RARE CANCERS TREATMENT:
THE CHALLENGES
The surgeon’s perspective

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no potential or actual conflicts of interest to declare
RARE CANCERS CHALLENGES

- EARLY AND CORRECT DIAGNOSIS
- CLINICAL EXPERTISE
- RESEARCH
- ACCESS TO NEW THERAPIES
- INEQUALITIES

European Society of Surgical Oncology
surgery → the mainstay of treatment of solid rare tumors

(11 out of 12 families)

- 2 patients out of 3 can be treated by surgery alone
- 30% more can receive a combined treatment of radio/chemotherapy and surgery
Rare cancers are not so rare: The rare cancer burden in Europe

Gemma Gatta a,*, Jan Maarten van der Zwan b, Paolo G. Casali c, Sabine Siesling b, Angelo Paolo Dei Tos d, Ian Kunkler e, Renée Otter b, Lisa Licitra f, Sandra Mallone g, Andrea Tavilla g, Annalisa Trama a, Riccardo Capocaccia g, The RARECARE working group

Fig. 4 – RARECARE estimates of relative survival for rare and common cancers in EU27 by age group.
The Burden of Rare Cancers in the United States

Carol E. DeSantis, MPH \(^1\)\(^*\); Joan L. Kramer, MD\(^2\); Ahmedin Jemal, DVM, PhD\(^3\)
The Burden of Rare Cancers in the United States

Carol E. DeSantis, MPH ° 1; Jean L. Kramer, MD; Ahmedin Jemal, DVM, PhD

![Bar chart showing the percentage of rare, common, and other cancers by system.]

Digestive System: 36% rare, 56% common, 8% other
Respiratory System: 12% rare, 68% common, 20% other
Breast: 5% rare, 85% common, 10% other
Female Genital System: 31% rare, 60% common, 9% other
Male Genital System: 5% rare, 92% common, 3% other
Urinary System: 6% rare, 89% common, 5% other
Endocrine System: 6% rare, 93% common, 11% other
Hematopoietic System: 38% rare, 51% common, 11% other
Improved survival using specialized multidisciplinary board in sarcoma patients


Presentation to a MDTB before treatment was associated with a better compliance to clinical practice guidelines, for example, biopsy before surgery, imaging, quality of initial surgery, and less reoperations (all P < 0.001). Local relapse-free survival and relapse-free survival were significantly better in patients presented to a MDTB before initiation of treatment, both in univariate and multivariate analysis.
## Improved survival using specialized multidisciplinary board in sarcoma patients

### Table 2. Patients' characteristics, procedures, and NETSARC MDTB

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>NETSARC MDTB before treatment</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes ($N = 5281$)</td>
<td>No ($N = 7247$)</td>
</tr>
<tr>
<td>Quality of first surgery$^b$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R0</td>
<td>1436 (52.6%)</td>
<td>1968 (32.2%)</td>
</tr>
<tr>
<td>R1</td>
<td>845 (30.9%)</td>
<td>1965 (32.1%)</td>
</tr>
<tr>
<td>R2</td>
<td>204 (7.1%)</td>
<td>1148 (18.8%)</td>
</tr>
<tr>
<td>NE</td>
<td>246 (9.1%)</td>
<td>1032 (16.9%)</td>
</tr>
<tr>
<td>Reexcision after first surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>165 (6.0%)</td>
<td>1065 (17.4%)</td>
</tr>
<tr>
<td>No</td>
<td>2320 (85.0%)</td>
<td>4916 (65.7%)</td>
</tr>
<tr>
<td>NE</td>
<td>246 (9.1%)</td>
<td>1032 (16.9%)</td>
</tr>
<tr>
<td>Quality of final surgery$^b$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R0</td>
<td>1571 (57.5%)</td>
<td>2845 (46.5%)</td>
</tr>
<tr>
<td>R1</td>
<td>773 (28.3%)</td>
<td>1529 (25.0%)</td>
</tr>
<tr>
<td>R2</td>
<td>141 (5.1%)</td>
<td>707 (11.5%)</td>
</tr>
<tr>
<td>NE</td>
<td>246 (9.1%)</td>
<td>1032 (16.9%)</td>
</tr>
</tbody>
</table>
A Local relapse free survival

- MDT before surgery
- MDT after surgery

B Relapse free survival

- MDT before surgery
- MDT after surgery

LRFS

RFS

P<0.0001
Retroperitoneal sarcomas: patterns of care at diagnosis, prognostic factors and focus on main histological subtypes: a multicenter analysis of the French Sarcoma Group

Adherence to Guidelines for Adult (Non-GIST) Soft Tissue Sarcoma in the Netherlands: A Plea for Dedicated Sarcoma Centers

Harald J. Hoekstra, MD, PhD¹, Rick L. M. Haas, MD, PhD², Cornelis Verhoef, MD, PhD³, Albert J. H. Suurmeijer, MD, PhD⁴, Carla S. P. van Rijswijk, MD, PhD⁵, Ben G. H. Bongers, MD¹, Winette T. van der Graaf, MD, PhD⁶, and Vincent K. Y. Ho, MSc, PhD⁷
there can be profound implications for a patient not diagnosed at a sarcoma centre, such as missing the chance of a timely diagnosis of a potentially curable disease, and being spared more extensive surgery.

The experience of the surgeon is a prognostic factor of overall survival in STS
The experienced sarcoma surgeon

- Must perform almost 50 sarcoma surgeries/year
- Must act within a multidisciplinary environment
- Must be able to coordinate collaborations when necessary (with a multidisciplinary surgical team) with the potential for local control weighted against the potential for long-term dysfunction
Overall survival after resection of retroperitoneal sarcoma at academic cancer centers versus community cancer centers: An analysis of the National Cancer Data Base

Nicholas G. Berger, MD, Jack P. Silva, BS, Harveshp Mogul, MD, Callisn N. Clarke, MD, Manpreet Bedi, MD, John Charlson, MD, Kathleen K. Christians, MD, Susan Tsai, MD, MHS, and T. Clark Gamblin, MD, MS, MBA, Milwaukee, WI

2762 patients: greater propensity for neoadjuvant treatments at ACCs compared with CCCs
Predictors of surgical quality for retroperitoneal sarcoma: Volume matters

Matthew J. Maurice MD\textsuperscript{1} | Jessica M. Yih MD\textsuperscript{2} | John B. Ammori MD\textsuperscript{3} | Robert Abouassaly MD, MS\textsuperscript{2,4}

Patients treated at high-volume centers has
1.9-fold higher odds of undergoing surgical management (P < 0.001),
2.5-fold higher odds of receiving a R0/R1 resection (P = 0.026),
1.8-fold higher odds of an R0 resection (P < 0.001).
A) surgical treatment (red) versus non-surgical treatment (blue)

B) R0/R1 resection (red) versus R2 resection (blue)
Impact of hospital case volume on testicular cancer outcomes and practice patterns

Solomon L. Woldu, M.D.\textsuperscript{a}, Justin T. Matulay, M.D.\textsuperscript{b}, Timothy N. Clinton, M.D.\textsuperscript{a}, Nirmish Singla, M.D.\textsuperscript{a}, Laura-Maria Krabbe, M.D.\textsuperscript{a}, Ryan C. Hutchinson, M.D.\textsuperscript{a}, Arthur Sagalowsky, M.D.\textsuperscript{a}, Yair Lotan, M.D.\textsuperscript{a}, Vitaly Margulis, M.D.\textsuperscript{a}, Aditya Bagrodia, M.D.\textsuperscript{a,*}

Results: A total of 33,417 patients with TGCT diagnosed from 1,239 institutions met inclusion criteria.

Conclusions: Our analysis of a nationwide cancer registry demonstrated that increased hospital TGCT case volume was associated with significant differences in management strategies and improved survival outcomes, in particular for more advanced disease. © 2017
POPULATION SURVIVING IN SEMINOMA

NON SEMINOMA GERM CELL TUMOR

LOW VOLUME

HIGH VOLUME
Aggressive Surgical Approach to the Management of Neuroendocrine Tumors: A Report of 1,000 Surgical Cytoreductions by a Single Institution

Eugene A Woltering, MD, FACS, Brianne A Voros, MS, David T Beyer, BSBE, Yi-Zarn Wang, DDS, MD, Ramcharan Thiagarajan, MD, FACS, Pamela Ryan, RN, BSN, Anne Wright, RN, BSN, Robert A Ramirez, DO, M Jennifer Ricks, J Philip Boudreaux, MD, FACS

Table 6. Summary of the 5-Year, 10-Year, 20-Year, and Median Overall Survival and 30-Day Postoperative Mortality Rates by Site-Specific Classifications

<table>
<thead>
<tr>
<th>Primary site</th>
<th>n</th>
<th>No. of procedures</th>
<th>30-d postoperative mortality*</th>
<th>Overall survival rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>All</td>
<td>800</td>
<td>1,001</td>
<td>24</td>
<td>2</td>
</tr>
<tr>
<td>Lung</td>
<td>11</td>
<td>15</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Stomach</td>
<td>31</td>
<td>36</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Duodenum</td>
<td>55</td>
<td>57</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Pancreas</td>
<td>89</td>
<td>108</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Small bowel</td>
<td>516</td>
<td>658</td>
<td>15</td>
<td>3</td>
</tr>
<tr>
<td>Appendix</td>
<td>19</td>
<td>19</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Colon</td>
<td>23</td>
<td>29</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Rectum</td>
<td>34</td>
<td>52</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Other</td>
<td>8</td>
<td>12</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Unknown</td>
<td>14</td>
<td>15</td>
<td>2</td>
<td>13</td>
</tr>
</tbody>
</table>

*For 30-d postoperative mortality, n is equal to the total number of deaths within 30 days of surgery. Percentages were calculated as the number of deaths (n) for each primary site divided by the total number of procedures performed for each primary site. NA, not applicable; NR, not reached.
In surgical area, it will be important the definition of the minimum number of surgical operations for HNC to be considered “credentialed” for this disease.

if performance is about practice, competence is a broader field, encompassing technical expertise, medical knowledge, and ability to judge and to make decisions.

So, the process of credentialing should encounter also these aspects in a more complex and articulate judgment
Table 1. Clinical studies investigating the relationship between surgery (hospital and/or surgeon-related) case volume and outcome in head and neck cancer patients

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study country</th>
<th>Analysis period</th>
<th>Disease subsite</th>
<th>Study population (N)</th>
<th>Object of analysis</th>
<th>Cut-off of “high” surgery case volume (hospital and/or Surgeon)</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>[7•]</td>
<td>USA</td>
<td>1998 to 2002</td>
<td>Oral cavity Parotid/other salivary glands Pharynx Larynx Hypopharynx</td>
<td>11,160</td>
<td>HCV</td>
<td>59.7 cases/year</td>
<td>Improved short-term (30-day after surgery) and long-term (5 and 10-year) survival&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>[8]</td>
<td>USA</td>
<td>2003 to 2007</td>
<td>Oral cavity Oropharynx Larynx</td>
<td>1195</td>
<td>HCV</td>
<td>≥ 15 cases/year</td>
<td>Improved survival&lt;sup&gt;b&lt;/sup&gt; (n.s.s.)</td>
</tr>
<tr>
<td>[9]</td>
<td>Taiwan</td>
<td>2005 to 2007</td>
<td>Oral cavity</td>
<td>1256</td>
<td>SCV</td>
<td>22–117 cases/year</td>
<td>Improved survival (3-year)</td>
</tr>
<tr>
<td>[10]</td>
<td>Taiwan</td>
<td>1997 to 1999</td>
<td>Oral cavity</td>
<td>6666</td>
<td>HCV SCV</td>
<td>HCV ≥ 531 cases/3 years SCV ≥ 142 cases/3 years</td>
<td>Not improved survival (5-year) for HCV Improved survival (5-year) for SCV</td>
</tr>
<tr>
<td>[11]</td>
<td>USA</td>
<td>1996 to 1998</td>
<td>Larynx&lt;sup&gt;c&lt;/sup&gt;</td>
<td>11,446</td>
<td>HCV</td>
<td>6 cases/year&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Improved survival (5-year)</td>
</tr>
<tr>
<td>[12]</td>
<td>USA</td>
<td>1996 to 2002</td>
<td>Larynx&lt;sup&gt;e&lt;/sup&gt;</td>
<td>19,326</td>
<td>HCV</td>
<td>≥ 3.6 cases/year (community hospitals) ≥ 8.7 cases/year (community Cancer Centers) ≥ 17.1 cases/year (Teaching/Research Centers)</td>
<td>Improved survival (90-day, 365-day, 4-year) for patients treated at Teaching/Research Centers</td>
</tr>
<tr>
<td>[13••]</td>
<td>Canada</td>
<td>1993 to 2010</td>
<td>Oral cavity Oropharynx Larynx Hypopharynx</td>
<td>5720</td>
<td>HCV SCV</td>
<td>HCV ≥ 138 cases/year SCV ≥ 30 cases/year</td>
<td>Improve survival (5 and 10-year) for HCV</td>
</tr>
</tbody>
</table>

HCV hospital-related case volume, n.s.s. not statistically significant, SCV surgeon-related case volume

<sup>a</sup>Patients with large (> 30 mm), high-grade, parotid, pharynx and larynx had better advantage to be addressed at high-volume centers

<sup>b</sup>Patients treated at high-volume hospitals were not more likely to receive multimodality therapy and cisplatin-based chemoradiotherapy

<sup>c</sup>Only early-stage (T1-T2 N0 M0) laryngeal cancers were included

<sup>d</sup>Mean value/year

<sup>e</sup>Only advanced-stage (III–IV stage) laryngeal cancers were included
high volume surgeons ↔ multidisciplinary team
In which way the expertise of a centre can be recognized?
Improving the quality of rare/complex cancer care requires to concentrate expertise and sophisticated infrastructure in reference centres.

The fundamental step is the translation of the recommendations into policy decisions: the best interest of the patient should prevail.
A MULTI-STAKEHOLDER PARTNERSHIP INITIATIVE

Joining forces for action
CENTRALIZATION IMPROVES OUTCOMES?
Potential criticism to a “referral centers” policy

delay induced by centralization and time to refer the patients

low quality of decision-making in multidisciplinary meetings due to the vastly increased numbers of cases needing review
networking between centers of advanced treatment and surroundings hospitals is a key element to ensure that expertise travels, rather than patients.
COLLABORATIVE RARE CANCER NETWORKS

Sub-networks

ERN

European Society of Surgical Oncology
crucial instruments to improve quality of surgical care for patients with rare cancers: research

- accrual in **multicentric** clinical trials, assuring data quality control

  *the low number of patients in rare cancers makes it difficult to build a comprehensive evidence-base for practice*
Rare Cancers Europe (RCE) methodological recommendations for clinical studies in rare cancers: a European consensus position paper

P. G. Casali¹*, P. Bruzzi², J. Bogaerts³ & J.-Y. Blay⁴ on behalf of the Rare Cancers Europe (RCE) Consensus Panel

¹Adult Mesenchymal Tumour Medical Oncology Unit, Fondazione Istituto Nazionale Tumori, Milan; ²Clinical Epidemiology Unit, National Institute for Cancer Research, Genova, Italy; ³European Organization for Research and Treatment of Cancer (EORTC), Brussels, Belgium; ⁴Department of Medical Oncology, Centre Léon Bérard, Centre de Recherche en Cancérologie, Université de Lyon, Lyon, France

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Clinical trial design for rare cancers - why a less conventional route may be required

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Memorial Sloan Kettering Cancer Center, Department of Epidemiology and Biostatistics, New York, NY 10017

EDITORIAL

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Should clinical trials be approached differently for rare cancers?

"...the methodologies to help compensate for the small patient numbers associated with rare cancers should be utilized to help provide evidence to optimize treatments."

Ian Oliver*  
First draft submitted: 19 January 2016; Accepted for publication: 28 January 2016; Published online: 4 March 2016
Original Article

Post-relapse Outcomes After Primary Extended Resection of Retroperitoneal Sarcoma: A Report From the Trans-Atlantic RPS Working Group

Andrea J. MacNeill, MD†; Rosalba Miceli, PhD‡; Dirk C. Strauss, MD, PhD; Sylvie Bonvalot, MD, PhD; Peter Hohenberger, MD; Peter Van Coeverden, MD; Jordi Bartolome, MD; John Hayes, MD, PhD; Charles Honore, MD; Mark Fairweather, MD; Amanda Cannell, BSc; Jens Jakobs, MD; Rick L. Haas, MD; Milena Szacht, MD; Marco Fiore, MD; Paolo G. Casali, MD; Raphael E. Pollock, MD, PhD; Chandrajit P. Raut, MD, MSc; and Carol J. Swallow, MD, PhD

original article - bone and soft tissue sarcomas

Management of Primary Retroperitoneal Sarcoma (RPS) in the Adult: A Consensus Approach From the Trans-Atlantic RPS Working Group

DOI 10.1245/s10434-016-5336-7

Annals of Surgical Oncology

original article - bone and soft tissue sarcomas

Management of Recurrent Retroperitoneal Sarcoma (RPS) in the Adult: A Consensus Approach from the Trans-Atlantic RPS Working Group

DOI 10.1245/s10434-016-5336-7

Annals of Surgical Oncology

clinical practice guidelines

Soft tissue and visceral sarcomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up

The ESMO/European Sarcoma Network Working Group
Papers from TARPSWG
15 August 2017 — 0 Comments

NEWS
South Korea is now part of TARPSWG!

Activation Track - RESAR Study
*Take home message*
Defining high quality centers and a network of care by a process of accreditation

a collaborative effort among disease thought-leaders, politicians, advocates and scientific societies.
In addition to regional expert centers, smaller local centers must be identified to deliver less complex care.

Sub-networking or integrated networks
integrated networks increase accessibility and minimize the burden of traveling long distances

low access to proper treatments is likely higher in underserved areas
Struggle to inequalities: well-structured training programs by high quality centers

creation of expert centers in underserved geographic areas

RARE CANCERS TREATMENT: THE CHALLENGES FROM THE SURGEON’S PERSPECTIVE
Actively involve **patient advocacies**

- *To improve patients’ knowledge and ability to take decisions*

- *To secure access to innovative or complex treatments*

- *To support research, such as by being involved in the design of clinical trials*

- *To advocate at national health policy level.*
That’s all...

THANK YOU.

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