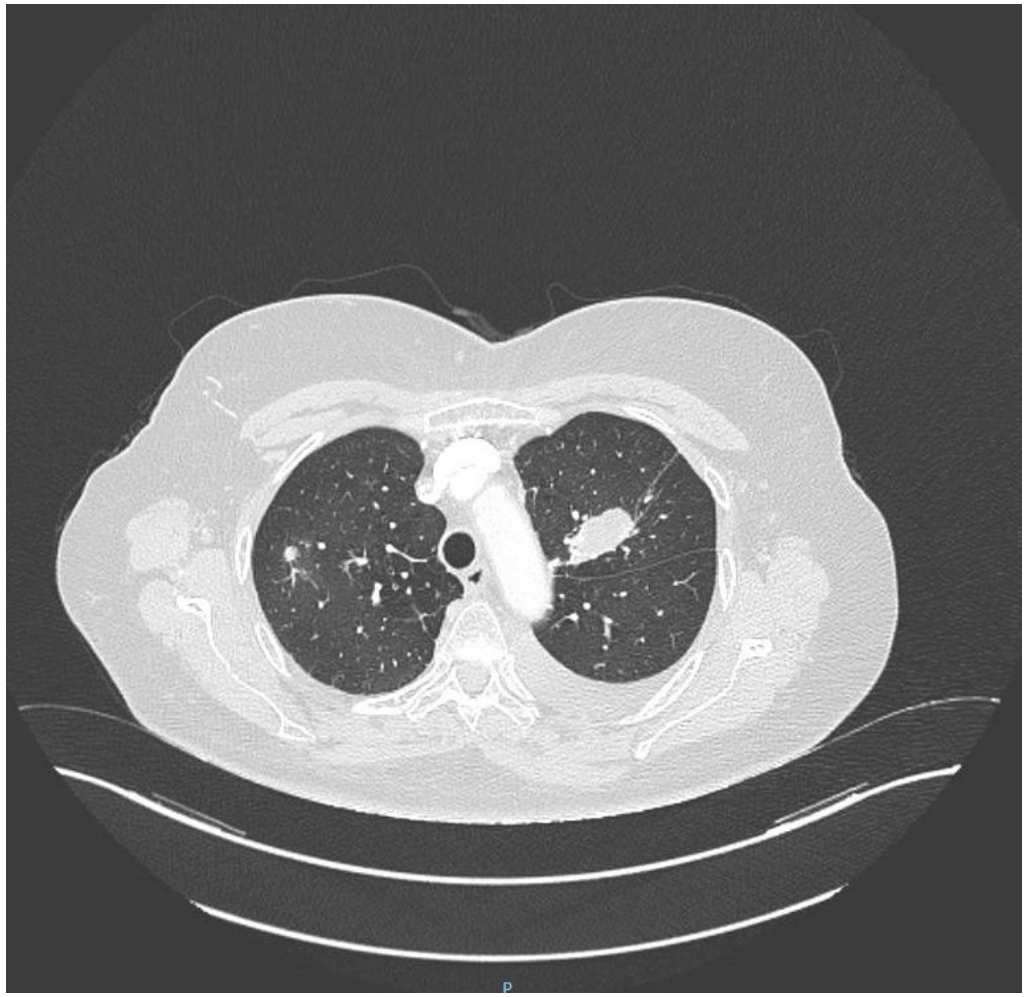
Fourth Line Treatment: Gemcitabine + Docetaxel

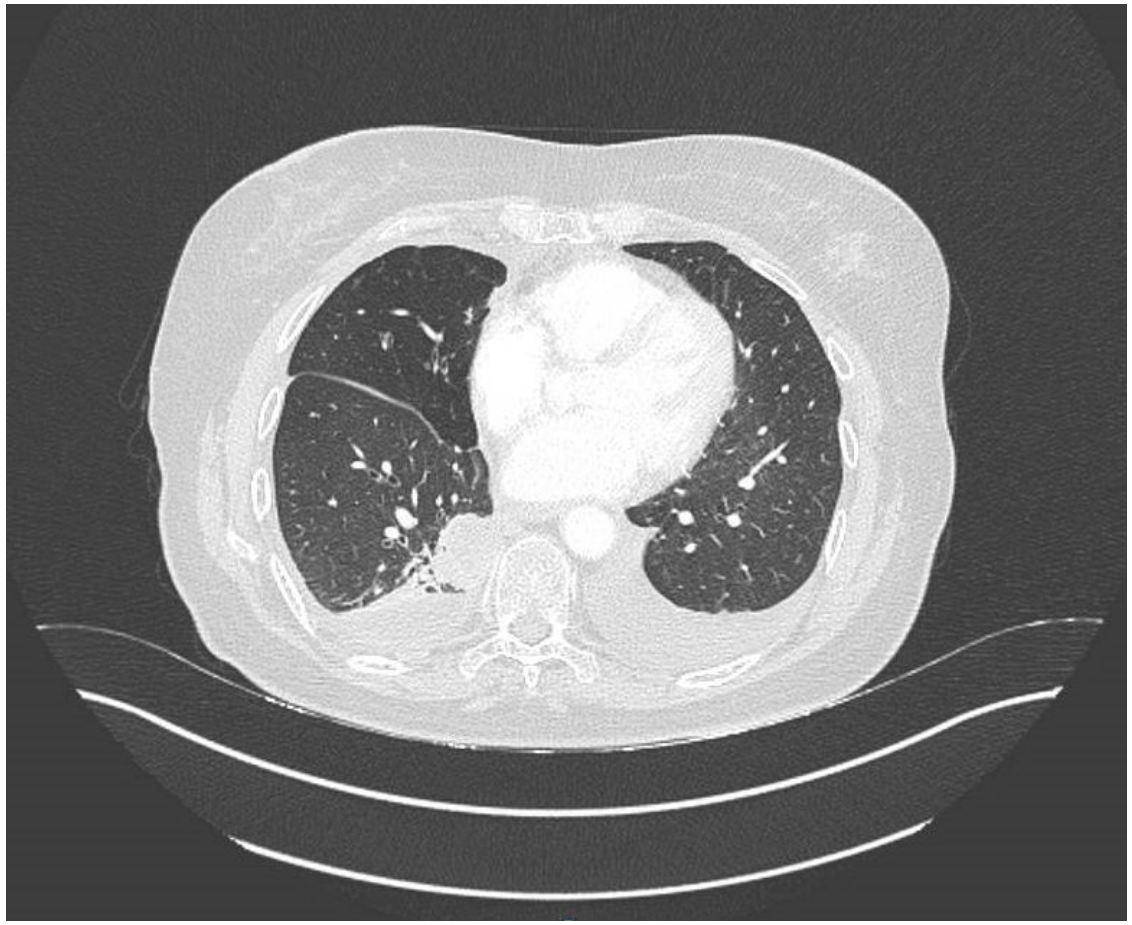
- From september/2023 to may/2024 **STABLE DISEASE** without any treatment.
- May/2024: **PROGRESSION DISEASE** (enlargement of known pulmonary lesions + local relapse 6.5 cm in semimembranous muscle)

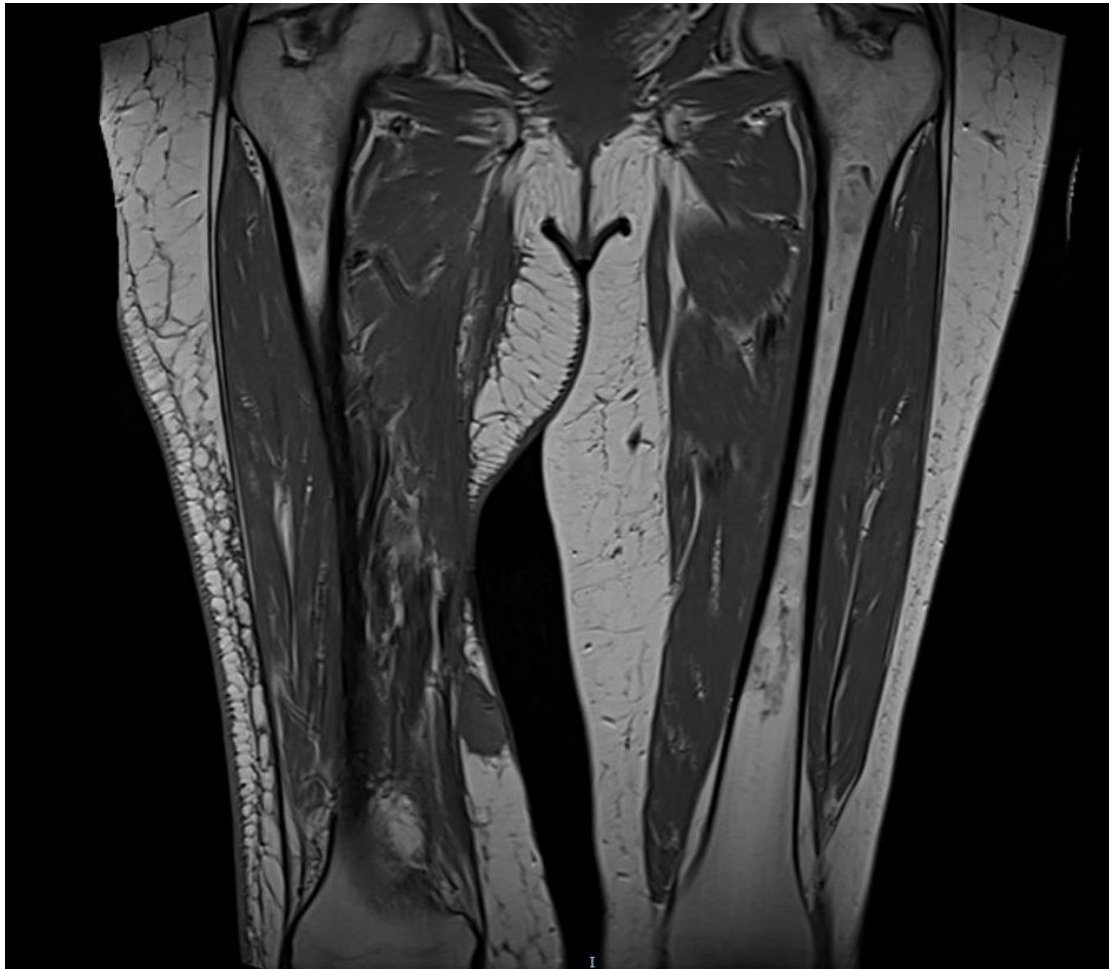
PFS

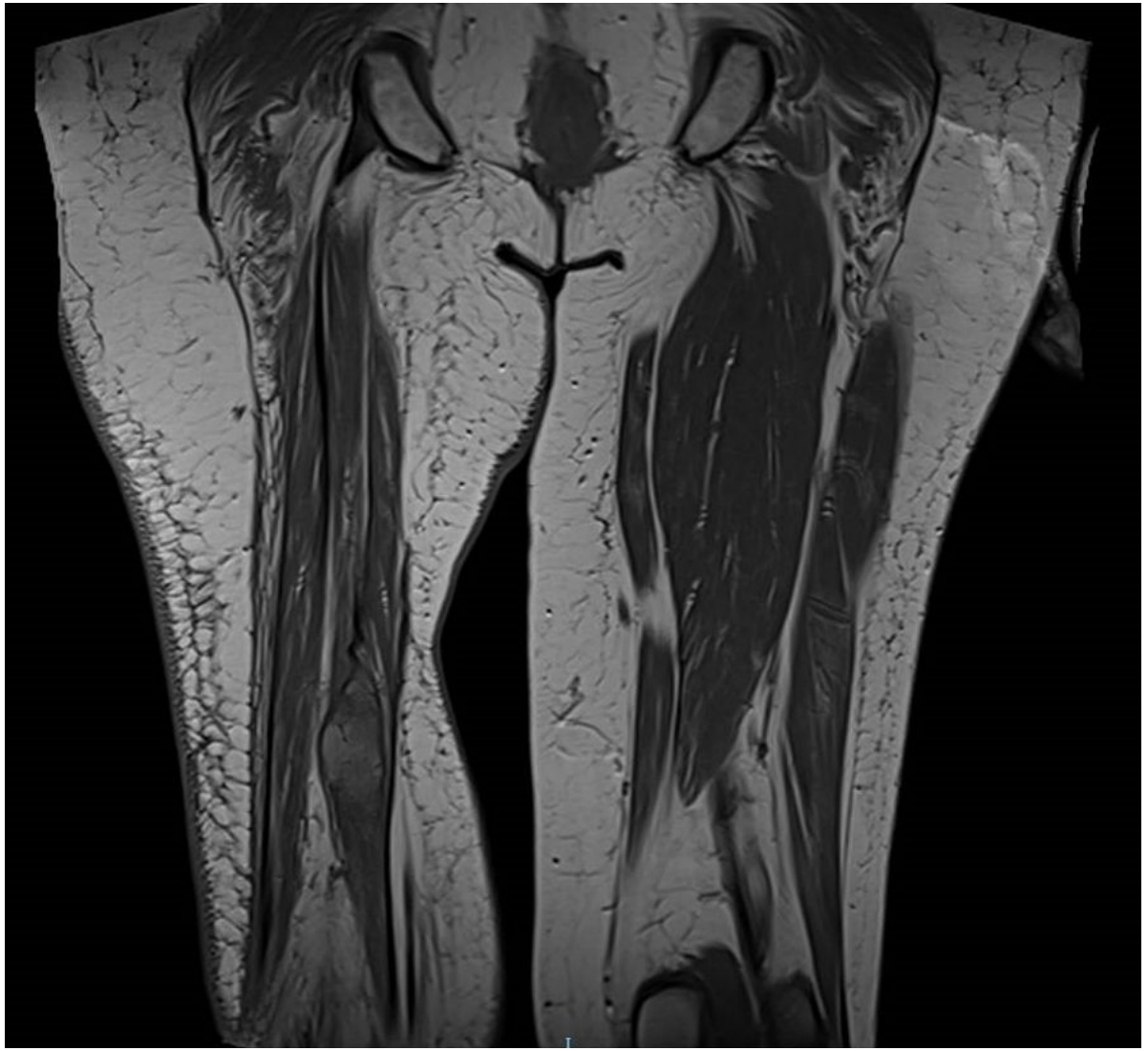
28 months under Gemcitabine/Docetaxel

- July 2024: Re-start gem-docetaxel (Doc 60mg/m2)□ gemcitabine monotherapy





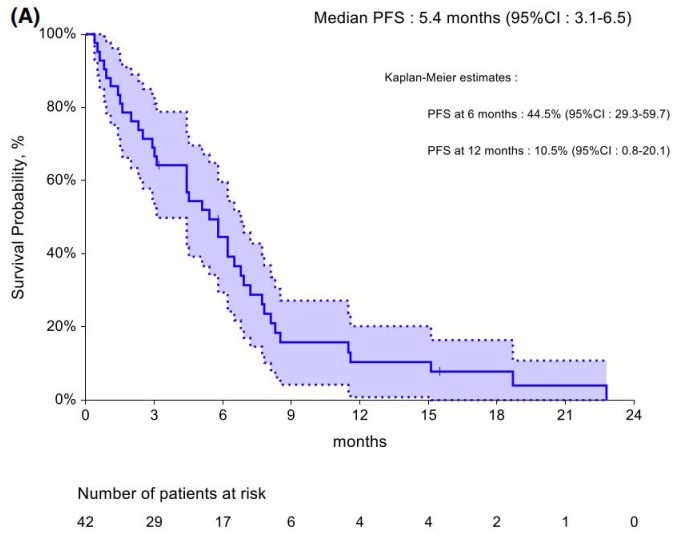




IN SUMMARY…

- Very long responder to gemcitabine-docetaxel (28 months) in 4th line in patient previously progressing to paclitaxel

- **Gemcitabine is relevant in angiosarcoma therapy**



mPFS 5.4 months
ORR 38%

N: 42
Series Gustave Roussy
Watson S. Cancer Med 2023

Retrospective data in adjuvant therapy from Italian Sarcoma Group (In press)

Open Questions

- Immediately previous line: immunotherapy (change in tumoral microenviroment? More prone to respond to chemo??

Thank you!

Obrigada!

Gracias!

Merci!

Grazie!