Early-stage locally advanced non-small cell lung cancer (NSCLC)

Clinical Case Discussion

Pieter Postmus
The Clatterbridge Cancer Centre
Liverpool Heart and Chest Hospital
Liverpool, United Kingdom
Early and locally advanced non-small-cell lung cancer (NSCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

P. E. Postmus¹, K. M. Kerr², M. Oudkerk³, S. Senan⁴, D. A. Waller⁵, J. Vansteenkiste⁶, C. Escrig¹ & S. Peters⁷, on behalf of the ESMO Guidelines Committee

¹The Clatterbridge Cancer Centre and Liverpool Heart and Chest Hospital, Liverpool; ²University of Aberdeen, Aberdeen, UK; ³Center for Medical Imaging, University of Groningen, Groningen; ⁴Department of Radiation Oncology, VU University Medical Center, Amsterdam, The Netherlands; ⁵Department of Thoracic Surgery, University Hospitals of Leicester NHS Trust, Leicester, UK; ⁶University Hospitals KU Leuven, Leuven, Belgium; ⁷Oncology Department, Service d'Oncologie Médicale, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland

*Correspondence to: ESMO Guidelines Committee, ESMO Head Office, Via L. Taddeli 4, CH-6962 Viganò-Lugano, Switzerland. E-mail: clinicalguidelines@esmo.org

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Symptoms

Question: Is there relation between pain left shoulder and tumour LLL?

LLL, left lower lobe
Diagnosis

Transthoracic CT guided biopsy

→ Squamous cell carcinoma p63 positive

MRI brain without metastases

cT2acN0cM0, Stage IB

T3 (invading parietal pleura)
or
T4 (invading diaphragm) ????
Algorithm lymph node staging

PET/CT-scan

- both CT and PET negative for mediastinal nodes and no central tumour or hilar N1 nodes
- CT or PET positive for mediastinal nodes or central tumour or hilar N1 nodes

CT or PET positive for mediastinal nodes or central tumour or hilar N1 nodes

- non-bulky mediastinal LN infiltration
  - EBUS/EUS
    - N0-N1
    - mediastinoscopy
      - N0-N1
      - N2-N3

- bulky mediastinal LN infiltration

upfront surgery

multimodality treatment

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1 Category description according to CT (and PET) imaging as in ACCP staging document [Chest 143 Suppl 5:211S-250S, 2013], see text for more details.
2 A negative result of EBUS/EUS is usually confirmed by mediastinoscopy, as the latter has the highest negative predictive value.
Tumour board

Comorbidities:

- Coronary heart disease
- COPD Stage 2, with severe diffusion impairment
Preoperative cardiac evaluation.

RCRI: at least 3 weighted factors* or
1) Any cardiac condition requiring medications
2) A newly suspected cardiac condition
3) Inability to climb two flights of stairs

Yes

Cardiac consultation with non-invasive cardiac testing treatments as per AHA/ACC guidelines

No

Need for coronary intervention (CABG or PCI)

Continue with ongoing cardiac care
Institute any needed new medical interventions (i.e. beta-blockers, anticoagulants or statins)

*RCRI weighted factors [138]:
- High risk surgery (including lobectomy or pneumonectomy)
- Ischaemic heart disease (prior myocardial infarction, angina pectoris)
- Heart failure
- Insulin-dependent diabetes
- Previous stroke or TIA
- Creatinine ≥ 2 mg.dL⁻¹

Postpone surgery for ≥ 6 weeks

Lung function tests (see Figure 3)

AHA/ACC, American Heart Association/American College of Cardiology; CABG, coronary artery bypass grafting; ECG, electrocardiogram; PCI, percutaneous coronary intervention; RCRI, revised cardiac risk index; TIA, transient ischaemic attack.
Preoperative respiratory evaluation

DLCO, diffusing capacity of the lungs for carbon monoxide; FEV1, forced expiratory volume in 1 second; ppo, predicted postoperative; VO2, oxygen consumption.
Algorithm for patients with stage I lung cancer and emphysema

CT, computed tomography; COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume 1; FVC, forced vital capacity; ILD, interstitial lung disease; IPF, idiopathic pulmonary fibrosis; LVRS, lung volume reduction surgery; RFA, radiofrequency ablation; RV, reserve volume; SBRT, stereotactic body radiotherapy; TLC, total lung capacity
<table>
<thead>
<tr>
<th>Weighted factors</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischaemic heart disease</td>
<td>1.5</td>
</tr>
<tr>
<td>History of cerebrovascular disease</td>
<td>1.5</td>
</tr>
<tr>
<td>Serum creatinine &gt; 2 mg/dL</td>
<td>1</td>
</tr>
<tr>
<td>Pneumonectomy planned</td>
<td>1.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Class groupings</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0</td>
</tr>
<tr>
<td>B</td>
<td>1–1.5</td>
</tr>
<tr>
<td>C</td>
<td>2–2.5</td>
</tr>
<tr>
<td>D</td>
<td>&gt; 2.5</td>
</tr>
</tbody>
</table>

Ischaemic heart disease: history of myocardial infarction, history of positive exercise test, current complaint of chest pain (myocardial ischaemia), nitrate therapy, ECG with pathological Q waves. Cerebrovascular disease: transient ischaemic attack, stroke. ECG, electrocardiogram.
Treatment

cT2acN0cM0, Stage IB
➢ Radiotherapy: 10x 6 Gy
Follow-up (3 years)
No symptoms
X-ray thorax as part of check-up
rEBUS (radial endobronchial ultrasound)

Biopsy lung: adenocarcinoma cells

EBUS done through 21G or 22G needle usually gives only aspirate, difficult for pathologist to classify adenocarcinoma further; 19G gives tissue core
# 2015 WHO terminology for small biopsies and cytology

<table>
<thead>
<tr>
<th>2015 WHO Resections</th>
<th>Small Biopsy/Cytology</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ADENOCARCINOMA</strong></td>
<td><strong>Morphologic adenocarcinoma patterns clearly present:</strong> Adenocarcinoma, describe identifiable patterns present</td>
</tr>
<tr>
<td>Lepidic</td>
<td></td>
</tr>
<tr>
<td>Acinar</td>
<td></td>
</tr>
<tr>
<td>Papillary</td>
<td></td>
</tr>
<tr>
<td>Micropapillary</td>
<td></td>
</tr>
<tr>
<td>Solid</td>
<td></td>
</tr>
<tr>
<td>No 2004 WHO counterpart – most will be solid adenocarcinomas</td>
<td>Morphologic adenocarcinoma patterns not present (supported by special stains; i.e. TTF-1 +; p40 -): Non-small cell carcinoma, favor adenocarcinoma</td>
</tr>
<tr>
<td><strong>SQUAMOUS CELL CARCINOMA</strong></td>
<td>Morphologic squamous cell patterns clearly present: Squamous cell carcinoma</td>
</tr>
<tr>
<td>Keratinizing</td>
<td></td>
</tr>
<tr>
<td>Nonkeratinizing</td>
<td></td>
</tr>
<tr>
<td>Basaloid</td>
<td></td>
</tr>
<tr>
<td>No 2004 WHO counterpart</td>
<td>Morphologic squamous cell patterns not present (supported by stains; i.e. p40+, TTF-1 -): Non-small cell carcinoma, favor squamous cell carcinoma</td>
</tr>
<tr>
<td><strong>LARGE CELL CARCINOMA</strong></td>
<td>Non-small cell carcinoma, not otherwise specified (NOS)</td>
</tr>
</tbody>
</table>
Adenocarcinoma

- Lepidic
- Acinar
- Solid
- Papillary
- Micropapillary
### Pathology and N involvement

<table>
<thead>
<tr>
<th>Type (predominant)</th>
<th>% with nodes</th>
<th>% N2</th>
</tr>
</thead>
<tbody>
<tr>
<td>solid (SOL)</td>
<td>47.5</td>
<td>23.1</td>
</tr>
<tr>
<td>micropapillary (MIP)</td>
<td>47.2</td>
<td>23.6</td>
</tr>
<tr>
<td>variants of invasive AC (VIA)</td>
<td>24.0</td>
<td>11.3</td>
</tr>
<tr>
<td>papillary (PAP)</td>
<td>18.9</td>
<td>8.7</td>
</tr>
<tr>
<td>acinar (ACI)</td>
<td>18.2</td>
<td>8.8</td>
</tr>
<tr>
<td>lepidic (LEP)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>minimally invasive AC (MIA)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>AC in situ (AIS)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Staging

Patient BU 1956

MRI brain, no metastases

Primary tumour

SUVmax 16.3

Lymphnodes

SUVmax hilum: 3.0

MRI, magnetic resonance imaging; SUVmax, maximum standardised uptake value
SUV, survival and lymph node involvement

<table>
<thead>
<tr>
<th>SUV_{max}</th>
<th>pN0</th>
<th>pN1-3</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 3.0</td>
<td>83 (91.2%)</td>
<td>8 (8.8%)</td>
</tr>
<tr>
<td>≥ 3.0</td>
<td>81 (68.6%)</td>
<td>37 (31.4%)</td>
</tr>
<tr>
<td>p</td>
<td>&lt; 0.001</td>
<td></td>
</tr>
</tbody>
</table>

Staging

TNM, tumour, node, metastasis

cT2acN1cM0, stage IIB
Treatment

**Resection:**
Left lower lobe resection with Lymphadenectomy
(position: left 9, 11, 8, 12 & 7, 5)

**Pathology report** (AJCC, 7th edition):
*Acinar Adenocarcinoma*
pT2a, pN2* (6/10), G3, R0; KRASmut, Stage IIIA

*N2: positive at level 11L & 7*
Treatment algorithm stage IIIA

ACCP, American College of Chest Physicians; CT, computed tomography; LN, lymph node; NSCLC, non-small-cell lung cancer; PET, positron-emission tomography
Benefit of adjuvant chemotherapy after resection

- 575 Resected Adenocarcinoma from LACE-Bio study

Disease-free survival:
Acinar/papillary subgroups
Chemotherapy versus observation

Disease-free survival:
Micropapillary/solid subgroups
Chemotherapy versus observation

Tsao MS et al. J Clin Oncol 2015