

Sarcoma Tumor Board

24th Multidisciplinary Management of Cancers: A Case-based Approach

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COMMERCIAL SUPPORT

None

Panelists

Dr. Robert Canter – Surgical Oncology, UC Davis

Dr. Brian Schulte – Medical Oncology, UCSF

Dr. Daniel DeLitto – Surgical Oncology, Stanford

Dr. Janai Carr-Ascher – Medical Oncology, UC Davis

Dr. Nam Bui – Medical Oncology, Stanford

Dr. Rosanna Wustrack – Orthopedic Oncology, UCSF

Dr. Varun Monga – Medical Oncology, UCSF

Dr. Everett Moding – Radiation Oncology, Stanford

Dr. Kathleen Doyle – Research Fellow, UC Davis

Deepti Behl, MD – Medical Oncology, Sutter Health

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Disclosures

Full Name	Role	Type of Financial Relationship	Company Name
Varun Monga	Panel	Advisory Board or Panel	Forma Therapeutics, Astex Pharmaceuticals
Varun Monga	Panel	Grants / Research	Rising Tide Clinical Cancer Research
Nam Bui	Panel	Consultant	Springworks Therapeutics, RAIN Oncology, Boehringer Ingelheim
Deepti Behl	Panel	Advisory Board or Panel	AZ, Janssen, Novartis, Ipsen, BMS, Boehringer

Case 1:

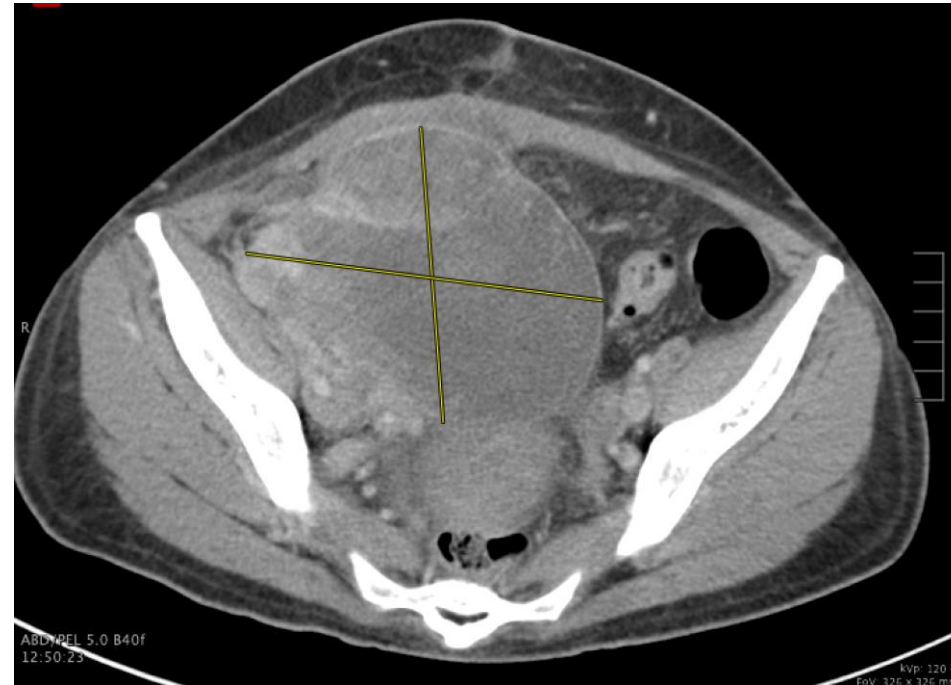
46 yo F presenting with abdominal pain for 3 weeks

PMHx: hyperlipidemia, depression

PSHx: cesarean section

Exam: palpable, firm, fixed lower abdominal mass in the right lower quadrant mildly tender to palpation, no peritoneal signs

Initial CT Images:



Work up:

- Admitted to GYN oncology service given concern for ovarian vs. adnexal origin of mass
- GI consulted given history of colon cancer in father
 - Colonoscopy: negative for concerning lesions
- OR with GYN for biopsy
 - Mass arising from pelvic sidewall encasing right common and external iliac vessels
 - Surgical oncology consulted intraoperatively for biopsy

Biopsy pathology: de-differentiated liposarcoma

- MDM2 amplification by FISH
- High histologic grade

Question: What is the next step in treatment?

1. Surgical Resection
2. Neoadjuvant chemotherapy
3. Neoadjuvant radiation
4. Radiofrequency ablation (RFA)

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1. Surgical Resection
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Patient received neoadjuvant chemotherapy: Adriamycin, Ifosamide, Mesna (AIM), 6 cycles

- Doxorubicin 25 mg/m² CIVI days 1-3
- Ifosamide 3000 mg/m² IV over 4 hours days 1-3
- Mesna 1000 mg/m² with ifosamide

6-month re-staging CT shows decrease in size from 7.5 x 7.8cm to 6.7 x 7.5cm



Question: What is the next step in treatment?

1. Surgical Resection
2. More chemotherapy
3. Radiation therapy
4. Palliative Care

Question: What is the next step in treatment?

1. Surgical Resection
2. More chemotherapy
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4. Palliative Care

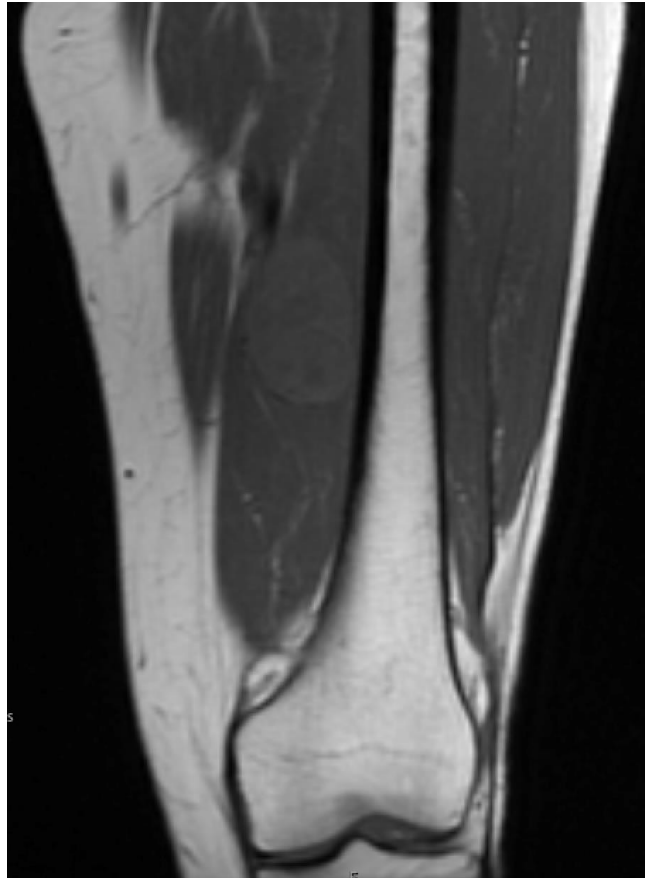
Patient undergoes extensive surgical resection of tumor and involved structures:

1. Radical resection pelvic sarcoma
2. Appendectomy
3. Right salpingo-oophorectomy
4. Ureterolysis
5. Ligation of external iliac vein
6. Neurolysis of femoral nerve
7. Omental flap

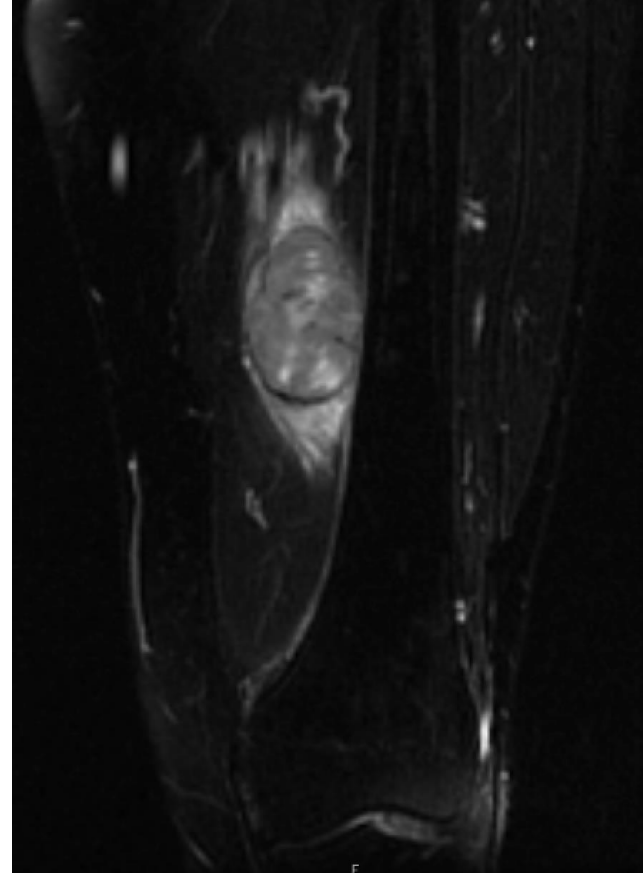
Final Pathology: de-differentiated liposarcoma, margins uninvolved, 70% necrosis

2.5 years post resection patient notes mass on anterior left thigh

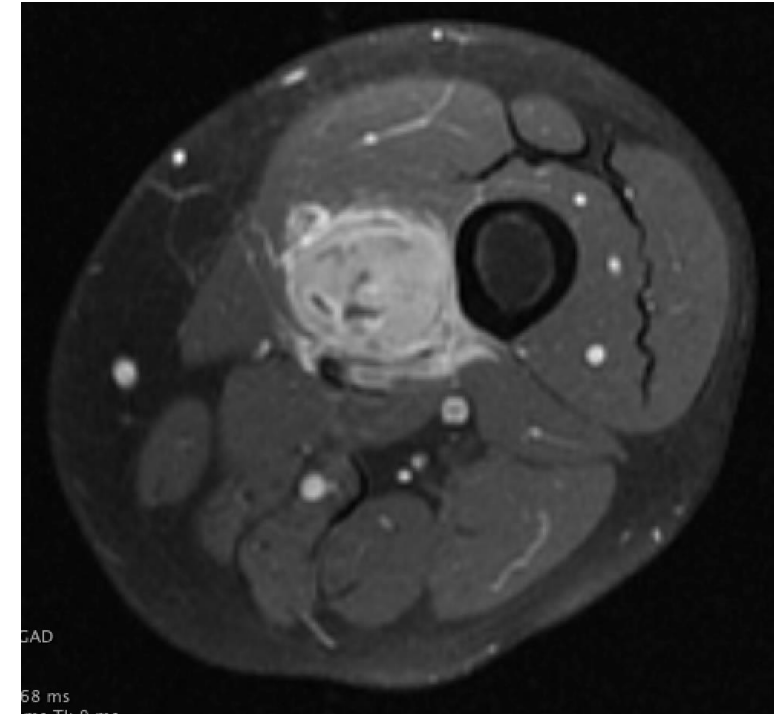
MRI shows:



T1



T2



T1 FS gadolinium

Question: What is the next step in treatment?

1. Surgical Resection
2. Preoperative chemotherapy
3. Preoperative radiation
4. Above Knee Amputation

Question: What is the next step in treatment?

1. Surgical Resection
2. Preoperative chemotherapy
3. Preoperative radiation
4. Above Knee Amputation

Treatment:

1. Neoadjuvant radiation therapy
 - 50 Gy in 25 fractions
2. Radical resection of tumor

Pathology: poorly differentiated pleomorphic sarcoma,

- MDM2 positive
- 10% necrosis
- Negative margins

Currently patient status is alive with no evidence of disease

What is the role of radiation in retroperitoneal sarcoma?



Preoperative radiotherapy plus surgery versus surgery alone for patients with primary retroperitoneal sarcoma (EORTC-62092: STRASS): a multicentre, open-label, randomised, phase 3 trial

STRASS 1

Conclusion:

- Preoperative XRT should not be considered standard of care for retroperitoneal sarcoma

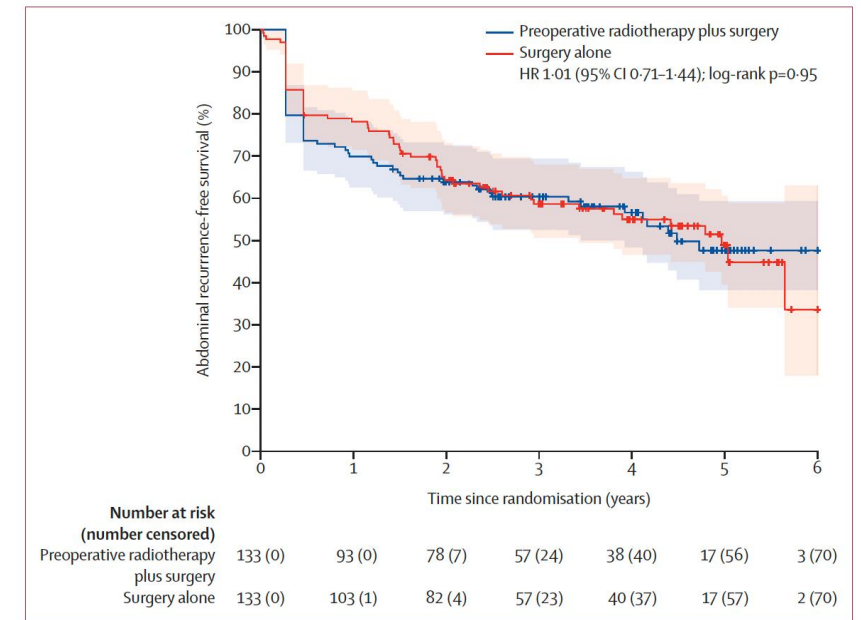


Figure 2: Abdominal recurrence-free survival in all patients
Shaded areas around the lines represent the 95% CI. HR=hazard ratio.

What is the role of chemotherapy in retroperitoneal sarcoma?

Now Enrolling: EA7211/STRASS 2 for Patients with High-Risk Retroperitoneal Sarcoma

🕒 August 25, 2023

Retroperitoneal sarcoma Sarcoma

STRASS 2

EA7211 – A Randomized Phase III Study of Neoadjuvant Chemotherapy Followed by Surgery Versus Surgery Alone for Patients with High-Risk Retroperitoneal Sarcoma (STRASS 2)

- High risk, resectable LPS (grade 3, some grade 2) or LMS (any grade) of retroperitoneal space or infra-peritoneal spaces of the pelvis that has not been previously treated
- Study is open and enrolling in Europe and North America

Take home points:

1. Preoperative XRT should not be considered standard of care for retroperitoneal sarcomas: **patients should undergo upfront resection when possible**
2. The role of XRT for liposarcoma should be further investigated
3. The role of preoperative chemotherapy for retroperitoneal sarcomas is currently under investigation

Questions?

Case 2:

38yo F presenting with painful, enlarging back mass

PMHx: none

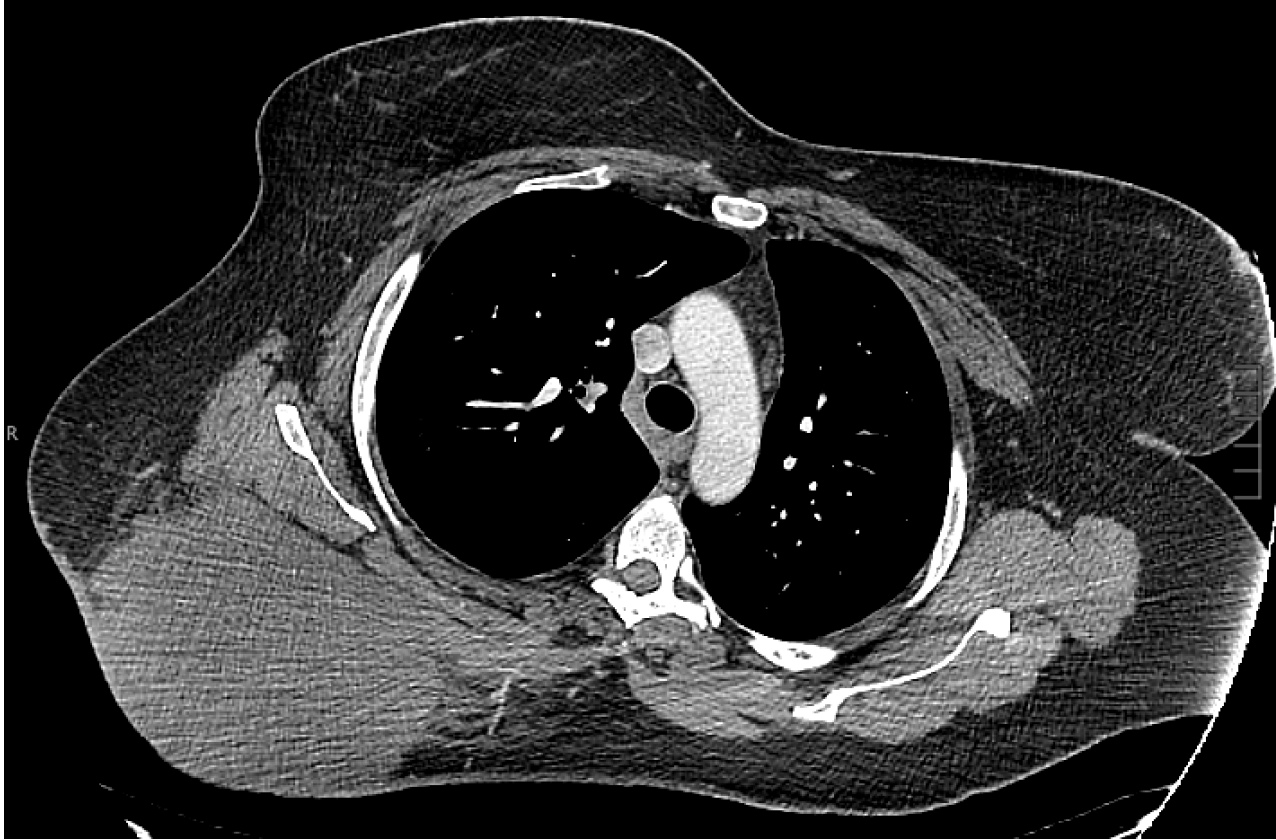
PSHx: none

PEx: Large grapefruit-sized hematoma to the upper right back with overlying purple-red skin. No fluctuance or drainage.

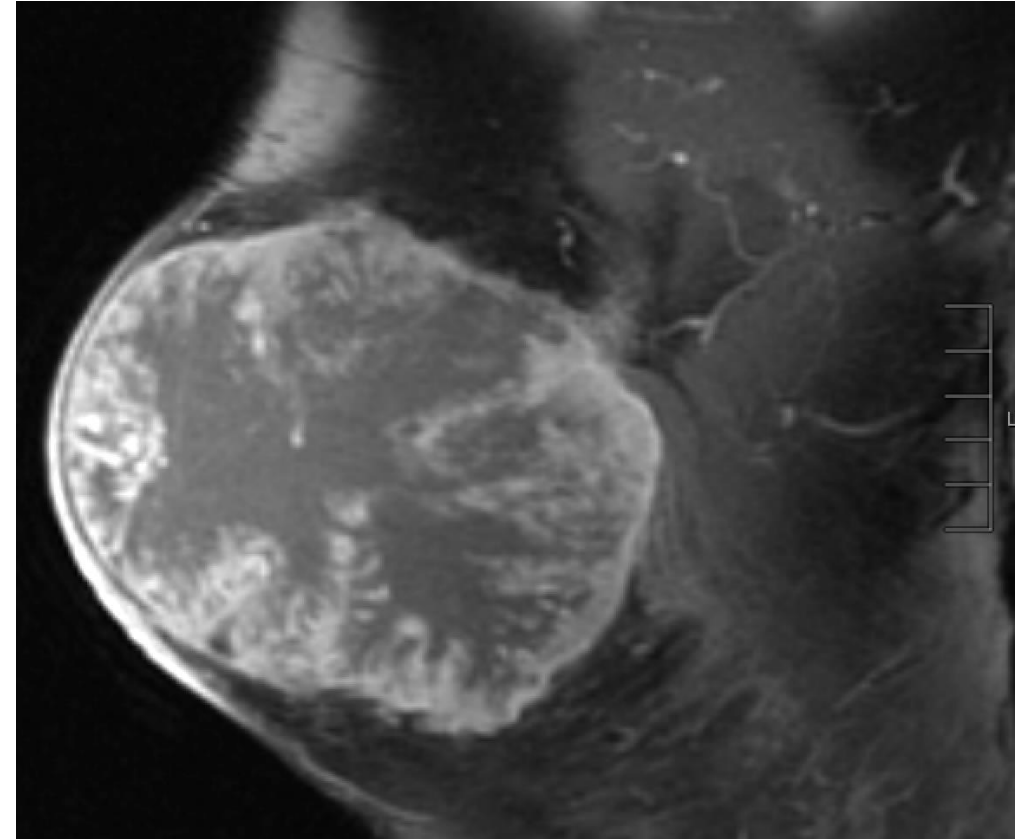


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Initial imaging:



CT chest



MRI upper extremity T1 post contrast

Core needle biopsy performed

Pathology results: high-grade undifferentiated round cell sarcoma

IHC: FLI-1 positive, CD31 positive, CD99 negative, EWSRI negative

Diagnosis: “Ewing-Like” Sarcoma

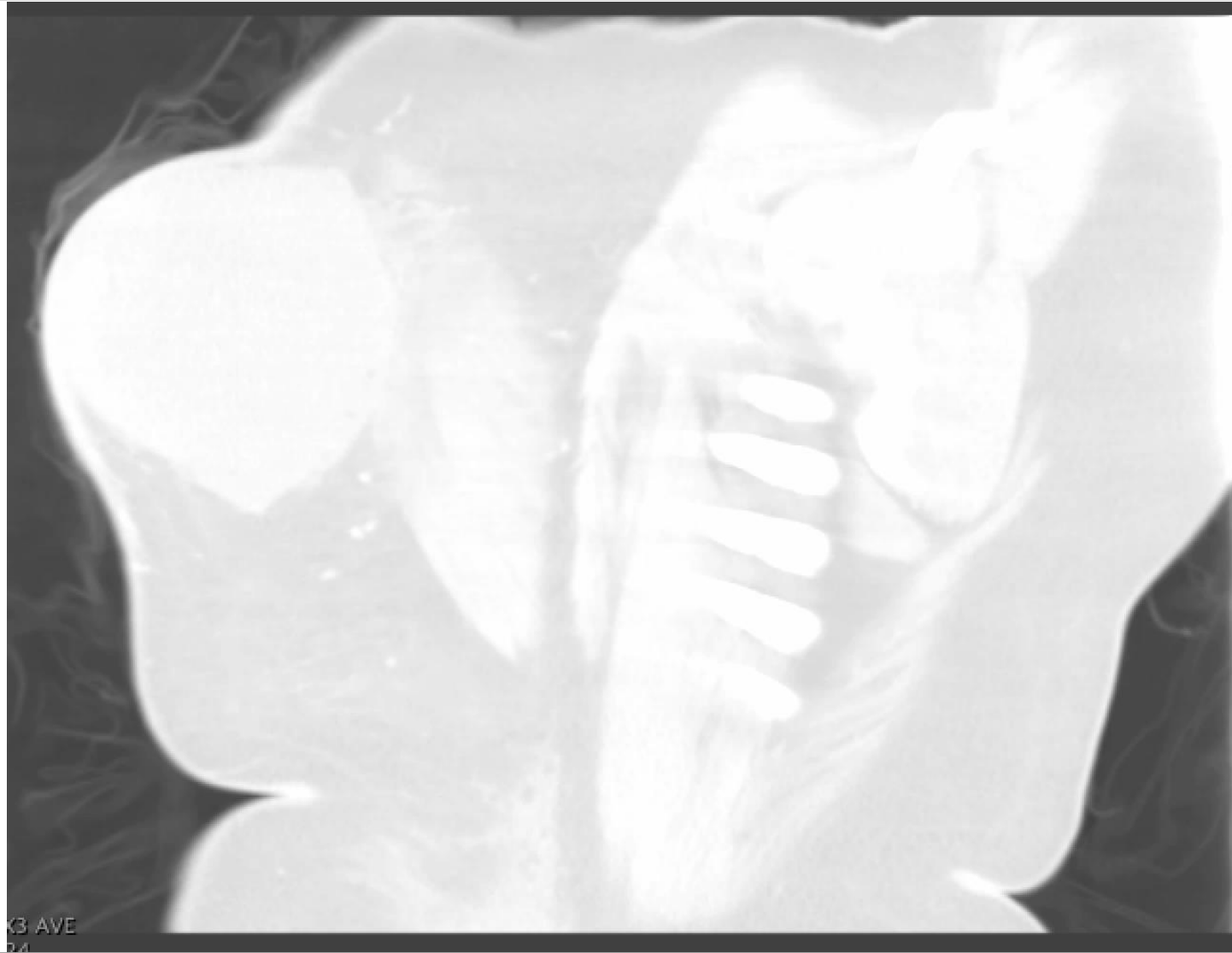
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Two weeks after initial presentation



Initial CT Chest
at time of
diagnosis:



Question: What is the next step in treatment?

1. Surgical resection
2. Preoperative chemotherapy
3. Preoperative radiation
4. Stem cell transplant

Question: What is the next step in treatment?

1. Surgical resection
2. Preoperative chemotherapy
3. Preoperative radiation
4. Stem cell transplant

Surgical Management:

Radical resection of tumor with wound vac placement

Margin re-excision and washout
2 weeks post-op

Split-thickness skin graft placed
1 week after washout and re-
excision

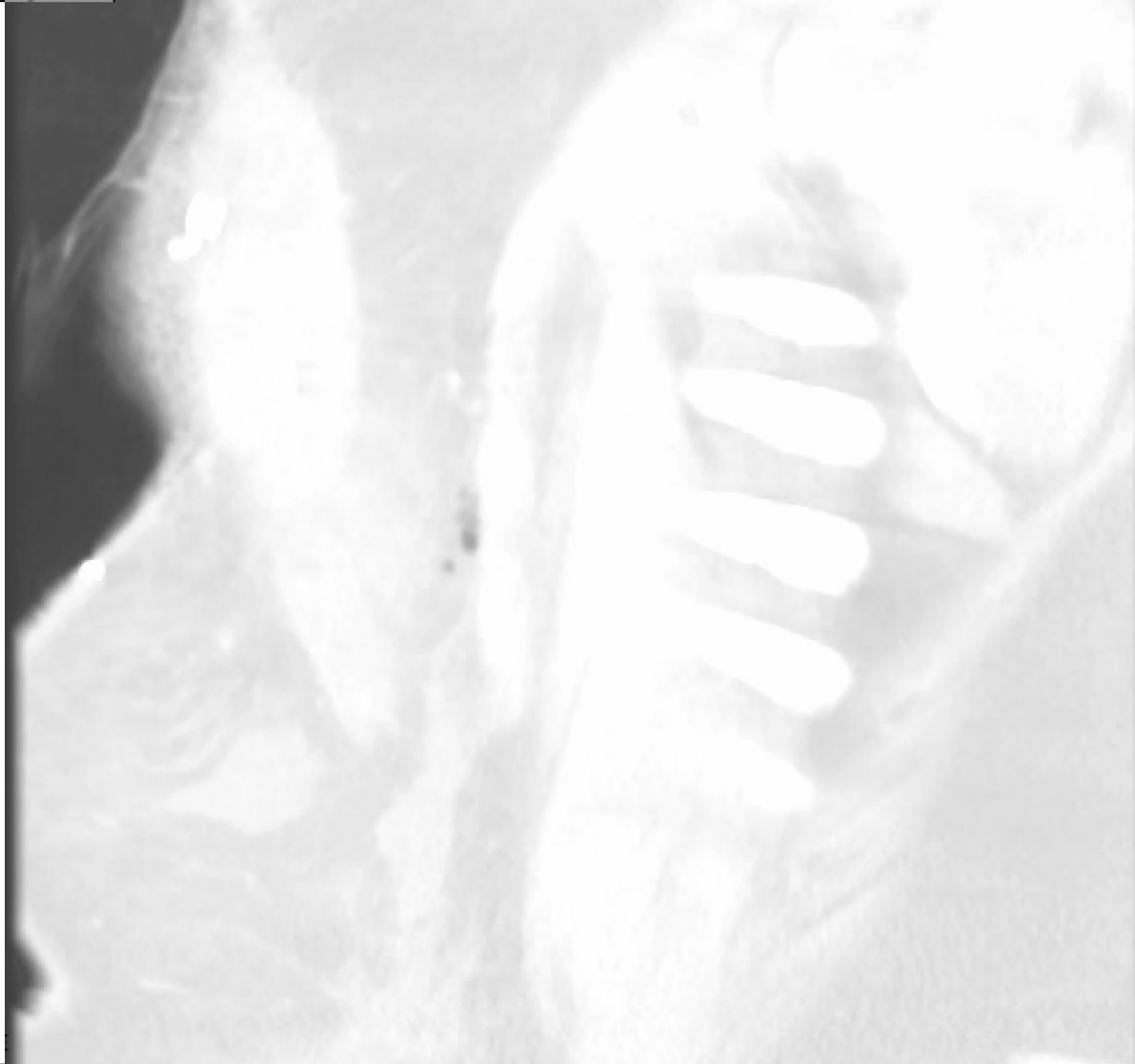


POD 2



POD 16

CT Chest 6 weeks
after initial
diagnosis (post
surgical resection):



Question: What is the next step in treatment?

1. Wait for wound to completely heal prior to initiating further treatments
2. Start chemotherapy now
3. Start radiation now
4. Allow for skin graft to show initial signs of successful engraftment prior to treatment

Question: What is the next step in treatment?

1. Wait for wound to completely heal prior to initiating further treatments
2. Start chemotherapy now
3. Start radiation now
4. Allow for skin graft to show initial signs of successful engraftment prior to treatment

Chemotherapy initiated: Regimen: VDCA/IE

Drug	Dose	Delivery
Vincristine	2 mg/m ² (max 2mg) day 1	Cycles 1, 3, 5, 7, 9, 11, 13, 15, 17
Doxorubicin	75 mg/m ² , day 1	Cycles 1, 3, 5, 7, 9
Cyclophosphamide +/- mesna	1200 mg/m ² , day 1	Cycles 1, 3, 5, 7, 9, 11, 13, 15, 17
Dactinomycin	1.25 mg/m ² , day 1*	Cycles 11, 13, 15, 17
Ifosfamide plus mesna	1800 mg/m ² daily, days 1-5	Cycles 2, 4, 6, 8, 10, 12, 14, 16
Etoposide	100 mg/m ² daily, days 1-5	Cycles 2, 4, 6, 8, 10, 12, 14, 16
GCSF support with every cycle		

Planned chemotherapy: 17 courses administered every 21 days. Odd-numbered cycles (non-infusional) can be administered as an outpt)

* Substitute dactinomycin for doxorubicin when cumulative doxorubicin dose is 375 mg/m².

Clinical Course:

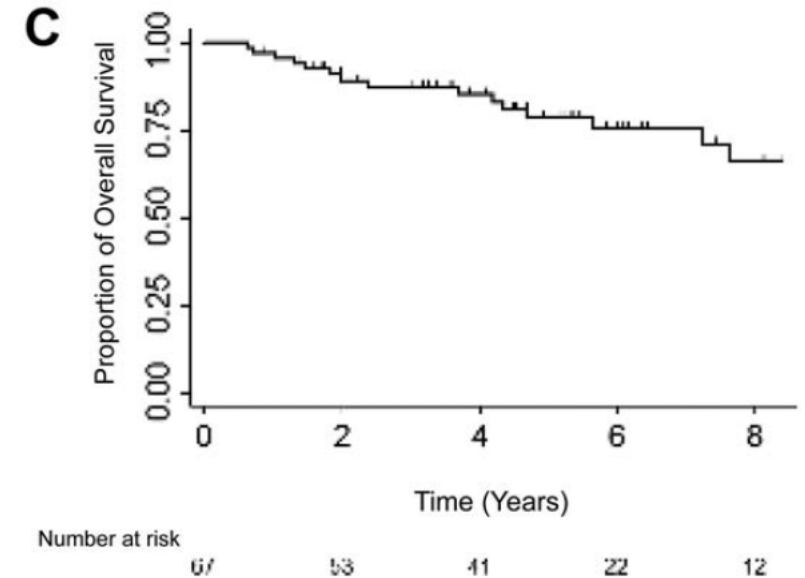
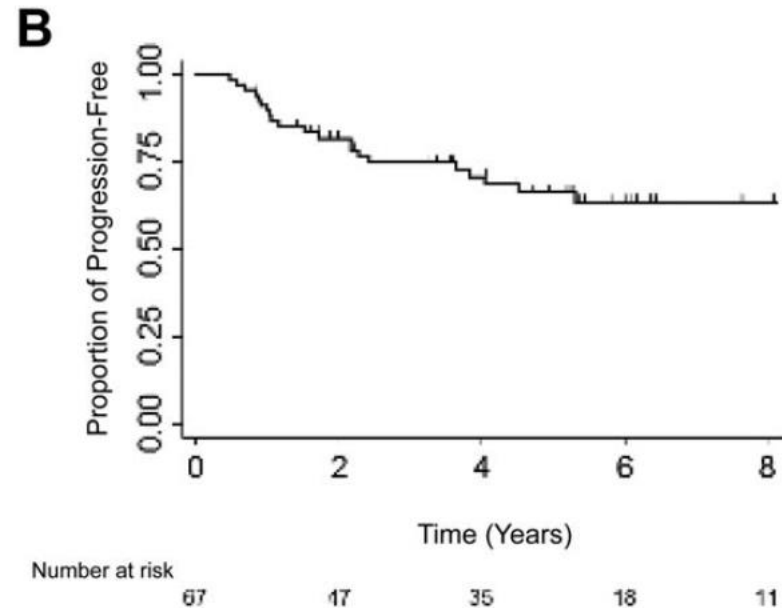
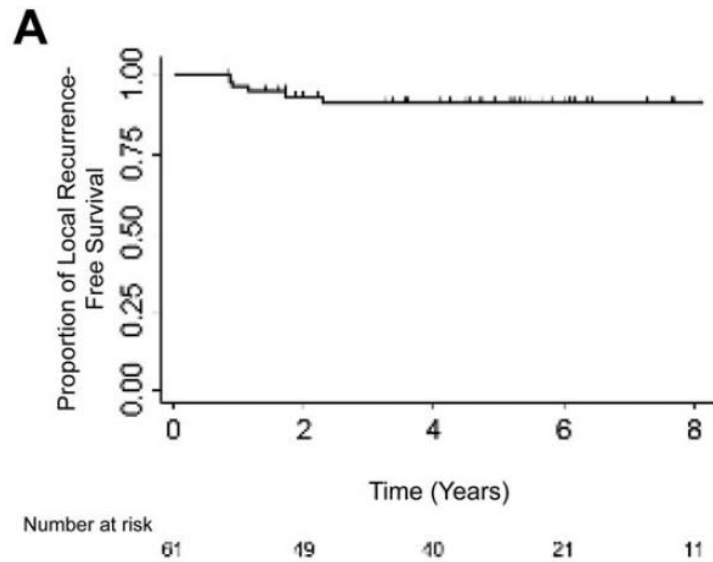
Tolerated 9 cycles of chemotherapy

Developed neutropenic fever, MRSA bacteremia, non-clostridium difficile diarrhea, and reduced ejection fraction so therapy was discontinued

Imaging demonstrates resolution of lung nodules, decision made to stop chemotherapy and begin disease surveillance imaging

Current status: no evidence of disease at 5 years

Localized Adult Ewing Sarcoma: Favorable Outcomes with Alternating Vincristine, Doxorubicin, Cyclophosphamide, and Ifosfamide, Etoposide (VDC/IE)-Based Multimodality Therapy



Take home points:

1. In the setting of a rapidly growing, fungating tumor, upfront resection before chemotherapy may be necessary for palliation and symptom control
2. VDC/IE chemotherapy appears to improve survival in adults similar to in children with Ewing sarcoma

Questions?

Case 3:

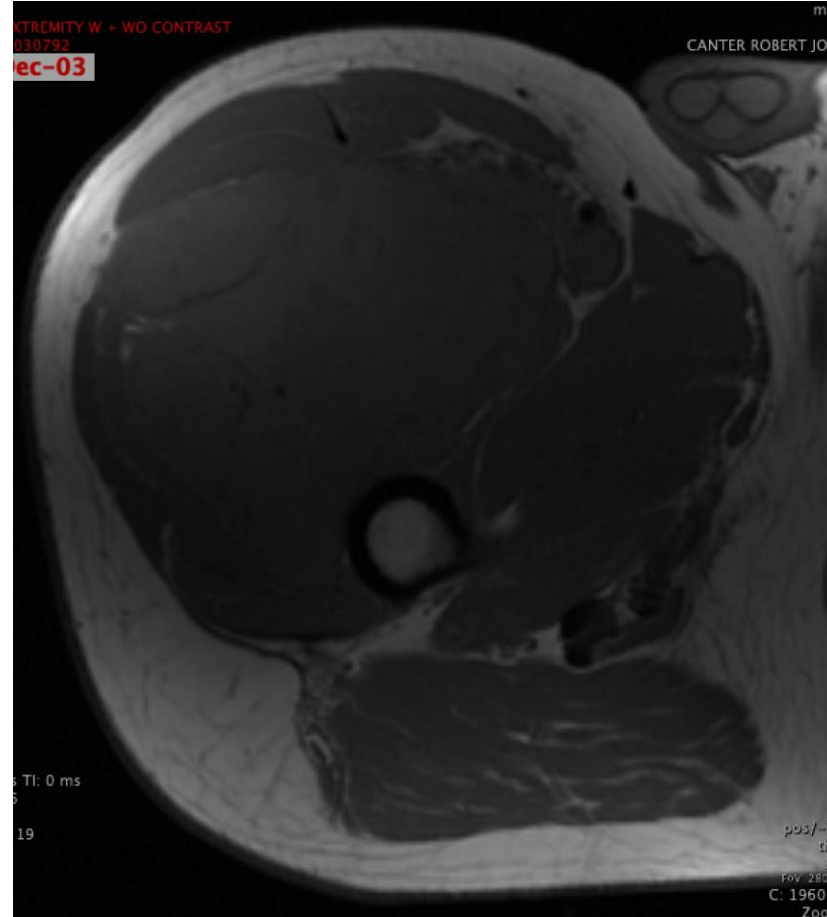
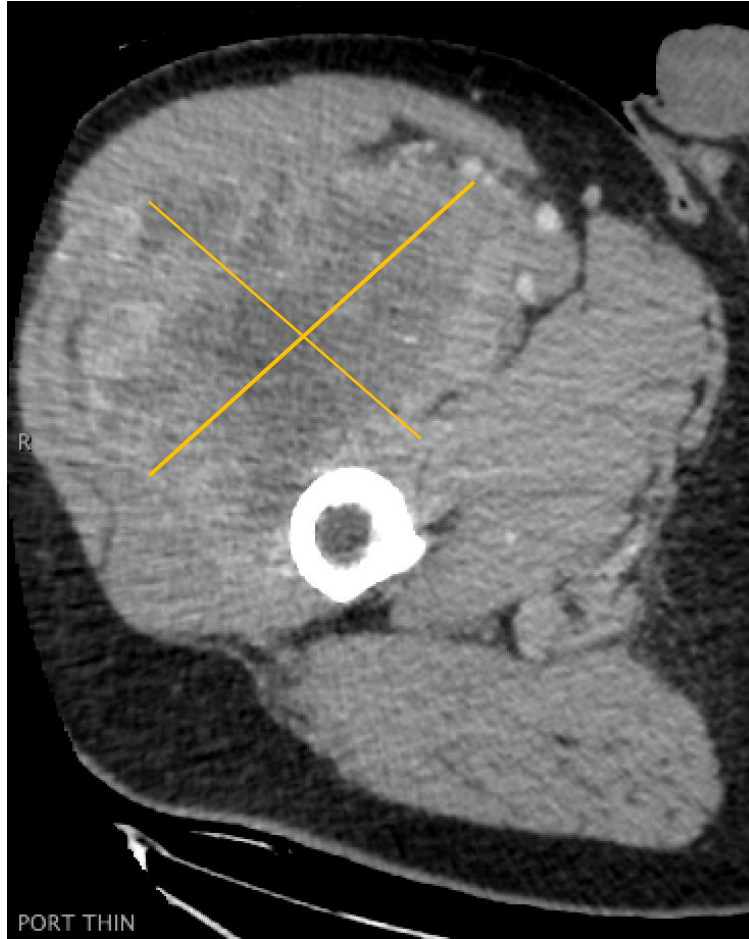
31 yo M presenting with right thigh swelling.

PMHx: recently diagnosed PE (now on Xarelto)

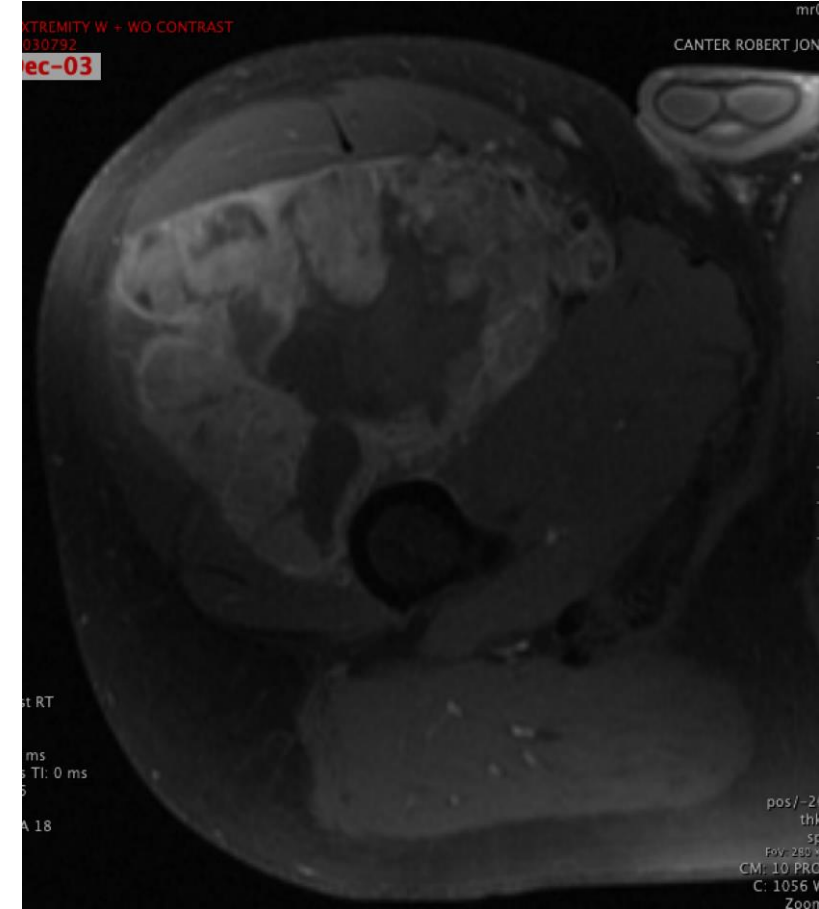
PSHx: none

Exam: Right anterior thigh with indurated immobile mass, approximately 10-14 cm diameter, no discoloration

Initial Imaging:

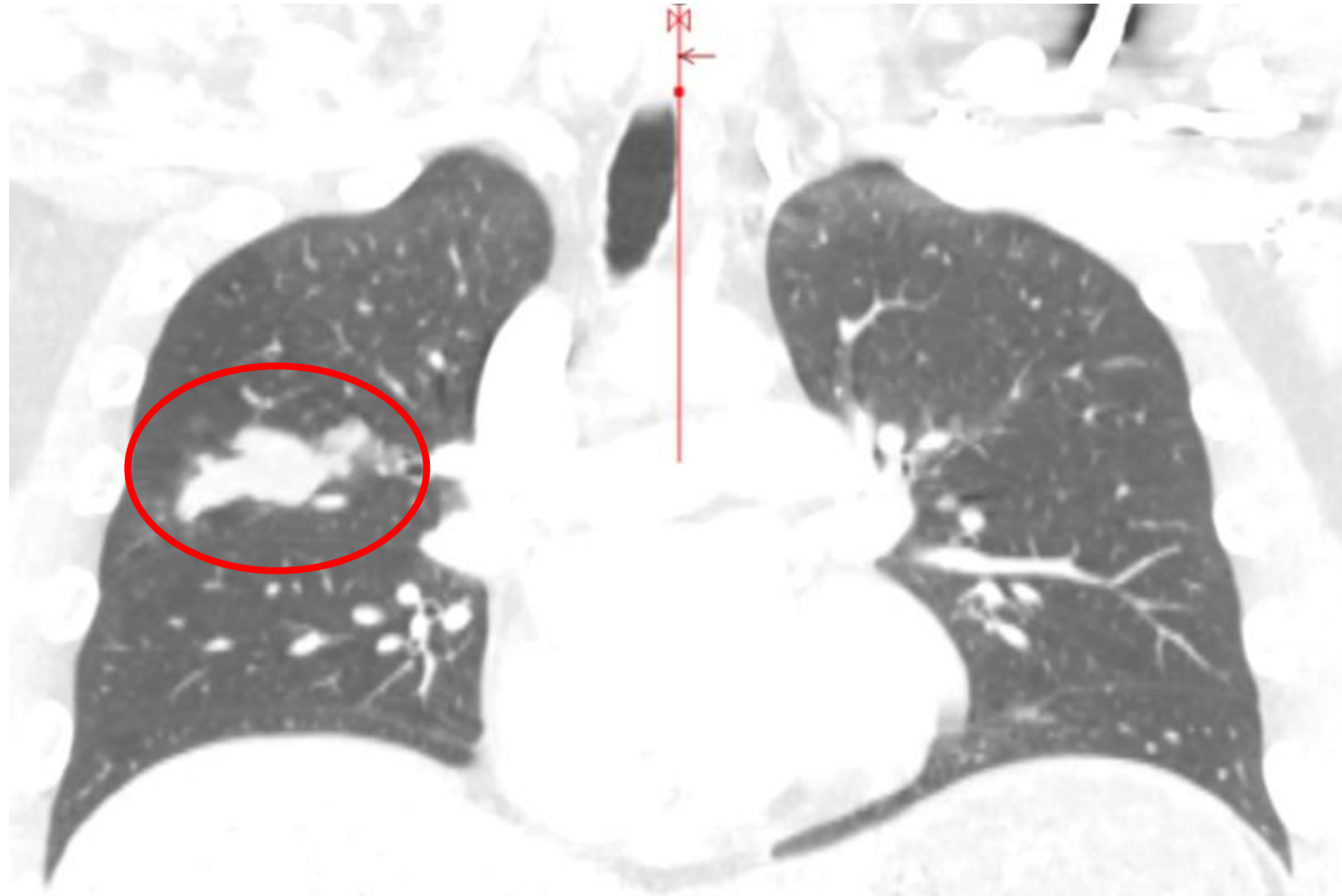


T1



T1 post contrast

Initial CT Chest



Clinical course:

Image-guided biopsy of thigh mass performed

Pathology: synovial sarcoma

Antibody testing:

BCL-2	Positive
CD99	Positive
AE1/AE3	Patchy positivity
EMA	Patchy positivity
S-100	Negative
STAT6	Negative
PD-L1 (22C3)	Negative (0% tumor cell membrane immunoreactivity)
Chromosome Results:	46,Y,t(X;18)(p11.2;q11.2)[12]/46,XY[3]

Question: What is the next step in treatment?

1. Surgical resection of thigh mass
2. Preoperative chemotherapy
3. Preoperative radiation
4. Lung metasectomy

Question: What is the next step in treatment?

1. Surgical resection of thigh mass
2. Preoperative chemotherapy
3. Preoperative radiation
4. Lung metasectomy

Clinical Course:

Underwent 6 total cycles of neoadjuvant chemotherapy (AIM with neulasta support)

- Doxorubicin 25mg/m² x 3 days, CI (total dose 75mg/m²)
- Ifosfamide 2,000mg/m² x 5 days, bolus (total dose 10g/m²)
- Mesna 2,000mg/m² x 5 days, CI (total dose 10g/m²)

Imaging after cycle 2 showed significant improvement in lung disease

Imaging after cycle 4 showed stable lung disease

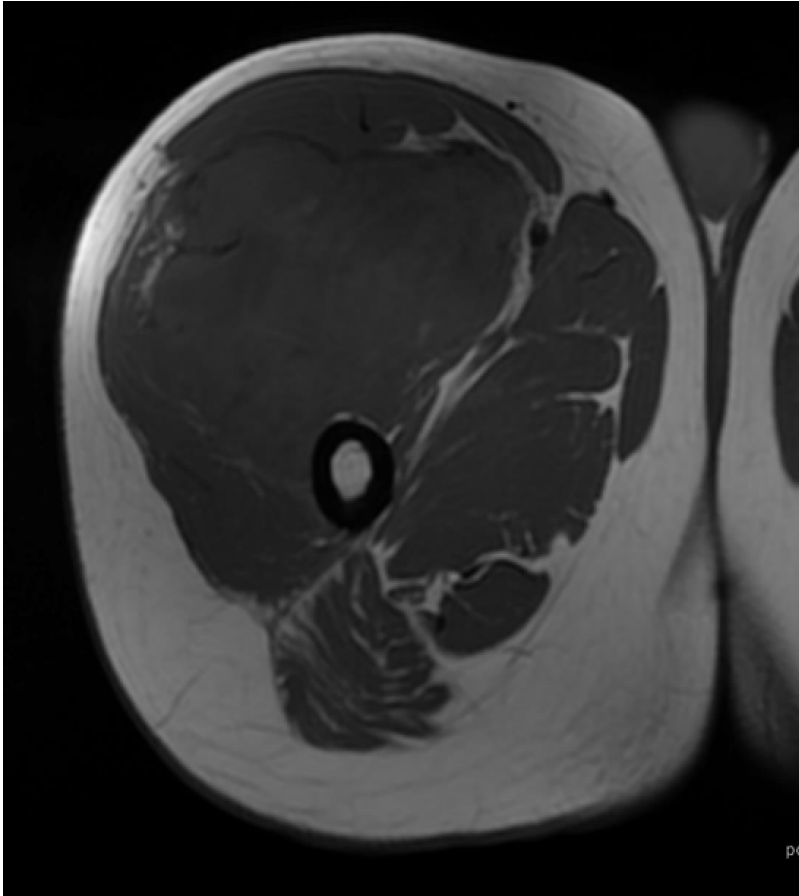
Question: What is the next step in treatment?

1. Surgical resection of thigh mass
2. Additional chemotherapy
3. Preoperative radiation
4. Concurrent radiation and chemotherapy

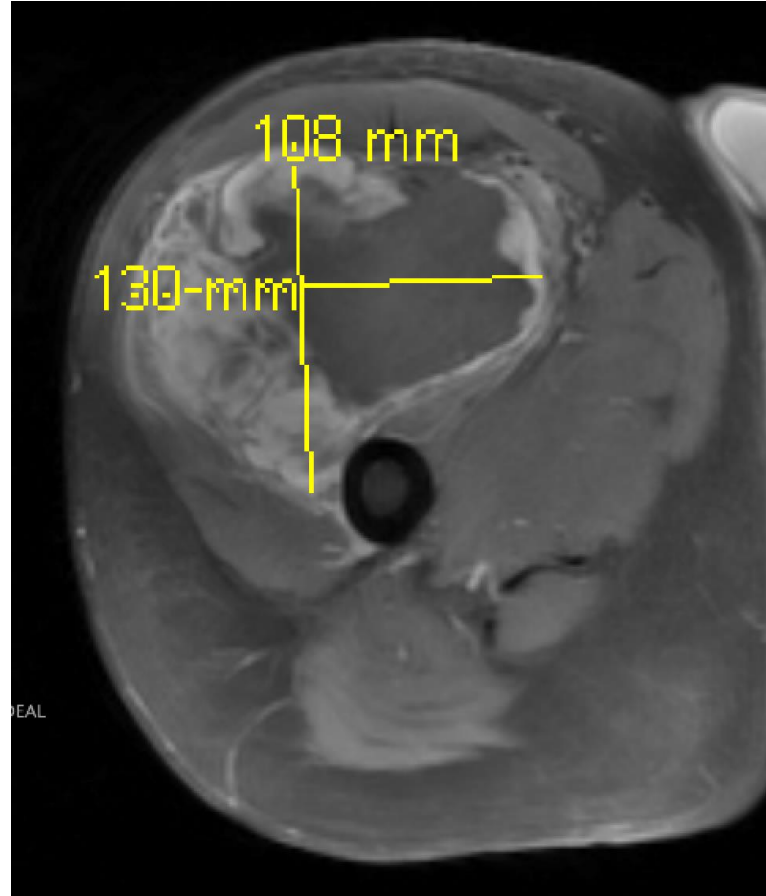
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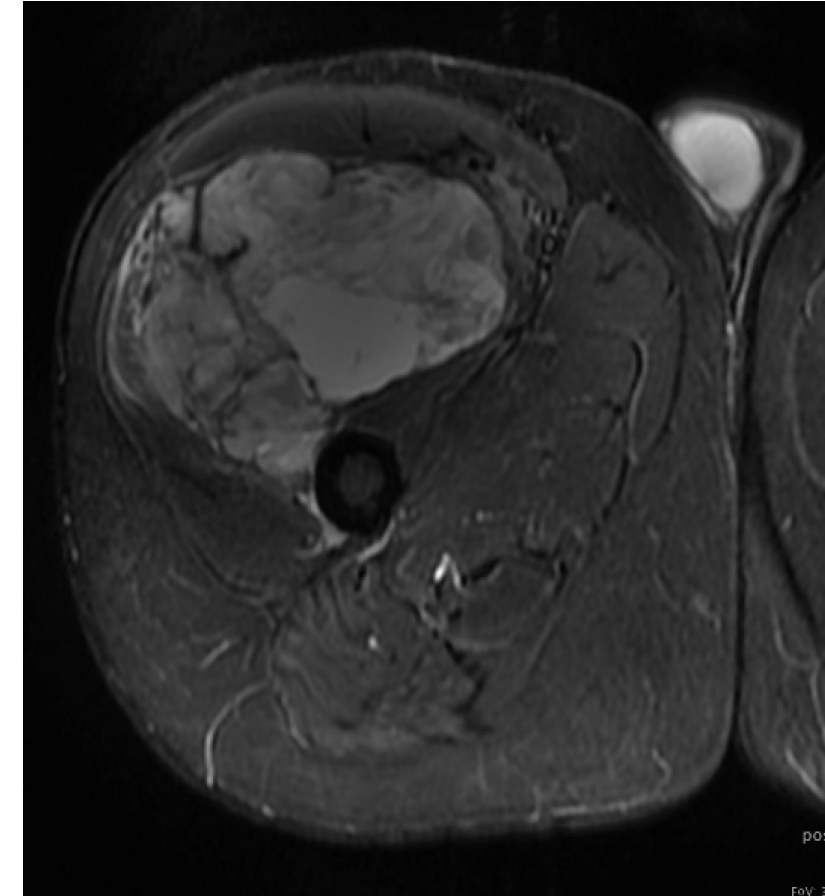
Post Chemo/XRT MRI:



T1



T1 Water



STIR

Clinical Course:

Surgical resection of thigh mass

Pathology demonstrates synovial sarcoma with negative margins and extensive necrosis (90%)

Post-surgery chemotherapy is held

Surveillance imaging demonstrated progression of lung nodules at 6 months.

Surveillance continues and shows progression of nodules at 12 months

Question: What is the next step in treatment?

1. SPEAR T-Cell Therapy
2. Stereotactic Body Radiation Therapy (SBRT)
3. Pulmonary metasectomy
4. Pazopanib

Question: What is the next step in treatment?

1. SPEAR T-Cell Therapy
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Question: What is the next step in treatment?

1. SPEAR T-Cell Therapy
2. Stereotactic Body Radiation Therapy (SBRT)
3. Pulmonary metasectomy
4. Pazopanib

Currently patient status is alive with active disease

A Systematic Meta-Analysis of Randomized Controlled Trials of Adjuvant Chemotherapy for Localized Resectable Soft-Tissue Sarcoma

Chemotherapy improves:

- Local recurrence
- Distant recurrence
- Overall recurrence
- Survival (when doxorubicin is used with ifosfamide)

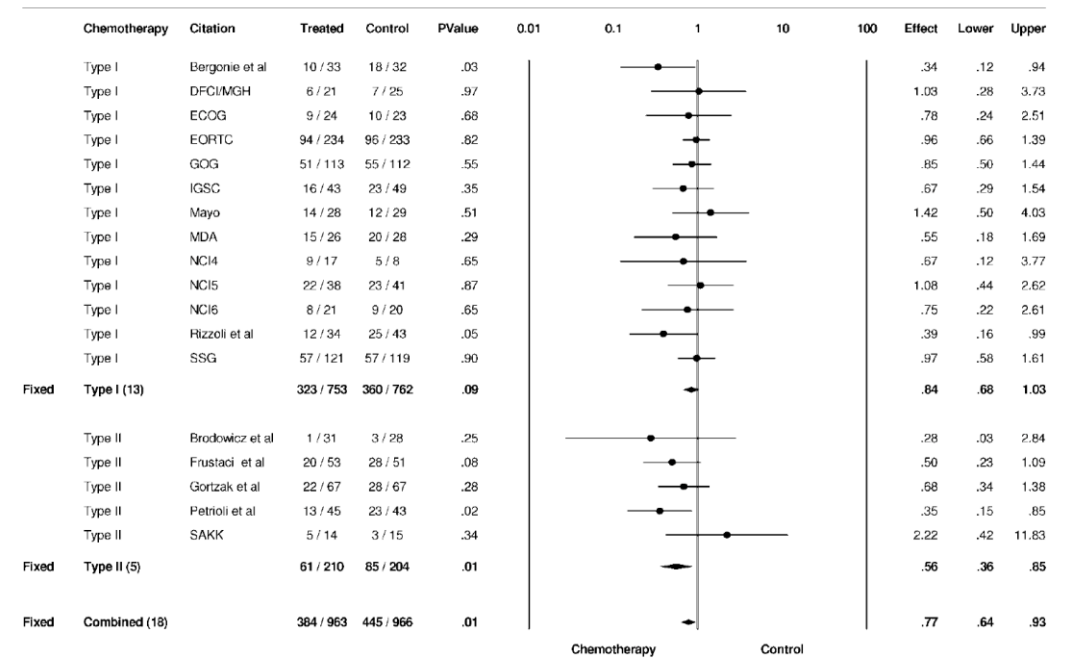


FIGURE 5. Hazard ratios of survival by type of chemotherapy regimen. Forest plot for hazard ratios of survival by type of chemotherapy regimen. Type I indicates adjuvant doxorubicin-based chemotherapy. Type II indicates adjuvant doxorubicin-based chemotherapy in combination with ifosfamide. Combined results are also provided.

Take home points:

1. Tri-modal therapy for synovial sarcoma is preferred (preoperative chemotherapy and radiation therapy)
2. Ifosfamide is used as a radiosensitizer and improves survival when given with doxorubicin
3. Management of metastatic disease is variable and multiple options exist

Questions?

Case 4:

46 yo F presenting with enlarging mass on the left forearm

PMHx: hypothyroidism

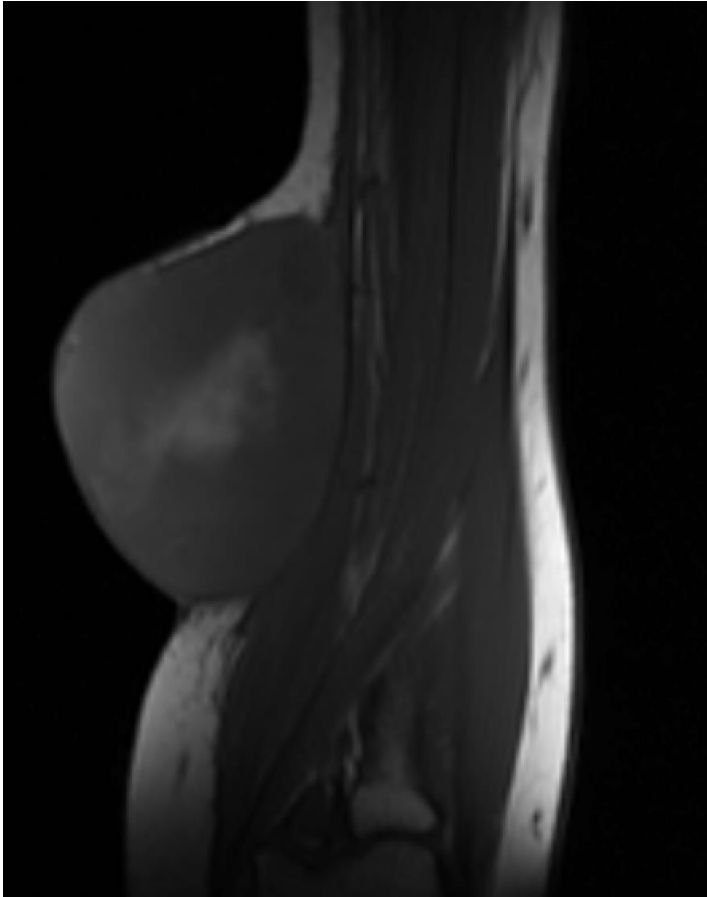
PSHx: prior resection of 2cm undifferentiated pleomorphic sarcoma (x2) four years prior to presentation

Exam: 8cm x 6cm x 4cm firm, fixed, indurated, ulcerative mass in the ulnar aspect of the left forearm

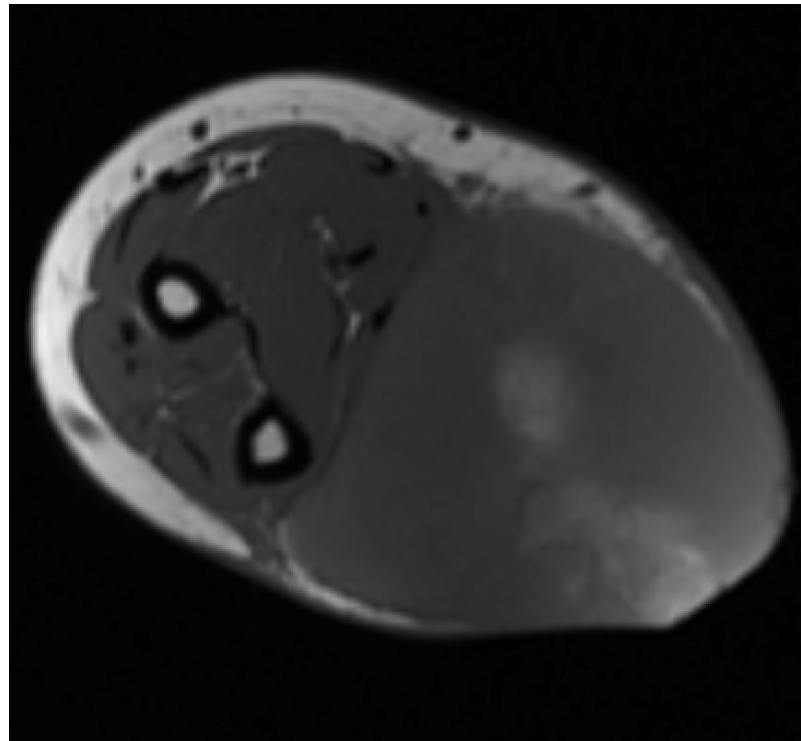
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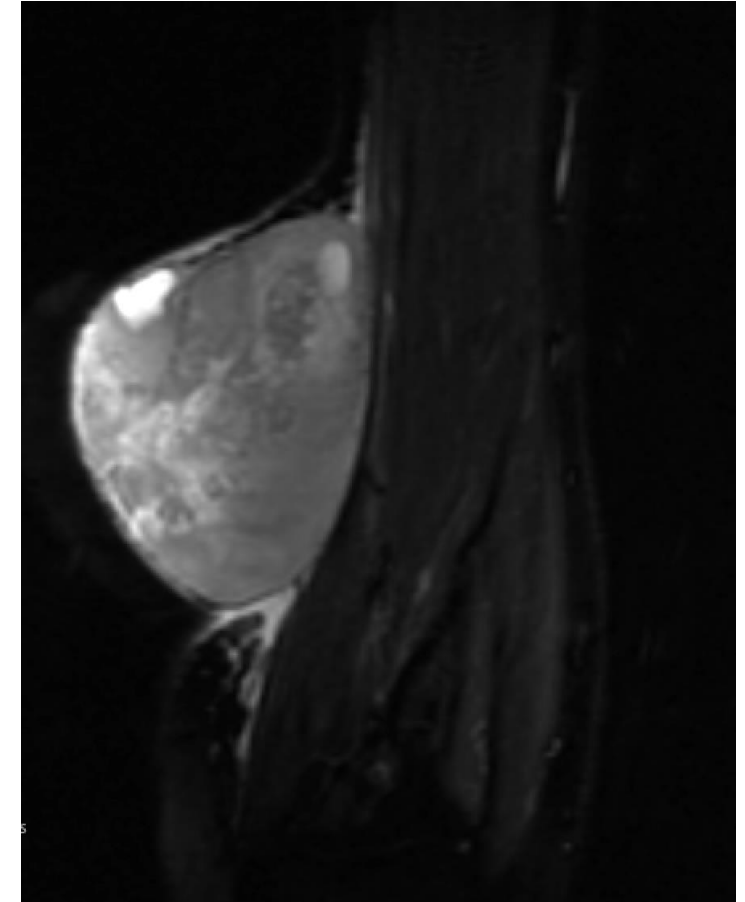
MRI:



T1



T1



STIR

Biopsy shows undifferentiated pleomorphic sarcoma

- Positive vimentin
- Negative actin, CD34, CD45, AE1/AE3, S-100

Staging CT chest shows no evidence of metastatic disease

Question: What is the next step in treatment?

1. Surgical Resection
2. Chemotherapy
3. Radiation therapy
4. Immunotherapy

Question: What is the next step in treatment?

1. Surgical Resection
2. Chemotherapy
3. Radiation therapy
4. Immunotherapy

Post-radiation exam:

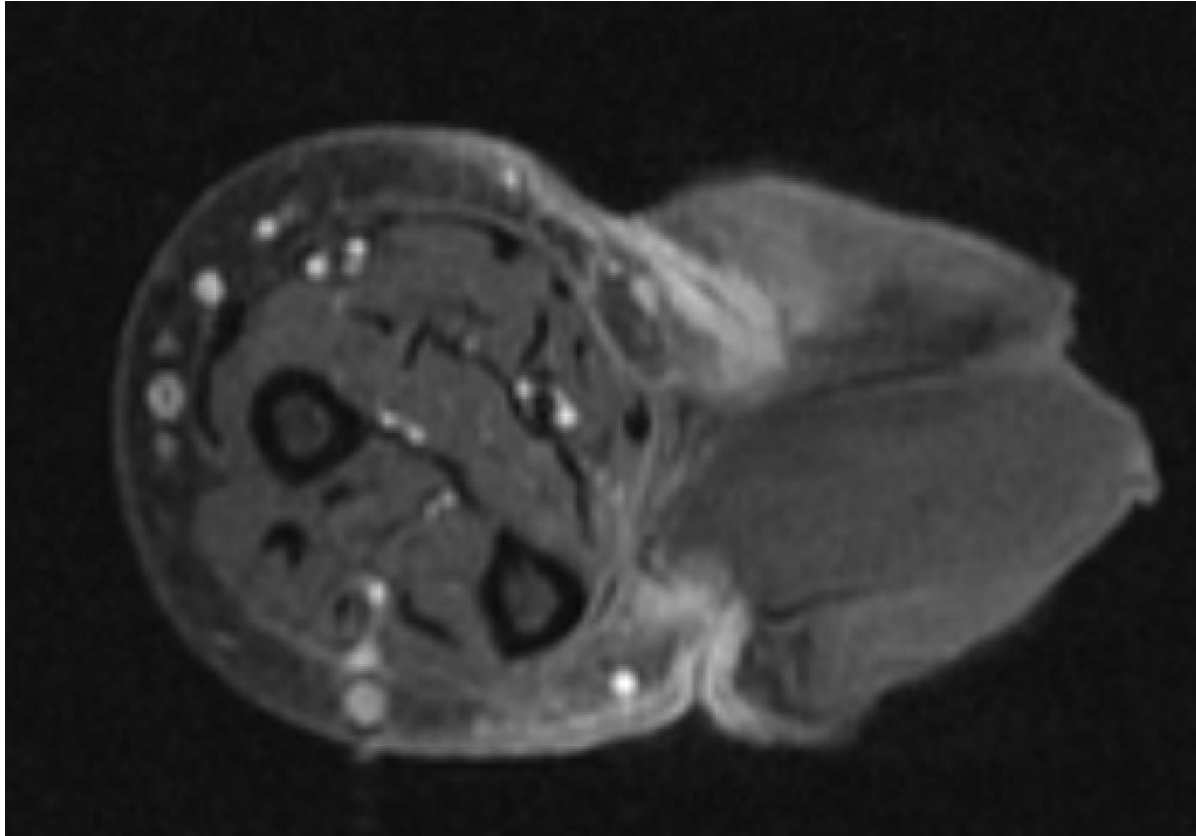


Last day of radiation therapy

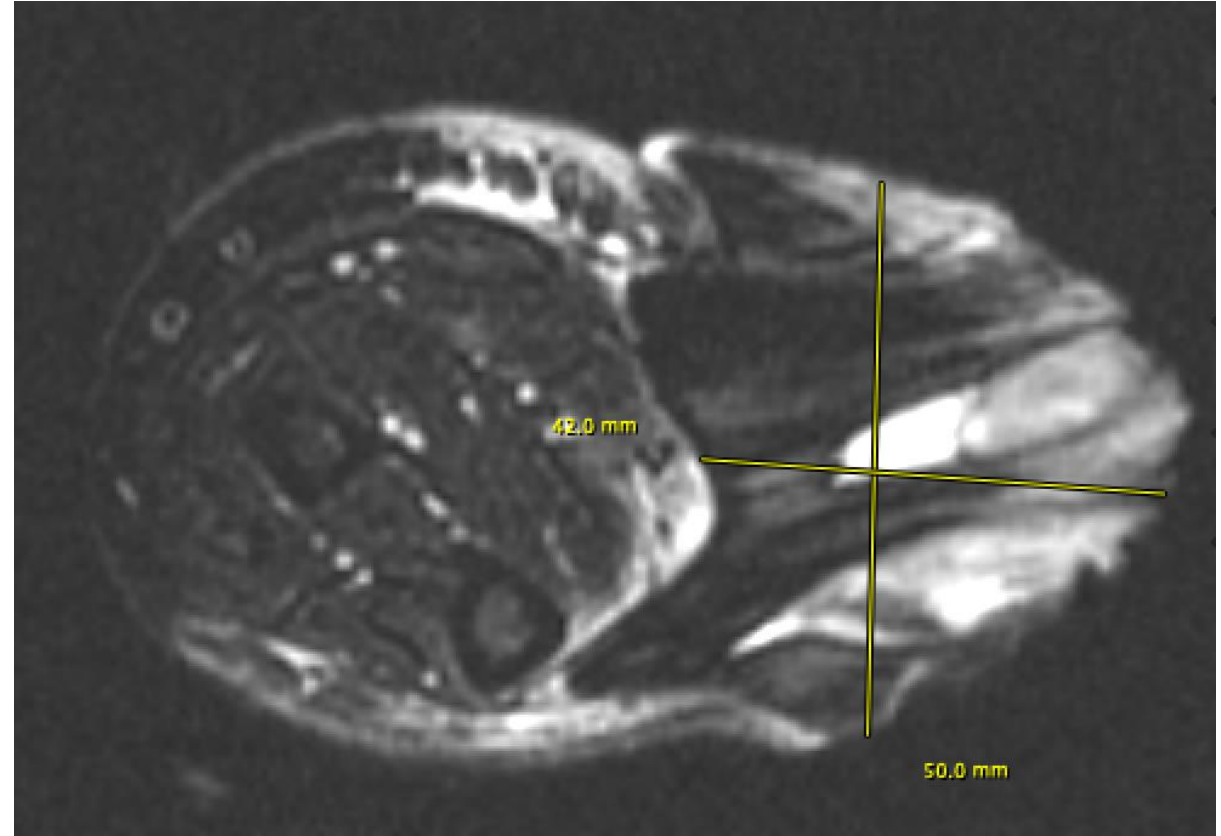


3 weeks post-radiation therapy

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T1 post contrast



T2

Question: What is the next step in treatment?

1. Surgical Resection
2. Chemotherapy
3. More radiation therapy
4. Immunotherapy

Question: What is the next step in treatment?

1. Surgical Resection
2. Chemotherapy
3. More radiation therapy
4. Immunotherapy

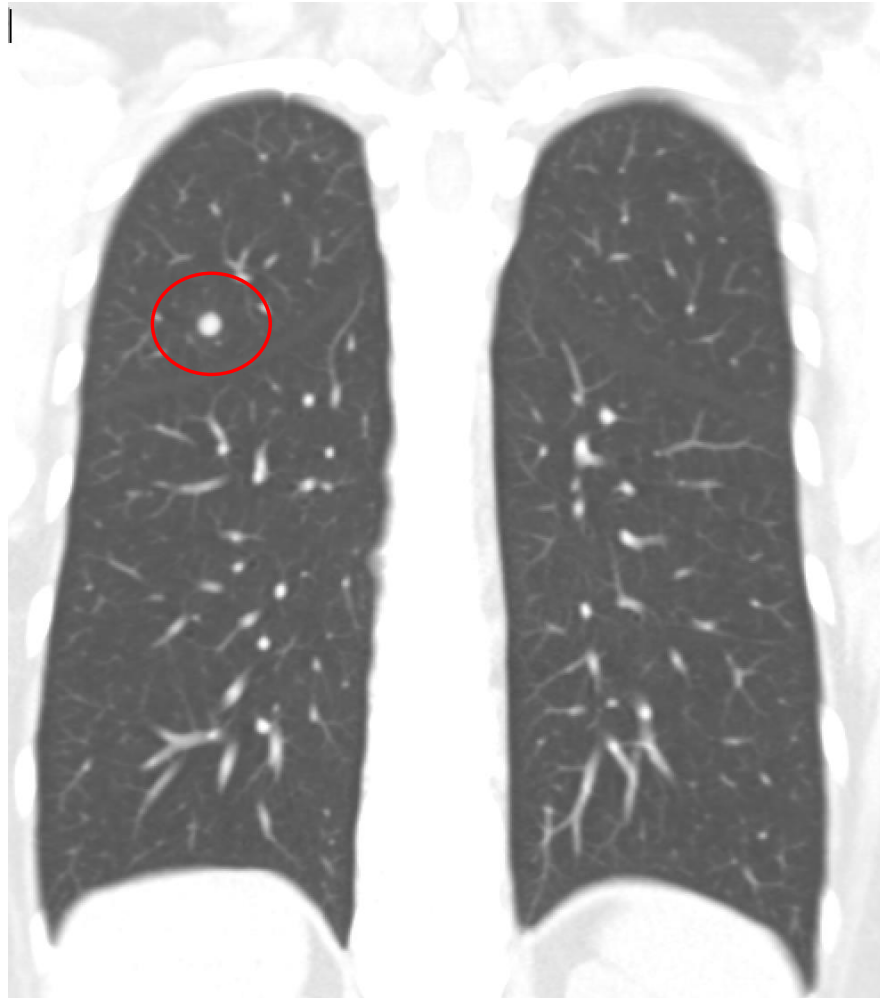
Clinical Course:

- Undergoes surgical resection of the mass, wound vac placement, and ultimately latissimus free flap placement with overlying skin graft
 - **Pathology: undifferentiated pleomorphic sarcoma with extensive necrosis and negative margins**
- Has wound breakdown with abscess requiring drainage and debridement, but ultimately does well
- Continues with post operative surveillance imaging

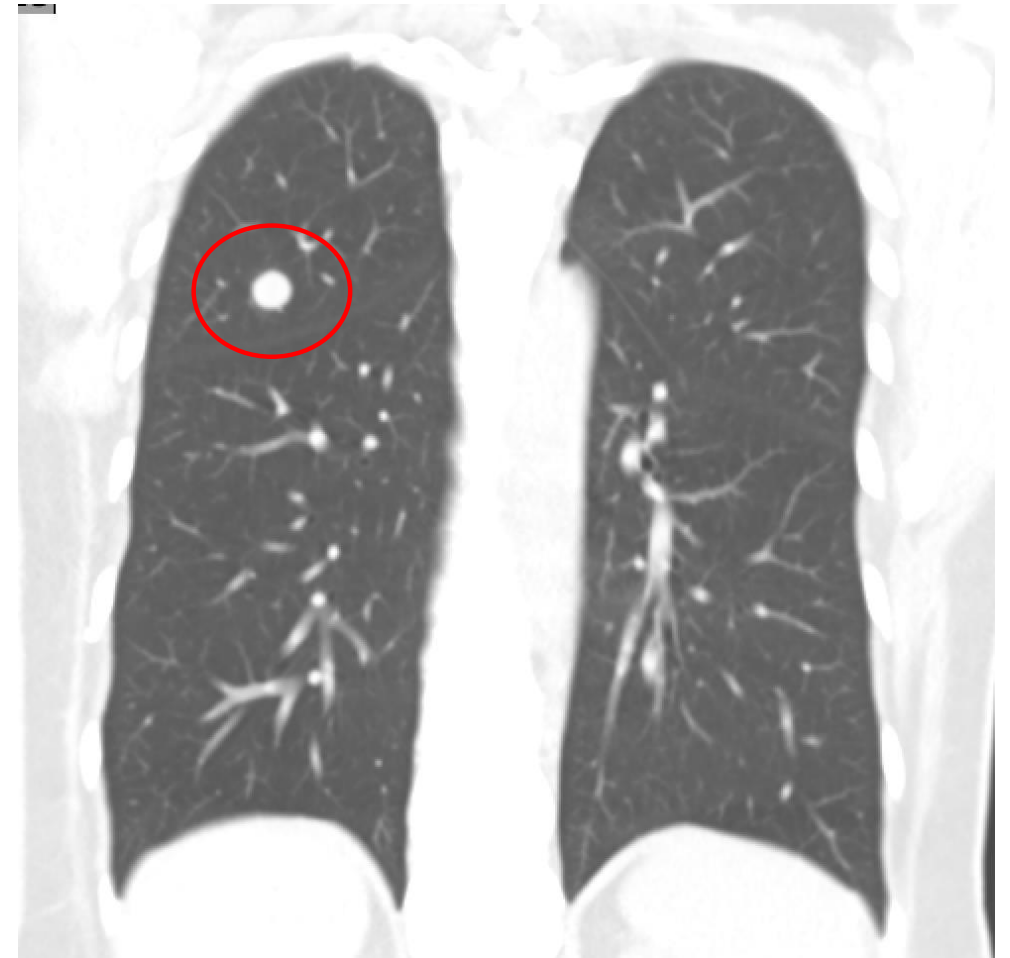


4 months post op

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6-month surveillance CT chest



1 month later

Clinical Course:

- Undergoes RUL wedge resection with thoracic surgery
- Pathology confirms metastatic sarcoma
- One year following later presents to outside facility ED with back pain without motor/sensory deficits
- Imaging demonstrates a large mass at L3-L5 with invasion at L4



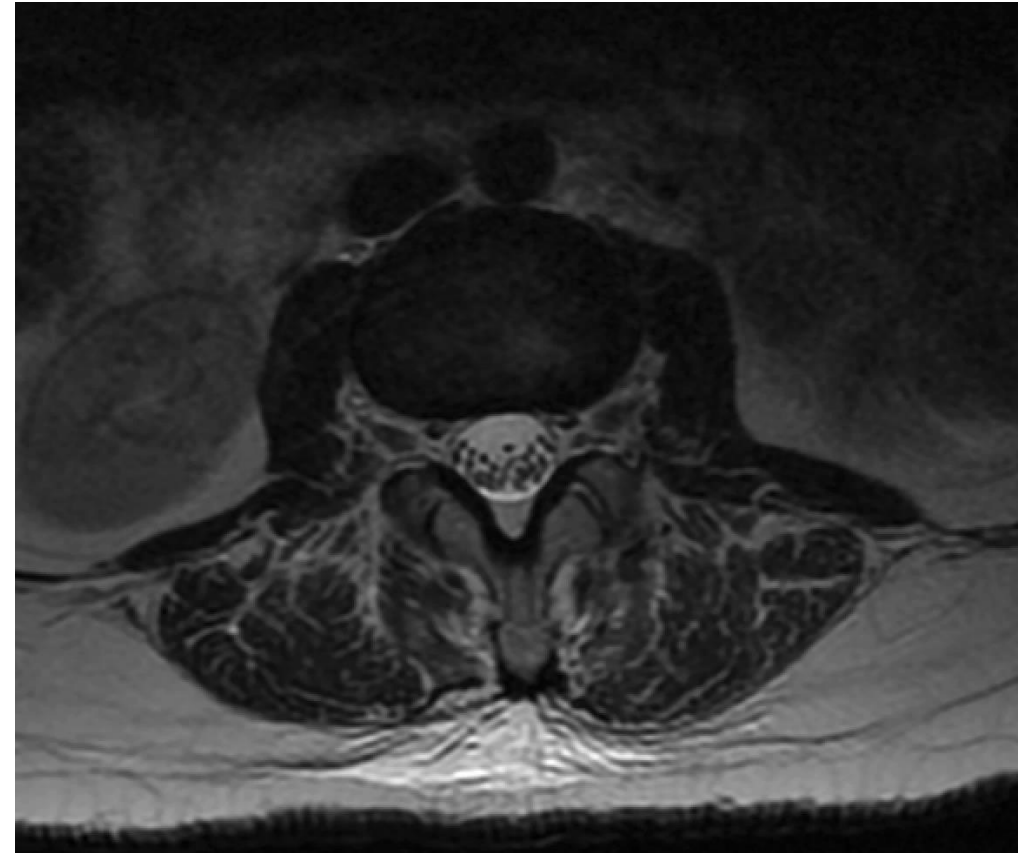
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STIR

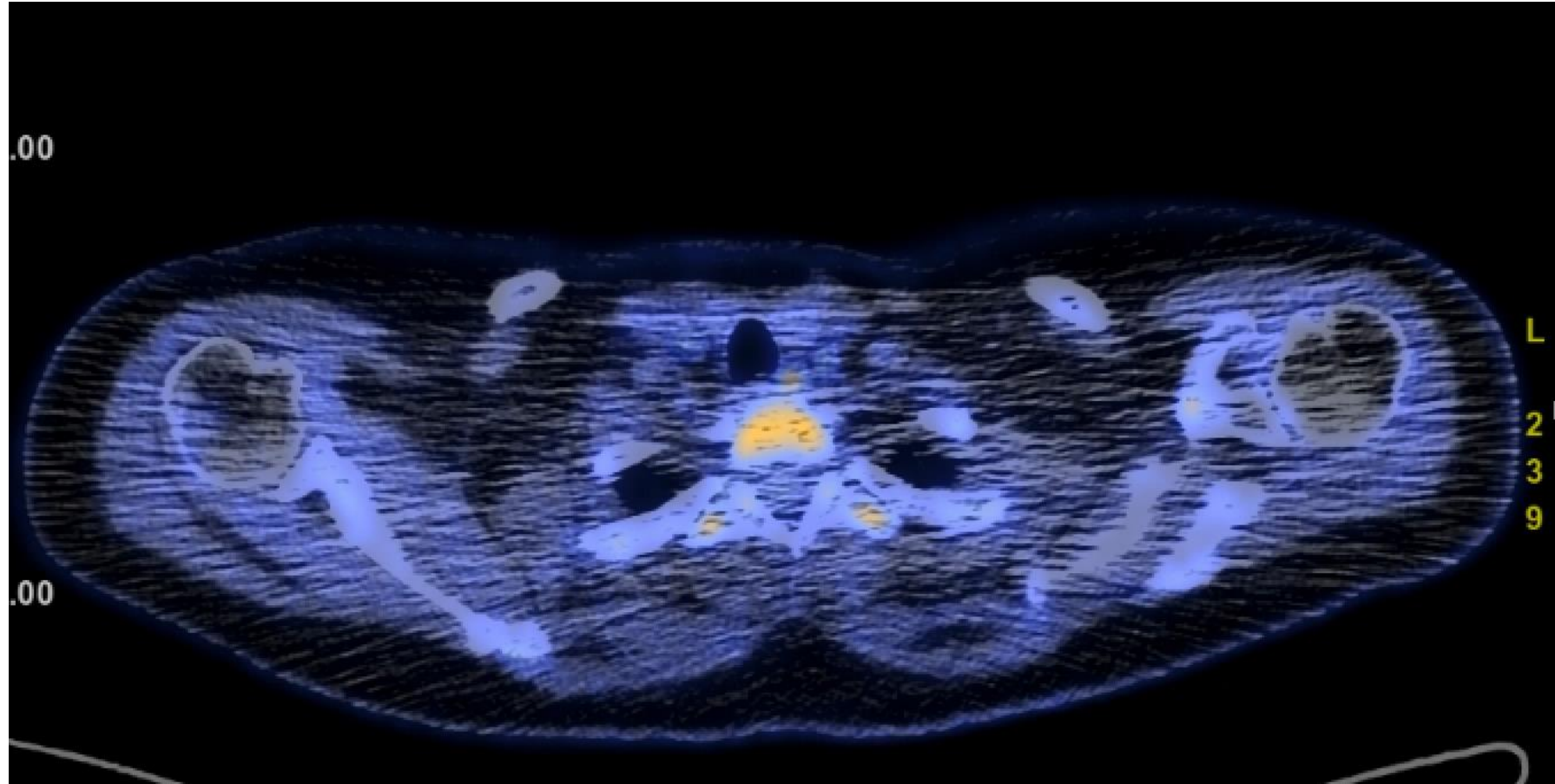


T1



T2

PET-CT Chest following spinal surgery:



Question: What is the next step in treatment?

1. Lung metasectomy
2. Chemotherapy
3. SBRT of lung lesions
4. Immunotherapy

Question: What is the next step in treatment?

1. Lung metasectomy
2. Chemotherapy
3. SBRT of lung lesions
4. Immunotherapy

Regimen: gemcitabine 800mg/m² on day 1 and day 8, docetaxel 75mg/m² on day 8

Clinical Course:

- Presents to an outside facility hospital for word-finding difficulties
- Found to have a subdural hematoma + metastatic lesion in the skull
- Undergoes left craniotomy for evacuation of subdural hematoma, right craniotomy for resection of tumor



Question: What is the next step in treatment?

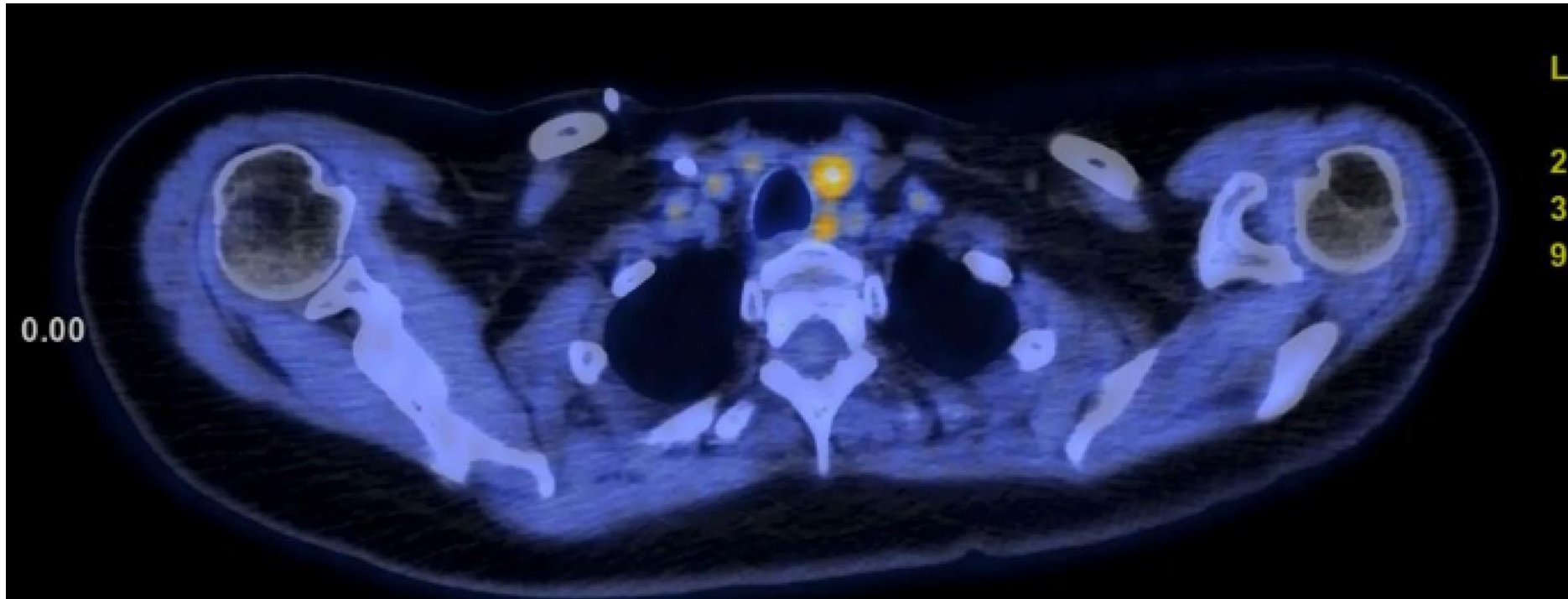
1. Continue current chemotherapy regimen
2. SBRT of lung lesions
3. Combination immunotherapy with axitinib and pembrolizumab
4. Palliative care only

Question: What is the next step in treatment?

1. Continue current chemotherapy regimen
2. SBRT of lung lesions
3. Combination immunotherapy with axitinib and pembrolizumab
4. Palliative care only

Clinical Course:

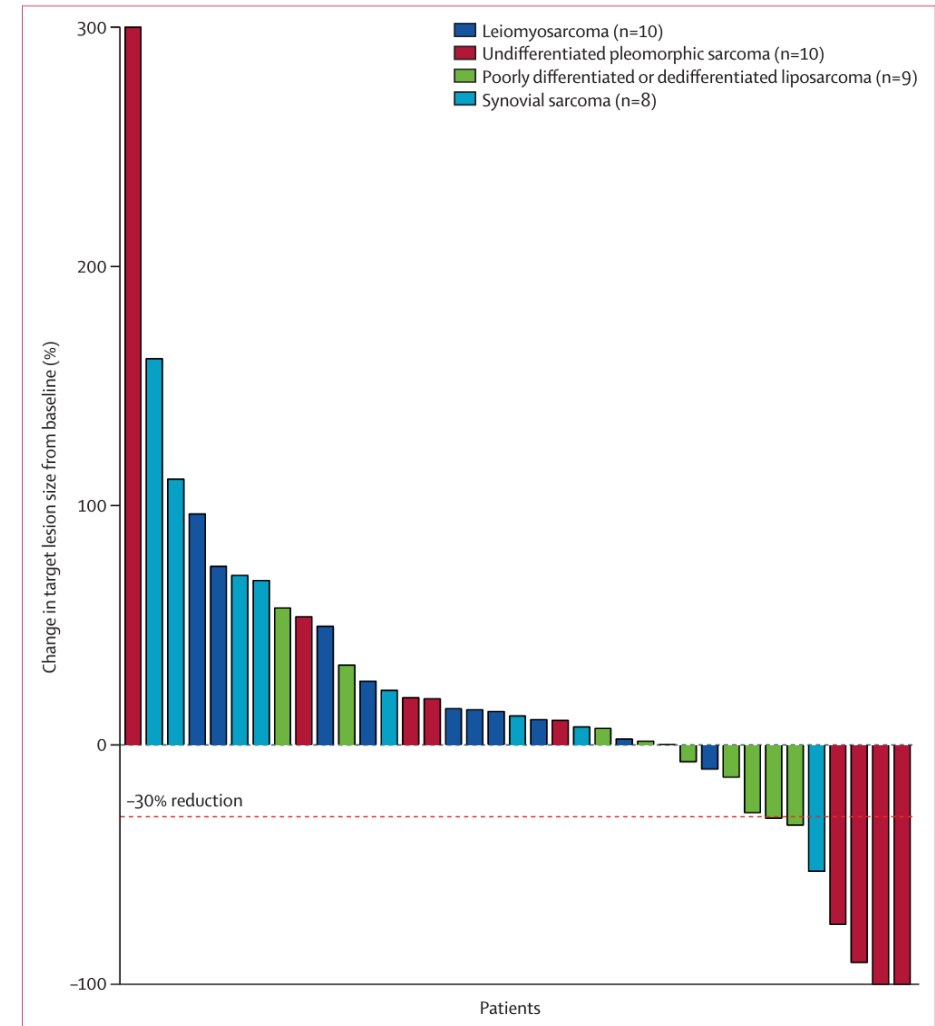
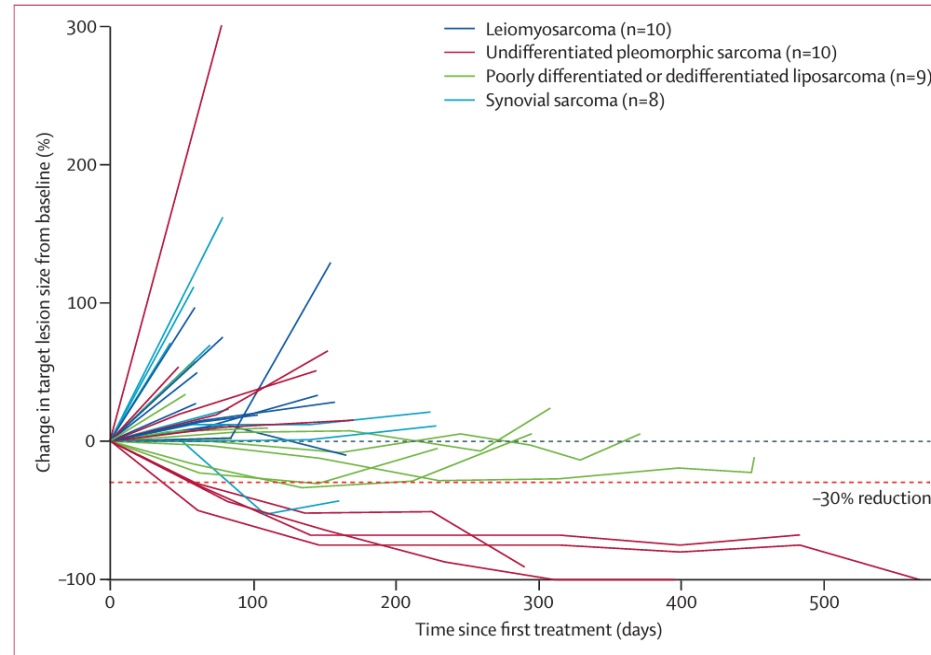
- Starts Axitinib 5mg BID and Pembro 200mg q3 weeks
- PET-CT after 3 cycles shows improvement in lung nodules



Pembrolizumab in advanced soft-tissue sarcoma and bone sarcoma (SARC028): a multicentre, two-cohort, single-arm, open-label, phase 2 trial

Conclusion:

Pembro produced a meaningful response seen in LPS and UPS



Take home points:

1. Pembrolizumab produces a meaningful clinical activity in UPS and LPS in patients who have previously received at least one systemic therapy
2. Additional trials looking at combination therapy with pembrolizumab and doxorubicin are ongoing

Questions?

Case 5:

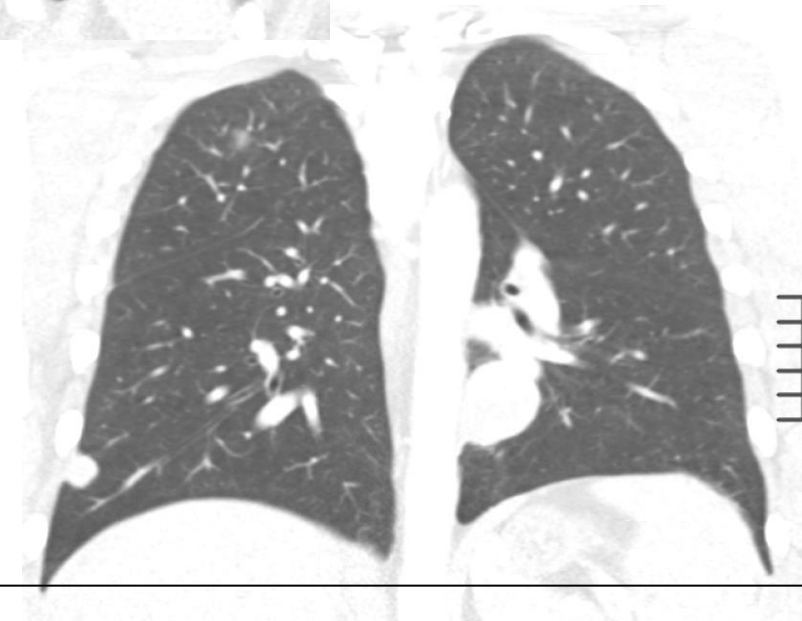
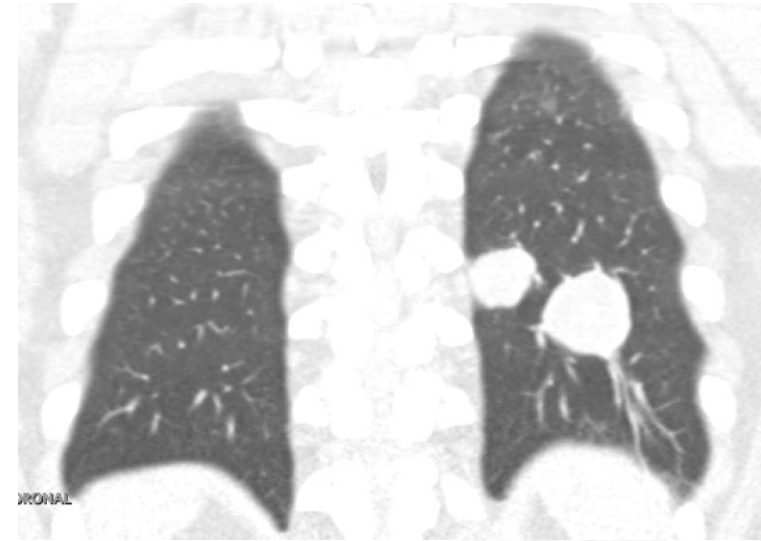
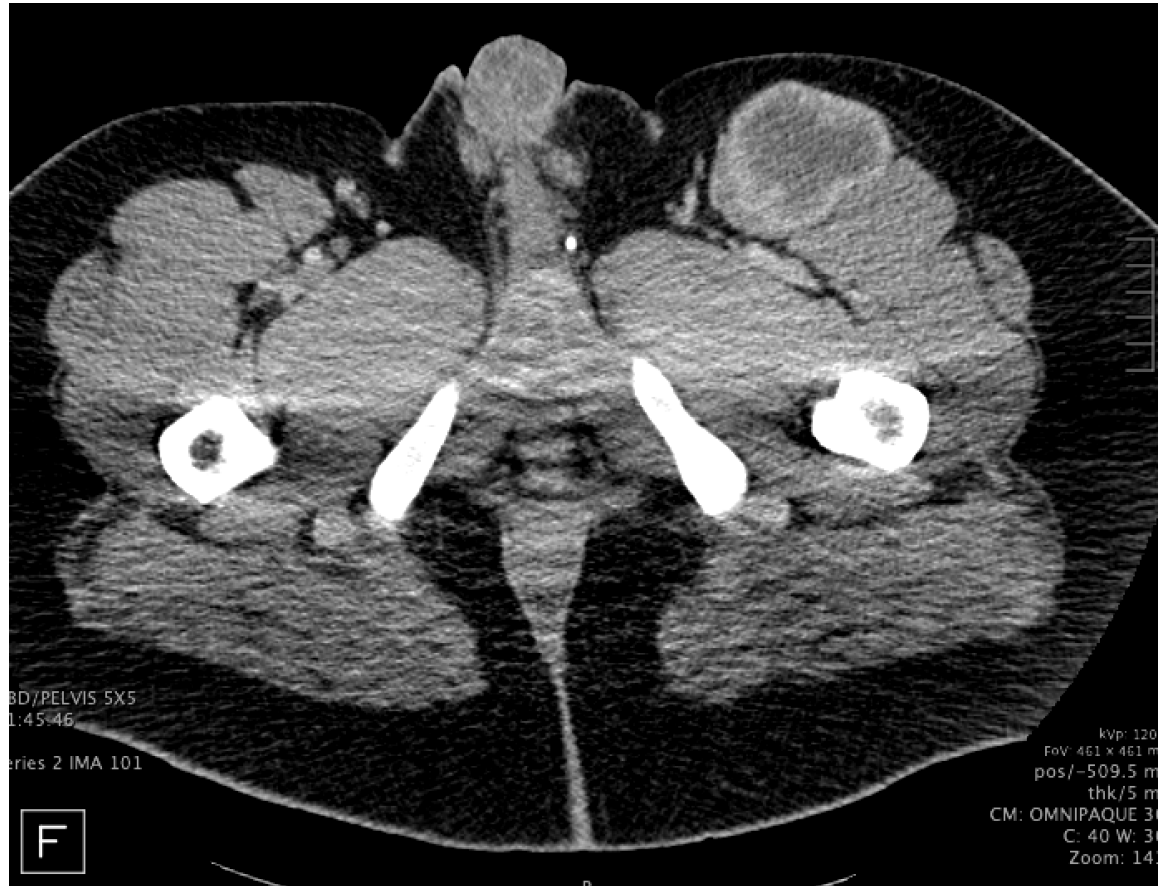
31 yo M presenting with progressively enlarging left thigh mass

PMHx: asthma

PSHx: benign cyst removal from scalp, tonsillectomy

Exam: LLE: 5x6 cm firm, non-tender, non-mobile mass in the left inguinal region. No mass appreciated in the left peritrochanteric/gluteal region

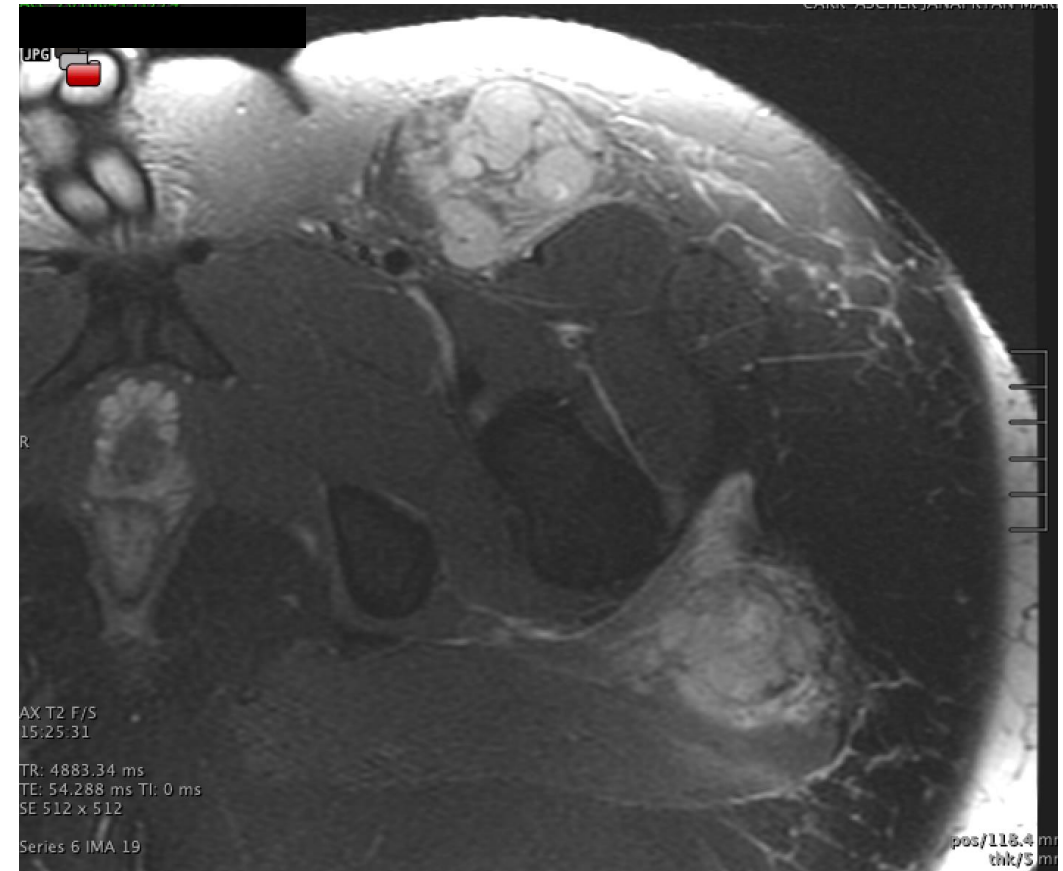
Imaging at time of diagnosis:



MR demonstrates additional left gluteal lesion

Core needle biopsy performed

Pathology: alveolar soft part sarcoma, FISH positive for TFE3 gene rearrangement



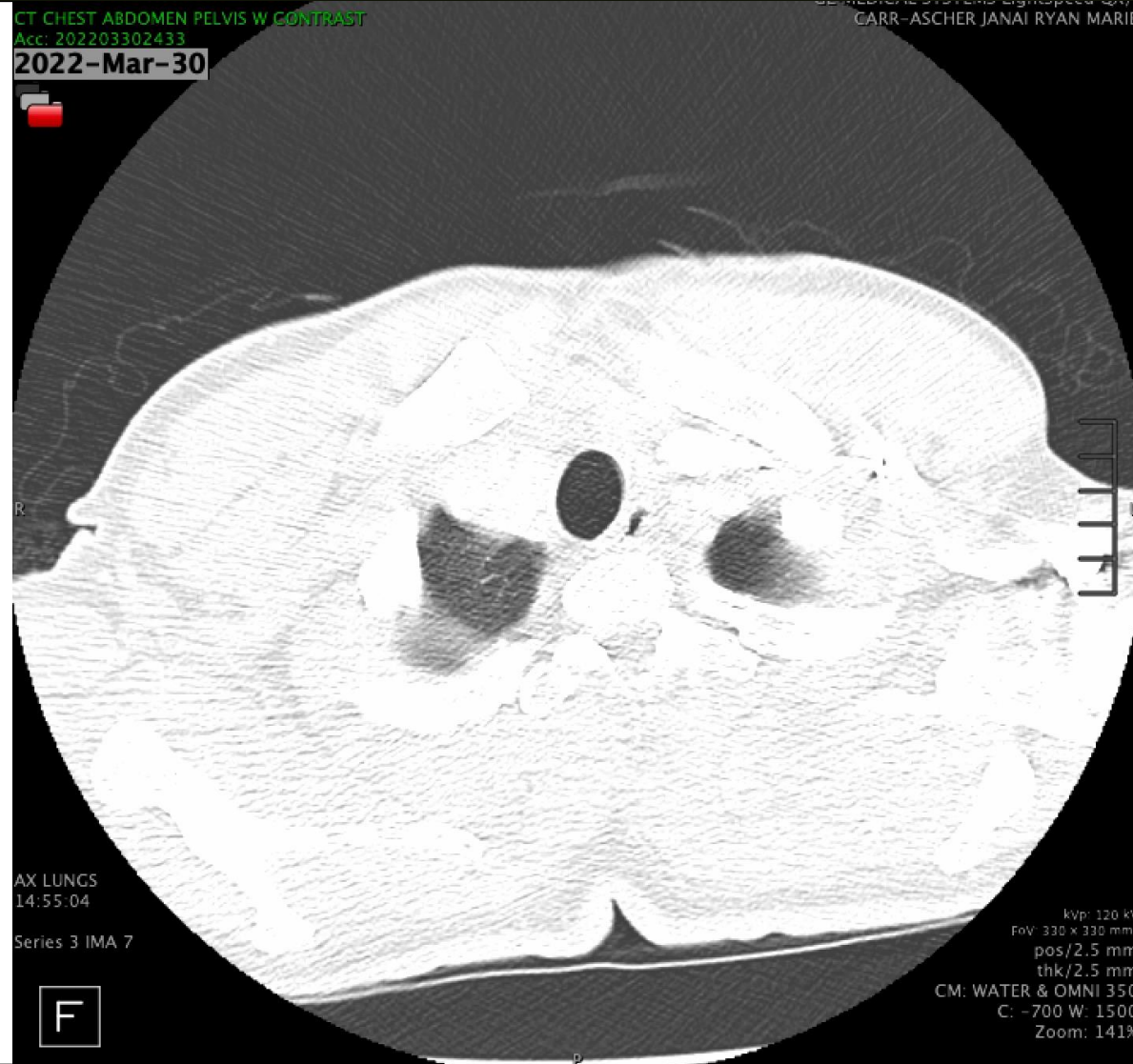
Initial treatment broken/inconsistent due to social reasons

Over 5-year period various treatments given including:

- Sunitinib
- Atezolizumab (clinical trial)
- Crizotinib (discontinued due to progression of disease)
- Radiation to the hip mass (13 fractions)

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Initial CT chest at presentation to our institution:



Question: What is the next step in treatment?

1. Lung metasectomy
2. Chemotherapy
3. SBRT of lung lesions
4. Immunotherapy

Question: What is the next step in treatment?

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Question: What is the next step in treatment?

1. Lung metasectomy
2. Chemotherapy
3. SBRT of lung lesions
4. Combination immunotherapy with axitinib and pembrolizumab

Clinical Course:

Receives 9 cycles of axitinib and pembrolizumab (10 cycles planned)

After cycle 9 has worsening LE swelling, shortness of breath, fatigue

Dose reduction discussed, deferred for now

Prior to cycle 10 patient presents to ED with “seizure-like” activity

Clinical Course:

Pembrolizumab held given toxicity

Interval imaging shows progression of disease

Restarted on axitinib only

Over next 6 months patient has significant progression of mediastinal disease

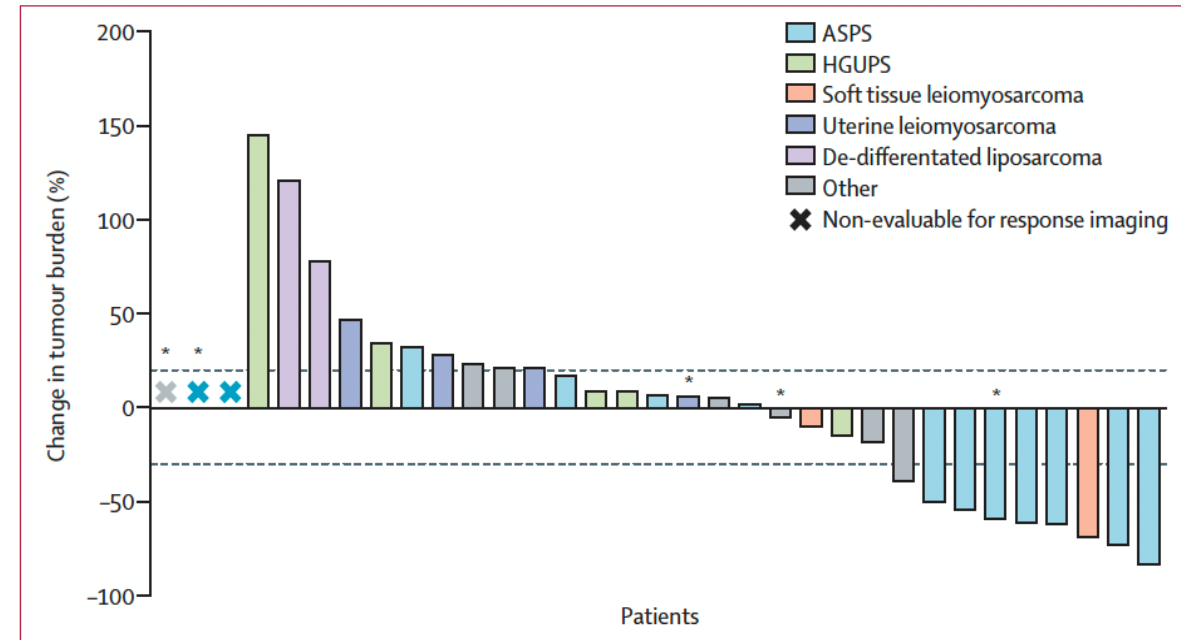
Ultimately stopped axitinib, started Pazopanib

Current status: Alive with disease

Axitinib plus pembrolizumab in patients with advanced sarcomas including alveolar soft-part sarcoma: a single-centre, single-arm, phase 2 trial

Breelyn A Wilky, Matteo M Trucco, Ty K Subhawong, Vaia Florou, Wungki Park, Deukwoo Kwon, Eric D Wieder, Despina Kolonias, Andrew E Rosenberg, Darcy A Kerr, Efrosyni Sfakianaki, Mark Foley, Jaime R Merchan, Krishna V Komanduri, Jonathan C Trent

3-month progression free survival was greater in ASPS group compared to entire cohort (72.7% in ASPS vs. 65.6% overall)



Take home points:

1. ASPS is a challenging disease entity to treat
2. Pembrolizumab + axitinib has shown efficacy in reducing tumor burden in advanced ASPS
3. Cardiomyopathy is a significant potential toxicity of pembrolizumab

24th Multidisciplinary Management of Cancers: A Case-based Approach

Disclosures

Thank you!