Guideline for the Treatment of Lung Cancer

Version History

<table>
<thead>
<tr>
<th>Version</th>
<th>Description</th>
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<tr>
<td>2.0</td>
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Summary of changes between version 2 and version 3

- The addition of a section on surgical treatment.
- Chemoradiotherapy and chemotherapy, first and second line have been radically updated
- The addition of a section on follow-up.

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1. Scope of the Guideline

1.1 This Guidance has been produced to make recommendations for:

- The treatment of lung cancer with radiotherapy.
- The treatment of lung cancer with chemotherapy.
- The treatment of non-small cell lung cancer with surgery.

2. Guideline Background

This document aims to combine up to date research, current thinking, and local expert opinion to generate Network Guidelines. Pan Birmingham Cancer Network has one centre for the surgical management of lung cancer at Heart of England NHS Foundation Trust (Heartlands site).

Guideline Statements – Non Small Cell Lung Cancer (NSCLC)

3. Surgery: NSCLC

3.1 Surgery should usually be performed with curative intent (or rarely with specific palliative intent).
3.2 Surgery should take place within 31 days of referral.
3.3 The following should be considered when referring for surgery:
   a. Those with NSCLC stages I and II
   b. In II B disease, involvement of chest wall or diaphragm does not necessarily preclude surgery. En-bloc resection of chest wall with adequate margins and consideration for radiotherapy produces good results.
   c. Although resectable, stage IIIa is not considered curable by surgery, however neo-adjuvant chemotherapy should be considered for these patients. Those who show a good response should be reconsidered for surgery.
   d. Patients with probable peripheral lung cancer where histology has not been obtained should be considered for surgery.
   e. Patients where surgical biopsy is needed to establish a diagnosis should be referred for the consideration of surgery.
   f. Patients needing assessment for operability or staging should be referred for the consideration of surgery.
   g. When pathological diagnosis has not been determined preoperatively, on table frozen section should be available and malignancy usually confirmed before proceeding to resection.
h. Patients with operable solitary brain metastases should be considered for neurosurgery prior to thoracic surgery.

i. Pleural effusion is a relative contraindication to surgery. Potentially operable patients with a pleural effusion should be investigated with pleural aspiration for cytology; closed pleural biopsies or thoracoscopy.

j. In T3 disease, involvement of the chest wall or diaphragm does not necessarily preclude surgery. En bloc resection of chest wall may be feasible for some patients.

3.4 Staging and assessment for suitability for surgery

3.4.1 Nature of the NSCLC.
- Site of tumour at bronchoscopy: tumour appears operable.
- The tumour should be more than 2cm from carina unless sleeve pneumonectomy or carinoplasty is to be considered.
- The tumour should only involve one lung.
- There should be no vocal cord paralysis.

3.4.2 Cardiac Status
If patients do not fulfil the criteria below, opinion from cardiologist must be sought and cardiac surgical referral made if necessary before considering for lung resection.
- There should be no clinical evidence of cardiac failure.
- There should be no myocardial infarction within the last 6 weeks.
- Where there is significant ischaemic heart disease a cardiological assessment should be arranged.
- Any patient with heart murmur must have an echocardiogram to assess valve gradients.

3.4.3 Respiratory Status
- All patients should have formal lung function tests prior to consideration for surgery.
- Predicted FEV1 is used as a guideline. A patient is considered suitable for surgery for lobectomy when FEV1 > 1.6 litres and pneumonectomy when FEV1 > 2.0 litres.
- Patients with FEV1 < 1.6 litres require more complex assessments including static lung volumes and transfer capacity. This may also include quantitative perfusion scan & CPET.
- Any patient who has excessive breathlessness i.e. cannot walk upstairs or more than 150 metres or whose FEV1 is < 1.6 litres may be assessed as follows:
  - Shuttle walk test. A shuttle greater than 150 metres correlates well with VO2 max of 15mls/kg/min.
- VO2 max:
  - Quantitative perfusion scan is used to delineate perfusion differentials between lungs and blood flow within each lung so as to determine postoperative lung function.
3.4.4 CT Scan
- All patients should have Staging CT scan of thorax and upper abdomen (neck as well if pancoast tumour).
- Mediastinal glands: superior mediastinal glands greater than 1.0cm in short axis if metabolically active on PET scan should be biopsied.

3.4.5 PET Scanning
- All patients should have a CT PET scan:
  - PET positive nodes in mediastinum should be biopsied prior to surgery by mediastinoscopy or mediastinotomy.
  - There should be no evidence of metastatic disease (other than solitary operable brain metastases – see 3.3 [h]).

3.4.6 Biochemical Screen (U&E, LFTs, glucose)
- Alkaline phospatase. If raised look for liver or bone metastases with an isotope scan and ultrasound.
- Low albumin <20 increases mortality and morbidity.

3.4.7 Haematology (FBC, clotting screen)
- All patients should have full blood count. HB below 10 carries poorer outcome.
- Any patient with abnormal counts or screen should be investigated further. Consider bone marrow if necessary.

3.4.8 Full Clinical Examination

4. Radiotherapy: NSCLC

4.1 Post operative radiotherapy may be offered after incomplete resection of the primary tumour.

4.2 Patients with good performance status (WHO 0, 1 and some 2) with adequate respiratory reserve (FEV1 > 0.8L) and medically inoperable stages I and II non-small cell cancer or III non-small cell lung cancer should be offered radical radiotherapy (55Gy in 20 fractions, CT planned with or without conformal technique).

4.3 Radiotherapy for stages I and II patients should start within four weeks of consent for treatment. Treatment technique will be CT based. The clinical target volume will not include uninvolved nodes. The planning target volume will be clinical target volume plus 1.5cm superiorly and inferiorly and 1cm circumferentially.

4.4 Radiotherapy for stages IIIa/b patients should start within four weeks of the last cycle of chemotherapy.

4.5 Palliative radiotherapy for patients unsuitable for chemotherapy should consist of 20Gy in 5 fractions schedule.
4.6 All patients for radical radiotherapy for inoperable stage I and II disease and chemoradiotherapy for stage IIIa disease must have a PET scan.

4.7 Currently, there are no facilities for CHART treatment in the West Midlands. The nearest centre for referral is Cheltenham General Hospital. Normally CHART would be available to those with stage I or II who are medically inoperable but suitable for radical radiotherapy, and those with stage IIIa or IIIb who are eligible for radical radiotherapy and who cannot tolerate or do not wish to have chemotherapy.

5. **Chemotherapy: NCSLC**

5.1 Adjuvant chemotherapy should be considered for all patients following complete resection for non-small cell lung cancer stage II - IIIa. Some patients with stage I disease should be considered for adjuvant chemotherapy i.e poor differentiation, vascular invasions, tumour larger than 4 cm.

5.2 Selection of drugs may depend on the cell type, such as Alimta for adenocarcinoma, taxotere for squamous cell carcinoma, Gemcitabine or Navelbine for unclassified NSCLC in conjunction with cisplatin.

5.3 Patients with locally advanced stage III disease and stage IV with good performance status (WHO 0, 1) should be offered palliative chemotherapy using a cisplatin based combination. As above, the selections of the combinations should be based on the cell type.

5.4 All adenocarcinoma histology should be tested for EGFR mutation (EXON 19 and 21). Mutation positive patients must be offered treatment with gefitinib (Iressa).

6. **Chemoradiotherapy: NSCLC**

PET staged IIIa patients with performance status of 0 and 1 should be considered for concurrent chemoradiotherapy where chemotherapy is given together with radiotherapy. Radiotherapy is started on the day of the second cycle of chemotherapy on Day 22. Radiotherapy must be delivered within one hour of the completion of the chemotherapy infusion. Gemcitabine and Navelbine are best avoided in this setting due to high incidence of grade III oesophagitis. Radiation dose per fraction is best reduced to 2 Gy leading to an overall does of 66 Gy in 33 fractions.

7. **Second Line Treatment: NSCLC**

7.1 On relapse, palliative second line chemotherapy can be offered to suitable patients with good performance status.
7.2 Docetaxol (taxotere), pemetrexed (Alimta) and Elotinib (Tarceva) are licensed and NICE approved in the second line setting.

Guideline Statements – Small Cell Lung Cancer (SCLC)

8. Limited Disease: SCLC

8.1 Intrathoracic disease considered suitable for radical treatment (T1 – T4, N1 and N2 M0) should be offered concurrent chemo-radiotherapy with Etoposide and Cisplatin or Carboplatin, and should commence radiotherapy (66Gy in 33) in cycle 2.

8.2 Patients who have been pre-treated with induction chemotherapy should be offered consolidation radical radiotherapy (55Gy in 20) if they achieved a radiological complete response following chemotherapy, taking into consideration the pre-chemotherapy tumour volume.

8.3 All patients should be offered prophylactic cranial irradiation (limited or extensive stage).

9. Extensive Disease: SCLC

9.1 Patients with extensive and extra-thoracic disease should receive palliative chemotherapy with carboplatin and etoposide.

9.2 There is no routine place for post-chemotherapy palliative radiotherapy, unless there is symptomatic residual disease.

10. Adjuvant Treatment: SCLC

Patients who have had surgery and are found to have small cell lung cancer should receive adjuvant chemotherapy with 6 cycles of a platinum agent and etoposide. They may then go on to receive prophylactic cranial irradiation.

11. Second Line Treatment: SCLC

11.1 On relapse, second line treatment may be considered for patients with good performance status. Patients with a disease free interval of 12 or more months could be re-induced with the same carboplatin/Etoposide regime.

11.2 Patients who relapse within 12 months of the previous chemotherapy should be considered for Vincristine, Adriamycin and Cyclophosphamide (VAC) regime or oral Topecan.
12. Radiotherapy: SCLC

All patients with small cell lung and non small cell lung cancer should be considered for palliative radiotherapy for symptomatic metastatic disease such as bone, spinal and brain metastases.

Guideline Statements – All Patients

13. Follow-up

13.1 NSCLC patients who have undergone surgery should have one post-operative follow-up appointment with the surgical team at 6-weeks and a further appointment 3 months later. Subsequent follow-up should be with the lung physician/oncologist up to 2 years. Disease free patients should be discharged at 2 years with a method of direct access back to the MDT should related problems occur.

13.2 All other lung cancer patients should be seen as their disease and condition dictates.

14. Patient Information and Counselling

14.1 All patients, and with their consent, their partners, will be given access to appropriate written information during their investigation and treatment, and on diagnosis will be given the opportunity to discuss their management with a clinical nurse specialist who is a member of the relevant MDT. The patient should have a method of access to the lung team at all times.

14.2 Access to psychological support will be available if required. All patients should be offered an holistic needs assessment and onward referral as required.

15. Palliative Care

Palliative care services will be made available to all patients as deemed appropriate by the MDT.

16. Clinical Trials

16.1 Wherever possible, patients who are eligible should be offered the opportunity to participate in National Institute for Health Research portfolio clinical trials and other well designed studies.
16.2 Where a study is only open at one Trust in the Network, patients should be referred for trial entry. A list of studies available at each Trust is available from Pan Birmingham Cancer Research Network. Email: PBCRN@westmidlands.nhs.uk.

16.3 Patients who have been recruited into a clinical trial will be followed up as defined in the protocol.

**Monitoring of the Guideline**
Implementation of the guidance will be considered as a topic for audit by the NSSG in 2012.

**References**
NICE 2005. Lung Cancer: The diagnosis and Treatment of Lung Cancer. Clinical Guideline 24. NB at the time of approval there are draft 2010 guidelines out from NICE.

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Date:

**Date Approved by the Clinical Governance Committee**
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