Retroperitoneal Sarcoma (RPS); what preoperative RT might add

Rick Haas

Department of Radiotherapy; NKI – AVL Amsterdam
Retroperitoneal Sarcoma (RPS);
what preoperative RT might add

Nothing to disclose
Outline

Clinical aspects of RPS

Predictive factors for local relapse

Why do RPS patients die?

RT issues and trials

EORTC 62092-22092 “STRASS”
The problem...

The opportunity to obtain negative margins in a tumor of this size is small
Table 1 - Summary of the 4 largest retrospective studies

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>cases</td>
<td>278</td>
<td>136</td>
<td>152</td>
<td>382</td>
</tr>
<tr>
<td>Median age (y.o.)</td>
<td>58 (16-88)</td>
<td>56 (46-65)</td>
<td>55 (47-67)</td>
<td>57 (14-87)</td>
</tr>
<tr>
<td>Median size (cm)</td>
<td>-</td>
<td>15 (10-28)</td>
<td>18 (10-26)</td>
<td>18 (3-60)</td>
</tr>
<tr>
<td>Grade</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>64%</td>
<td>33%</td>
<td>27%</td>
<td>32%</td>
</tr>
<tr>
<td>Intermediate</td>
<td>-</td>
<td>29%</td>
<td>39%</td>
<td>34%</td>
</tr>
<tr>
<td>Low</td>
<td>36%</td>
<td>38%</td>
<td>34%</td>
<td>29%</td>
</tr>
<tr>
<td>Not done</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>5%</td>
</tr>
<tr>
<td>Histology</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liposarcoma</td>
<td>41%</td>
<td>56%</td>
<td>59%</td>
<td>44%</td>
</tr>
<tr>
<td>Leiomyosarcoma</td>
<td>27%</td>
<td>15%</td>
<td>13%</td>
<td>18%</td>
</tr>
<tr>
<td>Others</td>
<td>32%</td>
<td>29%</td>
<td>28%</td>
<td>38%</td>
</tr>
<tr>
<td>5-y OS</td>
<td>? %</td>
<td>51%</td>
<td>60%</td>
<td>57%</td>
</tr>
<tr>
<td>5-y local recurrence free survival</td>
<td>59%</td>
<td>Not done</td>
<td>Not done</td>
<td>Not done</td>
</tr>
<tr>
<td>5-y probability of local recurrence</td>
<td>Not done</td>
<td>48%</td>
<td>29%</td>
<td>Not done</td>
</tr>
<tr>
<td>5-y abdominal recurrence free survival (*)</td>
<td>Not done</td>
<td>Not done</td>
<td>Not done</td>
<td>51%</td>
</tr>
</tbody>
</table>

(*) including peritoneal sarcomatosis and local relapse
RPS: clinical aspects

15% of all soft tissue sarcomas

generally asymptomatic

the average size at presentation: 15 to 18 cm

60% high grade

pathology: 70% = liposarcoma or leiomyosarcoma
RPS

Resection: R0 very difficult

Local failure 52-60% at 5 years

Continuous risk of local recurrences after five years especially those with low-grade sarcomas.
RPS

Resection:  R0    very difficult

Local failure 52-60% at 5 years

Table 2- Potential predictive factors for local recurrence indentified by multivariate analysis

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</tr>
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<td>165</td>
<td>177</td>
<td>97</td>
<td>382</td>
<td>500</td>
</tr>
<tr>
<td>Histology</td>
<td>No</td>
<td>-</td>
<td>No</td>
<td>No</td>
<td>Yes (Lipo)</td>
</tr>
<tr>
<td>Grade</td>
<td>Yes</td>
<td>No</td>
<td>-</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Margins</td>
<td>-</td>
<td>-</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
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<tr>
<td>Reference center</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Yes</td>
<td>-</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>Yes</td>
<td>-</td>
<td>-</td>
<td>Yes</td>
<td>-</td>
</tr>
</tbody>
</table>
RPS

most important for long-term tumor control:

✓ complete resection with gross negative margins

✓ aggressive en bloc resection of primary disease
  => management in a reference center

✓ possibly radiotherapy (retrospective series!)
  => need for a prospective randomized phase III trial
RPS

most important for long-term tumor control:

✓ complete resection with gross negative margins

✓ aggressive en bloc resection

=> management in a reference center

✓ possibly radiotherapy (retrospective series!)

=> need for a prospective randomized phase III trial
RPS

factors associated with tumor-related mortality after R0:

*Local relapse*

~75% die in the absence of metastatic disease.

Unlike extremity sarcomas; patients die of metastatic disease
Summary up to now:

Increased risk of local recurrence

If a local relapse occurs it is likely to become the cause of death
RPS: RT issues
RPS: RT issues

Can we extrapolate from extremity STS ?

Timing: 60-66 Gy postoperative feasible ?
  1 kidney
  intestinal adhesions
  => spacers

  50 Gy preoperative ?
  sarcoma is it’s own spacer

Brachytherapy ?
RPS: RT trials

RTOG 0124

ACOSOG

ISG chemoradiation trial
RPS: RT trials

RTOG 0124

Staging evaluation

Dox 75 mg/m² + Ifos 10 g/m² (up to 4 cycles)

Localized, potentially resectable T2, G2/3 retroperitoneal/pelvic STS

Surgical resection + radiation boost:
1. IO EB-IORT
2. IO HD BRT
3. PO HD BRT
4. PO LD BRT
5. PO EBRT

EBRT 45-50.4 Gy
RPS: RT trials
RTOG 0124

RTOG 0124 Protocol Information
A Phase II Study of Multimodality Therapy for Primary and Recurrent Retroperitoneal Sarcomas

Protocol Documents

Principal Investigator: Peter W. T. Pisters, M.D.

Primary Objective: To assess overall survival of retroperitoneal sarcomas after integrated chemotherapy, radiation, and surgery.

Patient Population: Histologically confirmed, non-metastatic, soft tissue sarcoma of the retroperitoneum and/or pelvis with measurable disease which has not been debulked High-grade disease (grade 3/3, 3/4, 4/4 primary or recurrent) > 5 cm or recurrent, moderate grade (grade 2).

Target Accrual: 48
Current Accrual: 5
Status: Terminated

Participating Sites:
RPS: RT trials

RTOG 0124

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**Current Accrual:** 5

**Date:**
RPS: RT trials

ACOSOG (ACOSOG-Z9031, ECOG-Z9031, NCT00091351)

Phase III Randomized Study of Surgery With or Without Preoperative Radiotherapy in Patients With Primary Soft Tissue Sarcoma of the Retroperitoneum or Pelvis.
RPS: RT trials

A C O S O G

American College of Surgeons Oncology Group

STUDY CHAIR  Peter W.T. Pisters, MD

TITLE  A Phase III Randomized Study of Preoperative Radiation Plus Surgery Versus Surgery Alone for Patients with Retroperitoneal Sarcomas (RPS).

SCHEMA

OBJECTIVES

Primary Objective:
To evaluate whether preoperative radiotherapy of 45.0-50.4 Gy plus surgery improves the PFS compared to surgery alone in patients with primary RPS.

Secondary Objectives:
1. To assess the toxicity and complications associated with preoperative radiotherapy and surgery.
2. To assess whether preoperative radiation increases the rates of microscopically complete surgical resection (R0).
3. To assess whether preoperative radiation increases the overall survival rate of patients with RPS.

*Including HIPAA authorization
RPS: RT trials

ISG

PREOPERATIVE CHEMO-RADIATION THERAPY FOR LOCALIZED RETROPERITONEAL SOFT TISSUE SARCOMA (STS): A PHASE II STUDY FROM THE ITALIAN SARCOMA GROUP

2011 Combined Meeting of the
Connective Tissue Oncology Society
and the Musculoskeletal Tumor Society

Thursday, October 27, 2011 4:15 PM

PAPER #16
PREOPERATIVE CHEMO-RADIATION THERAPY FOR LOCALIZED RETROPERITONEAL SOFT TISSUE SARCOMA (STS): A PHASE II STUDY FROM THE ITALIAN SARCOMA GROUP
Alessandro Gronchi, MD
RPS: RT trials

ISG

N = 86 RPS

Continuous Ifosfamide 14gr/m2, in 2 weeks

RT 28 x 1.8 Gy

4-6 weeks rest

Surgery

Completed total n = 61
CT n = 65, RT n = 74, surgery n = 80
RPS: RT trials

ISG

N = 86 RPS; median FU of 2 years

20 local recurrence
15 distant recurrence
17 patients died of disease.

3-yr LRFS 68%
DRFS 79%
OS 80%
RPS: RT trials

ISG
Int J Radiat Oncol Biol Phys. 2007

Intensity modulated radiation-therapy for preoperative posterior abdominal wall irradiation of retroperitoneal liposarcomas.

Bossi A, De Wever I, Van Limbergen E, Vanstraelen B.
RPS: study

Classical preoperative RT
RPS: study

Classical recurrence site
RPS: study

“Biological” preoperative RT
EORTC Soft Tissue and Bone Sarcoma Group

EORTC Radiation Oncology Group

A phase III randomized study of preoperative radiotherapy plus surgery versus surgery alone for patients with Retroperitoneal sarcoma (RPS)

EORTC protocol 62092-22092

STRASS

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Fax: +33 145115256
E-mail: bonvalot@igr.fr

Study Co-Coordinator: Rick Haas
Phone: +31 20 5122124
Fax: +31 20 6691101
E-mail: r.haas@nki.nl
RPS: trials

EORTC 62092-22092:

Primary endpoint: abdominal recurrence free survival

Statistics:
A 90% power to show an increase of 20% in the 5-year abdominal recurrence free survival rate from 50% to 70% (hazard ratio of 0.52) at the 2-sided 5% significance level:

256 patients will be randomized over 3-4 years.
Thanks for your attention

Orcas

Antarctica 2010