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Chemotherapy and Advances in Clinical Trials

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How to achieve optimal care

1) Multidisciplinary Approach

2) Complete and comprehensive Clinical Trial Portfolio

3) Integrated adult and pediatric Sarcoma Teams

4) Robust participation nationally and internationally:
NCCN, CTOS, AJCC, Alliance, SARC

Drugs Approved for Soft Tissue Sarcoma

- Cancer drugs approved by the Food and Drug Administration (FDA) for soft tissue sarcoma:
  - Dactinomycin
  - Doxorubicin
  - Imatinib
  - Pazopanib
  - Yondelis
  - Eribulin
  - Olaratumab
- Drugs commonly used include:
  - Ifosfamide
  - Dacarbazine
  - Gemcitabine
  - Taxotere
  - Paclitaxel
  - Vincristine
  - Temozolomide
  - Sorafenib/ Sutent

Impact of next-generation sequencing on diagnostic and therapeutic options in soft-tissue and bone sarcoma

Mrinal Gounder, Siraj Ali, Victoria Robinson, Mark Bailey, Richard Ferraro, Sherri Mills, Nirali Patel, Anita Krishnan, Sandra D'Angelo, Mark Dickson, Mary Lou Keohan, Vincent Miller, Gary Schwartz, Robert Maki and William Tap

PRESENTED AT: ASCO ANNUAL MEETING '17 | #ASCO17

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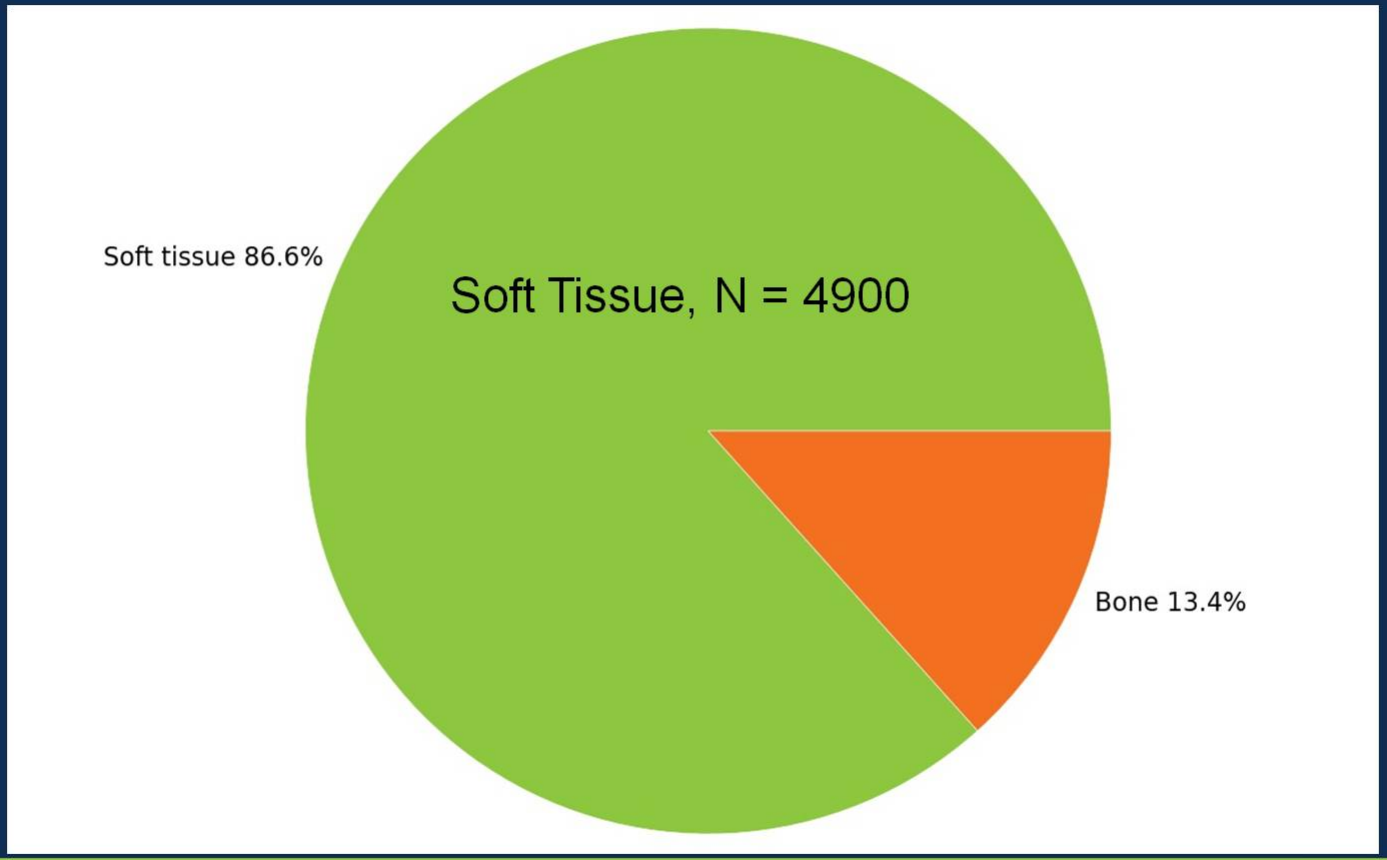
Questions:

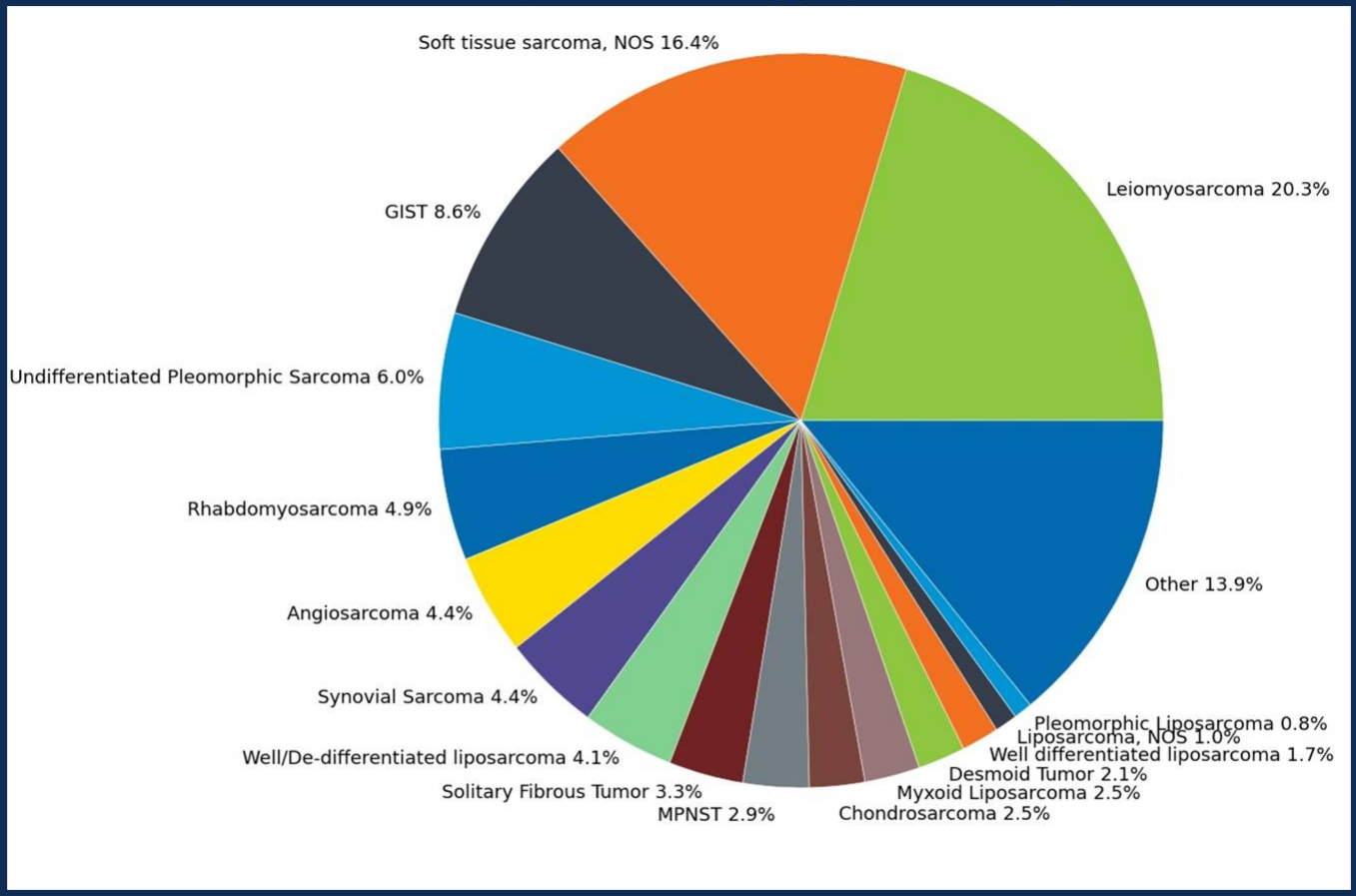
#1: Can genomic profiling aid/refine/modify diagnosis in sarcoma?

#2: Can genomic profiling identify therapeutic targets in sarcoma?

Distribution of Soft tissue versus Bone sarcoma (n = 5749)



56 unique histology (n = 5749)

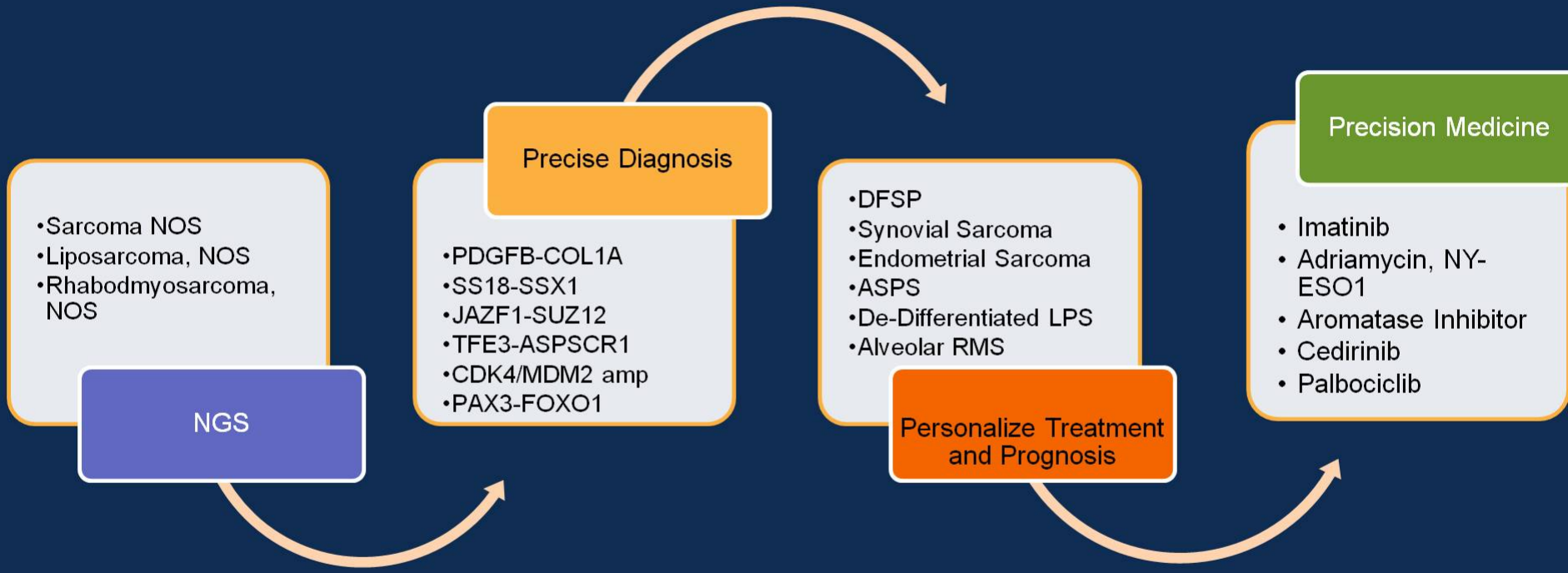


Question #1

Does genomic profiling aid/refine/modify diagnosis?

- YES, change/refine pathology diagnosis in 8% of the entire cohort (n = 460 patients)

Refine Diagnosis (n = 99, 2%)



Question #2

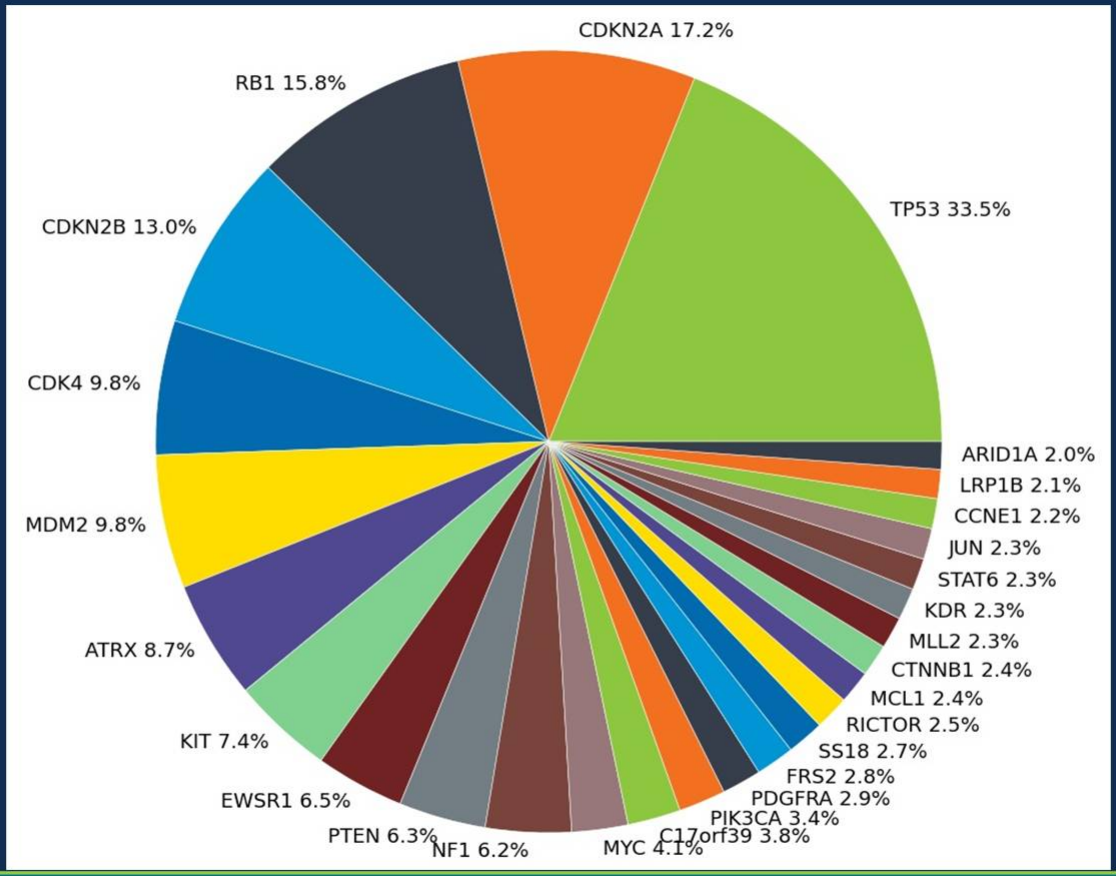
Does genomic profiling impact treatment decisions for sarcoma patients?

Landscape of Mutations (n = 5749)

634x depth

~62,000 mutations

~1200 fusions



Alliance A091401: A multi-center phase II study of nivolumab +/- ipilimumab for patients with metastatic sarcoma

Sandra P. D'Angelo[1], Michelle R. Mahoney[2], Brian A. Van Tine[3], James Atkins[4], Mohammed M. Milhem[5], William D. Tap[1], Cristina R. Antonescu[1], Elise Horvath[6], Gary K. Schwartz[7], Howard Streicher[8]

1. Memorial Sloan Kettering Cancer Center 2. Alliance Statistics and Data Center, Mayo Clinic 3. Washington University School of Medicine 4. Southeast Clinical Oncology Research Consortium NCORP, Winston-Salem, NC 5. University of Iowa/Holden Comprehensive Cancer Center 6. Astellas 7. Herbert Irving Comprehensive Cancer Center 8. National Cancer Institute, Cancer Therapy Evaluation Program, Investigational Drug Branch, Bethesda, MD

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Background

On-going need for more durable, effective and less toxic therapies

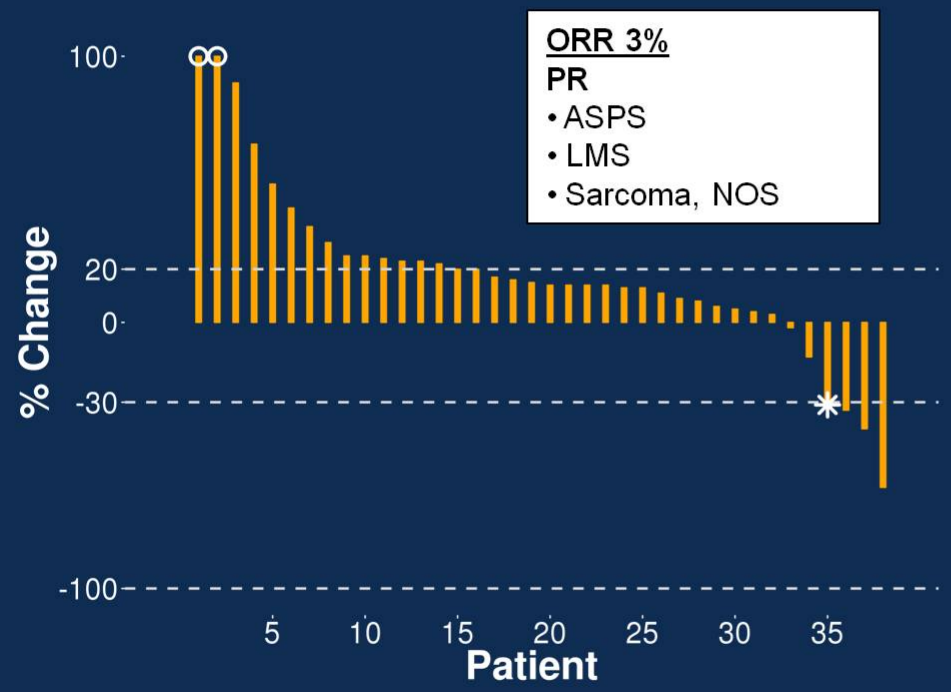
Immuno-oncology has emerged as a new promising approach

Pembrolizumab has demonstrated promising activity in selected sarcomas

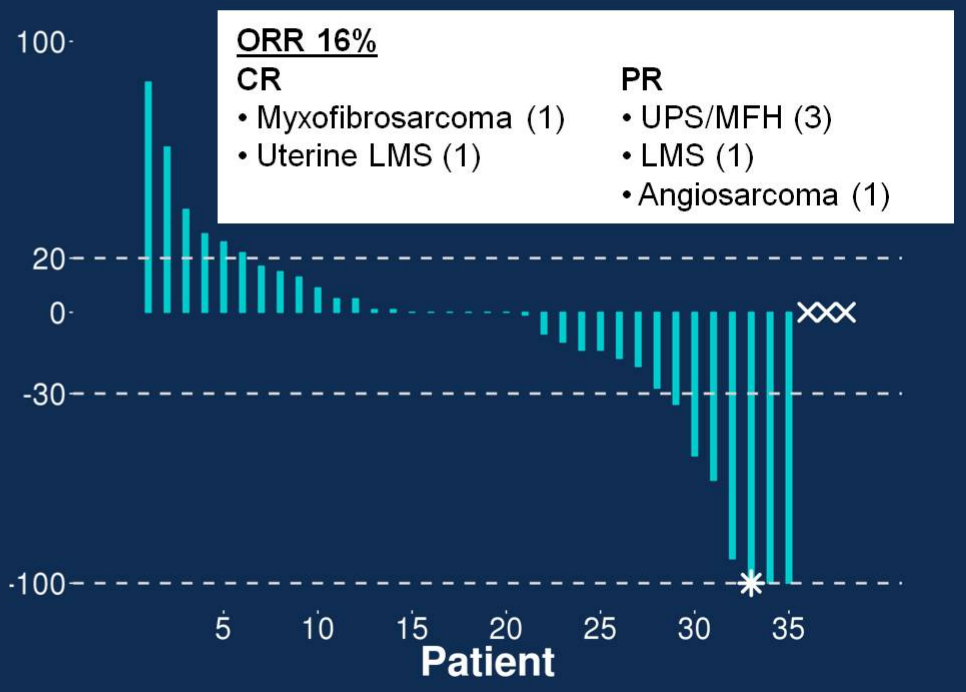
Combination checkpoint blockade with nivolumab and ipilimumab has improved efficacy in multiple malignancies

ORR: 3% Monotherapy, 16% Combination

Nivo 3



Nivo 3 + Ipi 1



Multicenter Phase II Study of Pembrolizumab in Advanced Soft Tissue and Bone Sarcomas: Final Results of SARC028 and Biomarker Analyses

Melissa A. Burgess, MD, Vanessa Bolejack, PhD, Brian A. Van Tine, MD, Scott Schuetze, MD, PhD, PhD, James Hu, MD, Sandra P. D'Angelo, MD, Steven Attia, DO, Dennis Priebat, MD, Scott H. Okuno, MD, Richard F. Riedel, MD, Lara E. Davis, MD, Sujana Movva, MD, Damon Reed, MD, Lisa H. Butterfield, PhD, Janos Roszik, PhD, Denise Reinke, NP, MBA, Laurence H. Baker, DO, Robert Maki, MD, PhD, Shreyaskumar Patel, MD, Hussein A. Tawbi, MD, PhD, on behalf of SARC028 Investigators

University of Pittsburgh, Cancer Research and Biostatistics, Washington University St Louis, University of Michigan, University of Southern California, Memorial Sloan Kettering Cancer Center, Mayo Clinic Florida, MedStar Research Institute, Mayo Clinic Rochester, Duke University, Oregon Health and Science University, Fox Chase Cancer Center, Moffitt Cancer Center, University of Pittsburgh, UT MD Anderson Cancer Center, SARC, University of Michigan, Mount Sinai Medical Center, UT MD Anderson Cancer Center

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Abstract Number: 11008

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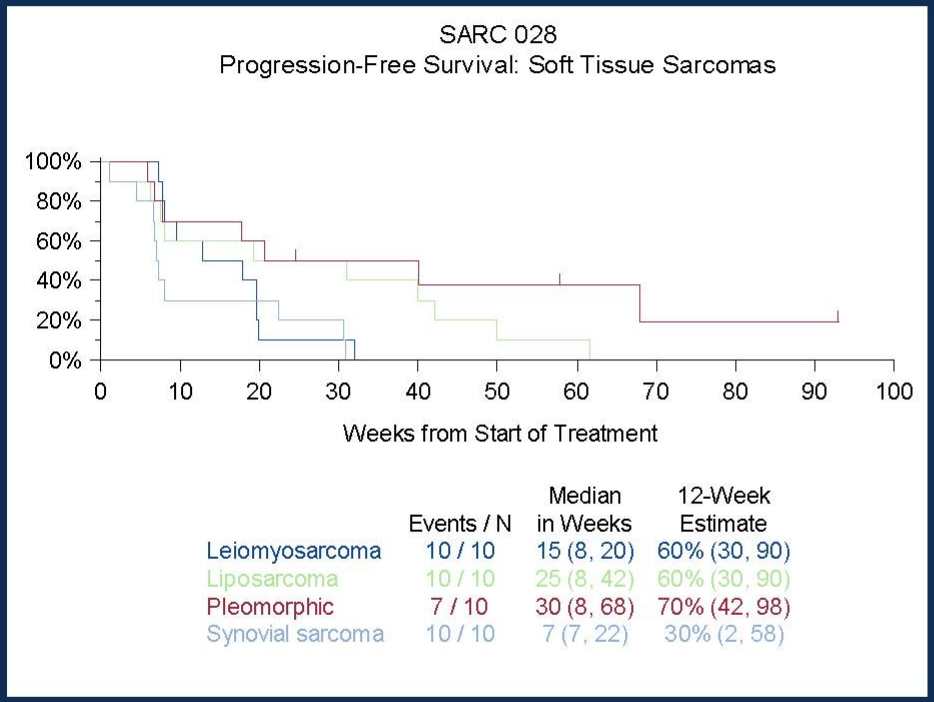
Enrollment

- 86 patients enrolled (6 patients were replaced)

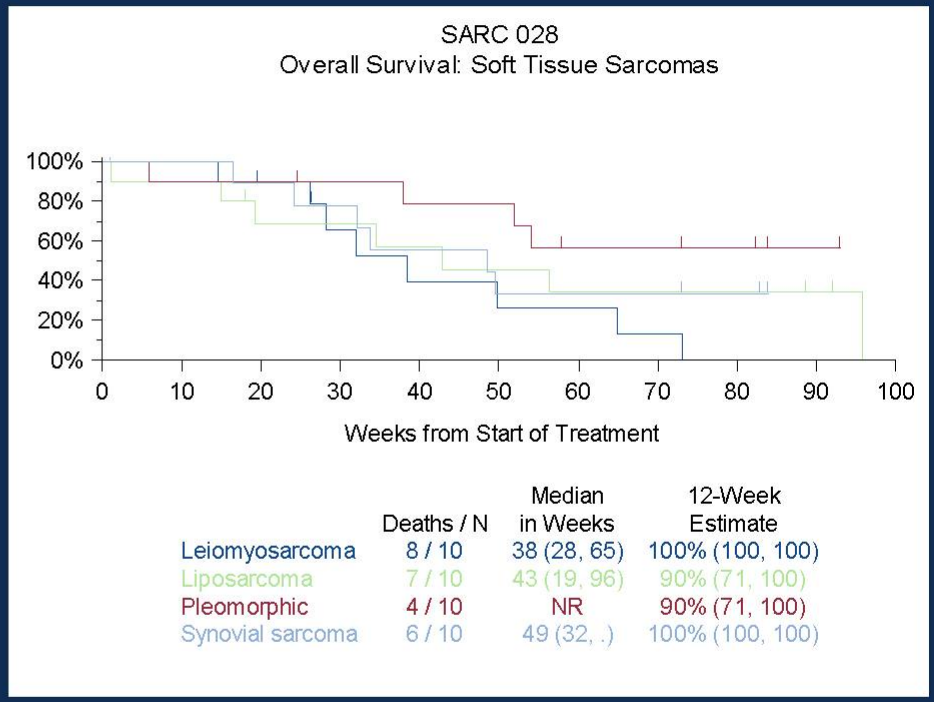
Soft Tissue Sarcoma	N = 40
Leiomyosarcoma	10
Liposarcoma	10
Synovial Sarcoma	10
Undiff. Pleomorphic Sarcoma	10

Bone Sarcoma	N=40
Osteosarcoma	22
Ewing's Sarcoma	13
Chondrosarcoma	5

PFS & OS by Soft Tissue Sarcoma Subtype



	Events / N	Median in Weeks	12-Week Estimate
Leiomyosarcoma	10 / 10	15 (8, 20)	60% (30, 90)
Liposarcoma	10 / 10	25 (8, 42)	60% (30, 90)
Pleomorphic	7 / 10	30 (8, 68)	70% (42, 98)
Synovial sarcoma	10 / 10	7 (7, 22)	30% (2, 58)



	Deaths / N	Median in Weeks	12-Week Estimate
Leiomyosarcoma	8 / 10	38 (28, 65)	100% (100, 100)
Liposarcoma	7 / 10	43 (19, 96)	90% (71, 100)
Pleomorphic	4 / 10	NR	90% (71, 100)
Synovial sarcoma	6 / 10	49 (32, .)	100% (100, 100)

Median PFS 18 weeks, 12-wk PFR 55%

Median OS 49 weeks

Conclusions

- Pembrolizumab is a potential viable treatment option in subset of sarcomas (UPS, LPS)
- Confirmatory activity with planned expansion study
  - Currently enrolling
  - Restricted to UPS and LPS cohorts (30 each)
  - 20 patients with mandatory bx
  - 10 patients without bx

Patterns of Response in STS