Updated Consensus Approach to Management of Metastatic Retroperitoneal Sarcoma

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Background

Management of metastatic retroperitoneal sarcoma: a consensus approach from the Trans-Atlantic Retroperitoneal Sarcoma Working Group (TARPSWG)†

Trans-Atlantic Retroperitoneal Sarcoma Working Group (TARPSWG)*

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†For Trans-Atlantic Retroperitoneal Sarcoma Group Collaborators see Appendix.

Annals of Oncology, 2018

Updated:
Primary RPS - 2021
Recurrent RPS - 2022

Background

43 Statements 2018

1. Evaluation in sarcoma centers with multidisciplinary team

Pretreatment Assessment

Clinical history and prior treatment (2.- 4.)

Imaging (5. – 9.)

Pathology (11. – 16.)

Patient Evaluation (17. – 21.)

Treatment

Local therapies (23. – 26.)

Pulmonary metastases (27. – 30.)

Hepatic metastases (31.)

Intra-abdominal metastases (32. – 33.)

Recurrent metastases (34. – 36.)

Palliation (37.)

Systemic therapy (38. – 43.)

Proposed Updates

- Histology-focused, upfront **– Included:**
  - Liposarcoma
  - Leiomyosarcoma
  - UPS
  - MPNST
  - SFT

→ Where are expected sites of disease?

When does metastasis / recurrence occur?

…What is expected outcome?*

Proposed Updates

- Histology-focused, upfront

- Separate:

  “Metastatic” (Visceral Organ, Distant) vs.

  “Multifocal” (Intraabdominal; Locoregional)

Systemic therapy - what is role and timing?

Surgery vs. other local therapies?

Leiomyosarcoma

- Distant metastasis!
- Metastasectomy?

Synchronous
vs.
Metachronous (DFI?)

Solitary
vs.
Multiple

Primary intact

Local recurrence?

Leiomyosarcoma

- Distant metastasis
- Metastasectomy?

Systemic therapy?

Other local therapy options?

- **Liver** directed therapies (Y90, HAI)…

Leiomyosarcoma

- Distant metastasis!
- Metastasectomy?

- **Liver** directed therapies (Y90, HAI)…

Liposarcoma

- Multifocal locoregional recurrence

Sarcomatosis?

- Multiple recurrences…

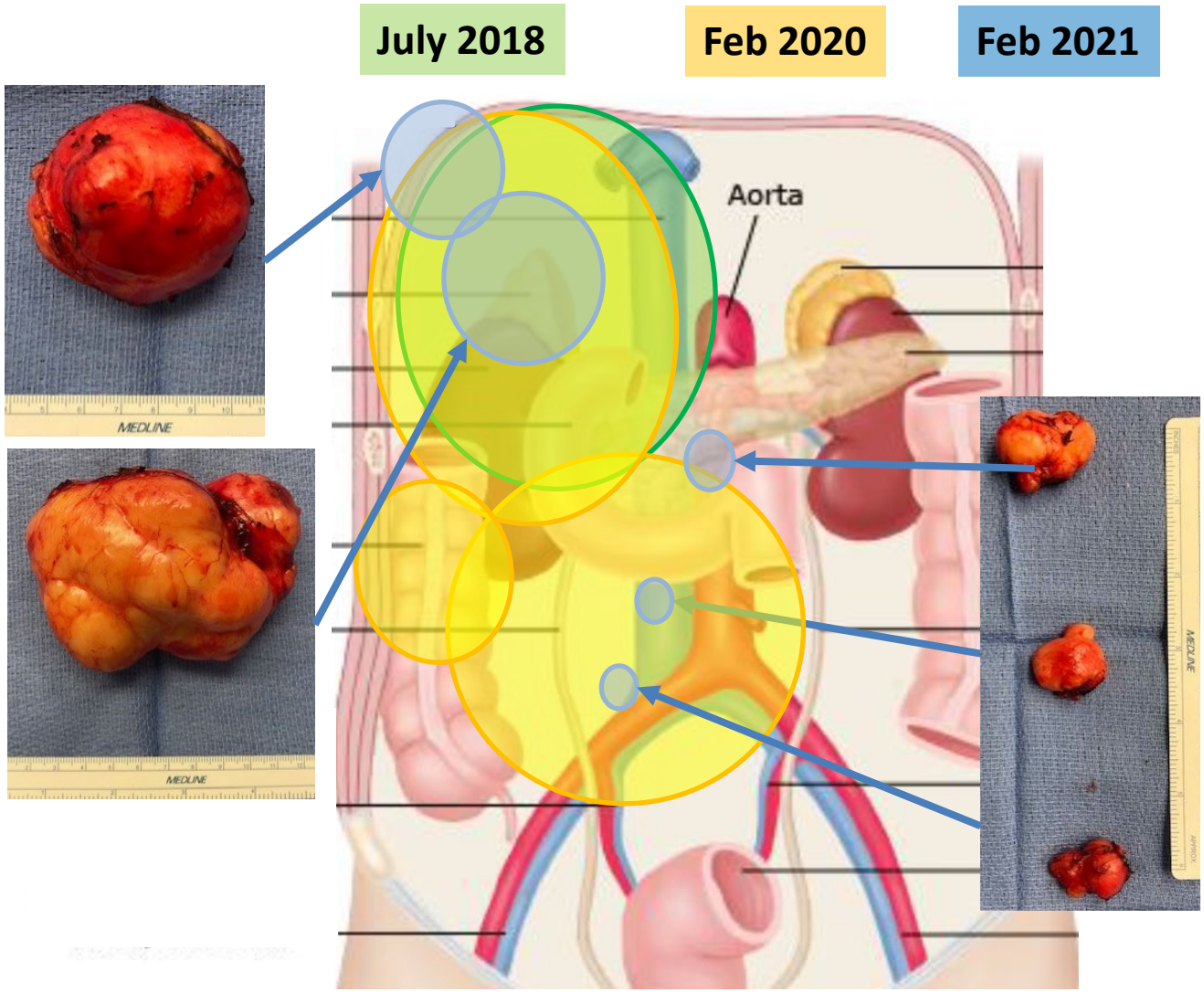
Systemic therapy?

Other local therapy options?

- Definitive radiation therapy
- Ablation

- Distant metastasis?

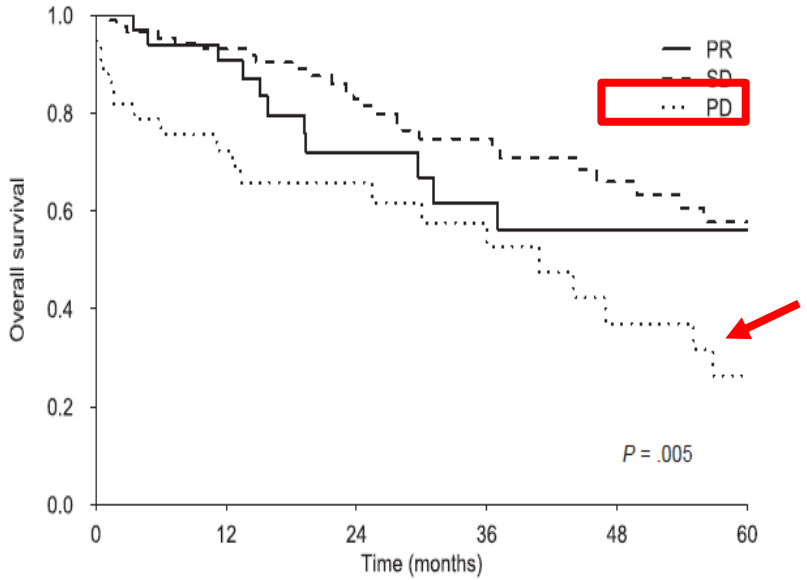
Liposarcoma



Systemic Therapy

- Can response to therapy be used to select patients who may or may not benefit from surgery?

Primary Disease



…keep on treating?

Tseng et al (TARPSWG), *Cancer* 2020

Systemic Therapy

2018

43. There is no clear agent of choice for second-, third- and higher-line treatment, or in the event that anthracycline-based therapy is contraindicated, but the following agents can be considered based on histologic subtype:

a. Single-agent ifosfamide can be used for selected subtypes [84]. An infusional schedule of ifosfamide (1 g/m^2 for 14 days followed by 14 days off) may be particularly effective for dedifferentiated liposarcoma (LPS), synovial sarcoma, and malignant peripheral nerve sheath tumor [85]. For synovial sarcoma in particular, high-dose (>10 g/m^2) ifosfamide can be effective [86]. (IB)
b. Trabectedin can be considered in sensitive histologies, such as LMS and LPS [87, 88]. (IB)
c. Eribulin has been shown to confer a survival advantage over treatment with DTIC in advanced pre-treated liposarcoma [89]. (IB)
d. For non-LPS, pazopanib can be considered based on the results of a randomized placebo-controlled trial in pre-treated STS [90]. (IB)
e. Gemcitabine can be used alone or in combination with docetaxel or DTIC for all subtypes, but especially LMS and undifferentiated pleomorphic sarcoma [79, 91–94]. (IB)
f. DTIC can be used alone or in combination with anthracyclines for LMS and SFT [72, 92, 95]. (IB)
g. Antiangiogenics, such as sunitinib, pazopanib, or temozolomide, can be considered for SFT [95]. (IVB)
h. Sirolimus and other mTOR inhibitors can be considered in PEComa [96]. (VB)
i. Crizotinib and other ALK inhibitors can be considered for inflammatory myofibroblastic tumor, although they are not yet approved for this application [97]. (VB)

Drug → Histology

Histology-Focused Systemic Therapy

Histology → Drug

National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2023
Soft Tissue Sarcoma

SYSTEMIC THERAPY AGENTS AND REGIMENS WITH ACTIVITY IN SOFT TISSUE SARCOMA SUBTYPES[d] AND AGGRESSIVE SOFT TISSUE NEOPLASMS

Desmoid Tumors (Aggressive Fibromatosis)[n]	Non-Pleomorphic Rhabdomyosarcoma
Preferred regimens • Nirogacestat (category 1)[43] • Sorafenib (category 1)[44]	**Preferred regimens** • Vincristine, dactinomycin, cyclophosphamide (VAC)[o,55] • Vincristine, dactinomycin, ifosfamide (VAI-Europe)[o,56]

- Liposarcoma
- Leiomyosarcoma
- UPS
- MPNST
- SFT

Retroperitoneal Well-Differentiated or Dedifferentiated Liposarcoma
Useful in certain circumstances • Palbociclib[s,110]

Solitary Fibrous Tumor
Preferred regimens • Bevacizumab[q] and temozolomide[103] • Sunitinib[82,104] • Sorafenib[105] • Pazopanib[106] **Other recommended regimens** • Anthracycline-based regimens: ▸ Doxorubicin[1,2,6,7] ▸ Epirubicin[8] ▸ Liposomal doxorubicin[9] ▸ AD (doxorubicin, dacarbazine)[1,2,10,11,12] ▸ AIM (doxorubicin, ifosfamide, mesna)[1-4,6] ▸ Ifosfamide, epirubicin, mesna[5] ▸ MAID (mesna, doxorubicin, ifosfamide, dacarbazine)[1,2,31,32] • Gemcitabine-based regimens: ▸ Gemcitabine ▸ Gemcitabine and docetaxel[20,21] ▸ Gemcitabine and vinorelbine[22] ▸ Gemcitabine and dacarbazine[23] • Trabectedin[j]

Logistics

"Committee"

- Will Tseng (Surgical Oncology), City of Hope
- Roberta Sanfillippo (Medical Oncology), INT Milan
- Chiara Fabbroni (Medical Oncology), INT Milan
- Jason Sicklick (Surgical Oncology), UCSD

- Radiation Oncologist?

- Interventional Radiologist?

Logistics

Proposed Timeline

- Draft circulation within Committee
- June 2024 (ASCO): Statement by statement – 2 mtgs
- November 2024 (CTOS): Near final draft – 2 mtgs
- Manuscript submission: end of 2024

~6-7 years
since original manuscript