Surgery for Small Cell Lung Cancer?

Basic Principles of Small Cell Lung Cancer (SCLC)

- SCLC accounts for ~13% of lung cancer in US
  - Declining over time
- Staging breakdown – 1/3 limited, 2/3 extensive
  - perhaps 5% “very limited” – stage I/II (no mediastinal nodes)
  - many suspected as node negative are upstaged at surgery
- Strong tendency to spread early
  - sensitive to chemo and radiation
  - chemo/radiation is standard for limited stage SCLC
  - surgery considered a reasonable option for very limited
Retrospective Reviews of Surgery in Patients with SCLC

- Multiple retrospective, single institution studies have shown that patients who undergo surgery for early stage SCLC have generally done well.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Inst.</th>
<th>N (St I)</th>
<th>Accrual Yrs</th>
<th>Surv (St I), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lim, JTCVS 2005</td>
<td>Royal Brompton</td>
<td>51 (18)</td>
<td>1980 – 2003</td>
<td>NR#</td>
</tr>
<tr>
<td>Brock, JTCVS 2005</td>
<td>Hopkins</td>
<td>82 (48)</td>
<td>1972 – 2002</td>
<td>42 (58)</td>
</tr>
</tbody>
</table>

*T1N0M0 only

- Far worse for SCLC vs other NE tumors

- But is it the treatment or the patients/cancers??

Is it the Treatment, or is it Patient Selection??

- Indolent bronchioloalveolar carcinoma

- Limited mesothelioma very responsive to pre-operative chemotherapy

- Locally advanced NSCLC that responds very well

- “Precocious metastases”/single focus
SEER Database Analysis of Surgery for SCLC

- 1560 patients with stage I SCLC, 1988-2004
- 205 underwent lobectomy without post-op RT
  - 5 year survival 50.3% after surgery
  - 5-year survival 21.3% for non-surgical patients
- However, non-surgical group probably includes many non-stage I patients (clinical vs. path staging)
- Surgery patients may very well have been younger, more fit, and had smaller cancers (unknown)

Yu, J Thor Oncol 2010

Concerns about Surgery for (Very)Limited Small Cell Lung Cancer

- Patients potentially well suited to surgery (node negative/stage I) are rare and hard to identify
- Many patients are upstaged at surgery
- Many surgeons are not that rigorous in staging
  - >11,000 surgical pts w/NSCLC in US (Little, ATS 2005)
    - 27.1% of patients had pre-operative mediastinoscopy
    - Of these, only 46.6% had any lymph nodes removed
    - Only 42.2% had any mediastinal nodes sampled during surgery
  - Good practice requires rigorous selection predicated on staging that too few surgeons are doing
Retrospective Reviews of Surgery in Patients with SCLC

- Surgery may compromise ability to administer chemo, which is extremely important in SCLC

<table>
<thead>
<tr>
<th>Trial</th>
<th>Cycle #</th>
<th>Completed Rx</th>
<th>Modified</th>
<th>Never Started</th>
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</thead>
<tbody>
<tr>
<td>ALPI</td>
<td>3 cycles</td>
<td>69%</td>
<td>51%</td>
<td>9%</td>
</tr>
<tr>
<td>IALT</td>
<td>3-4 cycles</td>
<td>NR*</td>
<td>NR</td>
<td>7.8%</td>
</tr>
<tr>
<td>BR 10</td>
<td>4 cycles</td>
<td>50%</td>
<td>NR</td>
<td>6%</td>
</tr>
<tr>
<td>CALGB</td>
<td>4 cycles</td>
<td>85%</td>
<td>35%</td>
<td>3%</td>
</tr>
<tr>
<td>ANITA</td>
<td>4 cycles</td>
<td>NR**</td>
<td>NR**</td>
<td>9.6%</td>
</tr>
<tr>
<td>JLCRG</td>
<td>2 years</td>
<td>61%</td>
<td>NR</td>
<td>3%</td>
</tr>
</tbody>
</table>

NR-not reported
* 74% of patients received 240mg/m² of cisplatin
** Median relative dose intensity* vinorelbine – 59%, cisplatin – 89%

Where are We Now? Will We Get More Information?

- SCLC numbers are decreasing
- Very limited SCLC accounts for <5%, typically <1 patient per year at most institutions
- Prospective randomized trial is infeasible
  - would require more than worldwide participation for yrs
  - many patients and physicians would resist randomization to surgery or not
- For now, surgery remains an option in rare, well-selected patients; benefit from surgery unclear
If you knew someone had a very early stage small cell lung cancer, would you recommend surgery?

How do you manage patients post-operatively after they have undergone surgery for a very limited small cell lung cancer?
Why is the incidence of small cell lung cancer declining over time?

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