

**Protocol for Planning and Treatment**

The process to be followed in the management of:

**SMALL CELL LUNG CANCER**

**Patient information given at each stage following agreed information pathway**

**1. DIAGNOSIS**

New cough; alteration in pre-existing cough; dyspnoea or worsening of previous dyspnoea; current pneumonia; symptoms from metastatic disease; paraneoplastic syndromes.

**2. STAGING**

Staging should be recorded using the UICC, TNM, 7<sup>th</sup> Edition 2009 definitions and the separate Veterans Administration Lung Group system which divides SCLC patients into either limited or extensive stages.

Using current staging procedures, 30-40% of SCLC patients have limited stage SCLC. After the diagnosis of SCLC, accurate staging should be completed as expediently as possible.

**Limited Stage Small Cell Lung Cancer**

The original operational definition of limited disease was tumour quantity and configuration that could be encompassed by a "reasonable" radiotherapy treatment volume including the primary tumour site and the adjacent hilar, mediastinal and ipsilateral supraclavicular lymph nodes. The presence of massive intrathoracic tumour may preclude a "reasonable" thoracic radiotherapy volume and allow palliative therapy only. The tumour volume may change in response to chemotherapy and so regular review is mandatory.

**Extensive Stage Small Cell Lung Cancer**

Disease beyond the limited stage criteria is defined as extensive stage. Patients with "regional" extensive stage disease (pleural effusion, contralateral supraclavicular nodes or cervical lymph nodes) have a prognosis that is intermediate between limited and extensive and may benefit from a limited stage type treatment plan.

**3. HISTOPATHOLOGY**

**WHO classification:**

Small cell carcinoma

Intermediate cell type carcinoma

Mixed small cell and non small cell carcinoma – should be treated initially with chemotherapy for small cell component and then radiotherapy, depending on results.

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**4. INVESTIGATIONS**

A full history and physical examination should precede any investigation.

Initial investigations should include full blood count, serum biochemistry and C reactive protein; a chest X-ray and CT thorax and upper abdomen.

Lung function testing (FEV1/FVC) should be performed.

Because lesions thought to be lung cancer radiologically are sometimes shown to be a benign process and because of the difference in treatment for non-small cell and small cell lung cancer, histological or cytological verification of the diagnosis should be obtained wherever possible.

Diagnostic procedures should be tailored to the individual patient and may include:

- i) Review of old chest X-rays to exclude a long-standing benign lesion or determine the rate of progression of a malignant lesion.
- ii) Bronchoscopy, biopsy of endobronchial lesions, brushings and washings, post-bronchoscopy sputum cytology.
- iii) Percutaneous fine needle or core biopsy in selected cases where bronchoscopy unhelpful or via endoscopic bronchial or oesophageal ultrasound (EBUS / EUS)
- iv) Excisional or needle biopsy of readily accessible secondary deposits
- v) CT brain prior to commencing radical treatment

**All patients should be discussed at the lung cancer MDT meeting to confirm staging and histological diagnosis and to determine an appropriate management plan which should be recorded in the patient's notes.**

**5. CHEMOTHERAPY/ RADIOTHERAPY**

**Limited stage disease:**

\* CONSIDER CLINICAL TRIALS \*

Options include :

**a) Concurrent chemo-irradiation <sup>(1)</sup>:**

**Rationale:**

Leads to 5% improvement in 3 year survival <sup>(1)</sup> vs. sequential

**Indications:**

Limited disease

PS 0, 1, or 2

Adequate pulmonary cardiac and renal function

Disease volume that can safely be encompassed in a radical radiotherapy volume.

**Chemotherapy:**

Day 1: Cisplatin 80mg/m<sup>2</sup> IV

Day 1 and 2: Etoposide 120mg/m<sup>2</sup> IV

Day 3: Etoposide 240mg/m<sup>2</sup> orally

Every 21 days for 4 cycles

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If cisplatin contraindicated (GFR<50ml/min, significant ischaemic heart disease, previous major vascular episode, neuropathy):

Day 1: Carboplatin AUC 6 (Cockcroft-Gault) or AUC5 (measured GFR)  
Days 1, 2: Etoposide 120mg/m<sup>2</sup> IV  
Day 3: Etoposide 240mg/m<sup>2</sup> orally

Radiotherapy:

Aim to start day 1 cycle 2 and no later than can be completed before end of last cycle of chemotherapy.

Dose:

45-50Gy in 20 fractions to a CT-planned volume.

**N.B. Thoracic irradiation should not be interrupted because of neutropenia (regardless of severity) in the absence of clinical evidence of infection.**

Prophylactic cranial irradiation (PCI) should be given following completion of chemotherapy

**b) Sequential chemo-irradiation <sup>(2)</sup>**

Rationale:

Improved median survival from 11.6 to 15 months <sup>(2)</sup>

Indication:

PS 2-3 patients thought unlikely to tolerate concurrent treatment

PS 0-1 patients with disease initially too bulky to encompass in a radical radiotherapy volume, and who have substantial tumour shrinkage following chemotherapy.

Adequate pulmonary, cardiac, renal function to tolerate chemotherapy and radiotherapy.

Chemotherapy:

Day 1: Cisplatin 80mg/m<sup>2</sup> IV  
Day 1 and 2: Etoposide 120mg/m<sup>2</sup> IV  
Day 3: Etoposide 240mg/m<sup>2</sup> orally  
Every 21 days for 4 cycles

If cisplatin contraindicated (GFR<50ml/min, significant ischaemic heart disease, previous major vascular episode, neuropathy): Carboplatin AUC 6 (Cockcroft-Gault) or AUC5 (measured GFR)

Day 1 and 2: Etoposide 120mg/m<sup>2</sup> IV  
Day 3: Etoposide 240mg/m<sup>2</sup> orally

Every 21 days for 4 cycles

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**Thoracic radiotherapy:**

40Gy in 15 fractions AP/PA to include tumour and mediastinum  
or 45-50Gy in 20 fractions to CT-planned volume

Aim to start no more than 4 weeks from day 1 of last cycle of chemotherapy.

Prophylactic cranial irradiation (PCI) should be considered and given concurrently with thoracic radiotherapy

**c) Prophylactic cranial irradiation (PCI) <sup>(3)</sup>**

**Rationale:**

Improves 3 year survival from 15% to 20% and halves incidence of brain metastases from 50% to 25%

**Indications:**

Limited stage SCLC without evidence of progression on chemotherapy  
PS 0-2

**Dose:**

25 - 30Gy in 10 fractions to whole brain

Aim to start no more than 4 weeks from day 1 last cycle chemotherapy.

NB – must NOT be given concurrently with chemotherapy.

**N.B. Post op:**

Rarely patients with small cell carcinoma undergo surgery. If so, consideration should be given to 4 cycles of consolidation chemotherapy as detailed above, followed by prophylactic cranial irradiation and thoracic radiotherapy, all detailed above.

**Extensive stage disease:**

\* CONSIDER CLINICAL TRIALS \*

Consider referral to Palliative Care for support and Information.

**a) First line palliative chemotherapy:**

**Rationale <sup>(4,5)</sup>**

Median survival of 8 months using EP or CAV

**Indications:**

Extensive stage SCLC

PS 0-2;

Adequate renal, cardiac, and liver function to tolerate chemotherapy

Day 1 Carboplatin AUC6 IV (AUC5 if EDTA GFR used)

Days 1, 2: Etoposide 120mg/m<sup>2</sup> IV

Day 3: Etoposide 240mg/m<sup>2</sup> orally

Every 21 days for up to 6 cycles if responding and well tolerated.

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If PS 3 consider  
Carboplatin AUC5 (Cockcroft-Gault)  
Etoposide 120 mg/m<sup>2</sup> IV d1, d2, 100 mg bd d3

In patients with poor renal function:

Day 1            Adriamycin 40 mg/m<sup>2</sup>  
Day 1            Cyclophosphamide 750 mg/m<sup>2</sup>  
Days 1, 2        Etoposide 120 mg/m<sup>2</sup> IV  
Day 3            Etoposide 240 mg/m<sup>2</sup> orally

**b) Prophylactic cranial irradiation**

Rationale:

Improves 1 year survival from 13% to 27%<sup>(6)</sup>

Indications:

Extensive stage SCLC and evidence of some response to chemotherapy on chest x-ray.  
Good PS (0-2).

Aim to start no more than 4-6 weeks from day 1 last cycle of chemotherapy

Dose:

20Gy in 5 fractions to whole brain

**c) Second line chemotherapy:**

Indications:

Selected patients of good PS (0-2)

If >3 months since first line treatment: re-challenge with same first-line drugs

If < 3 months since initial treatment:

i) PS 0-1

Day 1 Cyclophosphamide 1000 mg/m<sup>2</sup>  
Day 1 Adriamycin 40 mg/m<sup>2</sup>  
Days 1 and 2 Etoposide 120 mg/m<sup>2</sup> IV  
Day 3 Etoposide 240 mg/m<sup>2</sup> orally

ii) PS 2:

Day 1 Cyclophosphamide 750mg/m<sup>2</sup>  
Day 1 Adriamycin 40mg/m<sup>2</sup>,  
Day 1 Vincristine 1.4mg/m<sup>2</sup> (max 2mg)

Every 21 days for 4-6 cycles depending on response.

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iii) In relapsed patients where re-treatment with first line regimen is not considered appropriate due to toxicities and in whom CAV is contra-indicated due to toxicities and who at the Oncologist's discretion are not fit for iv chemotherapy, consider:

Oral Topotecan

Rationale: <sup>(7)</sup>

26 vs. 14 week median survival and improved symptom control vs. BSC <sup>(7)</sup>

Regime:

Topotecan 2.3mg /m<sup>2</sup> d1-5 q 21d orally up to 4 cycles

\* CONSIDER CLINICAL TRIALS \*

**d) Palliative thoracic radiotherapy:**

Indications

Progressive symptomatic disease during chemotherapy

Symptomatic relapse in patient not fit for further chemotherapy

Dose:

8Gy single fraction or 20Gy in 5 fractions over 5-7 days

\* CONSIDER CLINICAL TRIALS \*

**e) Palliative radiotherapy to other sites:**

As per non-small cell lung cancer except:

Fit patients who present with brain metastases from small cell lung cancer should be considered for chemotherapy as first line treatment with consolidation whole brain radiotherapy following this.

**References:**

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Chair: ..... Signature: ..... Date: .....  
(on behalf of OHMMG)

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