The definition of oligometastatic disease.

Christophe Dooms, MD, PhD.
Respiratory Division
University Hospitals Leuven
Belgium
I have no relevant financial relationships to disclose.
Clinical Practice Guidelines.

Evidence-based clinical practice guidelines 2013:

5.3.4.3.2. In patients with NSCLC and a contralateral lobe tumor nodule(s) (and no mediastinal or distant metastases), resection of each lesion is suggested, provided the patient has adequate pulmonary reserve (Grade 2C).

6.3.2. In patients with no other sites of metastases and a synchronous resectable N0,1 primary NSCLC, resection or radiosurgical ablation of an isolated brain metastasis is recommended (as well as resection of the primary tumor) (Grade 1C).

7.2.2. In patients with a synchronous resectable N0,1 primary NSCLC and an isolated adrenal metastasis with no other sites of metastases, resection of the primary tumor and the adrenal metastasis is recommended (Grade 1C).


No clear recommendations can be made regarding isolated distant metastases other than those involving the brain or adrenal gland.

Five-year survival rates of 10-20% have consistently been reported in patients who have undergone resection of a solitary metastasis (as well as resection of primary tumour).
Terminology.


- Intermediate biologic state of restricted metastatic capacity
- Limited number and organ sites of metastases
- Transitional state to dissemination


→ Spectrum model for oligometastases:
Stage I-III NSCLC: RCT of PET-CT vs CT.

- 11% of stage I-III is stage IV detected by PET-CT, of whom 63% is single organ oligometastatic.


Stage IV NSCLC: databases

- 7% of stage IV = 'solitary site' oligometastases.


- 23% of stage IV = 'single organ' oligometastases.


Incidence.

10-15% of all NSCLC = single organ oligometastatic disease.
<table>
<thead>
<tr>
<th>CT</th>
<th>PET-CT</th>
<th>WB-MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>cM0</td>
<td>cM1b (liver)</td>
<td>cM1b(liver and bone)</td>
</tr>
<tr>
<td>No lesions</td>
<td>2 lesions</td>
<td>≥5 lesions</td>
</tr>
</tbody>
</table>

**Incidence.**
Distinct cohorts.

- ‘oligometastases’ = diagnosed with oligometastatic disease
- ‘oligorecurrence’ = relapsed oligometastatic disease
- ‘oligoprogressive’ = status after cytoreductive therapy

→ These cohorts have probably different prognoses
## Inclusion criteria used in clinical trials.

<table>
<thead>
<tr>
<th>Published</th>
<th>N</th>
<th>RCT</th>
<th>Inclusion : N of metastases</th>
<th>Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salama 2011</td>
<td>62</td>
<td>no</td>
<td>1 in 55% ; 2 in 18% ; ≥3 in 27%</td>
<td>22% PFS at 2 yr</td>
</tr>
<tr>
<td>De Ruysscher 2012</td>
<td>39</td>
<td>no</td>
<td>1 in 87% ; 2 in 10% ; 3 in 3%</td>
<td>14% PFS at 3 yr</td>
</tr>
<tr>
<td>Milano 2012</td>
<td>17</td>
<td>no</td>
<td>1-2 in 89% ; 3-5 in 11%</td>
<td>12% OS at 5 yr</td>
</tr>
<tr>
<td>Griffoen 2013</td>
<td>61</td>
<td>no</td>
<td>1 in 82% ; 2 in 15% ; 3 in 3%</td>
<td>38% OS at 2 yr</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Prospective ongoing</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT00776100</td>
<td>98</td>
<td>yes</td>
<td>≤3 lesions</td>
<td>OS</td>
</tr>
<tr>
<td>NCT01185639</td>
<td>45</td>
<td>yes</td>
<td>≤3 extracranial lesions</td>
<td>PFS</td>
</tr>
<tr>
<td>NCT01345539</td>
<td>44</td>
<td>no</td>
<td>≤5 lesions in ≤3 organs</td>
<td>feasibility</td>
</tr>
<tr>
<td>NCT01446744</td>
<td>99</td>
<td>yes</td>
<td>≤5 lesions</td>
<td>OS</td>
</tr>
<tr>
<td>NCT01725165</td>
<td>94</td>
<td>yes</td>
<td>≤3 lesions (N1-3 counted as 1 lesion)</td>
<td>PFS</td>
</tr>
<tr>
<td>NCT01796288</td>
<td>200</td>
<td>yes</td>
<td>≤5 extracranial lesions</td>
<td>PFS</td>
</tr>
<tr>
<td>NCT02054819</td>
<td>20</td>
<td>no</td>
<td>≤5 lesions</td>
<td>OS</td>
</tr>
<tr>
<td>NCT02076477</td>
<td>420</td>
<td>yes</td>
<td>≤5 lesions</td>
<td>RR</td>
</tr>
</tbody>
</table>
Clinical features:

- Fit patient: PS 0-1
- Limited nodal involvement: N0/1.
- Disease radically treatable by surgery.
- Gross Tumour Volume <125cm³.
- Lung Planned Tumour Volume <639cm³.
- Lack of progression on systemic therapy.
- ≤3 distant metastases.

Lopez Guerra et al. IJROBP 2012;84:61.
Prognostic factors ~ outcome.

- 1 metastatic organ site
- 2 metastatic organs sites
- 3 metastatic organ sites

Oligometastatic disease.

Guidelines: none.
Oligometastatic disease.

Guidelines : none.

Recommendations : none.
Oligometastatic disease.

Guidelines: none.

Recommendations: none.

Multidisciplinary board: yes, but ...
“Multidisciplinary Tumour Board”

Oligometastatic NSCLC: a simulation expert multidisciplinary tumour board.

Christophe Dooms¹, Paul De Leyn¹, Christophe Deroose¹, Dirk De Ruysscher¹, Anne-Marie Dingemans², Joachim Pfannschmidt³, Keith Kerr⁴, Frank Lagerwaard⁵, Jose Luis Lopez-Guerra⁶, Ramon Mami-Porta⁷, Egbert Smit⁵, Johan Vansteenkiste¹.

University Hospitals Leuven Belgium¹, University Medical Center Maastricht Netherlands², Thoraxklinik Heidelberg Germany³, Aberdeen University Medical School Aberdeen United Kingdom⁴, VU Medical Center Amsterdam Netherlands⁵, Virgen del Rocio University Hospital Sevilla Spain⁶, Mutua Terrassa University Hospital Barcelona Spain⁷.

Presented at IASLC 2013: P3.09-004.

7 different centers

Radiation oncologist: 3  Thoracic Surgeon: 3
Pulmonologist: 3  Pathologist: 1
Nuclear medicine physician: 1
<table>
<thead>
<tr>
<th>Case</th>
<th>Oligometastatic Yes (%)</th>
<th>Treatment proposals (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>55</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>36</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>91</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>73</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>55</td>
<td>3</td>
</tr>
<tr>
<td>6</td>
<td>64</td>
<td>4</td>
</tr>
<tr>
<td>7</td>
<td>91</td>
<td>4</td>
</tr>
<tr>
<td>8</td>
<td>91</td>
<td>3</td>
</tr>
<tr>
<td>9</td>
<td>82</td>
<td>6</td>
</tr>
<tr>
<td>10</td>
<td>100</td>
<td>3</td>
</tr>
<tr>
<td><strong>Median</strong></td>
<td><strong>78% (36-100%)</strong></td>
<td><strong>4 (2-6)</strong></td>
</tr>
</tbody>
</table>
Male 54 yrs, PS 0, ex-smoker.

- TBLB + US-guided biopsy adrenal R & ischiorectal node: all proven EGFR-Wt ALK-negative lung adenocarcinoma
- Staging LLL cT2bN1M1b (adrenal R + pelvic node)

Oligometastatic disease? 55% Yes
Male 63 yrs, PS 0, ex-smoker.

- LungadenoCa LUL cT2aN0\textit{(mediastino neg)}M1b(1 RUL; 1 pancreas)

- Oligometastatic disease? 82% Yes
Male 56 yrs, PS 0, smoker.

- TBLB LUL: squamous cell Ca
- Staging LUL cT2aN0M1b(liver: CT one, KST three)

- Oligometastatic disease? 64% Yes

Whole body MRI:
- 3 liver metastases:
  - One in segment 8 of 25mm
  - One in segment 5 of 1mm
  - One in segment 2 of 1mm
Male 67 yrs, PS 0, ex-smoker.

- TBLB RLL lungadenoCa; EBUS station 11R(i) positive; mediastinoscopy micrometastasis in station 4R.
- Staging RLL adenoCa cT2aN2M1b(scapula R)

Oligometastatic disease? 91% Y
Definition.

“Synchronous” Oligometastases

- Definition has been merely based on personal opinion.
- At present: precise definition is lacking.
- Turning point between oligo-M⁺ and poly-M⁺ is somewhere between 1 and 5 distant metastases in ≤ 2 organs.
- Prerequisite: fit patient & disease radically treatable by surgical and/or radiotherapy modalities.
Thank you for your attention!