درمان‌های کمکی در سارکوم رتروپریتوئن

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• There is no "one size fits all" approach to treatment of RPS.

• Surgical resection has traditionally been the only potentially curative approach. Because of the typically large size and anatomic complexity, (R0 resection) is often not achieved, and locoregional recurrence is common, especially for low-grade tumors.

• Most sarcoma specialists would define complete resection of RPS as R0/R1, with ideally (R0), but with acceptance of the possibility of positive microscopic margins.
• Yet, the role of adjunctive therapy (radiation therapy, chemotherapy, either preoperatively or postoperatively) continues to be debated, and there is no consensus as to the best approach for all patients.

• Due to the rarity of these tumors and the complexity of treatment, there is widespread disagreement to optimal approach RPS and a lack of high-level evidence to support any approach. This is reflected in the widely disparate recommendations from expert groups.
• For all patients, it is suggested to participation in ongoing clinical trials, where available.
For treatment of well-differentiated liposarcoma with no areas concerning for higher grade histology on imaging, approach differs by tumor size:

- Initial surgery is reasonable for most patients with a small potentially resectable tumor.

- For larger tumors, treat aggressively with therapies that optimize local control (preoperative RT and aggressive surgery) because these patients tend to die from local recurrence and not distant disease, unless they dedifferentiate.
For patients with intermediate- and high-grade tumors with histologies that are chemotherapy sensitive (synovial sarcoma, myxoid/round cell liposarcoma, MPNST) and/or when the risk of distant metastatic disease is high (leiomyosarcoma of the inferior vena cava, large dedifferentiated liposarcoma), neoadjuvant chemotherapy, with/without preoperative RT.
• For intermediate- and high-grade tumors with histologies that are not chemotherapy sensitive or if the patient is not a suitable candidate for chemotherapy, preoperative RT alone (without chemotherapy) and aggressive surgery is offered.
• The use of adjuvant therapy following resection of an RPS without neoadjuvant therapy depends on the tumor grade and completeness of resection:
• Adjuvant RT for a low-grade grossly completely resected (R0/R1) tumor is not suggested.

• Postoperative RT could be considered for patients with a high- or intermediate-grade tumors who are at risk for local recurrence; however, in practice, most patients are just observed because it is rarely possible to deliver postoperative adjuvant RT with acceptable morbidity.
• Adjuvant chemotherapy cannot be considered a standard approach for STS at any site, including the retroperitoneum, and do not suggest its use outside of the context of a clinical trial.

• The benefit of adjuvant chemotherapy following surgical resection of an STS at any site is controversial.
• Delivery of RT prior to surgery, +/- IORT at the time of resection, permit the safe delivery of higher RT doses than possible in postop. setting, where RT doses to tumor bed are limited by large field size and proximity surrounding radiosensitive normal structures, (liver and bowel). In fact, many multidisciplinary sarcoma groups do not routinely offer postop. RT to patients with resected RPS because of significant concerns about the narrow therapeutic ratio.
- The theoretical advantages of preoperative, as compared with postoperative, RT for RPS:

  - The main advantage of preoperative RT is that the (GTV) can be precisely defined for radiation treatment planning, accurate targeting of radiation volume around the tumor.

  - The tumor itself can displace small bowel from the high-dose radiation treatment volume, resulting in safer and less toxic treatment.

  - Higher RT doses can be delivered to the actual tumor field since bowel adhesions to the tumor are less likely compared with the postoperative setting.
- The risk of intraperitoneal tumor dissemination at the time of the operation may be reduced by preop RT.

- Radiation is considered to be biologically more effective in the preoperative setting.

- It is possible that an initially unresectable tumor may be converted to one that is potentially resectable for cure.
• These advantages may result in an improvement in the therapeutic ratio when RT is administered preoperatively. Preoperative RT has been found to be very well tolerated.
• Intensity-modulated radiation therapy (IMRT) has the potential to further improve the therapeutic index by permitting dose escalation to the area of the tumor while minimizing the dose to normal tissues at risk for radiation toxicity (TI).
• IMRT was used to deliver RT (50 Gy in 25 daily 2 Gy fractions) to a preoperative clinical target volume (CTV).

• Or 45 Gy in 25 fractions (1.8 Gy per fraction) to the entire tumor and 57.5 Gy in 25 fractions (2.3 Gy per fraction) to the boosted retroperitoneal margin.
• Role of intraoperative radiation therapy:
  - If the surgeon anticipates a grossly incomplete resection, IORT for an additional dose of 10 to 15 Gy to areas of residual microscopic or gross disease is reasonable.
Concurrent chemoradiotherapy:

-A role for concurrent administration of preop RT and CHT(chemoradiotherapy) RPS is not established. There has been interest in this approach for RPS. However, given the lack of data from prospective trials that preop chemo/RT is more effective than preop. RT and the potential for toxicity, this approach should only be used for RPS in the context of a clinical trial.
• Pre OP CHT is safe and occasionally induces a radiographic response, which may impact surgical therapy in a few patients.
• (an anthracycline plus ifosfamide) .
-Microscopically positive margins increase the risk for local recurrence.
Following R1 resection, re-resection of tumor bed is typically not feasible without excessive morbidity. For these patients and for those who refuse further surgery, PORT can improve local control and long-term RFS. However, movement of viscera into the tumor bed after resection increases risk of radiation-associated morbidity, and these patients are frequently just observed, reserving RT for use (generally in conjunction with salvage surgery (+/-IORT) if develops local recurrence.
• Following complete surgical resection ( [R0] or [R1]), the NCCN guidelines suggest that PORT should not be administered routinely, with the exception of highly selected patients & unless a local recurrence would cause undue morbidity.

• For grossly incomplete (R2) resection margins (gross residual disease), re-resection is recommended if technically feasible.
• Given that late recurrences are common with RPS, long-term follow-up to at least 10 years is mandatory:
• For R0/R1 resections physical examination with abdominal/pelvic imaging every three to six months for two to three years, then every six months for the next two years, and then annually.

• A specific recommendation is not made by the NCCN for periodic chest imaging. However, higher rate of lung met. with RP and visceral leiomyosarcomas and pleomorphic undiff. sarcomas (as compared with other histologies), imaging of chest, on a regular schedule in these cases are done. Some clinicians routinely perform surveillance chest imaging for all patients with large, high-grade tumors, regardless of histology.
WORKUP

- Prior to the initiation of therapy, all patients should be evaluated and managed by a multidisciplinary team with expertise and experience in sarcoma.
- H&P
- Imaging
  - Image-guided core needle biopsy should be performed if preoperative therapy is being given or for suspicion of malignancy other than sarcoma.
  - Preresection biopsy is not necessarily required for well-differentiated liposarcoma.
- For patients with neurofibromatosis, see NCCN Guidelines for Central Nervous System Cancers (PSCT.3)
- For Li-Fraumeni syndrome, see NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic.
- For HNPCC or Lynch syndrome, see NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic.
- For patients with personal/family history suggestive of other cancer predisposition syndromes, consider further genetics assessment.

Diagram:
- Resectable → See Primary Treatment (RET SARC-2)
- Unresectable or Stage IV disease → See Primary Treatment (RET SARC-4)

Footnotes:
- These guidelines are intended to treat the adult population. For adolescent and young adult patients, refer to the See NCCN Guidelines for Adolescent and Young Adult (AYA) Oncology.
- See Principles of Imaging (SARC-A).
- Biopsy for retroperitoneal/intra-abdominal sarcomas should try to avoid the free intra-abdominal space. See Principles of Surgery (SARC-D).
PRIMARY TREATMENT

See NCCN Guidelines for Gastrointestinal Stromal Tumors (GISTs)

Resectable disease → Biopsy\textsuperscript{e,f,g} → GISTs

- Desmoid tumors (Aggressive fibromatosis) → See (DESM-1)
- Sarcoma\textsuperscript{h}

Surgery\textsuperscript{i,j} to obtain oncologically appropriate margins

or

Preoperative therapy
- RT\textsuperscript{k,l}
- Systemic therapy\textsuperscript{m}

\textsuperscript{e}See Principles of Pathologic Assessment of Sarcoma Specimens (SARC-B).
\textsuperscript{f}If considering preoperative therapy, biopsy required, including endoscopic ultrasound-guided biopsy for suspected GIST lesions.
\textsuperscript{g}Biopsy may not be required if diagnostic imaging is consistent with well-differentiated liposarcoma (WD-LPS).
\textsuperscript{h}For other soft tissue sarcomas such as Ewing sarcoma, see NCCN Guidelines for Bone Cancer; for RMS, see RMS-1.
\textsuperscript{i}See Principles of Surgery (SARC-D).

\textsuperscript{j}Consider postoperative systemic therapy for histologies with high risk for metastatic disease and/or high risk for local recurrence. Systemic therapy is not recommended for low-grade tumors.

\textsuperscript{k}If preoperative RT is anticipated, IMRT would be preferred to optimize sparing of nearby critical structures.

\textsuperscript{l}See Principles of Radiation Therapy (SARC-E).

\textsuperscript{m}See Systemic Therapy Agents and Regimens with Activity in Soft Tissue Sarcoma Subtypes (SARC-E).

See Postoperative Treatment (RETSARC-3)
## NCCN Guidelines Version 2.2021
### Retroperitoneal/Intra-Abdominal

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<th>SURGICAL OUTCOMES/CLINICAL PATHOLOGIC FINDINGS</th>
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<tr>
<td>R0</td>
<td>Post-op RT should not be administered routinely with the exception of highly selected patients and unless local recurrence would cause undue morbidity.</td>
<td>Consider postoperative systemic therapy for histologies with high risk for metastatic disease.</td>
<td>Physical exam with imaging every 3–6 mo for 2–3 y, then every 6 mo for next 2 y, then annually.</td>
</tr>
<tr>
<td>R1/R2</td>
<td>Post-op RT should not be administered routinely with the exception of highly selected patients and unless local recurrence would cause undue morbidity. In highly selected cases, consider boost (10–16 Gy) if preoperative RT was given. Consider re-resection if the biology of the cancer (grade, invasiveness), the technical aspects of the operation (R0 resection anticipated as a reasonable possibility), and the comorbidities of the patient allow for a safe intervention at the judgment of the operating surgeon.</td>
<td>Consider postoperative systemic therapy for histologies with high risk for metastatic disease.</td>
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*See Principles of Imaging (SARC-A).*  
*See Principles of Surgery (SARC-D).*  
*See Principles of Radiation Therapy (SARC-E).*  
*See Systemic Therapy Agents and Regimens with Activity in Soft Tissue Sarcomas (SARC-F).*

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For example, critical anatomic surface where recurrence would cause morbidity.*  
Systemic therapy not recommended for low-grade tumors.*  
If not previously administered, consider preoperative RT and/or systemic therapy.*
INITIAL THERAPY

Unresectable or Stage IV disease → Biopsy → Observation, if asymptomatic
• Systemic therapy\(^b,q\) and/or RT\(^l\)
• Surgery for symptom control → Imaging to assess treatment response\(^b\)

Resectable → See Treatment as per RETSARC-2

Unresectable or Progressive disease → Palliative or best supportive care (See NCCN Guidelines for Palliative Care)

\(^b\)See Principles of Imaging (SARC-A).
\(^q\)See Principles of Pathologic Assessment of Sarcoma Specimens (SARC-B).
\(^l\)See Principles of Radiation Therapy (SARC-E).
\(^b\)See Systemic Therapy Agents and Regimens with Activity in Soft Tissue Sarcoma Subtypes (SARC-F).
با تشکر از توجه شما