Small cell lung cancer makes up about 15 percent of all lung cancers. It occurs almost exclusively in smokers, particularly heavy smokers, and former smokers.

It is usually aggressive cancer that tends to grow and spread quickly.

Small cell lung cancer (SCLC) is distinguished from non-small cell lung cancer (NSCLC) by its rapid doubling time, high growth fraction, and the early development of metastases.

Although SCLC is highly responsive to both chemotherapy and radiotherapy (RT), it commonly relapses within months despite treatment.

Since SCLC usually presents with disseminated disease, treatment strategies are mainly systemic.

Although chemoradiation resulted in significant improvements in patient’s disease control for both the limited case and some of the extensive-stage disease, the long-term prognosis remains poor.

### Initial Evaluation and Workup

- History and clinical examination
- Pathology review
- Laboratory tests:
  - CBC,
  - Biochemistry including serum LDH. LDH elevation reflects the bulk of the tumor and considered an aversive prognostic feature.
- Imaging:
  - Chest radiography
  - Computed tomography (CT) scan chest and abdomen
  - Magnetic resonance imaging (MRI) or CT scan brain
- Bone scan/NAF Scan is the current modality to test for bone metastases

**Additional workup tools:**

- Bone marrow aspiration cytology and biopsy: if abnormalities as would be suggested clinically and/or by peripheral smear.
- Thoracentesis:
  - Diagnostic through a cell block
  - Therapeutic to relief patient’s symptoms.
- Pulmonary function tests, echocardiography as indicated for selected cases.
Staging of SCLC

- Patients with small-cell lung cancer are traditionally classified as having either:
  - Limited-stage or
  - Extensive-stage disease.
- Many experts recommended that small cell lung cancer should also be classified using the TNM staging system.

**Limited-stage disease (LD):**
- Limited-stage small cell lung cancer is defined as cancer that is encompassed within one radiation port.
- Limited-stage disease correlates with stage I, II, or III cancer and representing one-third of patients at the time of initial presentation.
- Most people with limited-stage small-cell lung cancer are treated with chemotherapy with introducing thoracic radiation therapy as early as possible, currently given along with the second cycle of chemotherapy.
- Those who achieved a good response will be offered the chance of prophylactic cranial irradiation (PCI).
- Recently, there has been a role of surgery in selected patients with limited-stage small-cell lung cancer after careful discussion at the thoracic MDT.

The Management Approach for Patients with Limited Stage LD Small Cell Lung Cancer

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*Adjvant chemotherapy* and *Concurrent chemoradiotherapy*
Surgery in Multimodality Treatment for LD-SCLC

Surgery as initial therapy:

- Surgery is recommended for patients who:
  - Present with a solitary pulmonary nodule;
  - Have no evidence of hilar or mediastinal nodal involvement;
  - Have no distant metastases; and
  - Have no contraindications to surgery.

- Patients who will be considered candidates for primary resection should undergo extensive evaluation for mediastinal involvement and distant metastases.

- This evaluation should include
  - PET-CT and
  - Brain imaging.

- Invasive staging of the mediastinum by:
  - Endobronchial ultrasound (EBUS) or
  - Mediastinoscopy even if there is no evidence of mediastinal involvement by imaging.

Chemotherapy

- The current standard of care for patients with LD-SCLC consists of:
  - Four to six cycles of combination chemotherapy of the current standard cisplatin plus etoposide [EP]
  - Concurrent thoracic radiotherapy, along with chemotherapy, usually administered with the second cycle.

- Carboplatin can be an alternative if cisplatin is contraindicated for reasons such as:
  - Preexisting neuropathy,
  - Hearing loss,
  - Renal insufficiency.

- The number of chemotherapy cycles would depend on:
  - Patient’s tolerance;
  - Disease responsiveness; and
  - Side effects of the treatment.

- Prophylactic cranial irradiation (PCI) is generally recommended for patients with a complete response or significant tumor regression at the completion of chemotherapy.
Extensive-Stage Disease (ED)

- It is defined as patients with small cell lung cancer spreading to the other lung, liver, adrenal glands, bones, or brain.

Treatment Options:

1) Palliative Chemotherapy:
   - Patients with extensive-stage small-cell lung cancer are generally treated with palliative chemotherapy utilizing cisplatin (or carboplatin) plus etoposide.

2) Palliative Radiotherapy:
   - Palliative radiation therapy would be offered for symptomatic metastatic sites.

3) Local Therapies:
   - Those who responded may be offered local therapies after discussion at thoracic MDT.

- Recently Atezolizumab has been combined to carboplatin and etoposide in the first-line setting as was shown on phase III trial with two months benefit on overall survival benefit as was outlined by IMpower 133 study.

Thoracic Radiation Therapy

- The plan of radiotherapy will be decided by our thoracic radiotherapy colleagues of the thoracic MDT.
- Prophylactic cranial irradiation:
  - Indicated for patients with a complete or very good partial response to their initial chemotherapy treatment.

Treatment of refractory and relapsed SCLC
Agents used on relapse:

- **Nivolumab** as a second-line regimen based on the phase II trial [Checkmate 331 trial] that gained an accelerated the Food and Drug Administration (FDA) approval yielding a response rate relative risk (RR) of 12%.

- **Treatment duration and further lines of therapy**
  - The optimal duration of second-line treatment has not been clearly established. A commonly employed and acceptable approach is to continue treatment until disease progression or unacceptable toxicity occurs.
  - Third-line chemotherapy may be offered to patients who still have:
    - Adequate performance status after progression on two lines of chemotherapy (ECOG 0 to 2),
    - The discretion of the treating clinician through thoracic MDT and patient preferences.

- **Late relapses (after six months)**
  - These patients may be challenged with the initial protocol provided that the patient maintains a good performance status (Eastern Cooperative Oncology Group [ECOG] 0 to 2 after having 6-12 relapse-free intervals and so considered potentially eligible to derive a greater benefit from this approach.
References


